Cecil R. Reynolds
Elaine Fletcher-Janzen
Editors

Handbook of

Clinical Child

Neuropsychology

② Springer

Handbook of Clinical Child Neuropsychology

Third Edition

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Edited by

Cecil R. Reynolds
Texas A&M University
College Station, TX, USA

and

Elaine Fletcher-Janzen
Private Practice
Cleveland, Ohio

Springer

Editors

Cecil R Reynolds
Department of Educational Psychology
Texas A&M University
College Station, TX, USA
crrh@earthlink.net

Elaine Fletcher-Janzen
Private Practice
Cleveland, Ohio
efj445@aol.com

Contributors

Priscilla A. Bade-White • College of Education, University of Arizona, Tucson, Arizona 85721, e-mail: pbadewhite@yahoo.com

Russell M. Bauer • Department of Clinical Health Psychology, University of Florida, Gainesville, Florida 32610-0165

Thomas L. Bennett • Department of Psychology, Colorado State University, Ft. Collins, Colorado 80523

Richard A. Berg • Private Practice, Wilmington Health Associates, Wilmington, North Carolina, 28401, e-mail: RBERG @ec.rr.com

T. Carter Bethea • Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27599

David Breiger • Department of Psychiatry and Behavioral Sciences, Children's Hospital and Regional Medical Center, University of Washington School of Medicine, Seattle, Washington 9810–2499

Ronald T. Brown • College of Health Professions, Temple University Health Sciences Center, Philadelphia, Pennsylvania 19140, e-mail: Ronald.brown@temple.edu

Melissa R. Bunner • Austin Neurological Clinic, Austin, Texas 78705

Margo A. Candelaria • Department of Pediatrics, University of Maryland School of Medicine, Baltimore, Maryland 21201

Manuel L. Cepeda • Department of Psychiatry, College of Medicine, University of South Alabama, Mobile, Alabama 36617-2293, e-mail: mcepeda@usouthal.edu

Cara Conway • Department of School Psychology, George Mason University, Fairfax, Virginia 22030

Rik Carl D'Amato • Department of Psychology, Faculty of Social Sciences and Humanities, Av. Padre Tomas Pereira, Taipa, Macau SAR, China

Brian P. Daly • College of Health Professions, Temple University Health Sciences Center, Philadelphia, Pennsylvania 19140

Jill M. Dorflinger • Alexian Brothers Behavioral Health System, Hoffman Estates, Illinois 60169

Laura Eckert • Department of Educational Psychology, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53201

Tywanda Ellison • Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27599

Bryan D. Fantie • Department of Psychology, American University, Washington, District of Columbia 20016-8062

Eileen B. Fennell • Department of Clinical Health Psychology, University of Florida, Gainesville, Florida 32610-0165, e-mail: efennell@phhp.ufl.edu

Elaine Fletcher-Janzen • San Angelo, Texas 76901

Charles J. Golden • Center for Psychological Services, Nova Southeastern University, Fort Lauderdale, Florida 33314, e-mail: goldench@nova.edu

Sam Goldstein • Department of School Psychology, George Mason University, Fairfax, Virginia 22030, e-mail: info@samgoldstein.com

Thalía Harmony • Instituto de Neurobiología, Universidad Nacional, Autónoma de México, Campus Juriquilla, 76230, Querétaro, Qro, Mexico, e-mail: thaliah@servidor.unam.mx

Lawrence C. Hartlage • Augusta Neuropsychology Center, Evans, Georgia 30809

Maile R. Ho • Department of Psychology, Colorado State University, Ft. Collins, Colorado 80523

Stephen R. Hooper • Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27599

Julie E. Horwitz • Department of Psychology, University at Albany, State University of New York, Albany, New York 12222

George W. Hynd • College of Education, Purdue University, West Lafayette, Indiana 47907, e-mail: ghynd@purdue.edu

H. Dennis Kade • Tidewater Child Development Services, Norfolk Department of Public Health, Norfolk, and Department of Psychology, Old Dominion University, Norfolk, Virginia, e-mail: doctorkade@gmail.com

Randy W. Kamphaus • Department of Educational Psychology, University of Georgia, Athens, Georgia 30602 and Department of Counseling and Psychological Services, Georgia State University, Atlanta, Georgia 30302

Kordell Kennemer • Oregon State Hospital, Portland, Oregon 97232

Marcel Kinsbourne • New School for Social Research, New York, New York 10011, e-mail: kinsbourne@aol.com

Bryan Kolb • Department of Psychology, University of Lethbridge, Lethbridge, Alberta T1K3M4, Canada, e-mail: kolb@uleth.ca

John C. Linton • Department of Behavioral Medicine, West Virginia University School of Medicine, Charleston, West Virginia 25326

Antolin M. Llorente • Department of Pediatrics, University of Maryland School of Medicine, Baltimore, Maryland 21209, e-mail: allorente@mwph.org

Charles J. Long • Psychology Department. The University of Memphis, Memphis, Tennessee 38152.

Christine LoPresti • Department of Psychiatry and Biobehavioral Sciences, University of California School of Medicine, Los Angeles, and Neuropsychiatric Institute and Hospital, Los Angeles, California 90024

Julie K. Lynch • Albany Neuropsychological Associates, Guilderland, New York 12084-1522

Robert J. McCaffrey • Department of Psychology, University at Albany, State University

of New York, Albany, New York 12222 and Albany Neurological Associates, Guilderland, New York 12084-1522, e-mail: rjmnpsy@aol.com

Frank McDonald • Our Children's House at Baylor, Dallas, Texas 75204

Arthur MacNeill Horton, Jr. • Psych Associates, Towson, Maryland 20814, e-mail: hortonn7@gmail.com

Arthur MacNeill Horton, III • Eastern Virginia Medical School, Norfolk, VA

Lawrence V. Majovski • Department of Psychiatry, University of Washington School of Medicine and Department of Psychiatry, Childrens Hospital, Seattle, Washington 98104, e-mail: majovski@u.washington.edu

Benjamin A. Mason • Department of Educational Psychology, Texas A&M University, College Station, Texas 77843

Kristen L. Mays • Department of Educational Psychology, University of Georgia, Athens, Georgia 30602

Joan W. Mayfield • Our Children's House at Baylor, Dallas, Texas 75204, e-mail: joanm@BaylorHealth.edu

Allison E. Morgan • Purdue University, West Lafayette, Indiana 47907

Jack A. Naglieri • Center for Cognitive Development, George Mason University, Fairfax, Virginia 22030, jnaglier@gmu.edu

Amy Nelson • Department of Educational Psychology, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53201

Nancy L. Nussbaum • Austin Neurological Clinic, Austin, Texas 78705, e-mail: nlnussbaum@austin.rr.com

John E. Obrzut • College of Education, University of Arizona, Tucson, Arizona 85721

Linda Pedersen • Lewisville Independent School District, Lewisville, Texas

Peter Platten • Department of Educational Psychology, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53201

Philip P. Randall • College of Education, University of Arizona, Tucson, Arizona 85721

Cecil R. Reynolds • Department of Educational Psychology, Texas A&M University, College Station, Texas 77843, e-mail: crrh@earthlink.net

Robert L. Rhodes • Special Education/ Communication Disorders Department, New Mexico State University, Las Cruces, New Mexico 88003-8001

Barbara A. Rothlisberg • Department of Educational Psychology, Ball State University, Muncie, Indiana 47306

Paul Satz • Department of Psychiatry and Biobehavioral Sciences, University of California School of Medicine, Los Angeles, and Neuropsychiatric Institute and Hospital, Los Angeles, California 90024

Adam Schwebach • Neurology, Learning and Behavior Center, University of Utah, Salt Lake City, Utah 84112-9057

Margaret Semrud-Clikeman • Department of Psychology, Michigan State University, East Lansing, Michigan 48824

Lisa D. Stanford • Department of Psychiatry and Neurology, University of Illinois Medical Center, Chicago, Illinois 60612, e-mail: LStanford @psych.uic.edu

Phyllis Anne Teeter Ellison • Department of Educational Psychology, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53201, e-mail: teeter@uwm.edu

Michael G. Tramontana • Vanderbilt Psychiatric Hospital and Departments of Psychiatry and

Neurology, Vanderbilt University, Nashville, Tennessee 37212-3133, e-mail: Michael.tramontana@vanderbilt.edu

Melanie Vaughn • Arizona State University, Tempe, Arizona, 85287

Judith K. Voress • Donald D. Hammill Institute on Disabilities, Austin, Texas 78757, e-mail: jvoress@hammill-institute.org

Marie L. Walker • Austin, Texas

Tiffany Watts-English • Department of Psychiatry and Behavioral Sciences, Duke University, Raleigh, North Carolina 27708

Timothy B. Whelan • Department of Psychiatry, Baystate Medical Center, Springfield, Massachusetts 01199, e-mail: timothy.Whelan@bhs.org

Preface to the Third Edition

In the more than 20 years since we conceptualized and outlined the first edition of the Handbook of Clinical Child Neuropsychology, much has changed in our field yet much has remained the same. There have been great strides in understanding both normal and pathognomic development of neural structures that have led us to greater depths of understanding the brain–behavior relationships in children. It seems that advances in neurobiology and related neurosciences continue to add impetus to the need for emphasizing the role of the brain in many forms of psychopathology that were once considered solely the domain of psychodynamics and behaviorism. We have implored the authors of this third edition to take careful note of the science that underlies the practice of clinical child neuropsychology and to integrate these advances wherever possible into the updates of their chapters as well as considering them in the chapters that are new to this volume. At the same time that our depth of understanding of brain–behavior relationships has improved, many of the methodological and statistical problems that have plagued research in the field remain. We continue to provide chapters on these issues in an attempt to improve research and research outcomes in the discipline in addition to providing chapters that give guidance to current best practices for the workhorse practitioner.

Unfortunately, one of the things that has not changed in our field is the presence of a dearth of qualified pediatric and child clinical neuropsychologists. While there are more qualified child practitioners now than ever before, children remain underserved. Every year, without fail, since the National Institute of Mental Health began issuing a list of underserved populations within the United States, children have appeared in the top 10 of all underserved populations. Our hope is that by continuing to provide information on current practice,

science, and thought about the practice of clinical child neuropsychology in a common location, we will continue to foster the development of the field and perhaps attract additional practitioners to obtain expertise with children.

In this third edition, updates of chapters from the second edition appear along with a variety of new chapters that present information on topics that have become more salient over the several decades we have toiled over this handbook. Those familiar with prior editions will note new works by Sam Goldstein and Adam Schwebach on the Neuropsychological Basis of Learning Disabilities; Antolin Llorente on the Neuropsychological Assessment of Spanish-Speaking Children and Youth; Arthur MacNeill Horton, Jr. and Arthur MacNeill Horton, III on the Child Clinical Neuropsychology of Drug Abuse; Sam Goldstein and Kordell Kennemer on Neuropsychological Aspects of ADHD; Robert McCaffrey, Julie Horwitz and Julie Lynch on Child Forensic Neuropsychology; Priscilla Bade-White, John Obrzut, and Philip Randall on Neuropsychological Aspects of Pervasive Developmental and Autism Spectrum Disorders; and Jack Naglieri, Cara Conway, and Sam Goldstein on Using the PASS Theory in Neuropsychological Assessment. We consider these to be central/main stream efforts that are central to understanding the field of clinical child neuropsychology and the broadening role of child practitioners in our discipline. As a strong example of the latter, Joan Mayfield's chapter on the role of the pediatric neuropsychologists in coma is a seminal work in the guidance it provides the child practitioner.

As we have noted in prior volumes, there are many individuals to whom we must express our appreciation and without whom this work could not have been completed. As the publishing industry has consolidated, this handbook has moved across publishers. We greatly appreciate the efforts of Sharon

Panulla and Janice Stern, of Springer, for continuing to appreciate the need for this volume as well as their guidance and ultimately bringing it to fruition at its new home. We also cannot forget Eliot Werner, our original editor from Plenum Publishing Company (now absorbed under the Springer umbrella), who had sufficient faith in us as well as the development of child clinical neuropsychology as a discipline to risk publishing a large, comprehensive handbook originally in this field. The dedication and efforts of all of our chapter authors are acknowledged and sincerely appreciated. Without their hard work and careful thought, this handbook would be a shallow effort on our part. Elaine wishes to express her gratitude to her family, David, Emma, and Leif for their support and encouragement. Cecil continues to note and appreciate Julia's contributions to his efforts not only through her confidence, emotional support, and companionship, but through her willingness to engage him in discussions particularly of the applicability of our science to the day-to-day problems of the clinical practitioner, of which she remains a superb example.

College Station, Texas   Cecil R. Reynolds
Cleveland, Ohio   Elaine Fletcher-Janzen

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Foundations and Current Issues

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Development of Neuropsychology as a Professional Psychological Specialty: History, Training, and Credentialing

LAWRENCE C. HARTLAGE AND **CHARLES J. LONG**

Background

Neuropsychology can be depicted as having a long history and a short past. As early as 400 BC, Hippocrates conjectured a correlation of behavioral observations with possible anatomic localizations, and later Galen related the anatomic localizations to the brain. Although there were occasional detours and distractions, Gall's early-19th-century chronological hypotheses served as the focus of exploration for a time. By the late 19th century more sophisticated experimental methodology laid the groundwork for the underpinnings of current scientific neuropsychology. The data from electrical stimulation of discrete cortical areas in animals by Fritsch and Hitzig around 1790, the clinical localization of expressive speech by Broca, and the localization of receptive language by Wernicke a century later laid the foundation for major breakthroughs in the 20th century. Indeed, during the 20th century, two major approaches to the study of brain–behavior relationships evolved. In Russia, a qualitative clinical evaluation evolved, characterized by the work of Luria

(Luria, 1970; Luria & Majovski, 1977) and Beehtereva (1978). This focused on the observation of cognitive functions such as content, replication, and flexibility of thinking (Puente, 1989).

In the United States, a number of different factors influenced early-20th-century approaches to the study of brain–behavior relationships. The influence of British scientists including Henry Head and Hughlings Jackson, unlike their Russian counterparts, supported use of psychometric tests and, unlike Luria's focus on localization, attended to behavioral/psychological features. In the first half of the 20th century—perhaps reflecting interest following two world wars and the differentiation of "functional" from "organic" sequelae of brain injuries resultant from both open and closed head injuries—there was a trend away from localization, instead addressing classification of behavioral deficits as a unitary phenomenon, i.e., was the problem "functional" or "organic" (Hartlage, 1966). This conceptual approach is reflected in the work of a number of well-recognized names from this era: Wechsler and others attempted configural organization of subscales to identify organic profiles; Bender developed a constructional praxis measure addressed to identification of brain injury (Bender, 1938); and Benton developed a combined constructional praxis/short-term memory test for identification of brain injury (Benton, 1955).

LAWRENCE C. HARTLAGE • Augusta Neuropsychology Center, Evans Georgia 30809. **CHARLES J. LONG** • Psychology Department, The University of Memphis, Memphis Tennessee 38152.

During the latter years of the first half of the 20th century, an approach for measuring biological bases of intellective functions was promulgated by Halstead (1947), but his untimely death curtailed his further development of these concepts. It was his student, Reitan, at Indiana University Medical Center, who was able to refine Halstead's measures and develop a number of his own, providing the solid scientific and experimental basis for neuropsychological practice based on a standardized, validated, comprehensive battery sensitive to brain dysfunctions. Reitan's seminal 1955 paper (Reitan, 1955) demonstrated differential (Wechsler) verbal and performance IQ scores resultant from unilateral brain injuries, and over the next half century, Reitan reported in a number of studies the ability of this neuropsychological battery to not only identify but differentiate among brain dysfunction resulting from a variety of etiologies. This work was largely based on assessment of adults with verifiable brain injury.

Following progress in the development of a scientific database for applied neuropsychology, there was an emerging recognition of psychology as a profession with potential applications dealing with both medical and societal issues.

During World War II, psychology was recognized for its potential in military manpower utilization, especially in fields such as selection and training of pilots. At war's end, focus shifted toward utilizing psychological procedures for determining whether war related problems in veterans represented difficulties of primarily psychological as opposed to neurologic origin, such as might be resultant from various types of head injuries.

In the early years of its emergence, a loosely constituted International Neuropsychological Society represented neuropsychology. This was an interesting group composed of psychologists, neurologists, and educators with an interest in brain–behavior relationships. The International Neuropsychological Society held its first program meeting in 1973, on a medical school campus in New Orleans, with approximately a hundred participants. The growth of interest in the field of neuropsychology and the need for some type of education and credentialing guidelines encouraged a small group of psychologists to organize the National Academy of Neuropsychologists (subsequently renamed the National Academy of Neuropsychology). Its first program meeting was in 1981, in Orlando, with approximately 350 participants. One of the early initiatives of the National Academy of Neuropsychology was to survey identifiable neuropsychologists to assess their perception of the need for some national credentialing body for neuropsychologist's practice. Following widespread agreement that such a body was indeed needed, the National Academy assigned an ex-president (L.C.H.) to organize such a board. In the early 1980s, a board constituted exclusively of individuals with (peer nominated) expertise in neuropsychology who were also credentialed by the American Board of Professional Psychology (typically board certification in clinical psychology) was organized to serve as a founding board to refine credentialing issues and procedures. This organization, as an outgrowth and product of the National Academy of Neuropsychology, was incorporated as the American Board of Professional Neuropsychology. Overtures were made to the American Board of Professional Psychology to offer neuropsychology as a new specialty. However, the American Board of Professional Psychology was not at that time willing to recognize a new specialty area. Instead the executive director (Margaret Ives) agreed offering neuropsychology as a super specialty (e.g., comparable with the American Board of Psychiatry and Neurology Certification in Child Psychiatry or Neurology, which was added to basic qualifications, in psychiatry or neurology, with the designation "with special competence in child"). At this point, a group of psychologists not formerly affiliated with any professional organization, who did not have ABPP qualifications, felt their qualifications in neuropsychology would be overlooked by this procedure. Accordingly, they organized a rival board that was subsequently incorporated as the American Board of Clinical Neuropsychology.

Following establishment of both scientific and professional facets of neuropsychology and with the increasing recognition of neuropsychological substrates of learning and adaptive behavior problems in adults with brain injury, there developed a progressive interest in some possible central processing dysfunctions as being etiologic in a wide variety of children's learning problems (e.g., Chalfant & Scheffelin, 1969). Given impetus and support by the focus of "The Great Society" programs on identification, description, and treatment of childhood learning problems,

neuropsychology was increasingly involved with the assessment of exceptional children.

The growing involvement of neuropsychology with children's problems raised a number of scientific and professional questions and issues. As the body of research relating known brain damage to specific learning and behavior problems had for the most part involved adults, one obvious scientific question involves the extent to which this research could be applied to children. Stemming from this scientific question arose a professional issue, namely, which tests or diagnostic approaches are appropriate for use with children? If findings from adults could be applied directly to children, then presumably a downward extension of a battery appropriate for use with adults might be adequate for this purpose. Conversely, if findings from adult neuropsychology could not be applied to children, it would be necessary to develop a new database for application to child neuropsychology.

Another specific question dealt with whether findings from individuals with known brain damage verified on neurological, neurosurgical, or neuroradiological criterion measures could be applied to children who were presumed to have neuropsychological impairments on the basis of neuropsychological assessment, but for whom there was no definitive evidence of structural or physiological damage. This scientific question translated into obvious professional issues. Because for many children whose neuropsychological examination findings suggested a clear central nervous system dysfunction, there was no external criterion that could validate such an impression, the misclassification of such children as "brain injured" could adversely influence their educational programming and management.

Assessment Approaches

In response to the demand for neuropsychological services for children, and in attempts to address the scientific and professional issues raised by this demand, two diverse approaches to the provision of neuropsychological services to children emerged. One approach involved modified versions of traditional neuropsychological batteries such as the Halstead–Reitan Neuropsychological Battery (Reitan, 1955; Reitan & Davison, 1974; Selz, 1981) and the Luria-Nebraska Neuropsychological Battery (Golden, 1981; Golden, Hamineke, & Purisch, 1980; Plaisted, Gustavson, Wilkening, & Golden, 1983), which standardized the adult battery items on a child sample. For the most part, this standardization took the form of deleting from the adult battery those items that were too difficult for children. There is reportedly good congruence between the adult and child batteries on classificatory accuracy, and also between the Reitan-Indiana Children's Battery and the Luria-Nebraska Neuropsychological Battery for Children (Berg et al., 1984; Geary, Schultz, Jennings, & Alper, 1984; Golden et al., 1981). Even among proponents of a standardized battery approach, there is disagreement concerning which battery is best for which population of patients (e.g., Adams, 1980a, 1980b; Spiers, 1981). The second emphasis is on interpretation of standard psychometric tests from a neuropsychological perspective, augmented by some measures of sensory and motor function, using relevant age-appropriate tests for children of given ages, ranging from preschool through adolescent ages (Hartlage, 1981, 1984; Hartlage & Telzrow, 1983; Telzrow & Hartlage, 1984). This approach uses standardized behavioral tests and interprets them according to the individual's strengths and weaknesses and in some cases makes inferences regarding neurological integrity. Such an approach is popular with psychologists working in school settings, and in many cases may be adequate for child neuropsychological assessment. Although there is little evidence that one approach is clearly superior, "turf skirmishes" often center on the issue of qualifications. Psychologists who have developed expertise in the use of a given neuropsychological test battery tend to support the view that the only legitimate neuropsychologists are those with a similar background and expertise. Psychologists who espoused diagnostic approaches involving traditional psychometric tests counter by questioning the relevance of a standardized battery developed for adults with known brain lesions for assessing children who often do not have evidence of brain lesions. They also question the redundancy involved in adding a standard neuropsychological battery to the array of psychometric instruments required by most school districts for psychoeducational assessment. The second approach appears to be preferred by most professionals. A survey of internship training programs suggests that most professionals prefer the second approach (interpretation of

standard psychometric tests from a neuropsychological perspective) (Goldberg & McNamara, 1984). Their survey results revealed that 78% employ nonstandardized assessment strategies, 63% the Halstead–Reitan Battery, and 35% the Luria-Nebraska. Even those individuals employing a neuropsychological battery frequently augment the battery with common psychological tests.

Recently, there has evolved a small following of practitioners who attempt to modify subparts of existing neuropsychological batteries, such as a fairly recent publication of a "revised" children's young adolescent's version of the Category Test (Boll, 1993), or modify administration of a standardized test commonly used as part of a neuropsychological battery (e.g., Kaplan, 1991). As there is nothing conceptually new or different in such modifications of existing text or procedures, such approaches can be classified, according to use, in one of these two schemata.

Professional Context of Child Neuropsychology

With the advent of the CAT scan, NMR, and other instruments, neuropsychological assessment has shifted away from simple yes/no "organic" diagnosis as a primary endeavor and has moved toward comprehensive assessment of the functional consequences of neurological damage (i.e., cognitive skills). The focus is on cognitive strengths and weaknesses and their relationship to academic performance and/or intervention strategies. Neurological integrity is only indirectly inferred as a contributing factor and the utility of such inferences is questioned. It continues to be argued that neuropsychodiagnosis has little or no relevance to education and/or rehabilitation, although it may be relevant to planning for intervention. While the data at present do not indicate that neuropsychological assessments are essential, it is often the case that this is the only assessment whereby a comprehensive investigation of a broad range of cognitive skills is evaluated in the context of emotional and situational factors.

Current interest in neuropsychological assessment has begun to focus on the ecological validity (predictive validity) of neuropsychological tests. While relating test scores to vocational performance and real-world behaviors is difficult because of the variability across jobs and across social situations, the academic environment affords a much more stable environment. Future research in this area may well hold substantial promise for the development of a better understanding of the relationship between neuropsychological performance in children in a learning environment as well as aid in the development of effective treatment strategies.

Levels of Inference

An important issue in training and credentialing in child neuropsychology involves the purposes for which neuropsychologically relevant data are to be used. A comparatively low level of inference involves a conclusion that impaired brain function may be etiologic or at least contributory to a given problem. An example of this level of inference might be a conclusion reached by a school psychologist that a child's failure to acquire a given academic skill is likely related to brain damage or dysfunction. At a considerably higher level of inference are diagnostic statements indicating specific localizing and etiologic phenomena. An example of this level of inference might be a statement, reached by a clinical child neuropsychologist working in a neurological setting, that a child appears to have an astrocytoma confined to anterior portions of the nondominant cerebral hemisphere. Perhaps the highest level of inference involves statements concerning some irreversible intervention. An example of this type of inference might involve a clinical child neuropsychologist working in conjunction with a pediatric neurosurgeon who concludes that removal of a major portion of a child's hippocampus will not impair memory or other mental function. Between these low and high levels of inference occur many intermediate levels involving such matters as optimal instructional mode, referral to a neurological specialist, prognostic statements based on inferred level of cortical integrity, or conclusions concerning whether (or the extent to which) a child's impaired cognitive performance may be related to an injury for which legal action is pending.

It is possible that a well-trained clinical child psychologist or school psychologist, with only moderate training (or credentials) in child neuropsychology, may make appropriate lower level inference concerning brain–behavior

relationships. For example, a school psychologist may, by training, experience, and clinical skill, be quite adequately prepared to develop perfectly appropriate academic intervention programs for a child with a chronic or acquired neurological impairment, and precluding such individuals from such practice on the grounds that they are not sophisticated in brain–behavior relationships may serve to deprive a child of a valuable professional resource. Conversely, it is not reasonable to expect such a professional to detect manifestations of an early stage neurodevelopmental disorder or a neoplasm of some slowly progressive type. On the one hand, it can be argued that, until the proper diagnosis is made, it is not possible to determine what level of inference may be required: This might suggest that all questions concerning possible brain involvement in children require the involvement of a qualified child neuropsychologist. On the other hand, in a typical school population, the base rate of neurodegenerative or slowly progressive neoplastic disorders is sufficiently low that such a requirement may be considered to be unrealistic.

Interactive with the level of inference is the issue of potential harm to the child. Some chronic neurological conditions, such as might be represented by chronic cerebral hemispheric functional asymmetry, can conceivably be overlooked without necessarily causing major problems. In cases where appropriate educational and counseling services are provided, overlooking the neurological substrates of uneven levels of academic performance may be only minimally handicapping to the child. Conversely, labeling the child "brain damaged" may deprive the child of needed educational support. Similarly, the mismatch between a child's neuropsychologically mediated abilities and deficits in an ongoing educational program that does not take these factors into account may cause harm to the child, both in terms of frustration and failure to achieve academically at ability levels. Obviously, individuals should only make higher-order inferences regarding brain–behavior relationships when their training, experience, and clinical skills qualify them for such inferences. Although guidelines concerning training and credentialing can and should address these issues, at the present time they have not been effectively addressed. Even if they are addressed in the future, it is not reasonable to hope that such guidelines can resolve them all.

Credentialing of Psychologists

Although the study of developmental brain–behavior relationships is a relatively recent endeavor in neuropsychology (Dean, 1982), it has already been argued that there is a need for some type of credentialing and certainly for more specialized training if one is to provide appropriate neuropsychological services to children.

Clinical psychologists have traditionally tended to function as generalists—setting few limits regarding credentialing and developing no formal method for identifying a particular area of expertise. They tend not to limit their practice to a specific problem area or specific age group (VandenBos, Stapp, & Kilburg, 1981). This state of affairs no longer appears appropriate for the current practice of psychology because of the dramatic change in the knowledge base. Certainly it is clear that neuropsychological assessment requires specific knowledge not generally obtained in traditional clinical psychology training programs. Furthermore, the techniques and issues in child psychology cannot simply be deduced from knowledge of adults. Specialty training in school psychology and specialization in child psychology also speak to the changes in training promoted to meet the needs of the child.

Although the American Psychological Association initially recognized only four specialty areas, a review in credentialing activities by Sales (1985) identified 31 specialty-credentialing boards; and at the time of this writing the American Board of Professional Psychology has added several more boards and is negotiating with others for inclusion under its umbrella approach to credentialing. The overall credentialing process continues to undergo review. In February 1994 the APA Council of Representatives voted to establish an APA College of Professional Psychology that will function as a credentialing body (APA Practice Directorate, 1994). Also in 1994, APA formed the Joint Interim Committee for the Recognition and Identification of Specialties and Proficiencies. These activities point out APA's awareness of organizing and clarifying the credentialing process. Even though psychologists are identifying areas of specialization and devising procedures for membership inclusion, clinical psychologists seem reluctant to limit their practice by establishing formal specialties within

clinical psychology and such activities are not likely to be readily endorsed. Indeed, clinical psychologists have been able to push legislation to enact state licensing and to specifically define diagnoses of brain damage, and the practice of neuropsychology, as within the specific purview of clinical psychology.

In the absence of credentialing, control is left to licensing activities, done at the state levels, resulting in a wide variety of requirements for practice in a specified area such as neuropsychology and a tendency to rely on the individual practitioner with respect to not making professional judgments at levels of inference for which the practitioner is not qualified. As has just been noted, however, in cases involving some neuropsychological problems, an otherwise well-trained clinician may not recognize the neuropsychological nature of the problem and at the same time feel justified by avoiding any inferential statements concerning CNS involvement. Although it could be argued that making no inferential statement concerning CNS deficit in such a case may in fact be inferring something about CNS integrity, such activities are extremely difficult to control within limitations of generic state licensing laws. Few states attempt to designate specialty training within psychology although recently Louisiana has identified a sub-specialty in neuropsychology with inclusion contingent on satisfying the requirements of either the American Board of Professional Neuropsychology or the American Board of Clinical Neuropsychology.

A national credentialing board, not limited by legislators who enact and amend licensing laws at the state level, is an accepted approach toward ensuring some level or degree of competence among practitioners who have met the requirements of that board. With credentialing requirements set by professionals, this obviously represents an approach with considerable potential for helping ensure such competence. As participation in the activities required for credentialing is entirely voluntary (and can entail a fair amount of energy, frustration, and money), there is no assurance that the only qualified neuropsychology practitioners are those who are board certified. As with generic state licensure, board certification in neuropsychology does not necessarily guarantee expertise in all areas of neuropsychology. Unlike the American Board of Neurology and Psychiatry, which adds "with special competence in child neurology" (or psychiatry) for practitioners who satisfy the required training and experience for this endorsement, neuropsychology issues only generic endorsement.

At the present time there are two boards in neuropsychology: the American Board of Professional Neuropsychology and the American Board of Clinical Neuropsychology. Although both boards are attempting to comprehensively evaluate professionals and award the diplomate status to those who are judged to be qualified, the number of individuals who can be evaluated by this comprehensive process is limited. Even though both credentialing boards have been in varying states of activity since 1984, it is estimated that only about 800 individuals have successfully completed the oral examination and have been awarded the diplomate in neuropsychology. Furthermore, both boards can only comprehensively evaluate 40–50 per year. The result is that it will be quite some time before the majority of qualified neuropsychologists can be identified. An even greater problem relates to the fact that both boards evaluate neuropsychologists as a broad category. While the individual outlines specific areas of competency within neuropsychology such as interest in children, there is no formal designation as to those who are specifically qualified in child neuropsychology.

The awareness of a lack of understanding of the specialty practices by third-party payers led the National Academy of Neuropsychology and the APA's Division of Clinical Neuropsychology to form a Joint Task Force in 1991. After numerous discussions several guidelines were proposed. This included the formation of new neuropsychological assessment codes and a definition of a neuropsychologist.

Definition of a Clinical Neuropsychologist

A. Level I Certification by examination by either the American Board of Clinical Neuropsychology or the American Board of Professional Neuropsychology

B. Level II

    1. Education—Doctorate degree in psychology from a regionally accredited institution with a program in psychology

2. Experience—Three years (minimum of 500 hours per year) of clinical neuropsychological experience at either predoctoral or postdoctoral levels
3. Supervision—Two years supervision in clinical neuropsychology satisfied by one or more of the following:

   a. Two years postdoctoral supervision
   b. One year predoctoral and one year postdoctoral supervision
   c. Successful completion of a postdoctoral fellowship

4. License
   State or province licensure at the level of independent practice
5. Definition

Clinical neuropsychology is defined as the study of brain–behavior relationships based on a combination of knowledge from basic neurosciences, functional neuroanatomy, neuropathology, clinical neurology, psychological assessment, psychopathology, and psychological interventions.

This was followed by a letter of October 1994 from Carl B. Dodrill, Ph.D., Division 40 president, in which he indicated that the above definition was in error and that the only definition of a clinical neuropsychologist approved by Division 40 was published in *The Clinical Neuropsychologist,* 1989, volume 3, p. 22 [see Appendix for guidelines for doctoral training in clinical neuropsychology], which is as follows:

A Clinical Neuropsychologist is a professional psychologist who applies principles of assessment and intervention based upon the scientific study of human behavior as it relates to normal and abnormal functioning of the central nervous system. The Clinical Neuropsychologist is a doctoral level psychology provider of diagnostic and intervention services who has demonstrated competence in the application of such principles for human welfare following:

A. Successful completion of systematic didactic and experiential training in neuropsychology and neuroscience at a regionally accredited university;
B. Two or more years of appropriate supervised training applying neuropsychological services in a clinical setting;
C. Licensing and certification to provide psychological services to the public by the laws of the state or province in which he or she practices;
D. Review by one's peers as a test of these competencies.

Attainment of the ABCN/ABPP Diploma in Clinical Neuropsychology is the clearest evidence of competence as a Clinical Neuropsychologist, assuring that all these criteria have been met.

As can be seen from the confusion in definitions, the issues are far from resolved regarding clinical neuropsychology in general, and the issue of specialization in child neuropsychology has not been addressed.

Further complicating the issue of board certification, usually designated as "diplomate" status, is the pervasive level of inference issue. Because only the best neuropsychological clinicians—for instance, those qualified to make the highest levels of neuropsychological inference—are likely to receive "diplomate" status, who is to do the lower level of inference work? As has been mentioned, whereas it might be considered optimal practice to have all children with any problem seen by a skilled child neuropsychologist, to ensure that problems of a neurological nature are not overlooked, this is obviously not realistic.

These problems raise the question of the use of technicians in neuropsychology. The Division 40 Task Force on Education, Accreditation, and Credentialing concluded that "the use of . . . technicians is a common and accepted practice when the supervising psychologist maintains and monitors high standards of quality assurance" (APA Task Force, 1989, p. 25). Surveys of practicing neuropsychologists indicate that 53% use technicians. It would appear that neuropsychologists can make effective use of technicians to provide more cost-effective services. Such use would not preclude the neuropsychologist spending time with the patient in obtaining the history, reevaluating questionable areas of weakness by the use of additional tests, or clarifying test findings during the debriefing with the patient.

It appears that specialty credentialing is unlikely to be accepted in the near future by the vast majority of clinical psychologists. Therefore, training must be designed and offered to best prepare these individuals for their designated area of clinical service. Universities offering specialty training in school psychology, child

psychology, and/or neuropsychology are meeting such needs.

General Issues in Child Clinical Training

With respect to educational context, clinical child neuropsychology can be viewed as a sub-area of clinical child psychology, and it is relevant to preface a review of issues in clinical child neuropsychology training with an overview of training issues in clinical child psychology. Presently, although there are seven formal predoctoral training programs in neuropsychology (Lubin & Sokoloff, 1983), few are specifically designed for child neuropsychology. In some programs, students are required to satisfy the requirements of the child clinical and neuropsychology training programs to be designated as trained in child neuropsychology. Without such arrangements, much of the specialty training in clinical child neuropsychology currently is provided by postdoctoral positions.

The report of the task force from Division 40 recommends that in the absence of formal accredited educational programs:

> (1) The entry level credentials for the practice of clinical neuropsychology shall be predicated on the license to practice at the independent professional level in the state or province in which the practitioner resides; (2) In addition, 1600 hours of clinical neuropsychological experience, supervised by a clinical neuropsychologist at the pre- or post-doctoral level, shall be required; (3) Persons receiving a doctoral degree in psychology before 1981 may substitute 4800 hours of post-doctoral experience in a neuropsychology setting involving a minimum of 2400 hours of direct clinical service. *(Newsletter 40,* 1984)

In the absence of formal training programs in child neuropsychology, specialization in child neuropsychology must either combine two existing areas or seek further postdoctoral training.

Because of the changing nature of the nervous system in the child and the impact of non-neurological factors on the child's behavior, the child neuropsychologist needs to be trained in basic psychological, developmental, and neuropsychological issues. In addition, the role of psychological assessment in clinical child neuropsychology needs to be well understood.

The reliance on standardized tests increases with decreasing experience of professionals in any discipline. Of primary importance is the issue to be addressed or the question to be answered. If the primary question relates to whether there is cerebral dysfunction, then regardless of the test employed, the evaluators' effectiveness depends on their training in brain–behavior relationships and their understanding of the nervous system and its contributions to behavior. Without such training, effective interpretation of behavior leading to decisions regarding brain dysfunction cannot be reached. If learning disability is of primary interest, then the evaluator needs to understand the relationship between test behavior and learning disability. The same argument holds for developmental delays, emotional disorders, retardation, and so on.

New graduates, individuals shifting their area of basic training, or researchers tend to depend on a fixed battery or evaluation strategy and rigorously defend it against all others. They thus exhibit a strong tendency to become method oriented, rather than problem oriented. With further education on the part of the professional and understanding of the relationship between areas of primary importance, less reliance is made on a specific test battery and a broad range of assessment devices may be employed in order to effectively assay the behaviors in question and outline an effective treatment plan.

Clinical neuropsychology as a specialty within psychology is a fairly new area that is continuing to undergo change and self-analysis in order to outline clinical courses most appropriate to the practice of neuropsychology. The database on neuropsychology has also served to shift psychologists into a designated specialty area as the knowledge base required to pursue neuropsychological assessment is sufficiently broad to make it difficult for traditionally trained psychologists to pursue effectively such clinical activities without extensive training or experience.

In 1977 it was recognized that a conference dealing with training in clinical child psychology was needed, and a preliminary working conference was held in 1983 with the principal conference held in May 1985. In general, the recommendations included three features involving general clinical psychology training, involving requirements for training in normal development; experience with normal children; and minimal competencies in assessment, psychopathology, and intervention with children (Johnson & Tuma, 1986; Tuma, 1986). Specific

to clinical child psychology graduate training were seven recommendations, the first of which endorsed the Boulder Model for clinical child psychology. Another recommendation endorsed the APA Division 27 Task Force-documented Guidelines for Training Psychologists to Work with Children, Youth and Families (Roberts, Erickson, & Tuma, 1985). In general, the other recommendations specific to clinical child psychology training dealt with such issues as recognizing cultural diversity and the multiple contexts in which psychologists working with children, youth, and families must function. Internship training was recommended as involving at least two-thirds of the training experience in child clinical activity, with research incorporated into the internship program. Postdoctoral and continuing education training in clinical child psychology was recommended, although specific guidelines concerning required background prerequisites or context areas were not proposed.

With respect to recognition of proficiencies and specialty areas in psychology, the APA Board of Professional Affairs (BPA) appointed a Committee on Specialty Practice from 1970 to 1980 to explore such issues. Specialty guidelines for clinical, counseling, industrial/organizational, and school psychology were approved by the APA Council in 1980, making APA's first detailed public statement concerning service provisions in specialty areas. The BPA appointed a Subcommittee on Specialization in 1980 to address the issues involved in criteria for specialty areas not covered by these four major areas, and in 1983 a second draft manual for the identification and continued recognition of proficiencies and new specialty areas in psychology was published (Sales, Bricklin, & Hall, 1983). Differentiation was made between proficiencies and specialties, on the basis of several major criteria. A specialty was recommended as involving a body of knowledge with (1) unique client populations, (2) specific techniques and technologies, (3) problems addressed, and (4) settings wherein the knowledge applied. Proficiency, on the other hand, would involve a body of knowledge and skills that provide the basis for services in one of these four parameters.

The requirements for the identification of a specialty area involved (1) a formal organization, recognized in the field that is responsible for managing the development of a specialty; (2) a definition of the specialty, including knowledge and skills required; and (3) an educational sequence of training and experience. Requirements for the identification of the proficiency involved (1) a formal organization, (2) a definition, (3) evidence of need and parameters of practice, (4) demonstrated efficiency, and (5) uniqueness. In this context, neuropsychology could be viewed as representing either a specialty or an area of proficiency, with clinical child neuropsychology a subarea of either a specialty or a proficiency.

In a related and somewhat parallel area, the APA Task Force on Education and Credentialing (1985) published a recommendation concerned with educational content required for designation as a psychology program. Although related in only a tangential way to clinical child neuropsychology, the designation system tends to discourage the graduate education of clinical child neuropsychologists in academic settings without a clear identification as part of a psychology program (e.g., freestanding clinical child neuropsychology programs in medical schools or professional schools would have difficulty meeting the designation criteria).

Focus on Training in Clinical Child Neuropsychology

Where does training in clinical child neuropsychology fit into this broader context? Training in clinical child neuropsychology is generally provided in one of three ways: graduate coursework, internship/practicum training, and postdoctoral training fellowships.

There has been a dramatic increase in training programs over the past decade, increasing from approximately 7 to approximately 40 programs offering a terminal degree in neuropsychology (Division 40 of the American Psychological Association, 2005). While graduate course offerings show considerable variability, many offer training as a subspecialty of clinical psychology; many more clinical programs offer some coursework in neuropsychology; and some clinical programs offer lectures on neuropsychology but no formal coursework (Golden & Kuperman, 1980). Thus, among the 60 or more APA-approved clinical programs that indicate they provide offerings in neuropsychology, these offerings may range from formal coursework to practica or even possible work placements.

Division 40 of the APA (Neuropsychology), aware of the need for establishing guidelines for neuropsychology training, has formed a task force to develop such guidelines (see Appendix). A preliminary report of their efforts was published in *Newsletter 40* (1984). According to those guidelines the major function of the clinical neuropsychologist is to assess current behavioral disturbances associated with neurological impairment. The report suggested that neuropsychological assessment should include measures of (1) abstract reasoning and categorical thinking, (2) cognitive flexibility and planning, (3) language communication, (4) learning and memory, (5) sensation and perception, (6) fine and gross motor functions, (7) initiation and attention, (8) affect and mood, and (9) psychosocial adaptation.

In order to effectively pursue these assessment goals, the diagnostician needs training in (1) functional neuroanatomy, (2) clinical diseases, (3) child development, (4) changes in behavior as a function of aging, (5) behavioral psychopharmacology, (6) psychophysiological principles underlying pathologies, (7) sociocultural factors, (8) personality assessment and interviewing skills, (9) principles of test construction and validation, and (10) test administration and interpretation. Properly trained neuropsychologists should be able to outline treatment plans and consult with family members, educators, employers, and so on, in order to assist in improving the behavioral adjustment of the individual in specific situations. Remediation by a clinical neuropsychologist focuses primarily on disability associated with cerebral dysfunction and secondarily on emotional or other maladaptive behaviors that are a consequence of the individual's primary disability.

The *Newsletter* outlined the needs of the child neuropsychology training to include much of the above with adjustment in training suggested to incorporate bodies of knowledge as well as techniques and resources specific to clinical child neuropsychology. Major issues such as child development, CNS plasticity, and the nature of the referral questions are seen as primary additional areas of competence. One of the primary distinctions between child and adult neuropsychology is the emphasis on description of processes in children, because the focus on process helps delineate specific treatment plans. More so than with adults, a multidisciplinary team often evaluates children; thus, child neuropsychologists must have knowledge of related professions so that they may effectively interface their findings in developing the final treatment plan.

Among practicum offerings that include child neuropsychology as an area of training, these offerings in many cases exist as ancillary options, such as being available on a limited basis within a child therapy practicum. Even in practicum or internship settings wherein neuropsychology is mentioned as an area of training emphasis, there is considerable variability. This variability appears to reflect both the differing concepts of neuropsychology as a specialty area within clinical neuropsychology and the unique backgrounds of the faculty who provide such training. In one grouping of 28 graduate settings that offered neuropsychology training, Golden and Kuperman (1980) found that the tests used most frequently were the Wechsler and Bender Gestalt.

Postdoctoral training programs in clinical child psychology are relatively rare. However, a number of postdoctoral programs in clinical neuropsychology offer some exposure to child neuropsychology, and a few provide some segment of the program devoted to work for children. Informal surveys of postdoctoral trainees who have had at least some postdoctoral training in clinical neuropsychology reveal a rather wide range of backgrounds. Some "retread" postdoctoral fellows, whose doctoral training is in nonclinical areas such as physiological psychology, have very little background in either child development or the special skills needed to evaluate children. Others with backgrounds in areas like school psychology may have excellent skills in child assessment and good knowledge of developmental phenomena, but little expertise in functional neuroanatomy or basic brain–behavior relationships. Yet others enter postdoctoral child neuropsychology training programs with good assessment skills involving both children and adults, with coursework in neuroanatomy and physiology, and prior exposure to neurologically impaired children from practicum or work experiences. Thus, the content of the "ideal" postdoctoral experience in clinical child neuropsychology may relate to the unique backgrounds that such postdoctoral fellows bring to the program.

Professional Context of Clinical Child Neuropsychology

Neuropsychologists assume that understanding brain–behavior relationships is necessary for both diagnosis and treatment planning. Such knowledge is not, however, sufficient, and therefore few neuropsychologists focus on the brain as the only contributing variable. Child neuropsychological assessment must include measures of personality/emotional well-being and identification of environmental influences. Given such a broad "systems" analysis, the child neuropsychologist can provide information of benefit to a number of other disciplines. For example, the interpretation of neurological dysfunction in the context of situational, learning, emotional, and other important dimensions provides the neurosurgeon with a more comprehensive picture of the role that a lesion or area of damage might exert on a child's behavior. This can assist teachers in the classroom and parents at home by identifying strengths and weaknesses and identifying those factors that appear to be most amenable to modification. The assumption is that one needs to identify factors that contribute to aberrant behaviors and prioritize them regarding those that would appear to require primary assistance as well as those that are most likely to change with remediation.

Unlike the adult brain, which is assumed to be developmentally static with fixed effects associated with injury, the child's brain is characterized by growth and differentiation that extends from conception up to young adulthood (Renis & Goldman, 1980; Rourke, Bakker, Fisk, & Strang, 1983). The effects of neurological damage are influenced by age, the locus of the injury, the nature of the damage, the sex and socioeconomic status of the individual, as well as the emotional adjustment, coping, and adaptive skills of the individual (Bolter & Long, 1985). Thus, even our limited understanding of chronogeneric localization can improve the assessment and remediation of neurologically impaired children. Neurological damage during the developmental years may produce permanent deficits, temporary deficits, and/or delayed-onset deficits (Teuber & Rudel, 1962). Understanding the neurological contribution to the overall behavioral complex is necessary to effectively identify barriers and plan for remediation.

Professional Relationships

Although all psychologists view behavior from a systems perspective, problems are viewed somewhat differently depending on the specialization. School psychologists focus primarily on academic problems and secondarily on how non-academic factors influence school performance (e.g., emotional, situational, neurological, genetic, developmental). Child psychologists focus primarily on emotional/behavioral problems with secondary focus on other areas. The child neuropsycho-logist focuses primarily on brain–behavior relationships with other factors being viewed "as" secondary.

Professionals in other specialties have challenged the approach of child neuropsychologists. School psychologists have argued that understanding neurological systems is not important for effective treatment (Senf, 1979). It is further argued that neurological labeling connotes irreversibility and mitigates responsibility for remediation (Sandoval & Haapanen, 1981). In fact, Hynd (1982) suggested that the neuropsychological evaluation might provide information that reduces the need for referral for expensive and nonproductive neurological evaluations.

There remain many unresolved issues regarding training and practice of clinical child neuropsychology. As outlined in this chapter, the clinical child neuropsychologist must possess a knowledge base that cuts across many existing areas of specialization. Perhaps for this reason, individuals from a number of specialty areas may function in the assessment and treatment of children with neurological dysfunction in the future. Hopefully, with improved awareness and education, effectiveness of communication will be enhanced across these specialties. This may lead us to recognize the requisite combination of broad skills in general child clinical areas and specific skills in child neuropsychology as constituting clinical child neuropsychology, both a specialty and an area of proficiency.

Appendix

Source: The Clinical Neuropsychologist 1987. Vol. 1, No. 1, pp. 29–34, Swets & Zeitlinger, Reports of the INS-Division 40 Task Force on Education, Accreditation, and Credentialing

Guidelines for Doctoral Training Programs in Clinical Neuropsychology

Doctoral training in clinical neuropsychology should ordinarily result in the awarding of a Ph.D. degree from a regionally accredited university. It may be accomplished through a Ph.D. program in clinical neuropsychology offered by a psychology department or medical faculty or through the completion of a Ph.D. program in a related specialty area (e.g., clinical psychology) which offers sufficient specialization in clinical neuropsychology.

Training programs in clinical neuropsychology prepare students for health service delivery, basic clinical research, teaching, and consultation. As such they must contain (a) a generic psychology core, (b) a generic clinical core, (c) specialized training in the neurosciences and basic human and animal neuropsychology, (d) specific training in clinical neuropsychology. This should include an 1800-hour internship which should be preceded by appropriate practicum experience.

(A) Generic psychology core

1. Statistics and methodology
2. Learning, cognition, and perception
3. Social psychology and personality
4. Physiological psychology
5. Life-span developmental
6. History

(B) Generic clinical core

1. Psychopathology
2. Psychometric theory
3. Interview and assessment techniques

    i. Interviewing
    ii. Intelligence assessment
    iii. Personality assessment

4. Intervention techniques

    i. Counseling and psychotherapy
    ii. Behavior therapy/modification
    iii. Consultation

5. Professional ethics

(C) Neurosciences and basic human and animal neuropsychology

1. Basic neurosciences
2. Advanced physiological psychology and pharmacology

3. Neuropsychology of perceptual, cognitive, and executive processes
4. Research design and research practicum in neuropsychology

(D) Specific clinical neuropsychological training

1. Clinical neurology and neuropathology
2. Specialized neuropsychological assessment techniques
3. Specialized neuropsychological intervention techniques
4. Assessment practicum (children and/or adults) in university-supervised assessment facility
5. Intervention practicum in university-supervised intervention facility
6. Clinical neuropsychological internship of 1800 hours preferably in noncaptive facility. (As per INS-Div. 40 Task Force guidelines). Ordinarily this internship will be completed in a single year, but in exceptional circumstance may be completed in a 2-year period.

(E) Doctoral dissertation

It is recognized that the completion of a Ph.D. in clinical neuropsychology prepares the person to begin work as a clinical neuropsychologist. In most jurisdictions, an additional year of supervised clinical practice will be required in order to qualify for licensure. Furthermore, training at the postdoctoral level to increase both general and subspecialty competencies is viewed as desirable.

Guidelines for Neuropsychology Internships in Clinical Neuropsychology

The following report summarizes the recommendations of the subcommittee on internships of the INS-Division 40 Task Force. The report was prepared by Linus Bieliauskas and Thomas Boll.

At the outset, it is recognized that the internship program is designed primarily for students with degrees in clinical psychology. Such internship programs are those accredited by the American Psychological Association and or those listed in the Directory of the Association of Psychology Internship Centers.

Entry into a psychology internship program is a minimum qualification in a neuropsychology internship. Such entry must be based on

completion of at least 2 years in a recognized psychology Ph.D. graduate training program in an area of health services delivery (e.g., clinical, clinical neuropsychology, counseling, or school psy-chology). Alternately, entry into a psychology internship program must be based on completion of a "retreading" program designed to meet equivalent criteria as a health services delivery program per se. Within the training programs described above, the student must also have completed a designated track, specialization, or concentration in neuropsychology.

There are generally two models for psychology internship training: (1) generic clinical psychology, and (2) specialty in clinical neuropsychology. The former does not concern us here since such training is not geared toward producing specialized experience or qualification. The latter type of internship program, when designed to provide specialized training in neuropsychology, is what constitutes a clinical neuropsychology internship.

A clinical neuropsychology Internship must devote at least 50% of a 1-year full-time training experience to neuropsychology. In addition, at least 20% of the training experience must be devoted to general clinical training to assure a competent background in clinical psychology. Such an internship should be associated with a hospital setting which has neurological and/or neurosurgical services to offer to the training background. Such an internship should not be associated only with a strictly psychiatric setting.

Experiences to Be Provided

The experiences to be provided to the intern in clinical neuropsychology should conform to the descriptions of professional activities in the Report of the Task Force on Education, Accreditation, and Credentialing of the International Neuropsychological Society and the American Psychological Association (1981). Necessary training should be provided in both a didactic and experiential format. Supervisors in such an internship should be board-certified clinical neuropsychologists.

Didactic Training.

A. Training in neurological diagnosis.
B. Training in consultation to neurological and neurosurgical services.
C. Training in direct consultation to psychiatric, pediatric, or general medical services.
D. Exposure to methods and practices of neurological and neurosurgical consultation (grand rounds, bed rounds, seminars, etc.).
E. Training in neuropsychological techniques, examination, interpretation of tests results, report writing.
F. Training in consultation to patients and referral sources.
G. Training in methods of intervention specific to clinical neuropsychology.

Experiential Training.

A. Neuropsychological examination and evaluation of patients with actual and suspected neurological diseases and disorders.
B. Neuropsychological examination and evaluation of patients with psychiatric disorders and/or pediatric or general medical patients with neurobehavioral disorders.
C. Participation in clinical activities with neurologists and neurosurgeons (bed rounds, grand rounds, etc.).
D. Direct consultation to patients involving neuropsychological issues.
E. Consultation to referral and treating professions.

Exit Criteria

At the end of the internship year, the intern in clinical neuropsychology should be able to undertake consultation to patients and professionals on an independent basis and meet minimal qualifications for competent practice of clinical neuropsychology as defined in Section B, Neuropsychological roles and functions of the Report of the Task Force (1981).

Guidelines for Postdoctoral Training in Clinical Neuropsychology

Postdoctoral training, as described herein, is designed to provide clinical training to produce an advanced level of competence in the specialty of clinical neuropsychology. It is recognized that clinical neuropsychology is a scientifically based and evolving discipline and that such training should also provide a significant research component. Thus, this report is concerned with postdoctoral training in clinical neuropsychology that is

specifically geared toward producing independent practitioner level competence which includes both necessary clinical and research skills. This report does not address training in neuropsychology which is focused solely on research.

Entry Criteria

Entry into a clinical neuropsychology postdoctoral training program ordinarily should be based on completion of a regionally accredited Ph.D. graduate training program in one of the health service delivery areas of psychology or a Ph.D. in psychology with additional completion of a "respecialization" program designed to meet equivalent criteria as a health services delivery program in psychology. In all cases, candidacy for postdoctoral training in clinical neuropsychology must be based on demonstration of training and research methodology designed to meet equivalent criteria as a health services delivery professional in the scientist-practitioner model. Ordinarily, a clinical internship, listed by the Association of Psychology Internship Centers, must also have been completed.

General Considerations

A postdoctoral training program in clinical neuropsychology should be directed by a board-certified clinical neuropsychologist. In most cases, the program should extend over at least a 2-year period. The only exception would be for individuals who have completed a specific clinical neuropsychology specialization in their graduate programs and/or a clinical neuropsychology internship (Subcommittee Report of the Task Force, 1984) provided the exit criteria are met (see below). As a general guideline, the postdoctoral training program should provide at least 50% time in clinical service and at least 25% time in clinical research. Variance within these guidelines should be tailored to the needs of the individual. Specific training in neuropsychology must be provided, including any areas where the individual is deemed to be deficient (testing, consultation, intervention, neurosciences, neurology, etc.).

Specific Considerations

Such a postdoctoral training program should be associated with hospital settings which have neurological and/or neurosurgical services to offer to the training background. Necessary training should be provided in both a didactic and experiential format and should include the following:

Didactic Training.

A. Training in neurological and psychiatric diagnosis.
B. Training in consultation to neurological and neurosurgical services.
C. Training in direct consultation to psychiatric, pediatric, or general medical services.
D. Exposure to methods and practices of neurological and neurosurgical consultation (grand rounds, bed rounds, seminars, etc.).
E. Observation of neurosurgical procedures and biomedical tests (revascularization procedures, cerebral blood flow, Wada testing, etc.).
F. Participation in seminars offered to neurology and neurosurgery residents (neuropharmacology, EEG, brain cutting, etc.).
G. Training in neuropsychological techniques, examination, interpretation of test results, report writing.
H. Training in consultation to patients and referral sources.
I. Training in methods of intervention specific to clinical neuropsychology.
J. Seminars, readings, etc., in neuropsychology (case conferences, journal discussion, topic-specific seminars).
K. Didactic training in neuroanatomy, neuropathology, and related neurosciences.

Experiential Training.

A. Neuropsychological examination and evaluation of patients with actual and suspected neurological diseases and disorders.
B. Neuropsychological examination and evaluation of patients with psychiatric disorders and/or pediatric or general medical patients with neurobehavioral disorders.
C. Participation in clinical activities with neurologists and neurosurgeons (bed rounds, grand rounds, etc.).
D. Experience at a specialty clinic, such as a dementia clinic or epilepsy clinic, which emphasizes multidisciplinary approaches to diagnosis and treatment.

E. Direct consultation to patients involving neuropsychological assessment.

F. Direct intervention with patients, specific to neuropsychological issues, and to include psychotherapy and/or family therapy where indicated.

G. Research in neuropsychology, i.e., collaboration on a research project or other scholarly academic activity, initiation of an independent research project or other scholarly academic activity and presentation or publication of research data where appropriate.

Exit Criteria

At the conclusion of the postdoctoral training program, the individual should be able to undertake consultation to patients and professionals on an independent basis. Accomplishment in research should also be demonstrated. The program is designed to produce a competent practitioner in the areas designated in Section B of the Task Force Report (1981) and to provide eligibility for external credentialing and licensure as designated in Section D of the Task Force Report (1981). The latter also includes training eligibility for certification in clinical neuropsychology by the American Board of Professional Psychology.

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2

Development of the Child's Brain and Behavior

BRYAN KOLB AND BRYAN D. FANTIE

Introduction

Perhaps the central issue in neuropsychology over the past 100 years has been the question of how psychological functions are represented in the brain. At the turn of the century, the debate was largely whether or not functions were actually localized in the cortex. Although today this is no longer a subject of major discussion, the general problem of determining *what* is localized in the cortex remains. One way to examine this issue is to look at the way function and structure emerge in the developing child.

As we look historically at the consideration of structure–function relationships in development, we are struck by the reluctance of researchers to engage in such analyses. Indeed, although Freud and Piaget were trained in biology, both carefully avoided inclusion of brain development in their theories of psychological development. It is likely that one major impediment to such theorists was an absence of biological data about developmental neuroscience (Segalowitz & Rose-Krasnor, 1992).

The development of structure–function relationships can be examined in three basic ways. First, we can look at the structural

development of the nervous system and correlate it with the emergence of specific behaviors. Initially this approach seems ideal, as the development of both the nervous system and behavior is orderly and consistent across individuals. Unfortunately, it is not as simple as it appears.

The nervous system matures in a relatively unremitting way, unfolding to the dictates of time. Behavioral change, on the other hand, is often more highly dependent on environmental factors. Thus, the degree of damage caused by sensory deprivation is largely determined by *when* it occurs during an animal's life (Hubel & Wiesel, 1970). In contrast, whether or not someone can ice-skate will be more easily predicted when one knows if the person was raised in Canada or Brazil. In addition, age-related neural changes are seldom immediately observable in vivo so it is extraordinarily difficult to correlate structural and functional variables directly. Furthermore, hypotheses regarding brain devel pment are hard to verify, especially because the human nervous system cannot be manipulated during development. Nevertheless, despite these impediments, this approach is still possible.

The second way to examine morphological and psychological development is to scrutinize behavior and then make inferences about neural maturation. For example, we might study the emergence of distinct cognitive stages carefully, as Piaget (1952) and his followers have done, and then predict what alterations must have occurred in the nervous system to account for

BRYAN KOLB • Department of Psychology, University of Lethbridge, Lethbridge, Alberta T1K3M4, Canada. **BRYAN D. FANTIE** • Department of Psychology, American University, Washington, DC 20016-8062, .

the behavioral change. This approach has not been widely used, largely because psychologists most interested in human development have not been very interested in brain function and many behaviors considered important to child development may not be related directly to neural growth. Nevertheless, this approach is promising and has been pursued actively by Gibson (1977).

There is a tendency to emphasize school-related skills as the most important for study in child neuropsychology. This is not surprising, given the lasting impact that educational success can have on one's entire life, professionally, socially, and, in terms of confidence and self-esteem, personally. In modern Western industrialized countries, the vast majority of a child's waking time is spent in school. Because of the sequential and cumulative nature of most of this type of learning, any impediment can result in a child being left with a widening academic gap between themselves and peers, a gap which, in the age of social promotion, can easily become insurmountable. Many types of childhood learning disabilities are likely related to abnormalities in neural development although this may not always be the case. We must remember that the human brain did not evolve in a classroom. In fact, the neural underpinnings of some learning disabilities may not actually be abnormal in anything other than the statistical sense of the term, and do not represent a true pathology of any kind; good news we hope given the large number of people who seem to receive the "learning disabled" diagnosis.

In light of the fact that, until fairly recently, only a very small proportion of the population was literate, it seems clear that reading, unlike spoken language, could not have been the result of direct evolutionary pressure on humans as a species. Therefore, the capacity to read is probably something akin to what Stephen Jay Gould and Richard Lewontin (1979) would call a "spandrel." Spandrels are traits that, themselves, "have no adaptive tale to tell, but reflect structural constraints imposed by an organism's development or by its quirky evolutionary history," (Dennett, 1995). So humans having the capacity to learn to read most likely came about as a sort of by-product of having developed other cognitive abilities. Therefore, although differences in the facility in learning to read might often be the direct result of the type and configuration of the neural structures one has, these differences may be the result of the normal variance in neuroanatomy that would not have any noticeable effect if one lived in a time or place where reading had not the preeminence as it does in our culture.

Albeit, reading is a very important function, especially for children, and it is essential that clinical neuropsychologists who work with children consider how variance across cognitive domains will affect how a child will fare in school. For the purpose of understanding how developmental neural changes underlie cognitive development, however, it might be better to look at more basic, elemental processes that likely map more closely on the functional neural architecture Thus, the basic functions that are related to neural development may not be found easily by studying scholastic behaviors such as reading. Rather, the neural mechanisms underlying reading ability may best be understood by examining fundamental visuospatial or visuomotor skills, which serve as components of higher-level, more complex cognitive behaviors such as reading.

The third way to study neural structure–function relationships is to relate brain malfunction to behavioral disorders. This method, which is prevalent in research dealing with adults, is difficult to apply to the developing brain. The major problem is that the function of a specific neural area may change over time. For instance, Goldman (1974) found that although juvenile rhesus monkeys that had sustained frontal cortex lesions in infancy could solve tasks sensitive to frontal lobe damage in adults, they subsequently lost this ability as they matured. This result can be interpreted as showing that some other structure, probably the striatum, initially controlled the behaviors necessary for the successful performance of the tasks. Through the natural course of development, this function is eventually transferred to the frontal cortex as the original structure takes some other role in the production of behavior. Because, in this case, the frontal cortex was damaged, it was unable to assume the function when required and the task could not be fulfilled. Therefore, because the association of functions and brain sites that is applicable at one age may be inappropriate at other ages, there is not just one form of the immature brain.

The plasticity of the immature brain poses another problem to inferring structure–function relations from malfunction in the developing nervous system. Brain damage occurring in infants may produce very different behavioral effects than in adults because early injury has also altered fundamental brain organization. The trauma does not affect the function of only the brain areas that are damaged directly. It also disrupts other neuroanatomical sites and circuitry appearing later, the subsequent normal development of which was dependent upon the intact structure and function of the regions damaged.

For example, Rasmussen and Milner (1977) showed that if neonatal speech zones, usually found in the left cerebral hemisphere, are damaged, language may develop in the right cerebral hemisphere. Similar damage at 5 years of age may cause the speech zones to move within the left hemisphere. In both cases, language would then occupy space normally serving other functions. The chronic behavioral loss would manifest itself in some other cognitive function, such as spatial orientation, even though the damage can be shown to have been in the cortical site that normally subserves language functions. Identical lesions could result in very different deficits depending on the age at which the damage occurred. Such effects do not occur in the adult.

We point out the pitfalls in developmental neuropsychology not to discourage the study of the child's brain, but to caution that what follows in this chapter must be considered in light of these problems. We shall summarize research on neocortical development using each of the three approaches outlined above. We begin by considering the anatomical development of the cerebral cortex. We then consider functional development and try to draw correlations between the emergence of particular behaviors and neural development. Finally, we examine factors affecting brain development.

Anatomical Development of the Child's Brain

The process of brain growth can be understood by considering the composition of the nervous system. The cortex is a laminated structure of approximately six layers made up of neurons and glial cells. Some glial cells in the brain, called oligodendrocytes, insulate certain portions of many neurons by wrapping around them. Other glial cells, mainly astrocytes and microcytes, are thought to perform basic maintenance and support functions for neighboring neurons. Neurons receive input from other neurons across tiny spaces known as synaptic gaps through processes called dendrites while sending output to other neurons via processes called axons. Cortical neurons exchange information with other cortical neurons as well as with neurons located in subcortical structures. Additionally, the many projections each neuron usually receives from other neurons often use different chemical substances to transmit information. Basically, these chemicals excite or inhibit the activity of the target cell, and it is the net total of these influences that determines whether or not the neuron fires. The successful development of the brain into a properly functioning, integrated organ requires that each component first be formed and then be correctly interrelated with the others.

The development of the different components of the nervous system can be categorized into distinct phases, illustrated in Figure 1. These include (1) the birth of neurons (neurogenesis), (2) the migration of neurons to their correct location, (3) the differentiation of neurons into different types and their subsequent maturation of connections, and (4) the pruning back of connections and cells themselves. Each of these stages is dependent on the production of specific molecules that act to facilitate the respective process. These molecules include various growth factors, hormones, and specific proteins that act as a sort of traffic signal for cells or their processes to follow. We will consider the development processes in turn.

Neural Generation

The human brain follows a general pattern of development, beginning as a neural tube and gradually acquiring the features of the adult brain (illustrated in Figure 2), that is typical of all mammals. The basic neural tube surrounds a single ventricle where cells are generated along the ventricular wall and then migrate out to their proper location. In humans, approximately 10^9 cells are required to eventually form the mature neocortex of a single cerebral hemisphere (Rakic, 1975). During development, the cortex
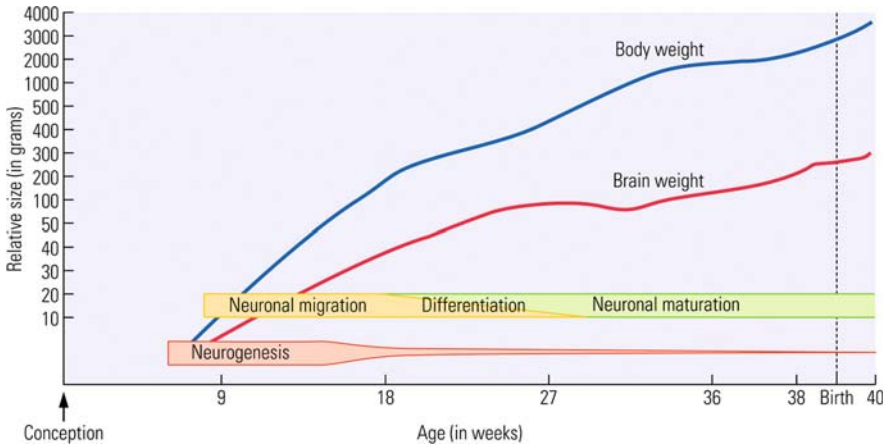
FIGURE 1. Stages of brain development.

is composed of four embryonic regions: the ventricular, marginal, intermediate, and sub-ventrical zones (as illustrated in Figure 3). These zones are transient features uniquely related to early development for each either disappears or becomes transformed so that they are no longer identifiable in the adult nervous system.

Sidman and Rakic (1973) combined the extensive studies of Poliakov (1949, 1961, 1965) with their own observations to produce a
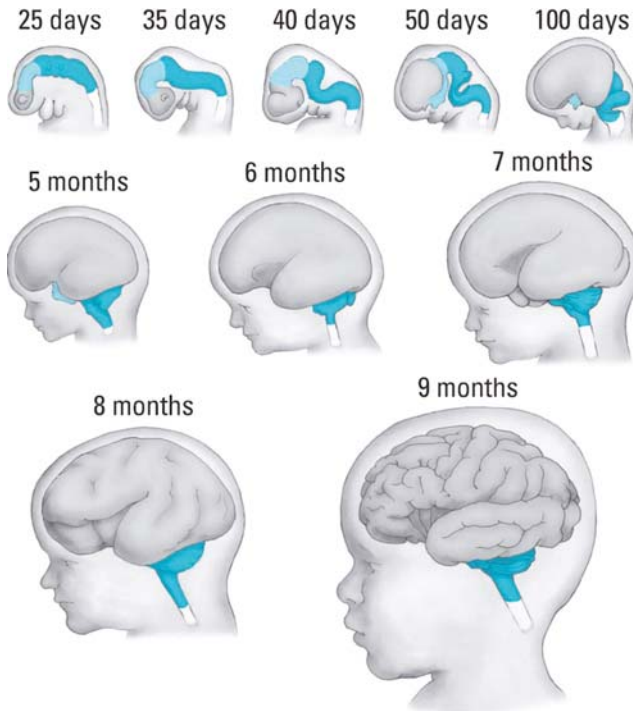
FIGURE 2. Prenatal development of the human brain showing a series of embryonic and fetal stages. (Adapted from Cowan, 1979.)
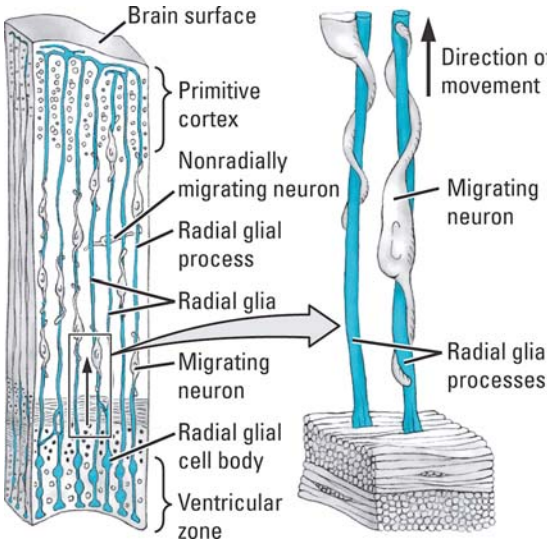
FIGURE 3. Schematic representations of the pattern of neural migration along the radial glial cells (after Rakic, 1981). Migrating neurons leave the ventricular and subventricular zones and travel to more superficial layers. En route they pass through the deeper neurons, which are already in place.

postnatally, and the cortical lamination continues to develop and differentiate until after birth.

One curious feature of cortical development is that it progresses in an "inside-out" progression. Neurons destined to form layer VI form first, followed in sequence by layers V to II. Marin-Padilla (1970, 1988) studied the sequential lamination of the human motor cortex in ontogenesis and found that by the fifth embryonic month, cortical layers V and VI are visible, although not yet completely mature. Over the ensuing months, the remaining layers develop (as summarized in Table 1). Thus, we see that successive waves of neurons pass earlier-arriving neurons to assume progressively more superficial positions. A second curious feature of brain development is that the cortex overproduces neurons, which are later lost through normal cell death. Layer IV in the motor cortex is a particularly clear example of this because cells that are visible there in the seventh month and at birth later degenerate, leaving an agranular layer.

As might be predicted, the precise timing of the development and migration of cells to different cytoarchitectonic regions varies with the particular area in question. For example, Rakic (1976) showed that while the ventricular zone is producing layer IV cells for area 17, the neighboring ventricular zone is generating layer III cells that will migrate to area 18. Thus, at any given moment during cortical ontogenesis, cells migrating from the ventricular zone are destined for different regions and layers of the cortex. One implication of this phenomenon is that

summary of the timing and phases of cortical development in humans. There is some disagreement over how long cells destined for the cortex divide and migrate in the human, but most cortical cell proliferation appears to be complete by the middle of gestation, although, at this stage, the cortex by no means appears like that of an adult. Cell migration may still proceed for some months after this time, possibly continuing

TABLE 1. Sequential Lamination of the Human Motor Cortex in Ontogenesis[a,b]

Case	I	II	III Upper	III Lower	IV	V	VI
5-month fetus	++	0	0	0	0	+	+
7-month fetus	++−+++	+	+	+−++	+	++	++
7½-month fetus	+++−++++	++	++	++−+++	++	+++	+++
Newborn infant	++++	+++	+++	++++	++++	++++	++++
2½-month-old infant	++++	+++	++++	++++	Very thin	++++	++++
8-month-old infant	++++	+++	++++	++++	Agranular	++++	++++

[a] From Marin-Padilla (1970)
[b] Key: 0, unrecognizable; +, immature; ++, developing; +++, established; ++++, fully developed.

events that might affect the fetus during cortical development, like the presence of a toxic agent such as heavy metals, will affect different cytoarchitectonic zones differently. For example, prenatal exposure to methylmercury can produce dendritic spine dysgenesis in the pyramidal neurons of the somatosensory cortex of rats (Stoltenburg-Didinger & Markwort, 1990). Furthermore, because specific populations of cells are migrating at different times to any given cortical laminae, it implies that toxic agents, or other environmental events, could perturb the development of a specific population of cells to a particular cytoarchitectonic area.

Finally, we must mention that there has been recent controversy over the presence of neurogenesis in the adult brain. There is agreement that neurogenesis continues in the hippocampus and olfactory bulb, but although neurogenesis has been reported in the neocortex, striatum, amygdala, and substantia nigra, the latter findings have been difficult to replicate consistently in the undamaged brain (for a review, see Gould, 2007).

Cell Migration

Because cortical cells are born distal to the cortical plate and must migrate there, one can ask how this occurs, particularly as cells traveling to the outer layers must traverse the cells and fibers of the inner layers. In a series of elegant studies, Rakic (1972, 1975, 1981, 1984) showed that neurons migrate to the appropriate laminae within the cortex along specialized filaments, known as radial glial fibers, which span the fetal cerebral wall at early ages. These radial glial cells originate in the ventricular zone and extend outward to the cortical plate. As the cortex develops, thickens, and sulci begin to appear, the radial glial fibers stretch and curve, guiding the migrating neurons to their correct location (see Figure 3). Interestingly, prenatal exposure to gamma radiation or alcohol during particular windows of vulnerability can either halt migration prematurely, or prolong it abnormally, respectively (Hicks, Damato, & Lowe 1959; Miller, 1986), thus causing an extensive disruption of brain function and structure by interfering with a single developmental process.

Axonal Development

As cells migrate along the radial glial fibers, they begin to develop axons that run to subcortical areas, other cortical areas, or across the midline as commissural fibers. The rate of axon development is extremely rapid, apparently on the order of 1 mm/day. In addition to axons of cortical cells growing out, axons from the thalamus enter the cortex after the principal cortical target cells complete their migrations and assume the appropriate positions within the developing cortical plate (Rakic, 1976).

Dendritic Development

Two processes occur during development of the dendrite: dendritic arborization and spine growth. The dendrites begin as individual processes protruding from the cell body. Later, they develop increasingly complex extensions, looking much like the branches of trees in winter. Spines are little appendages, resembling thorns on a rose stem that begin to appear in the seventh intrauterine month (Poliakov, 1961). Before birth, they are observed only on the biggest neurons (mainly those found in layer V). After birth, they can also be found on other neurons where they spread and densely cover the dendritic surface. Although dendritic development begins prenatally in the human, it continues for a long time postnatally. In laboratory animals, the development of both dendritic branches and spines has been shown to be influenced dramatically by environmental stimulation (Greenough, 1976), a phenomenon that is probably very important in relation to the human child's development. In addition, it is now clear that dendritic development is also affected by gonadal hormones, leading to the development of a male or female cerebral structure (Juraska, 1990). The influence of gonadal hormones is not limited to birth but continues into adulthood and may play an important role in the processes related to aging (Stewart & Kolb, 1994). In contrast to the development of axons, dendritic growth usually commences after the cell reaches its final position in the cortex and proceeds at a relatively slow rate, on the order of micrometers per day. The disparate developmental rates of axons and dendrite are important because the faster-growing axon can contact its target cell before the dendritic processes of that cell are
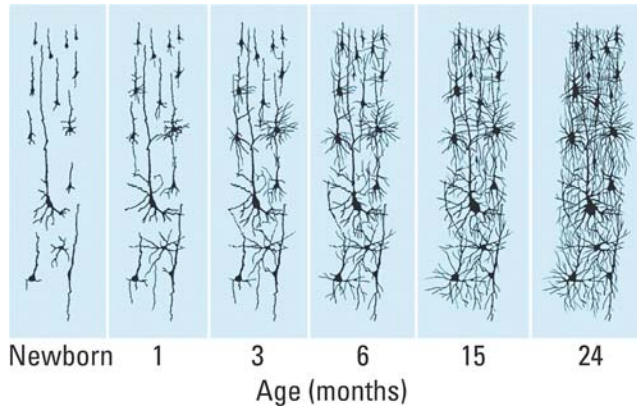
FIGURE 4. Postnatal development of human cerebral cortex around Broca's area as taken from camera lucida drawings of Golgi-Cox preparations (from Conel, 1939–1967)

elaborated, suggesting that the axon may play a role in dendritic differentiation (Berry, 1982). The morphological changes associated with dendritic growth in the frontal cortex are illustrated in Figure 4.

Synaptic Development

The mechanism that controls synapse formation is one of the major mysteries of developmental neurobiology, largely because synapses are perceptible only by electron microscopy, which does not allow direct observation of their sequence of development in living tissue. The onset of synaptogenesis is abrupt, and the appearance of synapses in any particular area is remarkably rapid although neurons may be juxtaposed for days before they actually make synaptic connections. Synapses usually form between the axon of one neuron and the dendrites, cell body, axons, or established synapses of other cells. Because synaptogenesis begins before neurogenesis is complete, neurons migrating to the superficial layers of the cortex must bypass cortical neurons on which synapses have already formed or are in the process of forming.

Although little is known about the details of synaptic development in humans, Bourgeois (2001) outlined five distinct phases of synapse formation in the cerebral cortex of primates, as illustrated in Figure 5 for the macaque. The first two phases take place in early embryonic life and are characterized by the generation of low-density synapses. The synapses formed in phases 1 and 2 differ in their origin, but both groups are believed to be generated independently of experience.

The number of synapses grows rapidly in phase 3, with the peak in the macaque at about 40,000 synapses per second. This phase begins before birth and continues until nearly 2 years of age in humans. Phase 4 is characterized by an initial plateau in synapse number followed by a rapid elimination of synapses that continues through puberty. Phase 5 is characterized by another plateau in synapse number through middle age followed by a drop in senescence.

The first developmental period of synapse reduction is dramatic, falling to 50% of the number present at age 2. And just as synapses can be formed very rapidly during development, they may be lost at a rate of as many as 100,000 per second in adolescence. It should not surprise us that teenagers are so moody when their brains are undergoing such rapid changes in organization.

In phases 3 and 4, the development (and elimination) of synapses is influenced by experience-expectant and experience-dependent mechanisms. Experience-expectant means that the synaptic development depends on the presence of certain sensory experiences. For example, in the visual cortex, the synapses depend on exposure to features such as line orientation, color, and movement. The general pattern of

(A) Monkey visual cortex

(B) Human cortex
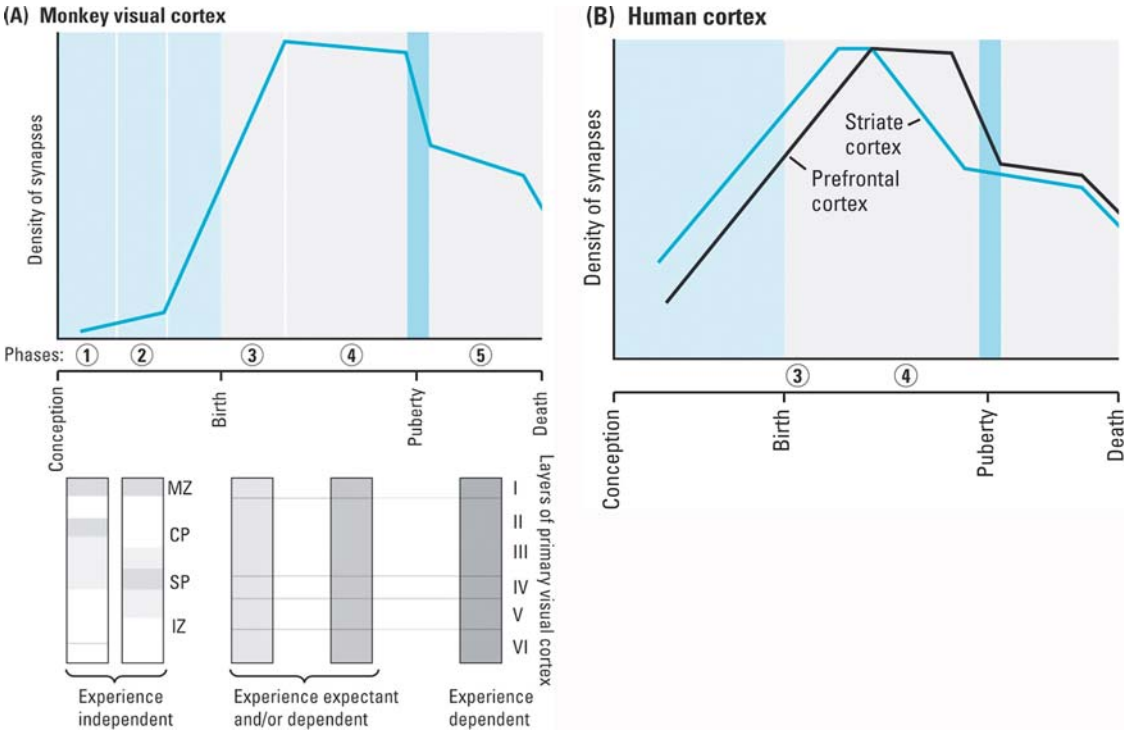
FIGURE 5. (A) Phases of synapse formation and pruning. Five different phases of synaptogenesis are identified between conception and death. The shading in the *vertical bars* indicates the areas of synapse formation during each phase. (B) Changes in the relative density of synapses in the visual cortex and prefrontal cortex as a function of days after conception. (After Bourgeois, 2001; Huttenlocher, 1984, 1990)

these synapses is presumed to be common to all members of a species—provided the individual members receive the appropriate experience. Experience-dependent refers to the generation of synapses that are unique to the individual. For example, in the visual system, these synapses can correspond to the learning of specific visual information such as the features of a particular face.

It is interesting that the synaptic density of infants appears to exceed that of adults, for it has generally been assumed that a larger number, or a greater density, of synapses implies a higher functional capacity. Evidence of decreasing synaptic density coincident with increasing cognitive skill is thus intriguing, especially because high numbers of synapses have been found in certain cases of mental retardation (Cragg, 1975). It is not surprising that intellectual ability cannot be predicted merely by its relation to the quantity of some anatomical feature, such as

synapses, and it is almost certain that the process involved in reducing synaptic density often represents some sort of qualitative refinement.

Glial Development

The differentiation and growth of neurons, which are generally produced before their associated glia, appear to play some role in stimulating the growth and proliferation of glial cells, but the mechanisms are unknown (Jacobsen, 1978). In contrast to neurons, which only relatively recently have been shown to continue to be born in very restricted brain areas, glial cells continue to proliferate throughout life.

Myelin Development

Myelination is the process by which the glial cells of the nervous system begin to surround axons and provide them with insulation.

Although nerves can become functional before they are myelinated, many researchers in the 1920s and 1930s assumed that neurons only reach adult functional levels after myelination is complete (Flechsig, 1920). This notion now appears to be an oversimplification but is, nonetheless, useful as a rough index of cerebral maturation. In contrast to other aspects of cortical development, myelin appears late, at a time when cellular proliferation and migration are virtually complete. The primary sensory and motor areas begin to myelinate just before term, whereas the frontal and parietal association areas, the last to myelinate, begin postnatally and continue until about age 15 years or, sometimes, even later. Because different regions of the cortex myelinate at different times, and myelination begins in the lower layers of each cortical area and gradually spreads upward, the upper layers of the motor and primary sensory areas are myelinating at the same time that the lower areas of some association areas are just beginning to myelinate.

Neurochemical Development

Chemical neurotransmitters serve as the primary means of interneuronal communication, yet virtually nothing is known about the neurochemical development of the human cortex. Although there are numerous studies of neurotransmitter development in the rat, knowledge about the relationships among transmitters in the adult neocortex is still limited, and the most completely described neurochemical systems make only a modest contribution to the overall synaptic activity of the neocortex (see Table 2). There are, however, some developmental studies using nonhuman primates that are worth reviewing as the human brain is likely to be similar (see also Parnavelas, Papadopoulos, & Cavanagh, 1988).

Goldman-Rakic and Brown (1981, 1982) investigated the regional distribution of catecholamines in rhesus monkeys ranging in age from newborns to young adults. Their overall findings were that although monoaminergic systems are present in the cortex at birth, these networks continue to develop for years. Catecholamine development varies greatly between different cortical regions, and the most striking postnatal increases in content were observed in the frontal and parietal association areas. Perhaps most

TABLE 2. Neocortical Neurotransmitters[a]

Transmitter type	Cell location
Afferents	
Norepinephrine	Locus coeruleus
Dopamine	Substantia nigra A10
Serotonin	Raphe
Acetylcholine	Globus pallidus magnocellular
Intrinsic	
GABA	Aspinous stellate (all layers)
Neuropeptides (somatostatin, neuropeptide Y, vasoactive intestinal polypeptide, cholecystokinin)	Aspinous bipolar stellates
Efferents	
Glutamate	Pyramidal cells (layer V corticostriatal)

[a]After Coyle (1982).

interesting was their observation that catecholamine development (especially that of the monoamines) parallels functional development in the prefrontal cortex over the first 2–3 years of life. These data support the suggestion that catecholamines may play an important role in the development of functional activity in the frontal cortex and likely affect the morphological development of various neuronal processes such as dendritic fields.

Postnatal Brain Development

After birth, the brain does not grow uniformly but rather tends to increase its mass during irregular periods commonly called growth spurts. In his analysis of brain/body weight ratios, Epstein (1978, 1979) found consistent spurts in brain growth at 3–10 months, accounting for an increase of 30% in brain weight by the age of 1 ½ years, as well as between ages 2 and 4, 6 and 8, 10 and 12, and 14 and 16+ years. The increments in brain weight were about 5–10% over each 2-year period. This expansion takes place without a concurrent increase in neuronal proliferation and is unlikely to be accounted for by increases in the number of glial cells. Rather, it most likely results from the growth of dendritic processes and myelination. Such an increase in cortical complexity would be expected to

correlate with increased complexity in behavioral functions, and it could be predicted that there would be significant, and perhaps qualitative, changes in cognitive function during each growth spurt. It may be significant that the first four brain growth stages coincide with the classically given ages of onset of the four main stages of intelligence development described by Piaget. We return to this later.

Cell Death

One of the most intriguing stages in brain development is cell death. Consider the following analogy. If one wanted to make a statue, it would be possible to do so either by starting with grains of sand and glueing them together to form the desired shape or by starting with a block of stone and chiseling the unwanted pieces away. The brain uses both the procedures but relies mainly on the latter to achieve the "final" form. We have already described how the brain creates the block to be sculpted, by generating an overabundance of neurons and connections. The "chisel" in the brain could be of several forms including genetic signal, environmental stimulation, gonadal hormones, stress, and so on. Similarly, the same processes are likely to affect the development of dendrites, axons, and synapses. Cell death does not end in infancy but continues well into adulthood (Bartzokis Beckson, Po, Nuechterlein, & Mintz, 2001). The possibility that environmental events may alter the brain by influencing cell death is intriguing because it implies a permanence to at least some effects of early experience.

One example of the effect of environmental stimulation on brain development comes from the work of Werker and Tees (1992). They studied the ability of infants to discriminate phonemes taken from widely disparate languages such as English, Hindi, and Salish. Their results showed that infants can discriminate speech sounds of different languages without previous experience, but there is a decline in this ability, over the first year of life, as a function of specific language experience. One might speculate that neurons in the auditory system that are not stimulated early in life may somehow be selected against and die, although there are other explanations.

Not only is there cell death during development but there is also a process of pruning
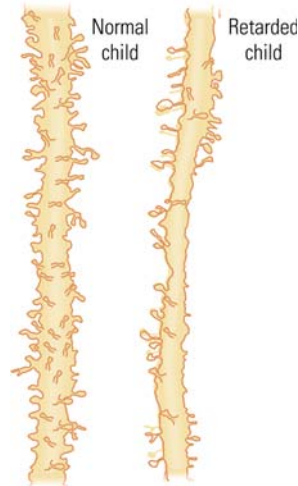
FIGURE 6. Camera lucida representations of Golgi preparations showing typical dendritic segments of medium-sized pyramidal neurons. *Left*: Example of apical segment from a normal 7-year-old child (accident case). *Right*: Example of apical segment from a 12-year-old profoundly retarded child. (After Purpura, 1974.)

synapses, as mentioned earlier. Recall that there is synapse elimination in the frontal lobe until adolescence (Figure 6). Thus, it seems likely that just as the nervous system uses the block-and-chisel method for choosing neurons, a similar process is used for selecting neuronal connections. The difference, however, is that it seems reasonable to expect that the brain could replace pruned connections later in life whereas the replacement of lost neurons is much less likely.

Imaging Studies of Brain Development

MRI and fMRI techniques are revolutionizing the study of human brain development. Early studies of gray-matter volumes showed that whereas a decline in gray-matter volume beginning around 6–7 years of age continues through adolescence, white matter volumes increase over the same time frame.

Gogtay et al. (2004) quantified the changes in gray-matter density at specific cortical points by using serial MRI scans of children followed over a 10-year period. The general finding was a shifting pattern of gray-matter loss, which presumably reflects neuron and synaptic pruning,

beginning in the dorsal parietal and sensorimotor regions and spreading laterally, caudally, and rostrally. The first regions to mature are primary cortical regions involved in basic sensory and motor functions. Parietal regions involved in space and language mature around puberty (age 11–13 years). Tertiary cortical areas such as the prefrontal cortex begin to mature last in late adolescence and continue well beyond.

Cortical Function at Birth

The extreme paucity of behavioral skill in the newborn leads to the notion that, shortly after birth, the cortex has not yet begun to function. Thus, the cortically injured infant was once thought to be indistinguishable from the normal child at birth (Peiper, 1963). Several lines of evidence suggest that the cortex is indeed functioning, although not like the adult brain. It is now known that cortically hemiplegic infants can be distinguished from normal babies on the basis of muscle tone (Gibson, 1977) and cortically damaged infants may also have abnormal sleep–waking cycles and abnormal cries (Robinson, 1966). There are also several measures of electrical activity that imply cortical activity is present at birth. EEG activity can be recorded from the fetal brain (Bergstrom, 1969), and epileptic seizures of cortical origin can occur in the neonate (Caveness, 1969). Perhaps the most compelling evidence of early cortical activity comes from the extensive work of Purpura (Purpura, 1976, 1982). In his study of cortical activity in premature human infants, Purpura took advantage of the fact that between 26 and 34 weeks of gestation, cortical pyramidal cells in primary visual cortex undergo significant growth and branching. These changes are associated with corresponding maturational changes in the electrophysiological characteristics of the visual evoked potentials (VEPs) in preterm infants. Although, even at birth, the VEPs are not identical to those of adults, they are present and indicate that at least primary visual cortex is functioning in some capacity.

Chugani and Phelps (1986) studied glucose utilization in the brain of infants using positron emission tomography. Their results showed that in infants 5 weeks of age or younger, glucose utilization, which can be taken as a crude measure of neural activity, was highest in the sensorimotor cortex, a result that is in accordance with anatomical evidence that this is the most mature cortical region at birth. By 3 months of age, glucose metabolism had increased in most other cortical regions, with subsequent increases in frontal and posterior association cortex occurring by 8 months. Thus, by about 8–9 months there is evidence of activity throughout the cerebral cortex, although it continues to change in the years to come.

Over the past decade, there has been an explosion of work on cognitive function in the developing brain including sensory functions (especially audition and vision), memory, face processing, spatial ability, and attention. The details of this work are beyond this chapter, but a recent volume summarizes much of this work (Nelson & Luciana, 2008).

Abnormal Development of the Child's Brain

We have seen that the anatomical development of the child's brain consists of the proliferation and migration of cells, the growth of axons and dendrites, synapse formation and loss, myelin growth, and so on. These processes begin early in embryonic development and continue until late adolescence. In view of the complexity of the cortex and its prolonged development, it is reasonable to expect that normal cortical development could be disrupted by any number of events. These include abnormalities in the normal genetic program of neural growth, the influences of exogenous factors such as psychoactive drugs (e.g., nicotine, antidepressants), toxic substances, or brain trauma, and nutritional or other environmental circumstances (e.g., maternal stress). We do not propose to discuss all of these possibilities, but will confine our discussion to those events that are most likely to be important to the neuropsychologist, namely abnormal neural differentiation and early brain damage.

Abnormal Neural Structure

In the event that either neurogenesis or neural migration is abnormal, one would expect gross abnormalities in cortical development. Clinically, a variety of conditions are recognized (Table 3), but little is known about the details of cell differentiation in these disorders. The major experimental study of disturbed migration in the cerebral cortex involves the reeler mouse

TABLE 3. Types of Abnormal Development

Type	Symptom
Anencephaly	Absence of cerebral hemispheres, diencephalon, and midbrain
Holoprosencephaly	Cortex forms as a single undifferentiated hemisphere
Lissencephaly	The brain fails to form sulci and gyri and corresponds to a 12-week embryo
Micropolygyria	Gyri are more numerous, smaller, and more poorly developed than normal
Macrogyria	Gyri are broader and less numerous than normal
Microencephaly	Development of the brain is rudimentary and the person has low-grade intelligence
Porencephaly	Symmetrical cavities in the cortex, where cortex and white matter should be
Heterotopia	Displaced islands of gray matter appear in the ventricular walls or white matter, caused by aborted cell migration
Agenesis of the corpus callosum	Complete or partial absence of the corpus callosum
Cerebellar agenesis	Portions of the cerebellum, basal ganglia, or spinal cord are absent or malformed

mutant. Caviness (Caviness, 1982; Caviness & Rakic, 1978; Caviness & Sidman, 1973) showed that in this animal the cortex is inverted relative to that of a normal mouse; the cells generated first lie nearest to the cortical surface and those generated last lie deepest. In addition, many of the pyramidal cells are abnormally oriented, in some cases with their major dendrites (the apical dendrites) oriented downward rather than upward as in the normal mouse. Despite their aberrant position, the cells develop connections as they would have had they been normally situated. Caviness and his colleagues studied the cortex of humans with various similar abnormalities, finding some of the same aberrant features (Caviness & Williams, 1979). Thus, in lissencephalic cortex, Williams, Ferrante, and Caviness (1975) found that cells failed to migrate into the appropriate layers and some cells were abnormally oriented, much as in the reeler mouse.

Injury and Brain Development

If the brain is damaged during development, it is reasonable to suppose that its development might be fundamentally altered. There are few studies of human brains with early lesions but there is a considerable literature from work with laboratory animals. In an extensive examination of monkeys with prenatal or perinatal frontal cortex injuries, Goldman-Rakic has shown a variety of changes in cortical development including abnormal gyral formation and abnormal corticostriatal connections (Goldman & Galkin, 1978; Goldman-Rakic,

Isseroff, Schwartz, & Bugbee, 1983). Similarly, Kolb and his colleagues have found abnormal corticostriatal and subcorticocortical connections, abnormal myelination, altered cortical catecholamine distribution, thalamic shrinkage, reduced gliosis relative to animals with similar injuries in adulthood, and markedly thinner cortex following early frontal lesions in rats (for a review, see Kolb, 1995). The thin cortex appears to result both from a loss in the number of cortical cells and from a loss in dendritic arborization. In sum, there is good reason to presume that early damage to the human brain produces significant changes in cortical morphology that extend far beyond the boundaries of the tissue directly traumatized.

One of the clearest abnormalities in the developing human brain can be seen in studies comparing the brains of normal and profoundly retarded subjects. Golgi studies have shown abnormally long, thin spines on dendrites of cortical neurons in retarded children with no known genetic abnormality (Figure 6). The degree of abnormality is related to the severity of retardation. The dendritic abnormalities in retarded children are strikingly similar to those seen in rats with cortical injuries around the time of birth and may reflect similar etiologies.

One of the difficulties in applying the results of studies of laboratory animals to humans is the difficulty in equating the developmental age of the brain in different species. For example, when rats are born, their brain is very immature relative to the human brain, which is reflected in the fact that their eyes and ears are not open, and not functional. Cats are somewhat older

developmentally than rats but still are much less mature than humans. In contrast, at birth rhesus monkeys are more mature than humans. Thus, as we try to compare developmental ages we must not be overly impressed by the "birth day" but rather we need to focus on the developmental age of the brain. Looking at rats and humans, if we compare the state of cortical development and injury effects, it appears that newborn humans are roughly equivalent to 10-day-old rats; newborn rats are probably roughly equivalent to 8-month-old fetuses (Kolb, 1995). We must note, however, that other criteria will lead to somewhat different timetables (Clancy et al., 2007).

Behavioral Correlates of Brain Development

Two types of behavior have been extensively studied and correlated with anatomical development, namely motor behavior and language. We shall consider each separately and then consider the development of their asymmetrical representation in the cortex. Finally, we will discuss the behavior of children on standardized tests typically used by clinical neuropsychologists. We shall not attempt to be exhaustive in our coverage of each, but rather try to give a flavor of the findings to date.

Motor Systems

The development of locomotion in human infants is quite familiar to most of us. Infants are, at first, unable to move about independently, but eventually they learn to crawl and then to walk. The way in which other motor patterns develop is less obvious, but one has been described in an elegant study by Twitchell (1965) who documented the stages an infant passes through while acquiring the ability to reach out with one limb and bring objects toward itself. Before birth, the fetus's movements involve essentially the whole body. Shortly after birth the infant can flex all of the joints of an arm in such a way that it could scoop something toward its body, but it is not clear that this movement is executed independent of other body movements. Between 1 and 3 months it orients its hand toward, and gropes for, objects that have contacted it. Between 8 and 11 months it develops the "pincer grasp," using

the index finger and thumb in opposition to each other. The development of the pincer grasp is extremely significant, because it allows the infant to make a very precise grasping movement that enables the manipulation of small objects. In summary, there is a sequential development of the grasping reaction: first scooping, then reaching and grasping with all fingers, then independent finger movements.

The fact that motor cortex lesions in adults abolish the grasp reaction with independent finger movements implies that there could be anatomical changes within the motor strip that correlate with the original development of the behavior. Although there are probably multiple changes occurring, especially in the development of dendritic arborizations, a correlation has been noted between myelin formation and the ability to grasp. In particular, the small motor fibers become myelinated at about the same time that reaching and grasping with the whole hand develop while the giant Betz cells of the motor cortex become myelinated at about the time the pincer grasp develops. These different types of motor fibers are thought to control arm and finger movements, respectively (Kolb and Whishaw, 1996).

The correlation between myelin development and motor behaviors can also be found in many other activities. Table 4 summarizes the development of a variety of behavioral patterns and myelin formation. It is difficult, of course, to be certain which correlations are meaningful, and, as we have noted, there are obviously many other anatomical changes occurring concurrently. Careful study of these data, however, does show some intriguing associations that warrant more detailed study.

Language Development

The onset of speech consists of a gradual appearance of generally well-circumscribed events that take place during the first 3 years of life (Tables 4 and 5). Language development is dependent not only on the development of appropriate perceptual abilities, such as the identification and categorization of speech sounds, but also on the development of motor capacities, especially those that control the lips and tongue. It therefore comes as little surprise that the precise movements of the lips and tongue needed for speech are fully developed well

TABLE 4. Summary of Postnatal Human Development[a]

Age	Visual and motor function	Average brain weight (g)[a]	Degree of myelination[b]
Birth	Reflex sucking, rooting, swallowing, and Moro reflexes; infantile grasping; blinks to light	350	Motor roots +++; sensory roots ++; medial lemniscus ++; superior cerebellar peduncle ++; optic tract ++; optic radiation ±
6 weeks	Extends and turns neck when prone; regards mother's face, follows objects	410	Optic tract ++; optic radiation +; middle cerebral peduncle ±; pyramidal tract +
3 months	Infantile grasp and suck modified by volition; keeps head above horizontal for long periods; turns to objects presented in visual field; may respond to sound	515	Sensory roots +++; optic tract and radiation +++; pyramidal tract ++; cingulum +; frontopontine tract +; middle cerebellar peduncle +; corpus callosum ±; reticular formation ±
6 months	Grasp objects with both hands, will place weight on forearms or hands when prone; rolls supine to prone; supports almost all weight on legs for very brief periods; sits briefly	660	Medial lemniscus +++; superior cerebellar peduncle +++; middle cerebellar peduncle ++; pyramidal tract ++; corpus callosum +; reticular formation +; associational areas ±; acoustic radiation +
9 months	Sits well and pulls self to sitting position; thumb–forefinger grasp; crawls	750	Cingulum +++; fornix ++; others as previously given
12 months	Able to release objects; cruises and walks with one hand held; plantar reflex flexor in 50% of children	925	Medial lemniscus +++; pyramidal tracts +++; frontopontine tract +++; fornix +++; corpus callosum +; intracortical neuropil ±; associational areas ±; acoustic radiation ++
24 months	Walks up and down stairs (two feet a step); bends over and picks up objects without falling; turns knob; can partially dress self; plantar reflex flexor in 100%	1065	Acoustic radiation +++; corpus callosum ++; associational areas +; nonspecific thalamic radiation ++
36 months	Goes up stairs (one foot a step); pedals tricycle; dresses fully except for shoelaces, belt, and buttons; visual acuity 20/20 OU	1140	Middle cerebellar peduncle +++
5 years	Skips; ties shoelaces; copies triangle; gives age correctly	1240	Nonspecific thalamic radiation +++; reticular formation ++; corpus callosum +++; intracortical neuropil and associational areas ++
Adult	–	1400	Intracortical neuropil and associational areas ++ to +++

[a]Source: Spreen, Tupper, Risser, Tuokko, & Edgell (1984).
[b]From Yakovlev and Lecours (1967). Estimates are made from their graphic data (±, minimal amounts; +, mild; ++, moderate; +++, heavy).

before the acquisition of finger and hand control.

The perceptual and motor processes necessary for language development are dependent on the maturation of the temporal and frontal lobes, which may be highly variable in developmental rate in some children. Thus, some children have a markedly delayed speech acquisition but later turn out to have normal intelligence and normal skeletal and gross motor development. For example, such children may not begin to speak in phrases until after age 4, in spite of an apparently normal environment and the absence of any obvious neurological signs that might suggest brain damage.

Experiential factors clearly influence speech development (e.g., Werker & Tees, 1992) so it could be argued that language development is

TABLE 5. Summary of Postnatal Development of Basic Social and Language Functions[a]

Approximate age	Basic social and language functions
Birth	Comforted by sound of human voice; reflexive smile. Most common sounds are discomfort and hunger cries and vegetative sounds; by the end of first month the cries become differentiated; noncrying speech-like sounds usually during feeding
6 weeks	Makes eye contact with mother; spontaneous smile. Responds to human voice and being held by quieting; smiles when played with; makes cooing and pleasure noises; cries to gain assistance
2 months	Begins to distinguish different speech sounds; cooing becomes more guttural or "throaty"; seeing people causes excitement; unselective social smile
3 months	Discriminates between some individuals; recognizes mother; selective social smile; orients head to voices; makes a vocal response to others' speech; "babbling"—a phase characterized by the "spontaneous" production of sounds. Usually begins in month 2 or 3 and continues to months 12–15 or later although typically decreasing as echolalia increases
4 months	Selective attention to faces; prefers to look at happy rather than angry expressions; localizes to sounds; can discriminate individual faces; smiles at other babies; varies pitch of vocalizations; imitates tones
6 months	Laughs aloud; conveys pleasure and displeasure in prosody; smiles at self in mirror; "echolalia," the imitation of sounds made by others, usually beginning at months 4–7. Imitation of prosody occurs long before that of articulated speech segments; forms the dominant linguistic activity through the second year with decreasing importance, except during the acquisition of new words, until at least months 30–36
9 months	Waves bye-bye; plays patty-cake; makes distinct intonational patterns; social gestures
12 months	May kiss on request. Sentences, the long and progressive process of learning the symbolic significance of speech sounds enabling the capacity to understand and generate meaningful words and sentences; in most individuals maximum capacity is probably not achieved until the middle of the second decade or later; a 12-month-old may have a vocabulary of 5–10 words that will double in the following 6 months
24 months	"Vocabulary" can be approximately 200–300 words by the second year; names most common everyday objects; "morphological–syntactical"—most of child's utterances will be unitary, i.e., single, nonassociated linguistic units up to 18–24 months and occasionally later; next 5–6 years, at least, will be devoted to the acquisition of the complex, multistaged process of developing a mastery of a morphological–syntactical system
36 months	Has vocabulary of 900–1000 words; 3- to 4-word simple construction sentences (subject–verb); can follow two-step commands; curses
4 years	Has a vocabulary of more than 1500 words; asks numerous questions; sentences become more complex
5 years	The typical 5-year-old may have a vocabulary of approximately 1500–2200 words; discusses feelings; the average 5- to 7year-old will be expected to have acquired a slow but fluent ability to read; handwriting will also likely be slow; graphism, however, should be well differentiated and regular; competent "phonetic" writing; the mastery of the orthographic system can be expected to extend for several more years
6 years	Expressive vocabulary of about 2600 words; receptive vocabulary of 20,000–24,000 words; uses all parts of speech
Adult	Has vocabulary of 50,000+ words by age 12

[a]Adapted from Lecours (1975) and Owens (1984).

not so much dependent on the maturation of some neural structure as it is on some form of environmental stimulation. Although this is possible, it is unlikely that speech development is constrained exclusively by some environmental event. Indeed, it is a common observation by parents that children may have markedly different histories of language acquisition. Furthermore, there is no evidence that training infants will significantly speed up language acquisition. Thus, the emergence of speech and language habits is most easily accounted for by assuming that there are maturational changes within the brain. The difficulty is in specifying what these changes might be. Indeed, in view of the complexity of the neural control of language, it is futile to look for any specific growth process that might explain language acquisition.

Nonetheless, it would be instructive to know in what ways the cortex is different before the onset of language (age 2) and after the majority of language acquisition is completed (about age 12).

As we described earlier in our discussion of neural maturation, by 2 years of age there is little neocortical neural cell division and most cells have migrated to their final location in the cortical laminae. The major changes that occur between the ages of 2 and 12 years are in the interconnection of neurons, largely through a decrease in the total number of synapses as well as an increase in the complexity of their dendritic arborizations. The latter increase implies a reorganization of networks and almost certainly reflects the development of some new synapses. If one assumes that language acquisition requires the development of *functional* connections between neurons, much as hypothesized by Hebb (1949) in his concept of cell assemblies, then these changes in synaptic density and dendritic detail may be logical candidates as constraints on speech development. The postnatal changes in dendritic complexity within the speech areas are among the most impressive in the brain. As illustrated in Figure 5, the dendrites are simple at birth and develop slowly until about 15 months when the major dendrites are present. Between 15 and 24 months, there is a dramatic increase in the density of the neuropil. A similar observation can be made from examination of the cortex of the posterior speech zone. Given the correlation between language development and maturation of the language areas, we can infer that language development may be constrained, at least in part, by the maturation of these areas and that individual differences in language acquisition may be accounted for by differences in this neural development. Furthermore, given the known effect of environmental stimulation on dendritic development, we might also predict that those differences in language acquisition that have some environmental influence may do so by changing the maturational rate of the dendritic fields within these areas.

Cerebral Asymmetry

Just as the asymmetrical function of the adult's brain has been a focal point for neurological study, the development of asymmetry has been a focal point of developmental studies. As asymmetry is the subject of another chapter in this volume (see Kinsbourne, this volume), we shall consider this topic only briefly.

Most of the research with children that has been designed to demonstrate lateralization of function has emphasized the age at which asymmetry first appears (see Molfese & Segalowitz, 1988). Table 6 gives examples of a number of representative functions, which hemisphere usually shows the relative advantage, and earliest age of demonstrated asymmetry. A central theoretical issue is whether or not functions are disproportionately represented in the two hemispheres because they depend on certain anatomical asymmetries that develop independent of environmental stimulation. The fact that anatomical asymmetries can be observed in the cortex prenatally (Chi, Dooling, & Gilles, 1977; Wada, Clarke, & Hamm, 1975) and, therefore, exist before the expression of the behaviors implies that asymmetry is relatively innate. Nevertheless, several major problems arise when we try to correlate functional and anatomical asymmetry. First, the functions that are most lateralized in adults are not easily assessed in children. For example, it is extremely difficult, if not impossible, to determine handedness for writing in infants, unless, of course, one is willing to assume that some other indirect measure, such as hand strength, in this case, will serve as a reliable predictor. Second, hand preference, based on general use, appears to change several times during infancy in many children. In addition, correlations between function and anatomical asymmetry in adults are far from perfect. Although the left planum temporale is thought to be the posterior substrate of language functions, it is larger in only about 70% of right-handed people, whereas speech is lateralized to the left hemisphere in about 99% of right-handers. What then does a similar anatomical asymmetry in the fetal brain imply?

Development of Problem-Solving Ability

As each cortical layer within an area develops, it interacts with and modifies the function of the existing structure. Gibson (1977), therefore, suggested that behavior patterns would be

TABLE 6. Studies Showing Age of Asymmetry for Different Behaviors

System	Age	Dominance	Reference
Auditory			
Speech syllables	Preterm	Right ear	Molfese and Molfese (1980)
Music	22–140 days	Left ear	Entus (1977)
Phonemes	22–140 days	Right ear	Entus (1977)
Words	4 years	Right ear	Kimura (1963)
Environmental sounds	5–8 years	Left ear	Knox and Kimura (1970)
Visual			
Rhythmic visual stimuli	Newborn	Right	Crowell, Jones, Kapuniai, and Nakagawa (1973)
Face recognition	7–9 years	Left field	Marcel and Rajan (1975)
	6–13 years	Left field	Witelson (1977)
	9–10 years	None	Diamond and Carey (1977)
Somatosensory			
Dichhaptic recognition	All ages	Left	Witelson (1977)
Motor			
Stepping	<3 months	Right	Peters and Petrie (1979)
Head turning	Neonates	Right	Turkewitz (1977)
Grasp duration	1–4 months	Right	Caplan and Kinsbourne (1976)
Finger tapping	3–5 years	Right	Ingram (1975)
Strength	3–5 years	Right	Ingram (1975)
Gesturing	3–5 years	Right	Ingram (1975)
Head orientation	Neonates	Right	Michel (1981)

expected to emerge exactly in the manner described by Piaget (1952):

> Behavior patterns characteristic of different stages do not succeed each other in a linear way (those of a given stage disappearing at the time when those of the following one take form) but in the manner of the layers of a pyramid (upright and upside down), the new behavior patterns simply being added to the old ones to complete, correct or combine with them. (p. 329)

Thus, for example, because the deepest layers of the cortex myelinate first, and these are the efferent or output layers, one would expect to observe motor responses preceding the development of perceptual capacity. Indeed, according to Piaget, motor actions must come first, as motor actions provide data from which to build perceptions. The question to consider is just how well the stage of cognitive development coincides with changes in neural maturation. This is a difficult question that has not been studied extensively. Nevertheless, there is at least suggestive evidence that there may be a significant relationship between cortical development and the classical Piagetian stages. [We note that the Piagetian stages of cognitive development are a source of some debate, and there are several other conceptual schemes to describe the development of cognition in children (Carey, 1984). We will restrict our discussion to Piaget, however, because we wish merely to demonstrate the type of study that can be done and because we are unaware of any attempt to correlate other schemes of cognitive development to cortical maturation.]

Piaget was a biologist by training and considered the acquisition of knowledge and thought to be closely related to brain function. He proposed that cognitive development was a continual process and that the child's strategies for exploring the world were constantly changing. These changes were not simply a result of the acquisition of specific pieces of knowledge but rather, at some specifiable points in development, were fundamental changes in the organization of the child's strategies for learning about the world. Piaget identified four major stages of cognitive development: stage I, Sensorimotor, birth to 18 months; stage II, Preoperational or Symbolic, 18 months to 7 years; stage III, Concrete Operational, 7–11 years; and stage IV,

Formal Operational, 11+ years). In stage I, the infant learns to differentiate itself from the external world, learns that objects exist when not visible, and gains some appreciation of cause and effect. In stage II, the child begins to represent things with something else, such as drawing. Stage III is characterized by the child's ability to mentally manipulate concrete ideas such as dimensions of objects and the like. Finally, in stage IV, the child is able to reason in the abstract. Having identified the stages, the challenge for the neuropsychologist is to identify those changes in neural structure that might underlie these apparent qualitative changes in cognitive activity.

The first four brain growth stages described earlier coincide with the usual given ages of onset of the four main Piagetian stages (Epstein, 1979). A fifth stage of development, which would correlate with the fifth brain growth stage, was not described by Piaget but has been proposed by Arlin (1975). The concordance of brain growth and Piagetian stage is intriguing but, to date, remains too superficial and oversimplified. We need to know what neural events are contributing to brain growth and just where they are occurring. Little is known of this in children after 6 years of age, but the question remains important to the neuropsychologist seeking to understand the maturation of cortical operations. Gibson (1977) presented a detailed hypothetical analysis of stage I.

Development of Neuropsychological Test Performance

Neuropsychologists have developed an amazing array of tests since World War II with which to assess the behavior of patients with cortical injuries (e.g., Lezak, Howieson, Loring, Hannay, & Fischer, 2004). In principle, it is logical to suppose that if a test is sensitive to restricted cortical lesions in adults, and if a normal child performs poorly on such a test, it could then be inferred that the requisite cortical tissue is not yet functioning normally. This logic is seductive but is not without difficulties. First, the method assumes that tests will be sensitive to focal lesions: Few tests are. Second, a child may perform poorly on a test for many reasons. For example, a child may have difficulty with a verbal test because the speech areas are slow to

develop or because he or she has an impoverished environment and has acquired only a limited vocabulary. Furthermore, just because a child does well on a test does not mean that the child's brain is solving the problem in the same manner as the adult brain. Indeed, there are examples of tests in which children do well, only to do more poorly the following year, followed later by improvement again. Thus, in their studies of facial recognition in children, Carey, Diamond, and Woods (1980) found that children improved in performance between ages 6 and 10, declined until age 14, and then attained adult levels by age 16. This result can be taken to imply that the younger children were solving the problem in a different manner than the older children and adults while, presumably, using different cortical tissues. In sum, although there are clear limitations to the inferences that can be made about the development of specific brain regions, we feel that much can be learned using this type of approach. We will illustrate this by focusing on our own studies using tasks that test frontal lobe function and the perception of faces and facial expression.

Frontal Lobe Tests

Segalowitz and Rose-Krasnor (1992) edited a special issue of *Brain and Cognition* that was devoted to the general premise that an understanding of cognitive development in children is dependent on understanding the role of the frontal lobe in development. Their argument is based on the idea that the frontal lobe plays a central role in generating cognitive strategies (as opposed to habits), evaluating those strategies, and monitoring both one's behaviors and the effects of one's behavior on other people. If their argument is correct, then an understanding of correlations between frontal lobe development and behavioral maturation is critical in developmental neuropsychology.

The idea that the frontal lobes play a special role in cognitive development is not new. Hebb (1949) speculated from his analyses of children with perinatal cerebral injuries that the frontal lobes were critical to cognitive development. In fact, Hebb believed that the frontal lobes played a more important role during development than in adulthood. More recently, Case (1992) has argued that between the ages of 1½ and

5 years, and again between the ages of 5 and 10 years, a sequence of changes take place in children's behavior that indicate a fundamental reorganization of their attentional and executive processes. Case correlates these functional changes with developmental changes in the frontal lobe (Stuss, 1992; Thatcher, 1992).

One way to investigate correlations between frontal lobe maturation and cognitive development is to study the behavior of children on tests performed poorly by people with acquired frontal lesions in adulthood. Two tests are especially sensitive to frontal lobe injury, namely the Wisconsin Card Sorting Test and the Chicago Word Fluency Test (Milner, 1964). In the first test, the subject is presented with four stimulus cards, bearing designs that differ in color, form, and number of elements. The subject's task is to sort the remaining cards into piles in front of one or another of the stimulus cards. The only help the subject is given is being told whether the choice is correct or incorrect. The test works on this principle: the correct solution is first to sort by color; once the subject has figured this out, the correct solution then becomes, without warning, to sort by form. Thus, the subject must now inhibit grouping the cards on the basis of color and shift to form. Once the subject has succeeded at sorting by form, the relevant feature again changes unexpectedly, this time to number of elements. This cycle of color, form, and number is repeated. The subject's score is the number of target categories completed after sorting 128 cards, and the task is terminated when all of the cards have been used or six categories have been completed, whichever comes first. Shifting strategies is particularly difficult for patients with left frontal lobe lesions.

In the second test, the subjects must write as many words as they can beginning with the letter "S" in 5 min. Following this, they must write as many four-letter words beginning with "C" as possible in 4 min and the final score is the total number of words generated. Frontal lobe patients do very poorly on this test. This deficit is not simply a problem of verbal ability, however, as frontal lobe patients perform at normal levels when asked to write the names of as many objects or animals as they can think of within a fixed time. We note that frontal lobe patients perform normally on many other tests as well. For example, on tests of visual recognition, which are performed poorly by patients with right posterior lesions, frontal lobe patients achieve normal levels of performance.

Kolb and Fantie (1989) tested children on the card sorting and verbal fluency tests and predicted that if the frontal lobes were slow to mature relative to other cortical areas, then children should reach adult levels very late, probably in adolescence on tests of frontal lobe function. In contrast, children should perform at adult levels much sooner on the tests performed normally by patients with frontal lobe lesions. This is indeed the case. Children perform poorly on all frontal lobe-sensitive tests when very young but improve as they develop. As predicted, performance on tests performed normally by adults with frontal lobe injuries improves more quickly, however, than performance on tests sensitive to frontal lobe injuries.

Frontal lobe patients are also notorious for their difficulties in social situations, although it is more difficult to quantify their behavior (Kolb & Whishaw, 2008). Kolb and Taylor (1981, 1990) showed that one way to analyze the unique frontal contributions to social interaction is to focus on the ability of frontal lobe patients to produce and recognize facial expressions. Kolb, Wilson, and Taylor (1992) gave children a series of tests of facial perception ranging from simple tests of facial recognition and closure to more complex tests in which facial expression had to be understood from the context of a cartoon. Children aged 5–6 years performed as well as normal adults on the tests of facial recognition but did not approach adult levels on the context-dependent facial perceptual tests until about age 14 years. Furthermore, in a small sample of adults with frontal lobe injuries in early childhood, we have shown abysmal performance on the context-related tests. This result is consistent with a series of case histories showing that children with frontal lobe injuries at the time of birth do not develop anything approaching normal strategies for coping with social situations (e.g., Ackerly, 1964; Eslinger & Damasio, 1985; Grattan & Eslinger, 1992).

Abnormal Brain Development and Behavior

Earlier we described abnormalities in neural migration that are probably found throughout the brain, but it is reasonable to

predict that there will be conditions in which such abnormalities might be restricted to relatively small zones of cortex. In fact, there is now reason to suppose that at least some forms of developmental dyslexia result from abnormal structural development. Drake (1968) examined the brain of a 12-year-old learning-disabled boy who died of cerebral hemorrhage. Autopsy showed that there were atypical gyral patterns in the parietal lobes, an atrophied corpus callosum, and neurons underlying the white matter that should have migrated to the cortex. More recently, Galaburda and his colleagues have reported analogous results from several dyslexic brains (Galaburda & Eidelberg, 1982; Galaburda & Kemper, 1979; Geschwind & Galaburda, 1985). Thus, in the brain of a 20-year-old male who previously had a reading disability despite average intelligence, they found an abnormal pattern of cytoarchitecture, especially in the posterior speech region of the temporal–parietal cortex. Although other details varied in these cases, the left posterior region was always abnormal. These abnormalities were believed to be the result of disordered neuronal migration and/or assembly. The right hemisphere was either completely or largely normal in all of these cases. Finally, Geschwind and Galaburda (1985) claimed to have evidence of similar anomalies in living dyslexic patients, with arteriovenous malformations in the left temporal region.

The finding of left temporal–parietal abnormality in dyslexics leads to the question of how these people, even as children, might perform on tests sensitive to focal cortical lesions. Few studies have compared dyslexic children directly to adults with left posterior lesions, but studies of dyslexic children have found behavioral deficits on tests that are particularly disrupted by left posterior lesions, including tests of short-term verbal memory, left/right differentiation, and verbal fluency (Sutherland, Kolb, Schoel, Whishaw, & Davies, 1982; Whishaw & Kolb, 1984). We must point out again that it is likely that not all children with learning disabilities have left posterior abnormalities. It would be interesting, however, to determine the correlation between neuropsychological test performance in learning-disabled children and the presence of left posterior abnormalities.

Early Brain Injury and Behavior

Perhaps the most dramatic evidence of recovery from brain injury comes from the observations that infants with damage to left-hemisphere language areas rarely have persistent aphasia. Indeed, shortly after he published his observations on the nature of aphasia from the left inferior frontal region in adults, Broca noted that children did not show long-lasting aphasia after similar injury, and he postulated that after injury to the left hemisphere language functions could shift to the right hemisphere (Broca, 1865). Barlow (1877) confirmed Broca's hypothesis in his investigation of a young boy who suffered a lesion of the left hemisphere, which led to only a transient speech disturbance, followed by a later lesion to the right hemisphere, which left the boy with a permanent loss of language. The simplest explanation of Broca's and Barlow's observations was that the developing brain was capable of functional reorganization that would allow development of relatively normal language abilities after injury to left-hemisphere language zones. Clinical studies over the next 100 years confirmed the general idea that the consequences of early focal lesions of the left hemisphere were minimal (e.g., Alajouanine & Lhermitte, 1965; Krashen, 1973; Lenneberg, 1967). In his comprehensive theory of language development, Lenneberg (1967) proposed that language-related processes in the left hemisphere developed rapidly from ages 2 to 5 years and then more slowly until puberty, by which time language development was complete. He reasoned that if brain damage occurred during the time of rapid development (up to 5 years), it would be possible to shift language functions to the intact right hemisphere, and there would be no chronic aphasia. By using Wada's sodium amobarbital procedure to determine the hemisphere mediating language, Rasmussen and Milner (1977) confirmed Lenneberg's speculation as they found that childhood injuries before 5 years of age allowed a shift in language processes to the right hemisphere. Injuries from about 6 to 10 years also allowed recovery from aphasia but this was sustained by a shift of language within the left hemisphere.

An additional important finding in the Rasmussen and Milner study was that many patients with injuries prior to age 5 had speech processes represented in both hemispheres.

Thus, if Broca's area was damaged, only those language-related functions subserved by Broca's area moved to the right hemisphere and, similarly, if only the posterior speech zone was damaged, only those processes moved to the right hemisphere. And, when both left frontal and temporal language areas were damaged, the functions of both regions shifted to the right hemisphere.

Given this clearly anomalous representation of speech in both hemispheres it would be surprising if there were not some type of disruption of nonlanguage functions, and, indeed, this is the case. For example, Woods and Teuber found that children with left-hemisphere injuries in the speech zones showed unexpected deficits in right-hemisphere functions as well as an overall drop in IQ (e.g., Woods, 1980; Woods & Teuber, 1973). Such results led to a reevaluation of the effects of early cortical injuries in children with a particular interest in looking at a broad range of cognitive functions, rather than just speech (e.g., Aram, 1988; Bates et al., 1997; Levin, Song, Chapman, & Howard, 2000; Stiles, 2000). The results of such studies make it clear that the advantages of having early, rather than later, cerebral injury may not be as great as once believed. In reviewing such results we can now reach the following conclusions.

1. *Children show significant sparing or recovery of language functions after early injury to known language areas, but these functions are not normal.* For example, Bates and colleagues (e.g., Bates & Thal, 1991; Bates et al., 1997; Reilly, Bates, & Marchman, 1998) provided detailed longitudinal descriptions of language impairment and development in a population of children with perinatal focal lesions. These children have delayed language development, but by kindergarten age most of these children have caught up in their lexical and syntactic abilities. Nonetheless, the children still have continuing linguistic impairments. Importantly, in contrast to adults with focal lesions of the language areas, the site of the lesion in the left hemisphere of children does not affect the pattern of linguistic deficits: the pattern of deficits is uniform across the lesion population. There was, however, a difference in the severity of deficits associated with different foci of damage because children with left temporal injuries had more severe deficits than children with other injuries.

2. *Perinatal lesions of either the left or right hemisphere produce significant language deficits during development*, a result that is quite different from what occurs in adults. In fact, Bates and colleagues (1997) found that depending on the language measure, early right-hemisphere lesions can produce greater receptive language impairments up to age 5 years than comparable early left-hemisphere lesions. This result is surprising and could be explained, in part, by suggesting that, if left-hemisphere language functions can shift to the right hemisphere, then perhaps some nonverbal functions can shift to the left hemisphere, which could lead to some disruption of normal language development.

3. *Children with focal right- or left-hemisphere injury show deficits in spatial processing, but like language functions, the spatial functions improve as the children develop.* Stiles and her colleagues (e.g., Akshoomoff et al., 2002; Stiles et al., 2005; Stiles Trauner, Engle, & Nass, 1997) followed a group of children with lesions (largely caused by stroke) incurred by 6 months of age and found deficits in visuospatial processing as early as children could be tested. The deficits abated over development and by puberty the deficits were markedly attenuated relative to children (or adults) with later injuries. One key point in the studies of Stiles is that the deficits observed in children are qualitatively similar to those seen in adults with similar focal lesions. This finding contrasts with the effects of early lesions on language functions (see above).

4. *The outcome from focal and diffuse lesions in early childhood is very different.* In an extensive series of studies of children with closed head injuries, Levin and his colleagues (e.g., Levin et al., 1996; 2000) have found that verbal and sensorimotor skills are more impaired in young children following severe closed head injuries than in older children sustaining comparable injuries. It appears that whereas functional outcome after focal lesions may be best if the injury is perinatal, diffuse damage at a similar age leads to a very poor functional outcome.

5. *Recovery from early cortical injury is task specific.* As we have noted, the best evidence of functional recovery or sparing after early injury can be seen in the domain of language. Compensation is not as extensive for nonlanguage functions, however. For example, in general, nonverbal functions are usually impaired after

early lesions, regardless of the location of the lesion (Carlsson & Hugdahl, 2000; LeVere, Gray-Silva, & Le Vere, 1988; Nass, de Coudres-Peterson, & Koch, 1989). Teuber (1975) argued that nonverbal deficits occur after left-hemisphere lesions because the shift of language to the right hemisphere "crowds" the right hemisphere, compromising the normal right-hemisphere functions (see also Satz, Strauss, Hunter, & Wada, 1994; Strauss, Satz, & Wada, 1990). And, of course, damage to the right hemisphere impairs nonverbal functions because that is the function of the right hemisphere.

But the task-specific nature of recovery can be seen in motor behaviors as well. Children with congenital hemiplegia show recovery of language functions but the hemiplegia remains (e.g., Carlsson & Hugdahl, 2000). Similarly, B. Kolb and B. Milner (unpublished) studied patients with early lesions of the language regions of the left temporal lobe who were shown by sodium amobarbital testing to have language functions represented in both hemispheres (that is, the posterior speech zone but not the anterior speech zone shifted to the right hemisphere). These patients later all had their damaged left temporal lobe removed for the relief of intractable seizures. In contrast to patients with similar removals, but with normal left-hemisphere speech representation, those patients with anomalous speech representation showed deficits on a task of copying sequences of arm movements, a deficit normally seen only in patients with left frontal or parietal injuries (Kolb & Milner, 1981). Thus, these patients paid a price for their good language functions but, in contrast to Teuber's suggestion that shifting language can interfere with right-hemisphere functions, in this case, it interfered with a left-hemisphere function.

6. *Deficits from perinatal lesions may not emerge until many years later*. Because infants have poorly developed perceptual, cognitive, and motor functions, it is often not possible to assess the effects of early injury until late childhood or even puberty. For example, Banich Cohen-Levine, Kim, and Huttenlocher (1990) studied the development of performance on two subtests of the Wechsler Intelligence Scale for Children, namely vocabulary and block design, in children with congenital cerebral injuries. They found that at 6 years of age there were

no differences in performance, but as the children aged, significant deficits emerged in the brain-injured children relative to age-matched controls. Given that many cognitive functions, and especially frontal lobe functions, are not mature until well into puberty (e.g., Kolb & Fantie, 1989; Kolb et al., 1992), it should not be surprising if some of the effects of frontal lobe injuries might not appear for over a decade after an infant injury, a result that was first noted by Hebb (1949).

7. *General intelligence is compromised by early cerebral injuries, and especially if there is a seizure disorder*. Although not all children with early brain injuries have general intelligence scores that fall below average, as a general rule of thumb, children with injuries in the first year (e.g., Riva & Cazzaniga, 1986) or children with a persistent seizure disorder (Vargha-Khadem & Polkey, 1992) have compromised IQs. This effect on IQ occurs even after perinatal frontal lobe lesions, lesions that do not normally affect IQ in adults with frontal injuries (Hebb, 1949; Kolb & Fantie, 1989).

8. *There is far less recovery from bilateral versus unilateral injuries*. One curious, but consistent, finding is that children with restricted bilateral injuries often have a worse functional outcome than children with a complete hemisphere removed. For example, children with complete removal of the left hemisphere usually show a shift of language functions to the right hemisphere. Vargha-Khadem, Watters, and O'Gorman (1985) found that even small lesions of the right hemisphere appear to be capable of blocking the shift of speech from the left to the right hemisphere in children with perinatal injuries to the speech zones of the left hemisphere, which resulted in severe and persisting language deficits. This effect of the right-hemisphere lesion is present even if the injury is well beyond the homologous language zones in the right hemisphere.

9. *Descending motor pathways can be reorganized following early damage and this reorganization may be functionally significant*. Using both functional magnetic resonance imaging (fMRI) and somatosensory evoked potentials (SEP), Holloway and colleagues (2000) investigated the sensorimotor functions of patients with childhood hemispherectomies. Many of these patients showed SEP in the normal hemisphere when the nerves of the limb opposite the

excised hemisphere were stimulated. Similarly, fMRI showed that for at least some of the patients, passive movement of the same limb produced activation in a region of somatosensory cortex in the normal hemisphere. The responses to the hand ipsilateral to the normal hemisphere must occur because direct ipsilateral pathways run from the normal hemisphere to the affected limb.

Similar conclusions have been made in studies showing that when patients with congenital hemiplegia move the hand opposite the intact hemisphere, they commonly show mirror movements of the hemiplegic hand (e.g., Farmer, Harrison, Ingram, Stephens 1991). Carr (2000) used transcranial magnetic stimulation to induce electromyographically measured movements in a group of 32 congenitally hemiplegic patients. Sixty-four percent of these patients showed EMG activity in the hemiplegic limb when the ipsilateral hemisphere was stimulated. No such movements were seen in control subjects or the other patients. All but two of the patients with anomalous ipsilateral pathways had prenatal injuries, whereas the lesions in the remaining patients were all postnatal, a result that suggests that age at injury may be critical in the development of functionally significant anomalous corticospinal pathways.

10. *The effects of early injury vary with age.* We have seen several clues that precise age at injury may be critical in predicting functional outcome, which leads us to several generalizations. First, prenatal lesions are more likely to lead to the development of functional ipsilateral motor pathways than lesions after birth, although the formation of such pathways is possible following postnatal injuries, especially in cases of hemispherectomy. The removal of most (or all) of a hemisphere may be important because large lesions alone, such as seen in congenital hemiplegia or cerebral palsy, appear unlikely to produce anomalous corticospinal pathways. Second, language appears to be the most plastic function if the brain is injured after birth, and the time course of this plasticity appears to be much longer than for other functions, lasting up to 10 years of age. The special plasticity of language functions may be related to its recent phylogenetic development and/or to the prolonged ontogenetic development of language functions in children. Third, although small focal lesions in the first few months of age do not appear to affect general cognitive functioning (i.e., IQ), as a rule of thumb lesions in the first year produce greater impairments in IQ than those occurring later. This appears to be especially true of frontal lobe lesions, a result that led Hebb (1949) to conclude that the earlier frontal lobe injury occurred in children, the worse the effect was on cognitive functioning.

Conclusion

The process of brain maturation is long, lasting at least into early adulthood. We have approached the problem of assessing the nature of functional localization in the cortex by examining the way in which structure and behavior emerge in the developing child. Neurons, the elementary components of the brain, are born, migrate, and, as their processes elaborate, establish connectional relationships with other neurons. Behavioral and cognitive capacities follow a similar sequence of development from the rudimentary to the complex. Structure–function relationships can be inferred by matching the developmental timetables of brain anatomy and physiology with those of behavior. In addition, we have demonstrated that neuropsychological tests that are sensitive to focal cortical damage in adults can be used to assess whether certain areas have reached functional maturity in normal, developing children. Furthermore, by studying the abnormal development of the brain and behavior, we may make inferences regarding the importance of particular developmental events on behavior.

The study of anatomical and behavioral development of the brain of the child is admittedly far from complete. However, we believe that the data obtained to date are beginning to answer the questions about the nature of the brain of the child. The continued study of developmental neuropsychology promises to change our understanding of the biological bases of the development of human behavior.

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3

Development of Cerebral Lateralization in Children

MARCEL KINSBOURNE

Lateral Asymmetry as a Pervasive Design Characteristic in Nature and the World

Lateral asymmetry prevails at levels of organization that range from subatomic particles to the human body and brain. At the subatomic level, asymmetry ("chirality") seems to be the default option (Hegstrom & Kondepudi, 1990). In nature, bilateral symmetry appears in response to species-specific selection pressures, not because there is something ideal about symmetry, as has been held since classical times. That functional representation in the brain is bisymmetric was taken for granted, until Paul Broca finally overcame this strong bias as recalcitrant unilateral data from his aphasic hemisphere-damaged patients kept appearing. In 1862, he reluctantly acknowledged in public that although speech is located in the anterior cerebrum, as the phrenologists had claimed, it is represented in the front left, rather than equally on both sides.

From then on, another equally unexamined assumption was substituted. It credited the left hemisphere with being the unique peak of the brain's functional hierarchy. It seemed obvious that there had to be a leading hemisphere. The left hemisphere was considered major or dominant. The right, minor or subdominant, hemisphere was like the left, at the "animal" level, but

unlike the left, it was devoid of those capabilities, like language, that elevate humans over animals. So while anatomical bisymmetry had to be abandoned, it took another century and much cultural change before Oliver Zangwill and his colleagues overthrew functional hierarchy in the late 1940s and early 1950s and established the current understanding that specialization is complementary between the hemispheres (Kinsbourne, 1982, 2000).

Whether asymmetries at the lower levels of organization interact to generate asymmetries at the higher levels is unknown. However, the above sequence of historical events puts us on notice that, counterintuitively, both in evolution and in development, asymmetry may be the base state or default option, and bisymmetry the design characteristic that needs additional explanation. More generally, in view of the fiercely defended but baseless premises mentioned above, we might wonder, "Does the current Zeitgeist, in turn, blind us to still more promising ways of conceiving cerebral function?" (Kinsbourne, 2000).

The Normative Adult Endpoint of Hemisphere Specialization

Cognitive development culminates in an endpoint of lateralization that in its broad definition is no longer in dispute. In the right-handed majority, language-related processes are left lateralized in almost every case. The

MARCEL KINSBOURNE • New School for Social Research, New York, New York 10011 KINSBOURNE@aol.com.

right hemisphere does contribute toward certain aspects of verbal behavior, notably comprehension of logical relationships, inference, metaphor, and humor, and at the output stage, intonation and the emotional tone of the utterance. The left hemisphere is also specialized for rapid sequential recognition of familiar input, as well as the recall and recognition of order information and the formulation of motor and conceptual action plans. Right-hemisphere dominance is best documented for certain spatial-relational processes, particularly in the visual modality, face recognition, vigilance and arousal, and the perception of emotional information.

Non-right-handers deviate from the dextral norm with respect to the relative incidence of right, left, and bilateral speech representation. Different methods for determining laterality offer somewhat different outcomes. The mean findings for speech lateralization of eight studies, using dichotic listening, intracarotid amytal, electroconvulsive therapy, functional magnetic resonance imaging, and functional transcranial Doppler sonography, respectively, were as follows: left lateralization: right-handers 94.5%, left-handers 64%; bilateral representation: 2.5% versus 11%; right lateralization: 3% versus 25%. In non-right-handers, spatial-relational functions are right lateralized as they are in right-handers, but also involve the left hemisphere in more than half of all instances (Bryden, Hécaen, & DeAgostini, 1983). Within each hemisphere the territory involved in cognitive function is more extensive in the left- than the right-hander (Kinsbourne, unpublished analysis of data from Bryden et al., 1983). Knecht, Draeger, and Deppe (2000) illuminate the relationship between hand preference and cerebral dominance by demonstrating that the incidence of right-hemisphere dominance for language increases linearly with the degree of left-handedness. In their large sample of 326 healthy individuals, only 4% of those with a handedness index of 100 (strongly right-handed) were right dominant, whereas 27% of strong left-handers (index –100) were right dominant. Gender-related differences in lateralization are not yet well substantiated.

The nature and neural basis of the relationship between hand preference and cerebral dominance remains mysterious, in spite of a spate of genetic and mechanical surmises. Both the brain and the body are implicated in handedness. A hint of the complexities of the issue is provided by the finding that when people with cleft lip have the cleft on the left, they are more often left-handed than when they have a right-sided cleft (Yorita, Melnick, Opitz, & Reynolds, 2005).

Development of Hemisphere Specialization: Competing Hypotheses

With respect to development, existing knowledge is virtually restricted to language and to a lesser extent, spatial-relational, prosodic, and emotional functions, in right-handed children. This discussion will therefore be confined to considering how peripheral laterality, notably hand preference, is established in the developing child and how the differential hemispheric representation of language and spatial-relational functions develops, in the normal case, and in certain developmental disabilities.

It is not yet clear how the changes in number, configuration, and connectivity of neurons in the two developing hemispheres relate to the nature or timing of emerging higher mental functions. One can time the origin of a lateralized mental skill only by when it appears at the behavioral level. Is the cerebral hemispheric substrate of the developing skill in its earliest stages the same as it is when the skill has fully matured? This is termed "invariant lateralization" hypothesis (Kinsbourne, 1975). The alternative "progressive lateralization" hypothesis (Lenneberg, 1967) proposes that initially mental functions (and language in particular) are based on the activity of both cerebral hemispheres, and that lateralization of verbal functions to the left and spatial-relational to the right occurs over time during childhood.

Lateralization and its development are subject to biological variation. Is a particular topography of hemispheric representation of function more conducive to efficient mental function than other topographies, as has been assumed for more than a century (Harrington, 1987)? If so, are there anomalous topographies in developmental disabilities, and if so, do they account for the behavioral deficits involved? These questions can be addressed most directly in the case of the fully mature nervous system,

but lags in achieving that endpoint can also be considered.

Asymmetrical function of the brain and the body are chiefly of interest for any implications they might have for adaptive performance and behavior. If they evolved from a bilateral base state, what adaptive advantage powered that emergence? If we could discover a role that asymmetry of function plays in adaptive behavior, then we could predict how lack or distortion of such asymmetries might affect the functioning of the human infant, child, and adult.

The Origin of Bisymmetry

Somatic bisymmetry is an adaptation to the needs of motile organisms. In addition to the obvious advantage of the streamlining that results, the bisymmetric organism is well adapted for the basic decision that organisms continuously make as they move from point to point: to turn right or to turn left (Loeb, 1918). Environmental opportunities and hazards are equally likely to arise on either side. Therefore the organism needs to be able to deploy its sensorimotor capabilities to either side with comparable speed and efficiency (Gardner, 1967). To meet this need, the receptor equipment and the musculature are both bilaterally arranged, and the corresponding control centers in the nervous system, crossed in the chordate (including vertebrate) phylum, uncrossed in the other phyla (Hyman, 1940), are reciprocally inhibitory opponent processors. In contrast, sessile organisms are not bisymmetric, and organisms that regress from a motile to a stationary (sessile) state concurrently lose their bisymmetric organization. Organisms whose life cycle divides into a motile larval and a sessile mature phase exhibit the relationship most strikingly. The motile larva is bisymmetric; the sessile adult is not. Fishes, which also freely swim up and down, usually exhibit dorsal–ventral somatic symmetry as well (Braitenberg, 1977).

Asymmetry (Somatic)

Minor asymmetries abound and have been documented in all species that have been studied in sufficient detail (Ludwig, 1932). An instructive example relates to the pelvic and pectoral fins of fishes. Fins, though bilateral, are asymmetric. The right-sided fins are generally more bony and muscular than the left (Hubbs & Hubbs, 1944). This is the case even though the fishes' musculature itself is bisymmetric. This appears to be because their asymmetry poses no problem for the function of fins as rudders to direct efficient swimming movements. This is an example of an asymmetry that does not appear to have evolved to meet a specific adaptive need, but rather exists because the engineering of exact bisymmetry was not needed to meet the adaptive pressures in the context of which the species evolved.

Asymmetry (Neural)

In behaviorally simple organisms the functions of the nervous system distribute across two domains: the regulation of the internal environment and the control of behavior that is oriented in space. The former does not call for bisymmetric control, and certain striking brain asymmetries in behaviorally limited species may relate to vegetative function (Braitenberg & Kemali, 1970). The repertoire of the more behaviorally sophisticated vertebrates, including mammals and birds, features a third domain: higher mental function as involved in communication, memory, and problem solving. Not being targeted toward specific locations in the physical environment, these processes can serve their purpose without being bilaterally represented. Whereas central representation of sensorimotor processes is topographic, representation of higher mental functions is abstract. If an abstract representation deviates, even substantially, from bisymmetry, this need not be because the asymmetric topography confers specific adaptive advantage. A diminished adaptive advantage of bisymmetrical organization may sufficiently account for deviation from bisymmetry (Kinsbourne, 1974). Ringo, Doty, Demeter, and Simard (1994) suggest that mammals with large brains benefit from lateralization because the nerve impulse takes as long as 25 ms to cross the corpus callosum, which interpolates an unacceptable time lag into the execution of complex fluent mental operations, if they have to be integrated between hemispheres. However, brains as small as those of rats are lateralized, whereas left-handed humans with bilateralized representations are cognitively unimpaired.

Dramatic functional asymmetry exists in the males of some species of songbirds whose song is largely controlled by the left brain (Nottebohm, 1971). The higher vocal control center is paralleled by a comparable area on the right side of the brain. If the left-sided control area for song is destroyed or disconnected from its vocal output mechanism, the right side assumes control over the bird song, but only if the lesion is made before singing has fully developed. Bird song is communicative. It is not directed toward any particular point in space but pervades ambient space. Bilateral control of such a function would not seem to be necessary and in fact unilateral control prevails. Nevertheless, the mirror image area does develop and is available as a reserve. This is not to suggest that it is in reserve in case of left-side brain damage. Rather, nature is conservative in the manner in which it refines neural control mechanisms, and there was perhaps no provision (or environmental adaptive trigger) to preclude the unutilized right-sided area from evolving in parallel with the left. There are human specializations that can be similarly interpreted, notably the left-sided control of speech. If the left speech area is totally destroyed, the right side is able to control speech output (Kinsbourne, 1998). Should we suppose that in the intact state the unilateral facility that controls behavior maintains its control by actively suppressing (inhibiting) its potential rival on the other side (Kinsbourne, 1974)? If so, it can also do so in the reverse direction in some species, and in yet other bird species, such as the parrot, control of song is bilateral (Hauser, 1996). The latter species are analogous to those left-handed humans who are bilateralized for language, without apparent detriment to their control of vocalizations. Thus, both in songbirds and in humans, lateralization of control of rapidly sequential utterances is prevalent, but evidently not indispensable for its efficient performance.

The analogy with the neural basis of bird song captures one attribute of human brain organization, but it fails to capture another attribute: the complementarity of human hemispheric specialization (Kinsbourne, 1982). A simple animal model illustrates complementary specialization. The paired claws of the lobster differentiate into a stout crusher, driven by slow muscle fibers, and a slender cutter, largely driven by faster muscle fibers (Govind &

Pearce, 1986). The asymmetry develops under central neuron control and is mediated by lateral differences in the degree of reflex activity. In humans, the cerebral hemispheres contribute differentiated but complementary components to skilled behavior, to the point that many real-life activities simply cannot be effectively controlled by one hemisphere alone. Bresson, Maury, Pierant-LeBonniec, and deSchonen (1977) found that human infants prefer the right hand for some activities, the left for others.

A child's first words are accompanied by pointing to the named object (Kinsbourne & Lempert, 1979; Lempert & Kinsbourne, 1985). It is doubtful that the side on which attention-attracting stimuli appear, or of the limb used to point, would override the genetically preprogrammed left-brain speech laterality. But if, as Annett (1973) suggested, sinistrals lack an overriding "right shift factor," it is quite possible that in them lateralization could be influenced by such environmental factors.

Lateralization of higher mental functions cannot be assumed to be adaptively necessary simply because it happens to be the general rule. Whether deviating from the norm of lateralization exacts a penalty in terms of behavioral control is an empirical issue not to be prejudged. Under what circumstances do humans deviate from the usual laterality patterns and, when they do, what if any are the consequences for adaptive behavior?

Morphological Asymmetries in the Human

The internal organs exhibit well-known major asymmetries. Deviation from the usual pattern has also been well documented, such as complete lateral reversal (situs inversus), reversal of a single organ (e.g., dextrocardia), and absence of asymmetry, as in horseshoe kidney in which a single bilaterally symmetric kidney straddles the midline. Abnormal position of the internal organs may compress adjacent structures, but how well the organs function does not depend on their location. In the human brain and musculature, a number of less radical asymmetries exist. None of them has been convincingly tied to function.

The right-hander's body is subtly asymmetric. Most bones and muscles are somewhat more massive on the right (Latimer & Lowrance, 1965) and this is not secondary to differential

use, as it already obtains in the infant (Pande & Singh, 1971). Asymmetries in fingerprints, hair whorls, and other ectodermal structures have been documented. More relevant to the brain, the skull, the shape of which is determined by the growth of the brain, protrudes on the right in front and on the left in back (LeMay, 1976; LeMay & Culebras, 1972). The parietal operculum is longer on the left. The right frontal lobe and the left occipital lobe are somewhat bulkier than the corresponding lobes on the opposite side.

Function could be inferred from these morphological findings (Galaburda, 1984) if the mass of a given area were to correlate with the efficiency with which the individual performs the activities it is specialized to control. Also, individuals who lack the asymmetry in question should have a correspondingly different profile of functional capabilities. The evidence is far from conclusive along either of these two lines. In particular, non-right-handers exhibit by far the greatest variability with respect to relative size of parts of the right and left brain (LeMay, 1992; McRae, Branch, & Milner, 1968) and the body in general (Hicks & Kinsbourne, 1978). No one has been able to attribute any functional differences between right-handers and non-right-handers (or among non-right-handers) to these morphological variations among the latter.

That the mere bulk of the brain may not be a good index of functional efficiency is not unexpected, since the amount of normal variance in intelligence accounted for by the overall brain size, though significant, is relatively slight. Also, the greater average bulk of the male than the female brain is not accompanied by an overall greater intellectual capability. A more refined measure of brain size would perhaps take account of local differences in the amount of infolding of cortex, the gray matter being layered around the folds. There is a dissociation between the size of Broca's area, which is greater on the right, and its infolding, which is greater on the left (Falzi, Perrone, & Vignolo, 1982). However, other areas are known to have more bulk on the left side in right-handers, notably the planum temporale (Geschwind & Levitsky, 1968; Witelson & Kigar, 1988). In any case, bulk of a brain area may not only reflect the number of its neurons. An area that is demarcated by gyral boundaries is not necessarily demarcated architectonically, or unitary in its function. There may be variation in how tightly packed neurons are, in the richness of their connections, or the precision of their organization and normality of their morphology. In the four cases of dyslexia documented by Galaburda, Sherman, Rosen, Aboitiz, and Geschwind (1985) in whom dysgenesis of neurons in various left cerebral areas was found at autopsy, brain bulk as observed on CT scan did not deviate from the norm. But a special case exists, a structure the cross-sectional area of which does reflect the number of nerve fibers it transmits: the corpus callosum. Its area in cross-section did correlate positively with performance in certain tests of laterality and attention in multiple sclerosis (Reinvang, Bakke, Hugdahl, Karesen, & Sundet, 1994) and in normals (Yazgan, Wexler, Kinsbourne, Peterson, & Leckman, 1995).

A further impediment to linking brain asymmetry with differential skill in higher mental functions derives from comparative data. Yeni-Komshian and Benson (1976) found that the planum temporale is larger on the left than on the right in chimpanzees, a species not noted for its verbal ability. In summary, although it is intriguing that morphological asymmetries are "invariant" across development, they have not been validated as indices of function, and correspondingly their existence in the newborn cannot be used as evidence that language precursors are lateralized.

A number of anatomical asymmetries are already present in the brain of the newborn infant (Spreen, Risser, & Edgell 1995). Although a host of specializations emerge as the child grows up, increasing size of their lateralized neural underpinnings is not a factor.

There has been a recent revival of the phrenological assumption, that more is better, driven by the availability of structural MRI and of generous research funding. This has led to an explosion of studies with the overall goal of identifying "biological markers" that demonstrate associations between diminished or increased size of parts of the brain in a host of diverse "dysfunctions." The theoretical basis for conclusions to be drawn is undermined by the fact that if the structure is too small, neurons, dendritic trees, and/or synapses can be thought to be depleted, and when it is too large, as the brains of people with autism often become in the course of the first year of life, synaptic pruning is held to have been lacking. Research advances

commensurate with resources expended on structural/volumetric imaging have yet to become available.

Peripheral Laterality

The infant cannot do things that are used to classify more mature individuals into those who are right-handed and those who are not. However, certain motor biases may predict hand preference. As early as 12 weeks of gestation, the fetus makes more right than left-hand movements. This indicates that motor asymmetry can arise under spinal control, before the higher centers have become functional (McCartney and Hepper, 1999). The newborn infant is not capable of behavior so differentiated as to involve the use of one hand and arm only. But within his or her repertoire is a lateral orienting synergism, the asymmetric tonic neck response, which includes turning of head and eyes to one side, extension of the ipsilateral arm and leg, and flexion of the contralateral arm and leg. Since head turning from side to side has been observed in the fetus, it must be under neural control at that early stage, and the asymmetries in head turning that are seen at birth are thought to reflect asymmetries in the neonatal nervous system (Ronnqvist and Hopkins, 1998).

Head turning can be seen as a precursor of locomotion toward one side, though the infant is lying supine. The outstretched arm may be a precursor for reaching and pointing. Be that as it may, Gesell and Ames (1947) first observed that spontaneous head turning in infants is more often to the right than to the left, and in a follow-up study with a small sample they found a relationship between the direction of the most frequent head turning in the infant and subsequent hand preference. Notably, all four of the infants who showed predominantly leftward head turning subsequently became left-handers. There is now good circumstantial evidence for a developmental sequence of peripheral laterality arising from the asymmetric tonic neck response that is first evident after the intrauterine age of 32 weeks (Turkewitz, 1977). Nevertheless, Liederman and Kinsbourne (1980a) found that asymmetry of head turning represents a motor, and not a sensory, bias. They observed an overall rightward turning bias in children of right-handed parents but not in children with one non-right-handed parent (Liederman & Kinsbourne, 1980b).

It is possible that asymmetric head turning takes place even in utero. The infant's head is most often turned to the right as it descends (headfirst and backward relative to the mother) through the birth canal. Churchill, Igna, and Senf (1962) reported that more LOA than ROA babies turn out to be right-handed at 2 years of age. They attributed this to hypothesized hemisphere injury by pressure against the pelvic floor—right hemisphere in LOA, left hemisphere in ROA. This does presuppose a staggering amount of birth-related cerebral damage. If the child who is predisposed to become dextral (and with a more prominent left than right occipital region; LeMay, 1992) has a more vigorous rightward turning tendency, even in utero, and vice versa, and this is one determinant of the presentation of the fetal head, the findings can be accounted for without invoking uncorroborated pathology.

Attempts to identify lateral biases in leg movements ("footedness") have yielded inconsistent results. However, 2- and 3-month-old infants grasp an object longer with the right than with the left hand (Caplan & Kinsbourne, 1976; Hawn & Harris, 1983) and at 5 months infants reach more frequently to the right (Cohen, 1966; Hawn & Harris, 1983; Seth, 1973). After pointing has emerged toward the end of the first year, it is more frequently accomplished with the right hand (Bates, O'Connell, Vaid, Sledge, & Oakes, 1986). The situation is complicated by evidence that the hand preferred for activities at the appropriate developmental level fluctuates, perhaps systematically, within a subject during the first year of life (Halverson, 1937; Liederman, 1983; Ramsey, 1984). The fluctuation may reflect epochs in which one or the other hemisphere is in a phase of relatively more active development. A mechanism that might relate actively developing brain to the frequency of corresponding hand use was provided by Kinsbourne (1970). He proposed an activational model by which activities in a given hemisphere overflow to hemispheric facilities not primarily involved in the activity in question. Contrary to the assumption that handedness emerges from diffuse movement patterns in infancy, its antecedents are already differentiated at birth. In summary, a motor bias that in most individuals is targeted rightward clearly

exists as early as at birth or even before and is a major determinant of the side of the subsequently preferred hand.

Infant Central Laterality

The asymmetry in size of the right and the left planum temporale has been documented in neonatal brains and in the fetus as early as 29 weeks of gestation (Chi, Dooling, & Gilles, 1977; Wada, Clark, & Hamm, 1975; Witelson & Pallie, 1973). With respect to function, several studies of infants have documented differential response to speech and non-speech input depending on its side of origin. Entus (1977) used the paradigm of high-amplitude non-nutritive sucking to indicate orienting to a change in stimulus state. When 2-month-old infants habituate to a constant sound they stop sucking. If that sound changed discriminably, the sucking is dishabituated and resumes. Entus presented tape-recorded speech and music. Given changing speech sounds, sucking stopped earlier if the changed sound was presented to the right ear. With music the same was true for the left. Although Vargha-Khadem and Corballis (1979) did not replicate these outcomes, Best, Hoffman, and Glanville (1982) presented similar findings using a heart rate dishabituation paradigm, as did Molfese, Freeman, and Palmero (1975) using amplitude of evoked potential. Amplitudes were higher over the left brain for speech, over the right brain for music, in newborns. MacKain, Studdert-Kennedy, Spieker, and Stern (1983) found infants better able to coordinate seen (lip) and heard aspects of an observed speech act when turning right toward the speaker than when turning left. Young and Gagnon (1990) reported that newborns turn more to the right than left when they hear speech. Segalowitz and Chapman (1980), studying premature infants, found that a verbal input caused a quieting of movements of the right arm and leg and musical input a quieting on the left.

These findings are fragmentary and qualitative and not always confirmed (Shucard, Shucard, Cummins, & Campos, 1981). Nevertheless, precursors of aspects of verbal behavior are observably present and lateralized as predicted by the invariant lateralization hypothesis as early as at or even before birth. Pena et al. (2003) played speech and backward speech to sleeping newborns and found a larger increase in left temporal blood flow, indicating increased metabolic activity of the neurons, for forward speech. Dehaene-Lambertz, Dehaene, and Hertz-Pannier (2002) compared speech (forward and backward) with silence. Speech generated strong left temporal activation as compared to silence. The left-hemisphere dominance for speech in early infancy was similar in degree to that of adults. Nor does the right hemisphere lag in specialization. Homae, Watanabe, Nakano, Asakawa, and Taga (2006) found increased right temporo-parietal blood flow when normal speech was subtracted from flattened speech. The prosodic element (intonation) generated right-hemisphere activation (again, as it does in adults). An intriguing finding relates to lateralization of perception of emotion, which is right-sided in adults (Schwartz, Davidson, & Maer, 1975). In infants less than 1-year old, Davidson and Fox (1982) monitored power spectrum EEG changes while they discriminated faces. Even at this early age the right hemisphere was more involved than the left in the discrimination of facial affect. Segalowitz and Berge (1995) reviewed research on the interaction of right versus left EEG activation with emotional state in infants.

Evidence that left thalamic nuclei are involved in verbal behavior and right thalamic nuclei in visual behavior (Ojemann, 1977) fits with the notion that there are lateralized selector mechanisms at a brain stem level that implement categorical (hemispheric) mental set (Kinsbourne, 1980). The subcortical mechanisms are perhaps involved, if not in the actual mental processing, of which the infant is not yet capable, then in facilitating its prospective occurrence, by implementing lateralized ascending activation of cortex.

Emergence of Hand Preference in Children

Asymmetries in movement patterns have been observed as early as the tenth week of gestation. McCartney and Hepper (1999) studied fetuses between 12 and 17 weeks of gestation. Significantly more right than left arm movements were observed. Therefore motor laterality appears well before cerebral laterality of structure and function become operational. When the child has become capable of reaching, grasping, and pointing, movements analogous to the activities based on which hand preference

is determined, the choice of hand used is under control of factors that will cease to operate as maturation proceeds. Notable is the tendency of infants not to cross the midline when they reach for things (Provine & Westerman, 1979). If the target is slightly to one side of the center, the child reaches with the ipsilateral limb regardless of hand preference. It is not that there is any motor constraint on reaching across the midline. If the child is already holding a desired object in the ipsilateral hand, he or she does cross the midline in picking up the target with the free hand (Hawn & Harris, 1983). Otherwise, the infant's "prewired" tendency to orient to the side of stimulation (use the hand ipsilateral to the target) overrides motor preference. This could explain why Goodwin (cited in Liederman, 1983) found that right-hand preference on a reaching task at 19 weeks strongly predicted hand preference at 3 years, but left-hand reaching preference did not. Unimanual preference for reaching at 7 weeks predicts the dominant hand for bimanual manipulation at 13 weeks (Ramsey, 1980).

Infants' tendency not to reach out and cross the midline seems to be a consequence of immature brain organization. When developmentally delayed individuals are slow to establish hand preference, that may be because they are still under the control of this more primitive mechanism. Even when it becomes possible to observe the child's choice of hand in a number of standard unimanual activities, the young child differs from the older individual in sometimes being inconsistent in which hand performs which activity (a factor separate from the question of which hand is preferred for activities overall). Palmer (1964) observed this "ambiguous" hand preference (Silva & Satz, 1984) in normal children. We will return to it when discussing children with mental retardation and autism.

Consistent hand preference tends to be established in the preschool years and to persist unless the individual is subjected to contrary cultural pressure. Children who showed left-handed tendencies used to be constrained to use the right hand instead, generating shifted sinistrals who would use the right hand at least for socially conspicuous activities like writing and holding tableware. Such people might still be more dexterous on the left, and giving them a novel activity to perform may reveal their left-hand preference. Nowadays this type of pressure

has been relaxed in the West (though it persists in east Asia) (Teng, Lee, Yang, & Chang, 1976). This is presumably the reason why Western offspring have a higher probability of being non-right-handed than their parents. Levy (1976) reported that left-handers constituted 2.2% of the US population in 1932, but more than 11% by 1972.

Using positron emission tomography while left-handed children who were "switched" were writing with their right hands, Siebner et al. (2002) observed persisting activation in the right hemisphere. They suggest that this represents the continued necessity to inhibit left-hand movements during the writing process.

Frequently documented within the left-handed population is the position of pen in hand, a distinction being made between the inverted position in which the point of the pen is held below the tip of the thumb and index finger and the non-inverted in which the pen is held in the same way as right-handers. Inverted handwriting posture is considerably more common in males. It develops during the grade-school period. It may reflect certain biological differences in brain organization (Levy & Reid, 1976). With respect to motor behavior the non-inverter exhibits a more bilateralized or right-hemispheric type of control and the inverter seems to be more ambidextrous (Parlow & Kinsbourne, 1981).

The prevalence of inverted writing position among left-handed developmentally disabled individuals is not known. It might be of interest, however, because Searleman, Porac, and Coren (1982) found it to be more common after birth stress.

Development of Central Laterality in Childhood

Most of the evidence derives from two sources, lateralized brain lesion effects and laterality testing in normal children, and relates to the language function. Laterality paradigms reveal the effects of functional lateralization on the control of behavior. Which hemisphere is dominant for a particular mental operation is revealed by a bias in how efficiently the relevant task is performed when the pertinent input originates from the right versus the left side of extrapersonal space. Each hemisphere also controls the elements of contralateral turning: faster orienting contralaterally, with consequent faster

information pickup, and faster response in that direction by limb or gaze. Thus, the task-specific activation of the specialized hemisphere introduces a slight but observable contralateral turning bias. Kinsbourne (1972) demonstrated that verbal thinking generates rightward orienting (gaze and head turning), whereas spatial thought occasions more left than right gaze shifts. Conversely, verbal learning during rightward head turning was greater than during left turning (Lempert & Kinsbourne, 1982). This method has as yet been little used in developmental studies. However, Barrera, Dalrymple, and Witelson (1978) did report more left gaze during visual processing of faces by infants, and MacKain et al. (1983) found infants better able to map visual on auditory components of speech signals when orienting rightward.

Dichotic listening and visual half-field viewing are the usual techniques for determining laterality of input processing. In dichotic listening, speech sounds, syllables, or words are simultaneously presented to both ears. The subject is asked either to report all stimuli ("whole report") or to listen separately to the right ear only and to the left ear only while ignoring words on the non-attended side ("selective listening"). In "whole report" a laterality index is computed to represent the extent to which the subject is able to correctly report input through the right ear as compared with the left. In selective listening the subject's ability to identify input from the specified ear is compared for the two ears, and so also is the incidence of responses that represent interference from the ear not to be attended. Normal right-handed adults as a group exhibit right-ear advantage (i.e., they are better able to identify material presented to the right ear than the left under both whole and selective reporting conditions). More intruding stimuli from the right ear are normally reported when selectively listening to the left than vice versa (Treisman & Geffen, 1968).

As early as 3 years of age, a right-ear advantage has been repeatedly demonstrated (Ingram, 1975, Kinsbourne & Hiscock, 1977; Nagafuchi, 1970; Piazza, 1977). Thus, a greater engagement of the left hemisphere in verbal auditory processing can be accepted. The question remains: Is the degree of this effect as great in children as in adults or is it that although lateralization has already occurred to some extent by age 3, it will subsequently increase further?

Whereas the direction of group mean ear advantage is an acceptable index of the side of the cortex that is dominant for the task in question, the degree of asymmetry is a dubious index for "degree of lateralization," which is itself a dubious concept. There are numerous factors that interact with differential hemispheric specialization to generate ear advantages that differ in degree, even when the same subject is tested under different circumstances or with different dichotic test materials. The test–retest reliability for dichotic listening ranges between about 0.5 and 0.8 (e.g., Bakker, Van der Vlugt, & Claushuis, 1978; Hiscock & Kinsbourne, 1980a). This degree of variability is hardly commensurate with an index that reflects a fixed structural characteristic. Direction of gaze and direction of movement in the visual environment can both influence the degree of right-ear advantage (Hiscock, Hampson, Wong, & Kinsbourne, 1985). Perhaps still more important is task difficulty. The extent to which items from one ear have to be held in memory while those from another are reported (Inglis & Sykes, 1967) can be a major factor if there is a bias to report stimuli from a particular ear first (Bryden & Allard, 1981). For these reasons it would not have been immediately clear how to interpret any interaction between age of child and degree of right-ear advantage for verbal material, had such been found. In fact, most competent studies failed to find such an interaction. Instead, the degree of ear advantage is roughly invariant, consistent with the invariant lateralization hypothesis. The proportion of interfering response from right versus left ear is also invariant across a wide age range in childhood (Geffen, 1978; Geffen & Wale, 1979; Hiscock & Kinsbourne, 1977, 1980a). Progressive lateralization gains little support from dichotic listening studies both in its original strong form, positing a gradient of lateralization culminating at puberty (Lenneberg, 1967), and in its weak form, restricting that gradient to the first 5 years of life (Krashen, 1973). If lateralization develops at all, its development is completed by age 3 (Porter & Berlin, 1975), the youngest age at which it is feasible to perform dichotic testing in the conventional manner. However, Lokker and Morais (1985) tested children aged 1–3 years dichotically, using selective reaching for an object rather than speech as the response. They

too found a right-ear advantage for children of right-handed parents.

The visual method of verbal laterality testing is less generally applicable to preschoolers because it relies on the written word. When grade-schoolers were presented with words that they could easily read, then the usual right half-field advantage was found, regardless of age (e.g., Marcel and Rajan, 1975).

The lateralization of speech output control in the intact individual can be determined by the method of verbal–manual interference (Kinsbourne & Cook, 1971; Kinsbourne & Hicks, 1978). Subjects perform a unimanual activity, such as speeded repetitive finger tapping, with one hand or the other, with or without concurrent speaking. If speech control is lateralized, speaking interferes disproportionately with the finger tapping when both activities are controlled by the same hemisphere (i.e., left lateralized speech interferes more with right than with left finger tapping). With this paradigm there is a differential interference with right-hand performance in children as young as 3 years. This indicates that speech is already lateralized to the left at that age, supporting invariance of lateralization for speech production (Hiscock & Kinsbourne, 1978, 1980b; White & Kinsbourne, 1980). The invariance hypothesis was recently supported by functional imaging (Wood et al., 2004).

Less is known about the ontogeny of lateralization for those non-verbal activities that are regarded as being right lateralized. Piazza (1977) found a left-ear advantage for the dichotic presentation of environmental sounds in 3-, 4-, and 5-year-olds, and Saxby and Bryden (1984) confirmed this for 5-year-olds (although in an earlier study, Knox and Kimura (1970) found somewhat weaker left-ear effects in 5- and 6- than in 7- and 8-year-olds). Sidtis, Sadler, and Nass (1987) found no interaction with age of left-ear advantage in the discrimination of complex tunes in children aged 7–12 years. For tachistoscopic face recognition, left visual field advantages are found in quite young children, unaffected in degree by age (Marcel, Katz, & Smith, 1974; Turkewitz & Ross-Kossak, 1984; Young & Bion, 1980; Young & Ellis, 1976). With respect to the ability to discriminate shapes by active touching (haptic perception), the typical left-hand advantage has been found as early as 2–3 years of age (Rose, 1984). Other studies revealed left-hand advantages for nonsense shapes in preschoolers (Etaugh & Levy, 1981) and grade-schoolers (Affleck & Joyce, 1979; Flanery & Balling, 1979; Klein & Rosenfield, 1980; Witelson, 1974, 1976), but only Flanery and Balling found a developmental trend.

Briefly exposed faces are equally well identified on either side of the midline until about age 7, when a left half-field advantage begins to emerge, earlier in boys than in girls (Carey & Diamond, 1994). This finding illustrates a fundamental issue in interpretation. Whereas the gradual emergence of an asymmetry could indeed imply progressive lateralization, it could as readily indicate the emergence of a processor that had not been functional in the less mature brain. If space perception calls for particular processing skills that normally only emerge toward the end of the first decade of life, then presenting a spatial-relational task to younger children will yield a lack of asymmetry by default, rather than indicate that at that age both hemispheres were processing the material in question to a comparable extent.

The absence of interaction between degree of lateral asymmetry and age in most studies simplifies the task of explanation. In addition to supporting lateralization invariance, it sidesteps the dilemma of interpreting between-group differences in the degree of laterality bias in the same direction. The assumption that degree of lateral asymmetry indexes degree of lateralization of the critical task-related mental operation (Shankweiler & Studdert-Kennedy, 1967) has never been substantiated. Indeed, it is unclear what is meant by greater or lesser degree of lateralization. Does the distinction assume that both hemispheres participate in the task, though to a varying extent unequally? If so, are they redundant in their contribution, or complementary? If unilateral brain damage occurs, should the function in question be compromised by damage on both sides, in proportion to the degree of lateralization on each side? If so, no such intimation from lateral brain injury exists. Given the many factors that, for instance, modify asymmetry in a dichotic test—task difficulty, task aptitude and motivation, the extent of stimulus dominance, and perhaps whatever else the subject is thinking about and how (happy or sad) he or she is feeling, it is hardly surprising that the literature on degree of lateralization is inconsistent in the extreme. Two related areas

to which the concept has been vigorously applied are gender differences and age at puberty difference in degree of lateralization. It is little wonder that the literature in both fields is a morass of inconsistencies. Operationally, laterality tests (and lateral brain damage effects) can only guide us in a choice between three alternatives: left lateralized, right lateralized, bilateralized.

Lateralization Probed by Lateral Cerebral Damage

If language lateralization is invariant, then left-brain damage should be equally likely, and right-brain damage equally unlikely, to cause aphasia or delayed language development in right-handed children as in adults (acutely—whether the probability or rate of compensation changes with increasing age is a separate issue). Contrary to earlier impressions (Basser, 1962), this is approximately the case. In Woods and Teuber's (1978) series, the incidence of aphasia in right-handed children aged 2–14 was about 70% versus 7% for left- and right-sided cerebral damage, respectively. The implication that the left hemisphere is specialized early for language is corroborated by series of children who suffered lateral cerebral damage before the emergence of language would be expected. The long-term language outcome is less favorable if the early damage was left-sided (Kershner & King, 1974; Kiessling, Denckla, & Carlton, 1983; Rankin, Aram, & Horwitz, 1981; Vargha-Khadem, O'Gorman, & Watters, 1985), at least in terms of syntactic proficiency (Aram, Ekelman, Rose, & Whitaker, 1985; Dennis & Kohn, 1975; Rankin et al., 1981). Left-sided brain injuries sustained before age 5 result in less favorable intellectual outcome than later injuries (Aram & Eisele, 1994) although the children still progress in the usual way through the stages of language development and score well within the normal range of IQ. It follows that brain organization is not strictly modular, but draws on distributed as well as focalized neural processing, at least during mental development.

Although lateralization of language remains invariant throughout its development, the locus of compensation after damage to the language area of the child's brain does not.

Penfield and Roberts (1959) reported on the incidence of aphasia after left temporal lobectomy in epileptic adults. When lesion onset was prior to 2 years of age, the probability of aphasia was much less than when the damage had occurred subsequently in childhood. It appears that territories in both hemispheres have the potential to compensate for injury to the language area. Right-sided territories are more likely to assume a compensatory role the earlier the lesion occurred, and perhaps the more extensive it is. Studying children with unilateral focal brain lesions, Chilosi et al. (2005) found both a rightward shift of language representation (inferred from dichotic listening) and inferior language development at 2 and 3 years of life in children whose lesions were left-sided. Perhaps right-hemisphere territories that normally control other processes are preempted for purposes of the compensatory functioning ("crowding hypothesis" of Teuber and Rudel, 1962) to the detriment of their customary role. Many adult aphasics program their residual or recovering speech from the uninjured right side of the brain (Kinsbourne, 1998). We conclude that language precursors rely on the same hemisphere that subserves language in its full maturity. The earliest manifestation is perhaps a selective activation of that hemisphere in a verbal context, well before its neural substrate has matured to the point that language processing is feasible. As language ability differentiates, language processing may involve, not a shrinking, but an expanding neural base within that same hemisphere (Satz, Strauss, & Whitaker, 1990).

Supportive evidence for early right-sided lateralization derives from studies of right-hemisphere lesion effects in childhood (Ferro, Martins, & Tavora, 1984; Kohn & Dennis, 1974; Stiles-Davis, Sugarman, & Nass, 1985). They all found spatial deficits analogous to those observed in adults after right-hemisphere damage. The fact that lateralization is invariant is not contradicted by the claim that lateralized findings emerge serially over time within each hemisphere (Satz, Strauss, & Whitaker, 1990). The latter phenomenon is better characterized as progressive intrahemispheric specialization than lateralization. Obviously different specialized central facilities become functional at different times throughout childhood. Whether their intrahemispheric base shrinks, expands, or

remains the same during this process has not been determined.

The impressively consistent evidence in favor of invariant lateralization for the major functions of both hemispheres offers a conveniently simple standard of reference against which to evaluate the frequently offered suggestion that children with a variety of developmental disabilities are anomalously lateralized, and that this causes the behavioral deficit.

Lateralization in Developmental Deficit

Introduction

Perhaps because developmental deficits offer so few clues beyond their surface phenomenology for their pathogenesis, lateralization has often been invoked as a possible factor. Allegedly, the normal lateralization of hemispherically specialized cognitive functions failed to occur, the assumption being that when cognitive processing is based on both hemispheres it is relatively primitive and necessarily inefficient. This logic depends crucially on the notion that lateralization is normally progressive and that when this progression is impaired, the end result is a cognitive deficit. As we have seen, the evidence for progressive lateralization is lacking; if anomalies of lateralization are to be found in developmental disabilities, some other explanation has to be sought. There is, in fact, a greater incidence of unusual forms of lateralization in developmental deficits, but the causes and implications of these differences remain quite obscure. They may be coincidental and non-specific. Furthermore, there is a coincidence between absence of the usual left lateralization of language in various disabilities and an increased prevalence of non-right-handedness in the same conditions (though the central and peripheral laterality anomalies by no means correlate perfectly). I first consider the data on hand preference.

Hand Preference in Developmental Disabilities

Not only is the non-right-handedness more common among the mentally retarded and language and learning delayed, but the non-right-handed subgroups of these populations tend to be more severely affected. For example, Hicks

and Barton (1975) found severe and profoundly mentally retarded individuals to be even more often non-right-handed than mild and moderate, who in turn were more often non-right-handed than the general population. Bradshaw-McAnulty, Hicks, and Kinsbourne (1984) confirmed this finding and related greater severity of the mental retardation to a greater probability of non-right-handedness in one or other parent. In infantile autism, non-right-handedness is particularly prevalent (Colby & Parkinson, 1977; Tsai, 1982), and several investigators have found the lower-functioning autistic individuals to be more often non-right-handed (e.g., Fein, Humes, Kaplan, & Lucci-Waterhouse, 1984). Indeed, in mental retardation, and particularly in autism, the hand preferred even for a single activity is apt to change from trial to trial (ambiguous handedness, according to Silva & Satz, 1984; see also Soper, Satz, Orsini, Van Gorp, & Gireer, 1987). Non-right-handedness is relatively common in stuttering and in language delay. In selective reading disability (dyslexia), non-right-handedness is relatively prevalent, again especially among the most severely affected children, who are to be found in clinical settings and in special schools for the learning disabled (Satz, 1976). An excess of non-right-handedness is generally not found among relatively poor readers as compared with good readers in the general school population.

Sharply contrasting explanations for this conjunction of findings have been offered. (1) Presuming that peripheral non-right-handedness implies a corresponding absence of central lateralization, the latter deficiency is incriminated as inducing a processing inefficiency (Orton, 1937). (2) Some left-handedness (Satz, 1972) or even all left-handedness (Bakan, 1971) is related to early left-hemisphere pathology (syndrome of pathological left-handedness of Satz, Orsini, Saslow, & Henry, 1985), and such early pathology is also likely to induce diverse developmental disabilities. (3) A postulated adverse influence early in development both diminishes language lateralization and impairs the evolving competence of the language hemisphere (Geschwind & Behan, 1982). (4) Becoming non-right-handed and suffering from a wide range of developmental disorders are consequences of an adverse influence on the fetal brain ("maternal immune attack") which is

generated by mothers who are susceptible to diseases of the immune system (Crawford, Kaplan, & Kinsbourne, 1994).

The second and third of these models are only applicable to those developmental deficits that can plausibly be attributed to malfunctioning of the left (language) hemisphere, rather than of the cerebral cortex as a whole. Language and reading disabilities are a case in point, and autism used to be so regarded (Rutter, Bartak, & Newman, 1971) although the evidence against this view is now very strong (Fein et al., 1984). However, it then also has to be explained why the right hemisphere does not compensate for the hypothesized left-sided malfunction, given its well-known ability to compensate for the effects of gross early left-hemisphere damage. For mental retardation and perhaps autism, in which conditions a more general cerebral deficit seems likely, explanations (2) and (3), targeted on the left hemisphere, lose force. However, conceivably more than one of the above-postulated mechanisms might come into play in the same individual. For instance, there is circumstantial evidence that right- as well as left-handed members of relatively sinistral families are more at risk for developmental deficit, or for having more severe deficit should early damage occur (Kinsbourne, 1986). The damage to which such individuals are vulnerable could in turn, when it implicates the left hemisphere, not only impair cognition, but also shift the hand preference phenotype to sinistral, in a genotypic dextral (pathological left-handedness). This would increase the prevalence of non-right-handedness among the affected family members beyond the level that prevails within their already relatively sinistral family (Bradshaw-McAnulty et al., 1984).

Central Laterality in Developmental Deficits

The measurement of central laterality requires a degree of cooperation from subjects, and perhaps for that reason, has most often been attempted in people whose developmental deficits are relatively mild, namely, the learning disabled. These consist of two main subgroups: children with attention deficit and children with central processing difficulties (Kinsbourne & Caplan, 1979). A sample of the former was found to be normally lateralized by a dichotic (Hiscock, Kinsbourne, Caplan, & Swanson, 1979) and a visual (Naylor, 1980) laterality test.

Therefore, studies have concentrated on the latter, and especially on the reading-disabled subgroup ("dyslexics"), under the influence of the persisting notion that dyslexia is the result of failure of left language lateralization (Orton, 1937; Zurif & Carson, 1970). But enough studies have found normal verbal laterality in learning-disabled children (e.g., Bouma & Legein, 1977; Caplan & Kinsbourne, 1982; McKeever & Van Deventer, 1975; Marcel et al., 1974; Marcel & Rajan, 1975) to indicate that failure of left-sided language lateralization is not a viable explanation for selective reading disability (reviewed by Hiscock & Kinsbourne, 1995).

The lack of evidence for abnormal laterality does not imply, however, that the left-sided language areas are normal in dyslexic children. Patchy microdysgenesis has been identified at autopsy (Galaburda et al., 1985). Alternatively, the left hemisphere might be undersupplied by ascending activation, rendering it hard for the child to muster verbal skills in full force to solve what is for him or her a difficult verbal problem (Kinsbourne, 1980). Such an activational insufficiency might also generate a relatively non-verbal (right-hemispheric) cognitive style in dyslexic children (Caplan & Kinsbourne, 1982). Obrzut, Hynd, Obrzut, and Pirozzolo (1981) found learning-disabled children better able than normally reading controls to listen selectively to left-ear input. Obrzut, Hynd, and Zellner (1983) obtained comparable results in visual laterality. The voluntary attentional shift could override a diminished rightward attentional bias engendered by the presumably relatively weak left-brain activation of the dyslexics. Yet another possibility is that dyslexic children fail to distribute verbal and spatial computation to different hemispheres (Obrzut, Boliek, Bryden, & Nicholson, 1994). If so, their behavior is analogous to that of normal adult left-handers, using the preferred direction of reflective lateral gaze as the dependent variable (Kinsbourne, 1972).

Bakker, Licht, Kok, & Bouma (1980) used an electrophysiological approach to distinguish subgroups of dyslexics that are deficient in right- and left-hemisphere functioning, respectively. Evoked potential studies lend support to the view that dyslexic children may exhibit abnormal responses in one hemisphere when tested, but the stability of those patterns has not been proven (Fried, Tanguay, Boder, Doubleday, &

Greensite, 1981; Mecacci, Sechi, & Levi, 1983). If stable, they could reflect lateralized activational deficiencies.

Absent and reversed anatomical cerebral asymmetries abound in dyslexics (reviewed by Hynd, Marshall, Hall, & Edmonds, 1995). As these authors point out, the significance of such findings is also qualified by their presence in many people in the general population. Either they are devoid of functional significance or, conversely, they account not only for extreme individual differences (as in learning disability) but also for individual differences considered to be within the normal range. Advances in quantitative MRI have now made the latter possibility amenable to study in the normal population.

Stuttering is an early arising deficit (3–5 years of age) in which maladaptive rivalry between the cerebral hemispheres for control of speech has long been suspected (Travis, 1927). The concept of stuttering as due to incomplete lateralization of speech was dramatically supported by case studies of four left-handed stutterers with lateralized cerebrovascular congenital anomalies (Jones, 1966). Intracarotid amytal testing before operation found them to be bilateralized for speech. After operation, repeat amytal testing showed that speech control had become restricted to the normal (unoperated) hemisphere. Also, after the operation, the patients ceased to stutter. This could be because the operation had titled rivalry in favor of a single hemisphere. However, comparable studies of three more right-handed stutterers without brain damage have not yielded comparable findings (Andrews, Quinn, & Sorby, 1972), and both behavioral and EEG laterality were normal in the stutterers (Pinsky & McAdam, 1980). As in dyslexia, it is more likely that in most stutterers any cerebral abnormality is of a dynamic rather than a static nature, for instance, contralateral interference with left-hemisphere activation for stuttered speech acts only. In the regional cerebral blood flow study of Wood, Stump, McKeehan, Sheldon, and Proctor (1980), stutterers were judged to have inadequate left-hemisphere activation (normalized when the stuttering was relieved by haloperidol). The influence of excessive right-hemisphere activation may explain the familiar fact that stuttering only appears, or is at its height, when the individual is anxious. Anxiety is associated with increased activation of the right frontal lobe

(Wiedeman et al., 1999), aggravating the distorted activation balance between the hemispheres.

Is the stuttered speech itself the cause of the diminished left-hemisphere activation? Blomgren, Nagarajan, Lee, Li, Aloord (2003) found that stuttered speech was associated with bilateral activation, rather than the usual left-sided activation, even when subjects made linguistic judgments without speaking.

For autistic spectrum disorders, both bilateral failure to lateralize and right-brain dominance have been proposed. But it seems more likely that heterogeneous patterns of cerebral specialization occur within the autistic population, and that no one pattern of lateralization constitutes a necessary condition for autistic symptomatology to appear (Kinsbourne, 1987). Among the heterogeneous mentally retarded population, Down syndrome individuals have been credited with anomalous perceptual laterality (Hartley, 1981; Pipe, 1983), indicating reversed cerebral dominance. But Tannock, Kershner, and Oliver (1984) found a right-ear advantage in Down syndrome, and Parlow, Kinsbourne, and Spencer (1996) found no laterality differences between Down and non-Down severely mentally retarded adults and an overall pattern for both laterality of verbal input and verbal output control that was comparable to the norm.

The scientific literature points to the following conclusions:

1. Laterality findings are compounded of two interlocking elements: localized areas of specialization and task-related activation. The two are usually congruent. However, activation for purposes of task performance may miss its topographical mark. Conversely, areas that are crucial to the performance of a practiced task may exhibit little or no extra activation. If only the topography is considered, the figures may not add up.
2. Asymmetrical representation of cognitive processes may not have evolved to meet adaptive needs, but may be the base state, or default option, without implications for the efficiency of the lateralized function.
3. Anomalous lateralization is not infrequent in diverse developmentally delayed

populations. But there is no evidence that failure to lateralize causes any of the developmental delays. Indeed, how well a cognitive process works has little or nothing to do with where it is represented in the human brain.

4. Specialized circuitry arises from precursors in the same half-brain. Hemisphere specialization is not the endpoint of modular function imported from elsewhere in the brain.

5. Behavioral patterns that unmistakably usher in language development appear at a stage of maturation at which there are few general cognitive operations to support their emergence. This makes it very unlikely that language development is compounded of the development of facilities in more general domains. Some brain circuitry can support language development, either primarily or in compensation. Other circuitry cannot (regardless of what non-language cognitive skills are at hand). If general-purpose mechanisms contribute to language development, a process that Marcus and Rabagliati (2006) have dubbed, after Darwin, "descent with modification," they do so in an accessory fashion, well after that development has begun.

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4

Development of Higher Brain Functions: Birth Through Adolescence

LAWRENCE V. MAJOVSKI AND DAVID BREIGER

Introduction

The bane of pain in understanding the healthy, normal, developing brain lay vainly in the unfolding story of life's unfinished experiment as to what we know and do not know regarding "what's going on age-wise" and how mapping structure onto function looks from birth through adolescence. Higher cortical functions in humans, birth through adolescence, proceed in defined age-related changes that influence structure–function relationships. In a five-year NIH-funded, multi-center project on "Normal (healthy) Brain Development (birth through 18)," findings from this report released in July 2006 are now available to the public via Brain Imaging Resource Network, which contains a comprehensive database on 500 human children with information collected from a wide variety of sources, e.g., MRI, neural, cognitive, intellectual, behavioral, and social demographic variables.

Significant limitations in our knowledge exist as to the processes involved in the normal developing human brain with respect to neurophysiological, neurochemical, neuroanatomical, metabolic, and other related neuroscience disciplines. Attempts have been made to correlate anatomical and behavioral data in a direct manner, leading to a surfeit of postulations in the literature against a shortage of supporting data for known brain–behavior relationships in children (Taylor, Fletcher, & Satz, 1984). Much emphasis tends to be placed on proposed neural mechanisms and theories accounting for changes regarding development of the human central nervous system (CNS) versus description of changes taking place with respect to normal development of the human brain. Major difficulties exist in drawing fixed conclusions because each human brain is unique with respect to its molecular blueprint, cellular differentiation pattern, acculturation factors, and neural growth patterns (Cooke, 1980; McConnell, 1991).

Luria (1969a, personal communication, 1977) stressed that what was lacking in the area of clinical child neuropsychology was an integrative scheme outlining a conceptual blueprint of normal brain development with concomitant motor, sensory, perceptual, and cognitive processes involved in children's higher cortical functions.

During the past 10 years, however, neuroimaging and brain metabolism (MRI, MRS, FMRI, MegEEG, MSI, PETT imaging) technologies are producing quantitative means of mapping human brain function onto brain structure (Kreis, Ernst, & Ross, 1993; Raichle, 1987; Raichle et al., 1994; Reynolds, McCormick, Roth, Edwards, & Wyatt, 1991; Stehling, Turner, & Mansfield, 1991; Tzika, Vigneron, Ball, Dunn, & Kirks, 1993).

LAWRENCE V. MAJOVSKI AND DAVID BREIGER • Department of Psychiatry and Behavioral Sciences, Children's Hospital and Regional Medical Center, University of Washington School of Medicine, Seattle, Washington 98104–2499.

Recent research reports have shown that the human brain continues to develop into the second and even third decades of life with different age-related changes from birth through 2; 2–4; 5–8; 9–12; 12–18+, involving at least two significant patterns in neuronal maturation, i.e., white and gray matter densities (Casey, Geidel, & Thomas, 2000; Giedd et al., 1999; Nelson, Thomas, de Hann, 2006; Kuhn, 2006).

The main goal of this chapter is to address highly significant facts and concepts related to the normal developing brain from the perspective of human conception through childhood. Major emphasis will be placed on the normal developmental perspective with selected pathological consequences that can result from abnormal influences for the clinical practitioner's interest. Recent advances in neuroimaging measurement and in vivo techniques of cerebral and cognitive developmental processes will be addressed in the final section of the chapter.

Development of the Human CNS

Throughout its development, one of the brain's many functions is to act in generating behavior. The question of how the brain effects control over behavior is central to the study of human developmental neuroscience. The brain can be viewed in one sense as a decision-making organ system for information processing (Hillyard, 1987). Understanding the development of the human CNS poses a basic problem of how inhibition brings about the regulation and integration of higher cortical processes involved in the brain's development. Two major themes of importance throughout the course of neuroembryological development are the integrative action of the component parts of the nervous system, and cellular differentiation, i.e., how the component parts are derived (Humphrey, 1978; McConnell, 1991; Nilsson, 1978).

A major problem in understanding the brain's development stems from the lack of a blueprint as to nature's original design. Completion of the human brain took place some 50,000 years ago. To date, knowledge is incomplete as to the original model. In studying the brain's development, neuroanatomists have discovered that the brain develops much more rapidly than other organs. Why this is so is not known. The influence of external signals in the environment, e.g., acculturation, on the brain is incalculable and is changing its structure more rapidly today than ever before (McConnell, 1991).

The human nervous system contains an estimated 10^9 neurons in the CNS, another 30×10^9 in the cerebellum itself, plus some 10^{11} granular cells within the cerebellum's macromolecular layers. There are an estimated 10^{12} glial cells crucial to the function and support of neurons. It is the association of these cells and their neurochemical communication links that makes humans human.

The human nervous system can be divided into three major aspects: central, peripheral, and autonomic. All three act in concert to control behavioral activities (e.g., motor, sensory, acoustic, optic). It is commonly held that the brain is the organ system that controls human behavior (Gottlieb, 1976a,b). A key element in attempting to understand how the brain works is the problem of inhibition and its role in human behavior. Exactly how the brain accomplishes control (inhibition) is not fully understood but part of the answer lies in the unfolding of the brain's morphology through the process of cellular differentiation.

Morphology

The CNS is usually defined as the brain (encephalon) and spinal cord (medulla spinalis) which develops from the *medullary plate* of the ectoderm. The brain lies in the cranial cavity surrounded by a bony capsule. The spinal cord is situated in the vertebral canal surrounded by vertebrae. Both are covered by cranial or spinal meninges that enclose a space filled with cerebrospinal fluid (CSF). The peripheral nervous system (PNS) is composed of cranial and spinal nerves (31 pairs) with associated ganglia consisting of motor fibers and sensory fibers. There are two types of motor fibers: (1) somatic motor fibers, which terminate in skeletal muscles, and (2) autonomic fibers, which furnish innervation to cardiac muscle, smooth muscles, and glands. Sensory fibers receive stimuli from receptive organs of various types. Nerves of the PNS supply the head, trunk, and limbs. The CNS and PNS together serve conscious perception, voluntary movement, and the processing of sensory-based messages and integration (Arey, 1974;

Kahle, Leonhardt, & Platzer, 1978; Moore & Persand, 1993a; Nilsson, 1978).

In the autonomic nervous system (ANS), there are two antagonistic components, the *sympathetic* and the *parasympathetic* systems. They are responsible for preserving a constant internal environment (homeostasis). All viscera, blood vessels, and glands are innervated by the ANS. The human nervous system, the organism, and the environment are functionally interrelated.

The human organism not only responds to its surroundings, it acts spontaneously on them as well through functional circuits. The action that is instigated by the CNS (transmitted via efferent nerves) is registered by the sense organs and information is then returned to the CNS via the efferent nerves. An integrative process follows until regulation occurs involving both *exteroceptive* and *proprioceptive* sensations (Afifi & Bergman, 1980; Carlson, 1994a).

The importance of the above phenomena is seen in the control and regulation of the muscular responses achieved via sensory cells in the muscles that provide a feedback circuit through sensory nerves to the CNS (Crelin, 1973; Kahle et al., 1978). Luria (1973a) and others have pointed out the functional interrelations between the nervous system, the organism, and the environment from which emerge higher cortical processes. These three components, together, serve conscious perception, voluntary movement, and the processing of messages through *polysensory integration*. To better appreciate the interplay between structure and function, it is useful to first understand the development of the brain, starting with the formation of the embryonic disc, the nervous system's point of origin (Humphrey, 1978; Moore & Persand, 1993a,b).

Neuroembryonic Structure Formation

The nervous system starts developing approximately 18–22 days after fertilization. The egg is composed of ectoderm and endoderm with mesoderm developing between the two. The nervous system is derived from the *ectodermal layer*. During embryological development, the neural plate, the neural tube, and the neural crest form. The neural crest becomes elevated to form the neural folds which, in turn, approximate each other in the midline and then fuse to form the neural tube. Cells at margins of the folds are not included in the wall of the neural tube. The partial fusion of the neural folds occurs approximately 23–24 days postfertilization (Crelin, 1974; Hamilton & Mossman, 1974; Kahle et al., 1978; Le Douarin, 1980; Lowrey, 1978; Moore & Persand, 1993a,b). In its formative stages, the neural tube appears as a straight structure. During its organogenesis, cervical somites deviate from the shape of the simple neural tube. This portion, destined to become the brain, forms various bulges and cavities, each of which has significance in the embryological plan of development (Jones & Cowan, 1978; Moore & Persand, 1993a).

Three primary bulges appear in the brain region of the neural tube: the forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon). When the development of the caudal end of the tube is completed, the *optic vesicles* appear and protrude from each side of the forebrain. Otic invagination also occurs at day 28 postfertilization. In terms of the ventricles of the future brain, a *cephalic flexure* and a *cervical flexure* become visible with cavities at sites of the prosocele of the forebrain, mesocele of the midbrain, and rhombocele of the hindbrain.

Each optic vesicle will differentiate to form a characteristic pattern: first, the optic cup; then stalk; and, later on, optic nerves that becomes part of the eyeball. The original connection of each optic vesicle becomes located in the diencephalon, a subdivision of the forebrain.

By day 36, the forebrain divides into two parts. The caudal subdivision becomes the *diencephalon*, and the anterior component further differentiates to form the *telencephalic vesicles* which eventually become the cerebral hemispheres (Carlson, 1994a; Hamilton & Mossman, 1974; Jones & Cowan, 1978; Moore, 1977). Simultaneous with the subdivision of the forebrain, the original cavity (the prosocele) undergoes subdivisions. Two telencephalic vesicles (teloceles) are formed and become the *lateral ventricles*. The median telocele, which lies between these two teloceles, together with the diocele, becomes the *third ventricle*. The mesocele develops into the *cerebral aqueduct*. As the forebrain divides into the telencephalon and diencephalon, the hindbrain forms into two structures: the *anterior metencephalon*, which becomes the *pons* and the *cerebellum*; and the posterior *myelencephalon*, which becomes the

medulla oblongata. The fourth ventricle forms from the cavity of the metencephalon (*metacele*), together with the cavity of the myelencephalon (*myelocele*).

By day 34, the cerebellar plate, cervical and mesencephalic flexures, lens invagination, otic vesicles, and olfactory placodes are visible. By day 45, olfactory evagination will have occurred as well as formation of the cerebral hemispheres. Lens fiber migration of retinal cells will begin in earnest at this point.

Growth and development by 3 months postfertilization take place in terms of the two smooth-walled telencephalic vesicles. These are easily identified as *cerebral hemispheres*. Each emerging hemisphere of the telencephalon will have divided by this time into three parts, each of which has different functions. The first component is the *rhinencephalon*; the second is the thick basal (*striatal*) region, which develops into the *basal ganglia*; and the third is a *suprastriatal region*, which forms the *cerebral cortex* and related underlying white matter (Arey, 1974; Crelin, 1974; Kahle et al., 1978; Moore & Persand, 1993a).

The rhinencephalon begins as an outgrowth from the telencephalon, e.g., the olfactory lobes. Each olfactory lobe forms part of the wall of the cerebral hemispheres. The second major portion of the rhinencephalon forms part of the wall of the cerebral hemispheres, e.g., the *hippocampus*, a bulging mass that appears on the medial wall of the lateral ventricles, bilaterally. In humans, the rhinencephalon includes, in addition to the bilaterally placed olfactory bulbs and hippocampi, such structures as the bilateral *pyriform lobes*, midline *septum pellucidum*, and midline *fornix*. The rhinencephalon differentiates into structures referred to as the *limbic lobe*, which contains interconnections with structures such as thalami, epithalamus, and hypothalamus. This constitutes the *limbic system*.

The functional significance of the limbic system lies in its association with emotional responses and the integration of olfactory information subserving both visceral and somatic information. The limbic system is involved in "emotional expression," whereas the hypothalamus is involved in the regulation "control" of emotions through hormonal substances. The thalamus serves as the "portal" to the cerebral cortex, which is inextricably bound together in the processing of sensory information leading to human conscious activity. Other bilaterally placed structures of the rhinencephalon include the *stria terminalis, septum, amygdaloid bodies, medial* and *lateral olfactory gyria, parahippocampal gyri, and cingulate gyri* (Carpenter, 1978; Crelin, 1974; Hamilton & Mossman, 1974; Kahle et al., 1978; Moore, 1977).

Basal Ganglia

The second part of the telencephalon that is formed is the *basal ganglia* (or *basal nuclei*). They are formed in the thickened portion of the striatal region of the telencephalic area, composed of several groups of neuronal cell bodies. One of the major groups of these *ganglia* (i.e., nerve cell bodies outside the brain and spinal cord) is the *corpus striatum*, which becomes related to the thalamus of the diencephalon. Up to the third month, the corpus striatum and thalamus are separated by a deep fissure. The corpus striatum bulges into the lateral ventricle while the thalamus protrudes into each side of the third ventricle. Beginning about the fourth month, the groove between these two structures will disappear and fuse into a common mass. When fully matured, the basal ganglia comprise the following main structures: *caudate nucleus, claustrum, amygdaloid body*, and *corpus striatum*. These structures will become involved with motor control (Carlson, 1994b; Carpenter, 1978; Kahle et al., 1978; Nauta, 1986a,b).

In the suprastriatal region, the third component of the telencephalon forms all of the externally visible cerebral hemispheres. The hemispheres increase in size and completely envelop the mesencephalon and the upper portion of the cerebellum, and the originally smooth surfaces begin to show convolutions at around 7 weeks. The formation of the surface convolutions, known as *sulci*, and the deeper depressions, termed *fissures*, allows the outer layer of neurons (the six cell layers in the cerebral cortex) to increase greatly in depth without a major change in the overall size of the brain in relation to its final volume. By the completion of its development, the cerebral cortex will range in thickness from approximately 1.5–4.0 mm with a surface area of $2.3–2.5 \times 10^3$ cm^2 (Crelin, 1973, 1974).

The first major fissure to appear on the lateral aspect of each cerebral hemisphere is the *lateral Sylvian sulcus* (or *fissure*) which becomes

evident by the third month. The slowly growing floor of the sulcus, which is lateral to the corpus striatum of the basal ganglia, is the *insula*. It eventually becomes completely covered by adjacent areas of the hemisphere. Beneath the convolutions of the cerebral cortex lies the substrate of the highest centers of the cortical integration in the human nervous system. Cortical layers I–VI subserve *higher cortical functions* involving conscious activity, memory processing of information, decision-making, planning, voluntary action, and ultimately reflection (Luria, 1966, 1969b, 1970, 1973a,b; Posner & Rothbart, 1992).

Ventricle Formation and CSF

Important changes are also occurring in various parts of the brain after the third month, particularly ventricle formation. The lateral ventricles each develop three horns that protrude into the various lobes of the cerebral hemispheres: the *anterior* horn projects into the frontal lobe, the *inferior* horn into the temporal lobe, and the *posterior* horn into the occipital lobe. Each lateral ventricle occupies a more lateral position relative to the third ventricle and the formerly broad *interventricular foramen* (*foramen of Monro*) becomes a narrow canal. The third ventricle connects with the lateral ventricles of each hemisphere by the foramen of Monro and continues caudally into the *cerebral aqueduct of Sylvius,* expanding beneath the cerebellum to form the fourth ventricle (Humphrey, 1978; Moore & Persand, 1993a).

Simultaneously, the egg-shaped thalami bulge into a third ventricle. Eventually the two thalami, with normal development, bridge this ventricle, come into contact with each other, fuse, and produce an interthalamic bridge. The *cerebral aqueduct of Sylvius* becomes a long, slender tube connecting the third and fourth ventricles. Two major foramina become prominent: the left lateral opening (*foramen of Luschka*) and the median opening (*foramen of Magendie*), both comprising the fourth ventricle (Kahle et al., 1978; Moore & Persand, 1993a,b).

A region of invagination, the *choroid plexus,* will occur along the choroid fissure of the lateral ventricle. Functionally, the choroid plexus serves as a source of CSF, the three main functions of which are (1) to support the weight of the brain in the skull, (2) to protect the brain from physical trauma during injury to the skull, and (3) to provide a stable chemical environment for the CNS, despite plasma's chemical composition changes (Afifi & Bergman, 1980; Carlson, 1994b).

Ependymal cells lining the brain's ventricles form the medial surfaces of each lateral ventricle, the roofs of the third and fourth ventricles, and portions of the plexus. As these cells grow and invaginate, they are accompanied by blood vessels known as *choroidal vessels*. CSF escapes through the median (foramen of Magendie) and lateral (foramen of Luschka) openings of the fourth ventricle into the *subarachnoid* space surrounding the brain and spinal medulla. The lining of the choroid plexus also forms a physiological barrier known as the *blood–brain barrier system* between the CSF and the blood supply to the brain.

The blood–brain barrier system is more permeable in newborns than in adults, becoming less permeable as the brain matures. Bilirubin, for example, in high concentration in infants can cause brain damage because it passes through the brain barrier system. Conversely, high levels of bilirubin do not affect the adult brain (Carlson, 1994a; Moore, 1977; Moore & Persand, 1993b).

Spinal Cord Formation, Alar and Basal Plates

During neuroembryological development, the neural tube is divided into longitudinal zones; the ventral half of the lateral wall differentiates early into the *basal plate*. It is thought to be the site of origin of the motor nerve cells. The dorsal portion of the lateral wall differentiates later and is termed the *alar plate*. It is the site of origin of sensory nerve cells. Between the alar and the basal plates lies an area from which autonomic nerve cells are thought to arise. Viewing the structural plan of the spinal cord and brain stem in this fashion aids in understanding how various parts of the brain are organized. Because it is held that the basal plate does not participate in the formation of the brain areas beyond the midbrain (metencephalon), the diencephalic and telencephalic vesicles are thought to arise from the alar plate (Kahle et al., 1978). Alar plate cell bodies are composed of *sensory* and *coordinating* (internuncial) neurons. These are located in the layer of gray matter (*mantle layer*). Gray matter is the region of the brain and cord that contains aggregates of nerve cell bodies, as distinct from *ganglia*, which are nerve

cell bodies that lie outside the brain and spinal cord. Differentiation of the diencephalon from the alar plate results in division into dorsal and ventral portions. The dorsal portion becomes the thalamus and consists of cell bodies of sensory and coordinating neurons. These *nuclei* are nerve cell groups within the brain. The ventral portion of the alar plate develops into the hypothalamus, which is composed of motor control neurons. The dorsal (alar) plate thus becomes the site of sensory and coordinating neuronal cell bodies. The ventral basal plate becomes the site of motor control neuronal cell bodies (Crelin, 1973, 1974; Moore, 1977; Moore & Persand, 1993b).

The thalamus exerts control through its *projectional* (internuncial) neurons, which synapse with parts of the brain other than the cerebral hemispheres, and in particular, with the hypothalamus. Thalamocortical interaction exists in what is known as the *thalamocortical projection system*. Two major structures of importance in terms of cortical–cortical and cortical–subcortical interneuronal connections are the major fiber tracts that arise in the *internal capsule* and the *median forebrain bundle* (MFB). The last projectional pathway from thalami to cerebral cortex takes place through the *nuclealis reticularis thalami*. It is thought that through this projection pathway, there is ongoing monitoring and modulation of information from lower levels of nervous activity to the upper cortical regions of the CNS. The thalami also serve a role in pacemaking activities seen in the electroencephalogram (EEG). Another important function is *selective awareness* involved in conscious activity (Bear, 1986; Bloom, 1979; Crelin, 1973; Hamilton & Mossman, 1974; Scheibel & Scheibel, 1961, 1963). A significant portion of the human thalami is composed of a group of nuclei that receive proprioceptive and general cutaneous, visceral, visual, and acoustic impulses, which are relayed to the cerebral cortex via other projectional (internuncial) neurons. The structural and functional relationships of the component parts of thalamic nuclei are inextricably comingled (Riss, 1972; Scheibel & Scheibel, 1966, 1972).

The hypothalamus, derived from the alar plate of the diencephalon, is part of the limbic system and is considered to be the headquarters for central motor control of the ANS. It regulates emotional responses and certain visceral functions, such as appetite, thirst, digestion, sleep, sexual drive, heart rate, body temperature, general smooth muscle action of internal organs, and control of the anterior lobe of the hypophysis. The hypothalamus is involved in the releasing of neuroregulatory factors.

By the seventh week, the *infundibulum* (posterior lobe of the hypophysis) appears and develops as an extension of the hypothalamus. The *parathyroid* structure appears in association with the *thyroid* gland. During the eighth to tenth weeks, thyroid follicles emerge as well as production of adrenaline and noradrenaline (Crelin, 1974; Hamilton & Mossman, 1974; Lemire, Loeser, Alvord, & Leech, 1975).

The basal portion of each cerebral hemisphere, situated anterior and lateral to the hypothalamus, is derived from the ventral portion of the *alar plate*. This basal area contains the *basal ganglia*. Other important anatomical structures that emerge from the telencephalon include the cerebral cortex and the septal–hippocampal–amygdaloid nuclei complex.

Fiber tract systems are also developing with nerve fibers of the brain and spinal cord that have a common origin and destination. This anatomical feature should be kept in mind when thinking about the development and differentiation of white matter versus fiber tract systems. It is the cell bodies of neurons (the functional and anatomical unit of the human nervous system) that are involved in human thought, memory, and voluntary and regulatory motor control over the entire nervous system. These neurons are localized in the cerebral cortex and are responsible for executing higher cortical functions (Afifi & Bergman, 1980; Kahle et al., 1978; McConnell, 1988; Szentagothai, 1975, 1978).

Hippocampi

The hippocampi have been described in recent as well as past studies going back to Santiago Ramón y Cajal (Anderson, 1975; Ramón y Cajal, 1911; O'Keefe & Nadel, 1978; Storm-Mathisen, 1979). The hippocampi play a significant role in the generation and retrieval of memory processes. They also serve a key role in the generation of conscious activity in humans. Studies on active memory capabilities of infants have shown that this feature of cognition occurs as early as 6 months after birth (Kagan, 1985; Kagan & Moss, 1983). The hippocampal

commissure (fornix) is the second set of major connections to appear in the *lamina terminalis*, a major component of the early telencephalon (the first set to appear is the *anterior commissure* and the third commissure will be the *corpus callosum*). These connections begin to cross from one cerebral hemisphere to the other toward the end of the first trimester of fetal life (Carlson, 1994a; Altman, Brunner, & Bayer, 1973).

Findings from magnetic resonance imaging (MRI) of human cortical development in autistic 8-year olds to 53-year olds, support the observation that brain abnormalities responsible for autism likely occur in the first 6 months of gestation (Courchesne, Townsend, & Saitoh, 1994; Saitoh, Courchesne, Egaas, Lincoln, & Schreibrion, 1995; Piven, Berthier, Storkstein, & Nehme, 1990). Brain stem auditory-evoked responses (BAER) of young children with autism suggest brain stem dysfunction affecting the processing of sensory input through the auditory pathway. Viewed from this perspective, an anomalous development of brain stem or posterior fossa may be only part of a generalized process of neurodevelopmental dysfunction that might account for deviant language, cognitive, and social development in the spectrum of autistic disorder (Wong & Wong, 1991). The hippocampal commissure could be a key maturational component of compromise, along with other structures (telencephalic) involved in the cognitive informational processing pathways forming during the sixth month of fetal brain development.

Cellular Differentiation of the Nervous System

Structural and functional organization of the nervous system is based on cellular organization in which the neuron is the basic building block of the nervous system. In terms of the nervous system's network, neurons are interconnected in a specialized array of systems via synaptic connections (Crelin, 1973, 1974; Hebb, 1949; Kuffler & Nicholls, 1977; Lund, 1978; McConnell, 1988; Szentagothai, 1978). Inhibitory synapses are important as excitatory ones. Inhibitory synapses limit and select continual impulse inflow. Selected signals are transmitted for further information processing and unimportant signals are suppressed.

Spinal Medulla. As the neural tube forms, three cell layers develop and differentiate from its walls: the ependymal layer, the mantle layer, and the marginal layer. These layers form distinct zones: the ependymal zone, the mantle zone (gray matter), and the marginal zone (white matter). The outermost layer becomes the *pia mater* derived from pial cells. The organizational patterns formed from these zones are best seen from the viewpoints of the spinal medulla (cord), the cerebellar hemispheres, and the cerebral hemispheres (Arey, 1974; Crelin, 1974; Kahle et al., 1978; Moore & Persand, 1993a,b).

The basic three-zone pattern of the spinal medulla structure will be retained in maturity as follows: The ependymal zone remains as columnar cells lining the lumen of the central canal; the cells of the mantle zone form the gray matter; and the marginal zone becomes the white matter. The gray matter of the spinal medulla assumes the anatomical appearance of an H-shaped mass surrounded by white matter. The *association* and *commissural* (internuncial) neurons of the gray matter of the spinal medulla are formed by other mantle zone neurons. The white matter lacks neurons. Instead, there are bundles of axons arising from those nerve cells located throughout all levels of the spinal medulla and brain to form various fiber tract systems. White matter, in contrast to gray matter's large number of cell bodies (neurons), contains only scattered bodies of cells, which are chiefly supportive in nature, e.g., *glial* cells, which outnumber neurons in the nervous system by a ratio of 10:1. With increased specialization of the brain, more complex arrangements of the axonal tracts occur constituting brain white matter.

Cerebellum. Research in the past decade indicates that an enormous amount of integration occurs within the cerebellum, specifically with the bursting of Purkinje fibers and the quenching of Purkinje cells (Ito, 1984; Thach, Goodkin, & Keating, 1992). The organizational pattern in the cerebellum shows pronounced deviation, neurohistologically, from the basic structural pattern of the mesencephalon, metencephalon, and medulla oblongata, which develop from neuroblasts of the dorsal portion of the mantle layer. Cells of the cerebellum are involved in motor control and have interconnections via the basal ganglia that may serve a role in monitoring and coordinating muscle activity in relation to all forms of sensory input (Carpenter, 1978; Kahle et al., 1978; Thach et al., 1992).

The cerebellum serves many functions. It repeats activities in a regulated, precise manner;

smooths out all motor activities; plays a role in sensory activity; and may even be involved in affective responses. It is the center for the smooth coordination of muscular responses, especially those involved with subconscious maintenance of normal posture. Because of its primitive three-layer system, i.e., molecular, Purkinje, and granular cells, it is also involved in feedback and dampening circuits that operate as a "servomechanistic system" to control complicated integrative movements such as talking and writing. Many cerebellar cells serve an inhibitory role, e.g., "turn off" cells such as Mugwump and Golgi II cells. The cerebellum may even be viewed as similar to a computer in that it may be able to generate programs on its own (Scheibel, 1978).

Thalamocortical Fiber System. The thalami receive all types of sensory input relayed by projectional neurons either to various nuclei of the brain stem or to the cerebral cortex. Nearly all of the axons conveying sensory input to each thalamus cross from the opposite side of the spinal medulla or brain stem. Those fibers that have not crossed include half of optic nerve fibers entering the thalami from the same side. From each thalamus, projectional neurons relay sensory impulses to the cerebral cortex for which there is a corresponding area in each thalamus. Activation of a minute portion of the thalamus will stimulate the corresponding (and much larger) portion of cerebral cortex via the axons from the *thalamocortical projectional neurons.* The cerebral cortex contains cell bodies of *associational neurons*, which send their axons through the white matter of the hemisphere and in another part of the cortex of the same side. The cortex also contains cell bodies of *commissural neurons*, which send their axons via the hemisphere's white matter ending on the opposite cerebral hemisphere. It is via the commissures (originating from the *lamina terminalis*) that a bridge is formed to allow the *functional integration* between the two sides of the brain (Arey, 1974; Carlson, 1994a; Carpenter, 1978; Crelin, 1973; Kahle et al., 1978).

During development, the first commissure to appear is the anterior commissure. It interconnects the olfactory amygdaloid nuclei and cortical portions of the cerebral hemispheres. Second to appear is the hippocampal commissure (region of the fornix), which will unite the two hippocampal olfactory portions of the hemispheres. Then, posteriorly, in the region of the pineal body, the *habenular* and *posterior commissures* interconnect with the diencephalon. The last of the commissures to form (and the largest of all) is the *corpus callosum*. It is known that myelination begins in the brain at about embryonic week 16 and typical layers in the cerebral cortex are observed around week 24. At birth, there will be continuing organization of axonal networks, cerebral corticospinal tract development, motor coordination, and myelination pattern formation (Carlson, 1994a; Moore, 1977).

Glial Cells. White matter and gray matter are made up almost entirely of cell constituents: White matter consists chiefly of bundles of axons, glial cells, and blood vessels; and gray matter is composed primarily of neuronal cell bodies, dendrites, axons, glial cells, and blood vessels (Afifi & Bergman, 1980; Carlson, 1994b). Glial cells are the supporting structures of the CNS. There are three types of glial cells in the human CNS: *astrocytes, oligodendrocytes*, and *microglia* cells. Glial cells outnumber neurons by 10:1. Type II astrocytes are thought to derive from oligodendrocytes. The latter are derived from either precursor cells in the neural tube or neural crest precursor cells. Microglia cells primarily arise from mesodermal embryonic connective tissue from which *all* layers of blood vessels of the brain and spinal medulla arise. They serve a phagocytic function after damage to the brain and are not found in the developing brain until blood vessels are present (Carlson, 1994b).

Astrocytes are composed principally of two different functional forms. The first are the fibrous *astrocytes*, which are abundant in white matter, providing both support and binding for the tracts of nerve fibers. The second, *type II astrocytes* (*radial glial cells*), are present in large numbers in the gray matter and serve many different purposes. They establish close contacts with neuronal cell bodies, blood capillaries, and pia mater. In conjunction with endothelial cells of capillaries, they form a highly selective blood–brain barrier (Crelin, 1973, 1974; Hamilton & Mossman, 1974; Moore & Persand, 1993a,b).

Cerebral Hemispheres. Beginning at approximately the third fetal month, migrating neuroblasts from the mantle zone pass into the marginal zone, giving rise to the cerebral cortex. Stratification within the cortex proceeds at an

ever-increasing rate. At approximately 6 months, the six layers of cell bodies and their associated interconnections that characterize the cerebral cortex become identifiable. Final differentiation of the outer layers continues through the second decade of life (and perhaps even longer). The outer layers (I–III) become more highly developed in humans than in any other mammalian species (Arey, 1974; Crelin, 1973, 1974; Moore, 1977; Moore & Persand, 1993a,b).

The pattern of neuronal development in the cerebral cortex during infancy is integral to the complex functions of the cortex, which ultimately consists of a vast information storage and processing ensemble, e.g., cognitive reasoning abilities, memory, communication, reflective thinking, and individual mental performance skills. From infancy through the first 3–5 years of life, the subcortical–cortical connections serve prominent roles in the storage of the myriad patterns of motor responses that can be elicited at will in order to control motor functions of the developing human body. It is the neocortex that gives humans voluntary control over how they will react to sensory–perceptual stimuli, integrate information, and decide whether or not to act on it in a deliberate manner (Scheibel & Scheibel, 1973).

In humans, voluntary control of muscles is almost exclusively regulated through the descending projectional tract systems arising from neurons in the cerebral motor cortex, e.g., the *pyramidal motor system*. One major system is the *corticospinal* tract that begins to form during embryonic week 9, reaching its outer limits by week 29. Fibers from the projectional neurons located in the cerebral cortex form fiber tracts and pass from the cerebral cortex to the other parts of the CNS (Bear, 1986; Carpenter, 1978; Kahle et al., 1978; Majovski & Jacques, 1982; Nauta, 1986a,b).

Axons of the pyramidal neurons pass from each cerebral hemisphere to form the corticospinal tract portion of each *internal capsule* situated in the *basal ganglia*. These two corticospinal tracts pass through the mesencephalon as part of the cerebral peduncles through the lower portion of the medulla oblongata. It is at the level of the medulla oblongata that most of the fibers of the tracts will *decussate* across the midline to pass down to the opposite side of the spinal medulla and become the *lateral corticospinal tract*. The uncrossed fibers, which remain ipsilateral, make up the *ventral corticospinal* tract and eventually cross to the opposite side at the lower levels of the spinal medulla. It is estimated that approximately 30% of the corticospinal tract fibers remain uncrossed, and that 70% are involved in decussation. Axons of the pyramidal motor control neurons of the cerebral cortex synapse with ventral gray column motor neurons (Arey, 1974; Carpenter, 1978). Functionally, the cerebral hemisphere on one side, from the decussation pattern manifested, exerts voluntary motor control over the opposite side of the body and also receives sensory inputs from the opposite side of the body via fibers that are crossed to enter each thalamus (Crelin, 1974; Lund, 1978).

Axons, whether myelinated or unmyelinated, become surrounded by glial cells (oligodendrocytes). Within the CNS, commissural, projectional, somatic, associational, and autonomic motor neurons become encapsulated by parts of other cells. The only exceptions are the *boutons* at synapses and nodes of Ranvier. From the PNS, the neurons become completely encapsulated parts of other cells, except at the terminal endings and at the nodes of Ranvier (Kahle et al., 1978).

Unmyelinated axons are those that are surrounded (sheathed) by parts of either oligodendrocytes (those within the CNS) or neurilemmal cells (those peripheral to the CNS). In contrast, myelinated axons are those that are sheathed by numerous layers of the cell membranes of either oligodendrocytes or neurilemmal (Schwann) cells. Major differences, neurohistologically, exist between the myelin sheath formed by each type. Oligodendrocytes and neurilemmal cells form myelin sheaths by similar processes but at different times.

Myelin Sheath Formation. Sheath cells become wrapped around the axon many times, with the sheath cell, the axon, or both, causing the spiraling motion. Fiber tracts begin to function maturely at the time they are covered with myelin. The process of myelination in the human brain begins 3 months postfertilization in peripheral site nerve fibers produced by adjacent Schwann cells. Myelination of nerve fibers in the CNS starts later and is produced by oligodendrocytes (Dietrich & Hoffman, 1992; Dietrich et al., 1988; Yakovlev & Lecours, 1967). However, at birth, only a few areas of the brain and tract systems are completely myelinated, e.g., brain stem centers serving

subcortical functions such as certain primitive reflexes. Generally, tracts become myelinated at the same time they become functional.

As the wrapping process occurs around the axon, the cytoplasm of the sheath cell retracts such that it is extruded so that the two layers of plasma membrane of the sheath cell fuse together. Myelin is actually formed by numerous fused layers of lipoprotein membrane composed of 70–80% lipid and 20–30% protein (Valk & Van der Knapp, 1989). Tracts of white, myelinated axons make up the majority of white matter of the nervous system. The majority of *preganglionic sympathetic* axons are myelinated and are responsible for the appearance of the white *ramus communicans*. In contrast, the majority of *postganglionic sympathetic* axons are unmyelinated.

Myelination is a process closely associated with the development of the functional capacity of neurons. One of its chief characteristics is the promotion of impulse conduction, which enhances the functional efficiency of the neurons. Unmyelinated neurons tend to have a low conduction velocity and show fatigue earlier, whereas myelinated neurons fire rapidly and have long periods of activity before fatiguing occurs. Neurons that are capable of rapid transmission of impulses become fully functional at about the time their axons are completely insulated with myelin (Carlson, 1994a,b; Crelin, 1974; Lemire et al., 1975; Valk & Van der Knapp, 1989).

Formation of myelin in the spinal medulla begins during the middle of fetal life but is not completed until puberty. The last spinal tracts to be myelinated are the descending motor tracts, such as the corticospinal (pyramidal) and the tectospinal tracts. These become myelinated during the first 2 years of life. At birth, only a few of the 15 dissectable descending tracts are completely myelinated (Crelin, 1974; Kahle et al., 1978; Yakovlev & Lecours, 1967). In the human brain, myelination continues into the fourth decade of life and even beyond (Dietrich & Hoffman, 1992; Valk & Van der Knapp, 1989; Yakovlev, 1962; Yakovlev & Lecours, 1967). The increased staining of myelin during the first and second decades occurs in the subicular region. During the fourth through sixth decades, it progressively shows lateralization along the surface of the presubiculum (including cingulum bundle projections). Data point to the importance of both early and late postnatal increases of myelination which occur in a key cortical limbic relay area of the human brain. This holds importance when applying a neurodevelopmental perspective to the study of normal versus psychopathological processes during early childhood and even adulthood (Bennes, Turtle, Khan, & Farol, 1994).

Motor neurons of the cranial nerves show myelination patterns before their sensory counterparts. Optic nerve fibers begin to show early myelination at birth and will be completed by the end of the third month including optic tracts, lateral geniculate body, optic radiations, and calcarine cortex.

Axons of the cerebral hemispheres are among the last to become myelinated, beginning around birth. At first, only the axons of cortical neurons of the olfactory, optic, and acoustic areas are myelinated, followed by those arising from cell bodies in the somesthetic and motor cortices. Fibers that become myelinated after birth are those of the projectional, commissural, and associational axons of the cerebral hemispheres. By 4–6 months of life, the splenium of the corpus callosum becomes myelinated. The infant will now begin to develop binocular vision and visual accommodation in order to identify objects. These skills, however, require interhemispheric connections and myelination of the fiber tracts between the visual cortex and associational areas of the brain. Myelination of axons of the associational cortices of the cerebral cortex will continue into adulthood (Carpenter, 1978; Crelin, 1973, 1974; Yakovlev & Lecours, 1967).

Neurotransmitters and Neurohormones. Neurons secrete specific neurotransmitters, neuropeptides, or neurohormone substances at the axonal terminal endings (boutons). Boutons are the sites where information is transferred from one neuron to the next and where electrochemical changes in the release properties of the presynaptic terminals take place. This might be thought of as a "chemical language" system within the brain. Neurohormones attach to the membrane of the cell on which the axon terminates and induce internal changes in that cell. Neurotransmitter substances serve as neurotransmitters, i.e., to either stimulate or inhibit the secretory process in concert with other neuromodulators. Once the secretory process is stimulated, physiochemical changes occur within the cell that are intimately related to the changes

in the permeability of the cell's membrane (Cooper & Bloom, 1991; Lehninger, 1968, 1993; Zucker & Lando, 1986).

Neurohistologically, many neurons that become highly specialized evolved from glandular cells. Certain cells of the body are structurally and functionally intermediate to typical endocrine cells and neurons. These cells possess axon terminations in the posterior lobe of the hypophysis (pituitary gland), rich in both cytoplasmic material and hormones. Hormones are produced by the neurons and pass along the axons to the hypophysis, where they are stored for release as required (Halasz, 1994). After being released, these posterior lobe hormones pass to the responsive tissues of the body through the vascular system. Other similar hypothalamic cells secrete hypophysiotropic substances that pass on to the endocrine cells of the anterior lobe of the hypophysis through the blood vessels and regulate endocrine hormone secretion. The sympathetic and parasympathetic components of the ANS are under the regulation of the neuroendocrine system via the pituitary gland (Daughaday, 1981; Imura, 1994; Kaplan, Grumbach, & Aubert, 1976; Kuffler & Nicholls, 1977; Snyder, 1980).

In the region of the *substantia nigra*, the dopaminergic (DA) nigrostriatal system affects motor balance and affectual response. This site also is implicated in the etiology of schizophrenia and parkinsonism (Majovski, Jacques, Hartz, & Fogwell, 1981). Different ascending arousal activating systems are located in the basal forebrain, upper brain stem, and hypothalamus releasing various neurotransmitters, as follows.

Serotonin (5-hydroxytryptamine) molecules are found in the raphe nuclei of the brain stem. The pathways that originate from them are distributed in a manner similar to those for adrenergic neurons. Serotonin (5-HT) can produce both inhibition and excitation of neuronal activity as well as depression of behavioral activity in the mature brain (Jacobs, 1994; Smith & Sweet, 1978a,b).

γ-Aminobutyric acid (GABA) is a transmitter substance released by inhibitory interneurons, as well as by cerebellar Purkinje cells. High concentrations of GABA are present in the striatonigral pathway within the substantia nigra, reticular thalamic nuclei, thalamocortical nuclei, and cortical pyramidal cells. The reticular nucleus is an important GABA-containing neuronal structure in that it is thought to influence the flow of information between the thalamus and cerebral cortex. GABA release in the ascending activating system, putatively, is implicated as having a role in helping to achieve and maintain the waking state.

Acetylcholine (ACh) is released at both excitatory terminals in the sensorimotor cortex, as well as visual cortex, and inhibitory terminals such as the olivocochlear bundle. In addition, it has been found in the *nucleus basalis of Meynert* (Dunn, 1980; Steriade, McCormick, & Sejnowski, 1993). ACh is involved in the dreaming state and plays a major role in influencing the cortex, thalamus, and forebrain structures (Cooper & Bloom, 1991; Steriade et al., 1993).

Monoamine transmitter substances can produce excitation or inhibition of neuronal activity. When this effect is exerted on inhibitory neurons, the net result is often facilitation via noradrenaline. Such a mechanism may account for the behavioral arousal produced by the catecholamines (i.e., noradrenaline and DA), which are believed to be involved in the facilitation of inhibition (Bloom, 1973, 1979, 1994; Cooper & Bloom, 1991; Majovski et al., 1981; Smith & Sweet, 1978b).

It has been theorized that DA and other peptides may play a role in the mechanisms of memory. A large body of evidence implicates pituitary hormones, particularly adrenocorticotropic hormone (ACTH), melanocyte-stimulating hormone (MSH), and vasopressin, in learning. The action of ACTH, MSH, and vasopressin may improve memory processes by modifying motivational and attentional factors. ACTH may act to stimulate the metabolism of DA and/or norepinephrine (NE). It is also thought by some that vasopressin may act to affect catecholamine metabolism in a rather complex manner. In this regard, arousal is thought to be associated with the activation of central NE systems and the release of hormones such as ACTH, vasopressin, and glucocorticoids. In the neonate's brain, modulators (neuropeptides) may play a role in terms of the mode of information storage and not necessarily have a direct effect on information stored. Even though not completely understood, it is currently thought that catecholaminergic as well as neurohormonal factors may play some type of role in the storage of memory (Bloom, 1994).

Some have suggested that opiate receptors may even play a role in the filtering of sensory stimuli at the cortical level involved with emotion-induced selective attention. This suggestion offers the possibility that neural mechanisms may exist whereby the limbic-mediated emotional states, essential for individual and species survival, may influence which sensory stimuli are selected for attention (Bear, 1986; Dunn, 1976; Kety, 1970). By implication, endogenous opiates may exert progressively greater influences at higher levels of sensory information processing in the cortex. Whether this holds true in the neonate's brain over the course of the earliest years of development is unknown. However, sensory stimuli at the cortical level may play a role in selective attention, which can have a significant bearing on the processes of cognition and learning mechanisms since they involve ACh, GABA, 5-HT, NE, glutamate, glycine, and aspartate, all of which can stimulate neurons. These substances, collectively, act to innervate the entire regions of the cerebral cortex and have a major influence on forebrain functioning (Steriade et al., 1993).

Neuroanatomical specific sites with neurotransmitter systems regulate attentional networks that have connections with subcortical areas. The latter structures and their diversity affect the developing brain by influencing orientation to sensory input, maintaining wakefulness, or carrying out various cognitive operations. Also involved in this modulatory neurotransmitter–neurohormone system is the fine tuning aspect of the state and level of excitability of the different parts of the nervous system so that analysis of sensory, cognitive processing and memory storage can lead to performance and behavioral responses once learned (Bloom, 1994; Posner & Petersen, 1990; Posner & Rothbart, 1992; Zola-Morgan & Squire, 1993).

Sex Differences in Brain Structure

The male human cerebrum is about 9% larger in adult men, and also found to be larger in boys, too (Giedd et al., 1996). This difference may be affected by a greater density of white matter than gray matter (Allen et al., 2003). The ratio of corpus callosum (CC) to total cerebral volume using 3D morphometry shows that the ratio is smaller in males, which suggests that larger human brains have proportionately smaller CC (Jancke et al.,

1997). Other differences in neuroanatomical microarchitecture of childhood male brain development shows that the male amygdala undergoes prolonged development during childhood and is larger in boys versus girls. Of the 10 billion neurons in the human cerebral cortex, more are found in the male cerebral cortex, densely packed, with some areas of exception. One interpretation from the above findings regarding larger neuronal mass, increased neuronal density, and greater white matter connections projecting from neurons is that of increased local network connections and decreased long-ranged connections. Studies involving language activation (Shaywitz et al., 1995) in female brains shows a bilateral distribution pattern suggesting greater interhemispheric connections, i.e., long-range connections (Baxter et al., 2003; Haier, Jung, Yeo, Head & Alkire, 2005). These recent studies demonstrate male brains tend to be more lateralized than females, morphologically, in their development.

Fetal Sex Steroid Hormones and Neural Development

A key biological mechanism that influences sex differences in a developing brain includes androgens, a class of steroid hormones associated with the development and maintenance of male sex characteristics and sexual differentiation. Testosterone also acts on the fetal brain producing sex differences in regard to neural structures and functions. Testosterone influences the transcription process, affects neural development and connectivity, and acts as a neuromodulator influencing various neurochemical processes, e.g., 5-HT and GABA transmission. Testosterone and 17-β-estradiol molecules both influence dendritic arborization in axons in concert with another important neurotropic factor BDNF (Goldstein et al., 2001). Current strategies and methods for research on sex differences in brain and behavior involving both laboratory animals and humans has been reviewed with regards to early development (Becker et al., 2005).

Summary

Phylogenetically, the brain can be thought of as a blueprint of nature's original design in which we currently lack the original complete set

of plans. To understand the brain's architectural plan today is like looking into a house in which additions have been made but without having access to the original plans to guide us. Clues that have been left behind concerning the functional aspects of the additions to the phylogenetic blueprint of the brain appear as follows. At the midbrain level, for example, children born with anencephaly will be able to live for only a few days or weeks, but they can nonetheless exhibit laughing and crying responses.

Another clue to understanding the functional neuroanatomy of the developing brain is in terms of its serving as a communication system where there is biological (neurochemical) information transfer. The principal components involved in this communication network are axonal conduction, synaptic transmission, and local cell processes. Another clue is the phenomenon of *supersegmental control* over lower processes of the human nervous system which also occurs at the midbrain level. The spinal cord as a mode of neural organization is yet another clue. Its chief characteristics are seen in *segmental* and *suprasegmental reflexes*.

The functional anatomy of sensation is another important clue in understanding the human CNS and its development. Distinguishing aspects are as follows: receptors and transduction processes; pain systems; discriminative sensory systems; and systems for automatic adjustment. Other important aspects are the descending motor control systems such as commissural, associational, and projectional fiber systems; basal ganglia; extrapyramidal mechanisms; and brain stem control centers of behaviors essential in development. The cerebellum is another system crucial in the functional understanding of the developing brain's neuroanatomy. It is involved in the modulation of motor and sensory mechanisms and may even have a role in decision-making responses as well, including perhaps emotional expression.

Other major clues are the brain stem and internal states. Both play a prominent role in the regulation and maintenance of sleep, wakefulness, emotional affect, pain, pleasure, and suppression of pain. In addition, there are various support systems and the internal milieu, e.g., the autonomic and endocrinological mechanisms that influence neuronal activity and ultimately human behavior.

The developing brain's higher cortical functions are the ultimate expression of human information processing consisting of an array of psychological processes (Luria, 1973a,b, 1980; Posner, 1993; Posner & Petersen, 1990; Zola-Morgan & Squire, 1993).

Factors Affecting Normal Brain Development and Higher Cortical Functions

There are six major events of significance that occur in normal human brain development: (1) dorsal induction, (2) ventral induction, (3) neuronal proliferation, (4) neuronal migration, (5) neural cell assembly organization, and (6) myelination. Any disruption in these processes will result in maturational dysfunction in the brain's early pattern of organization. The significance of this fact for developmental/pediatric/child clinical neuropsychology as a discipline is that the incidence of all major CNS anomalies diagnosed at or after birth is approximately 33%. It has only been in the last 15 years that myelogenesis and dysmyelination patterns could be studied and quantitatively measured in vivo or sequentially in the same child (Cohen & Roesmann, 1994; Dietrich, 1990; Dietrich et al., 1988; Dietrich & Hoffman, 1992; Valk & Van der Knapp, 1989; Zimmerman, Bilaniuk. & Grossman, 1983; Zimmerman, Bilaniuk, & Gusnard, 1992).

The development of higher cortical pathways used to the best advantage of the neonate rests on the above six maturational processes that affect conscious and unconscious programs of behavior. The formation of higher (cortical) mental processes involved in concept acquisition during early development is limited by unmaturated neural organizational and myelination patterns that are affected by several variables: timing, nutrition, environment, teratogenicity, and genetics, among others. Knowledge about these factors with regard to normal infant development of mental abilities and cognitive development is an essential aspect in the clinical exercise of diagnosis and establishment of remediation/intervention programs for neuropsychological deficits in young children (Gaddes, 1980; Rourke, Bakker, Fisk, & Strang, 1983; Spreen, Tupper, Risser, Tuokko, & Edgell, 1984).

General Factors Involved in Human Brain Growth

At the time of adult maturation, the human brain accounts for approximately 2–3% of the body's weight, but utilizes about 20% of cardiac output (oxygen consumption), and 70% of the body's glucose, which is almost exclusively dependent on the *oxidative phosphorylation* process (Davison & Dobbing, 1968; Humphrey, 1978; Lemire et al., 1975; Nilsson, 1978). Even though the body may be starving, the brain receives a disproportionate share of nutrients, thriving almost exclusively on oxygen and glucose. Because of these metabolic requirements and dependence on the above two principal constituents, and the fact that the human neocortex is poorly vascularized, states of anoxia, hypoxia, and hypoglycemia can seriously damage the brain's normal functions during early infancy. A child may suffer from extreme malnutrition and weigh only half of his or her normal weight and yet the brain may only be 15% underweight.

Ninety percent of neurons are located in the brain. It is an electrochemical network of some $10–15 \times 10^9$ nerve cells, all present at birth, that regulate sensory–perceptual, motor, language, and other functions, as well as the higher psychological processes that we define as human behavior. Brain work occurs whether we are awake or not. For example, breathing alone requires the complex coordination of some 90 muscles that must be regulated precisely in order to execute one breath.

Processing over approximately 10^2 bits of information per second, simultaneously, the human brain distinguishes between aspects of reality, memory (declarative and procedural), and fantasy as it matures. As the brain develops in its inhibitory capacity to effect control over behavior, it regulates the various human drives and emotions that it spawns throughout its development course. In some brain regions, 10^7 cell bodies can fit into a cubic inch; each one of them can be connected by their arborization pattern to as many as perhaps 6×10^4 neurons and none of them are exactly alike (Scheibel & Scheibel, 1973; Szentagothai, 1975, 1978; Szentagothai & Arbib, 1974). The neuroelectrochemical pulses reaching the inner ear, for example, pass through at least four increasingly elaborate stages of analysis and refinement before any sound reaches conscious awareness for perceptual discrimination.

Insults to the brain early in gestation may arrest development with resulting gross malformations, such as anencephaly (failure to develop a prosencephalic outpouching), holoprosencephaly (failure of the forebrain to separate and develop normal commissures), and lissencephaly (failure of fissures to occur, resulting in a smooth surface of the brain) (Dietrich & Hoffman, 1992; Langman, 1975; Smith, 1976; Zimmerman et al., 1992). There are very few recorded cases in which the timing of a damaging stimulus to the fetus can be determined accurately. In a recent report (Cohen & Roesmann, 1994), brain damage caused by fetal injury showed a dual pattern involving the globus pallidus (basal ganglia) during the second trimester and thalamic nuclei during the third. This pattern of prenatal insult to the brain in various gestational periods is essential in relation to timing of sensitive regions for normal versus anomalous brain growth patterns.

Nutritional requirements, as well as effects of malnutrition (especially protein deficiency, which can affect brain weight and result in cognitive deficiencies later in life), are critical during postnatal months 6–18. Throughout childhood (and well into adult life), brain function increases tremendously, despite a brain weight gain during this time that remains relatively low, i.e., 350– 400 g (Dodge, Prensky, & Feigin, 1975; Hamilton & Mossman, 1974).

Mass Growth of the Brain

Brain weight has been used as a quantitative index of brain growth, as well as a traditional indicator of quantitative aspects of CNS development. The brain of the newborn weighs approximately 300–350 g. By 12 months, the weight has more than doubled since birth and is approximately two-thirds that of the adult. The average weight of the adult brain is 1300–1500 g and is related to body size. Larger people usually have heavier brains although there is no proven correlation between brain weight and intelligence. Growth of the CNS during early fetal life reflects an increase in volume in the first trimester from 4 to 16%, compared to 42% at birth. The brain's weight is 21% that of the body at the sixth fetal month, 15% at birth, and approximately 3% at adulthood (Dodge et al., 1975; Hamilton &

Mossman, 1974; Yakovlev, 1962; Yakovlev & Lecours, 1967).

The increase in volume of the cerebral hemispheres is slow and steady between fetal months 2 and 6 but rapidly accelerates thereafter. The postnatal growth of the cerebral hemispheres results mainly from an increase in myelination. Myelination has begun in most areas by 8 months of age reaching its greatest deposit in the first 2 years of life. After this period, the process will continue at a slower rate into adulthood. The brain stem grows most rapidly between fetal months 2 and 6 and less rapidly thereafter. The cerebellum grows slowly between fetal months 2 and 5, followed by an exceptionally rapid increase in volume commencing at fetal month 6 and continuing until postnatal month 6. The weight of the brain more than doubles during the first 9 months postnatally, and reaches 90% of its adult weight by age 6.

The hemispheric surface of the brain more than doubles during the postnatal growth to reach an adult value of approximately $1600\,m^2$. This growth is accompanied by an increase in the size and number of gyri so that the intrasulcal portion of the adult cortex is about the same as that in the newborn. The adult cortical surface area is reached by the second year of life. The entire hemispheric surface is gyrated by approximately fetal week 32, despite the fact that these gyri are less numerous than in the adult brain.

Normal thickness of brain tissue between the ventricles and the cortical surface is approximately 4.5 mm. There are many reports in the literature that people of normal or above-average intelligence, on CT scans, have only a thin layer of mantle between ventricles and cortical surfaces measuring 1 mm versus the normal 4.5 mm. Several such cases have been documented in the medical literature (Lorber, 1980).

White Matter Development

Hemispheric white matter develops slower than cortical gray matter during gestation. Postnatally, white matter will continue to develop long after gray matter has reached a specified volume. The growth of the cortex subsides by the second year of life while hemispheric white matter continues even through the second decade as a result of accumulation of myelinated fibers with their increased diameters. Myelination is closely associated with development of the functional capacity of neurons; they fire more rapidly and have a longer refractory period. Different fiber tracts show myelination patterns at different developmental periods. The component populations of a given tract system may differ as to the timing of myelination (Davison & Peter, 1970; Dobbing, 1975; Dobbing & Sands, 1973; Valk & Van der Knapp, 1989; Zimmerman et al., 1983).

Myelination of tracts typically follows in a caudorostral direction, the cortical association fibers being the last to myelinate. The schedule for myelination was first elaborated by Flechsig (1883). Around fetal month 4, myelinated fibers appear in the ventral and dorsal spinal roots. Last to receive this investment are the associational fibers of higher cortical centers, e.g., the cerebral cortex's thalami. Some tracts are not fully myelinated until several years after birth (Crelin, 1973, 1974; Dobbing & Sands, 1970; Dobbing & Smart, 1974; Yakovlev & Lecours, 1967).

Cortical Development and Timing: A Link to IQ

Shaw et al. (2006) a neuroscientist at NIMH, reported on MRI findings of 300 healthy children, 5–18 years old, who were scanned and administered IQ testing. Their findings report that highest IQ scoring children had a delayed but prolonged growth spurt in the cerebral cortex. Three groups were studied as to IQ ranges as follows: Average (83–108), High (109–120), and Superior (121+). The overall sequence of cortical development was found to be similar in all three IQ groups, i.e., the cortex developmentally thickens during childhood and then reaches a peak and subsequently becomes thinner. The *timing* of these events was notably different in the Superior IQ group, revealing a trend that started out thinner, on average, when compared to the other two groups, and then showed a rapid thickening at approximately age 7 and peaking around 11 before showing decline in volume. The other IQ groups peaked earlier. They reported that when the subjects reached early adulthood, the cortex in all three groups reached approximately the same thickness. A striking observation made was that of cortical development disparity noted between the Superior IQ versus the other two groups in

the region of the frontal cortex, mainly the prefrontal area which involves reflection, organization, planning, extraction activities.

Some questions that emerge from these findings (Shaw et al., 2006) of prolonged cortical maturation, developmental timing, and its link to IQ development requiring further investigation are as follows: (1) What are the cellular events involved in the cortical processes that cause thickening and shrinking? (2) Is the trend observed in these three IQ groups susceptible to genetic, environmental influences, or birth? (3) Does parental IQ education and teaching styles influence the extended component in the Superior IQ versus High and Average IQ groups? (4) Is there evidence for a growth trend followed by a pruning process between neuronal connections that in a time-ordered sequence of events is affected by the above set of influences?

When addressing the question of, "What does normal human brain development look like in infants, children, and adolescents?" we simply do not as yet have a complete picture. However, a very important step has been made in the NIH Brain Database Project, providing information on 500 healthy subjects, birth through 18, which is a collaborative effort of several study groups, i.e., NIH, NICHD, NIMH, NINCDS, NIDA, Washington University (St. Louis), Boston University, and UCLA. The information contained in the database released in July 2006 is available to institutions through the Brain Imaging Resource Network (BIRN). The database provides information on healthy (not to be strictly equated with the notion of typical or normal) subjects *without* psychopathology, neuropathology, or neuropathophysiological conditions. The subject selection, inclusion criteria, methodologies, etc., are available for review (http://www.brain-child.org). This project is a first-time NIH-sponsored study comprised of six major investigation centers collecting data to address the question, "What is going on age-wise in healthy brains, birth through 18?" This project has looked into age-related structural changes regarding neural structures that involve white matter (WM) densities; gray matter (GM) changes over age span; thickness versus age and gender changes; SES; age; gender; parental education correlates with cortical thickness by neural regions. The studies conducted measuring WM and GM volume by densities are related to what changes occur in *structure–functional*

relationships influenced by age. Caution is needed in any serious discussion when attempting to draw fixed, causal-relationship-based conclusions in addressing structure-to-function in the developing human brain due to many significant and as yet unknown effects that can exert influences in this process, neuronal shifts, pruning of neuronal connections, local volume mass (NM versus GM), neuromodulators, experiencing of environment to name a few.

Intelligence, IQ, Spearman's "g" and Cortical Development

What are the practical benefits of IQ measurement beyond that of test-taking ability and predicting academic and job performances? At least one major psychological trait that IQ tends to strongly predict is the range and extent of social outcomes from mental tests. Research has shown individuals with higher IQs demonstrate an ability to manipulate information more efficiently, including reasoning, abstraction, learning, problem-solving (g) abilities which are involved in every phase of life's mental tasks (Spearman, 1904, 1927). High IQ scoring individuals in one study (Colom, Jung & Haier, 2006) used PETT showing less cerebral metabolism demand performing a mental task. Haier and colleagues studied individuals with high versus low IQs engaged in a video-watching exercise. Differences were shown in these two groups when doing a task (passive viewing of videos) requiring little mental effort. Brain activation during the watching of the videos showed a correlation between an area in the occipital lobe, involved in processing vision and language, and an area in the prefrontal lobe which subserves attention and reflection activities. This correlation was not observed in the low IQ group. The frontal cortex, which is involved in decision-making and complex problem-solving, is thought to play a key role in selecting which brain regions are "activated" in the posterior cortex. From these findings, it may be posited that high IQ scoring individuals are more efficient at quick, flexible thinking (fluid reasoning involving information processing) versus lower IQ scoring subjects. An earlier research study reported that larger brains show a weak relationship to higher IQ, but Colom, Jung & Haier, in press claimed to be first to demonstrate that GM

in specific regions in the brain is more related to IQ than is overall volume, i.e., multiple ares are related to IQ with various combinations of areas (neural networks?) which also can account for IQ scores. With respect to the GM volumes, the researchers were surprised to find that only 6% of all GM in the brains studied, appeared to be related to IQ.

Frontal Lobes and Executive Processes

Spearman's "g" (Spearman, 1927) is the psychometric concept ascribed to human general intelligence. The link between the frontal lobes (FL) and Spearman's "g" lies in the general cognitive role it involves and "g" being associated with some but not necessarily all frontal lobe regions, neuroanatomically. Research in the past decade has shown that there are important aspects within the FL different categories, e.g., inhibition, selective attention, behavior-emotion, metacognitive processes, not all of which are strictly speaking FL functions in the "executive" sense since they may be considered involving several different domain-specific modules with varying processes that are organized in differing networks of the working brain (Stuss, 2006).

Sensorimotor Functions and the Appearance of Neurological Reflexes

Motor control behavior of the newborn is largely under the control of the spinal cord and medulla, whereas motor control in adults occurs at different levels of the nervous system. At birth, several neurological responses are present. The appearance and disappearance of neurological (primitive reflex) signs are essentially transient mechanisms either subserving life-sustaining functions or forming preliminary patterns of future voluntary activity, e.g., the stepping reaction that precedes voluntary step-walking. The most important responses that appear and disappear in early postnatal life are reflexes of position and movement, e.g., the Moro reflex, asymmetric tonic neck reflex (TNR), neck righting reflex, Landau response, palmar grasp reflex, abductor spread of knee jerk, plantar grasp reflex, Babinski response, and parachute reaction. The Landau response and the neck righting

reflex are the first to appear around the time of birth and the last to disappear (at 1–2 years) (Siqueland & Lipsitt, 1966). Reflexes to sound that appear at the time of birth include the blinking response and the turning response. The reflexes of vision include blinking to threat, horizontal following, vertical following, opticokinetic nystagmus, postrotational nystagmus, lid closure to light, and macular light reflex (Barnet, 1966; Franz, 1963). The feeding reflexes include rooting response-awake, rooting response-asleep, and sucking response, all of which appear at the time of birth; the last to disappear is the sucking response at approximately 12 months.

The level of neural functioning during the neonatal period can be determined only with great approximation. Some of these reflexes will drop out of an infant's behavioral repertoire at around postnatal month 3 or 4. This is presumably the result of increasing cortical inhibition of lower centers in the brain. Reflex arcs exist below the cortical level, and before integration occurs between subcortical and cortical structures, stimulation of the infant elicits an involuntary, subcortically mediated reflex response. As the maturing cortical centers become integrated with subcortical areas, primitive reflex behavior then becomes inhibited. The fact that most of the activity of a normal newborn can be observed in an anencephalic infant possessing only a brain stem and certain components of the basal ganglia indicates that cerebral cortex participates very little, if at all, in the function of the CNS during this stage of life. Children with these morphogenetic anomalies do not survive usually more than 2 months, but while alive, they do show reflex development similar to the patterns of normal infants of the same age (Davison & Dobbing, 1968; Dodgson, 1962; Humphrey, 1964; Moore, 1977; Smith, 1976).

Concerning development of the cerebral cortex, upper, central, and hindmost regions tend to mature early, such as those concerned with bodily sensations involved in the control of movements, hearing, and vision. Frontal and lower sides (frontal lobe area) in the region of the temporal lobe mature at a slower rate. In the motor strip area, for example, parts that control trunk and arm movements appear in advance of parts that will control leg and finger movements.

Prematurity and Low Birth Weight

The fact that babies who are born prematurely but go on to develop without complications suggests that only when the brain is ready, and not before, will it start to develop in earnest. Infants who are 4 weeks preterm, generally speaking, will tend to "catch up" after 12 months. Judging by the immature state of the cerebral cortex, it can be speculated that the latter phenomenon plays a minor role in the life of the child at the time of birth. Support for this notion comes from recent studies showing correlation of myelin deposition with measurements of local glucose metabolism from ^{18}FDG-PETT research which is an indication of functional activity (Chugani & Phelps, 1986). The infant may be completely dependent on the inner regions of the brain, especially subcortical structures, since not until postnatal month 3 does the roof of the brain begin to intervene in a dominant manner, e.g., control of arm movements involved with the first signs of coordination of hand and eye movements (Davies & Stewart, 1975; Lemire et al., 1975; Levene & Dubowitz, 1982).

Studies in the past 10 years have shown that babies of very low birth weights (LBW < 1500 g) are at high risk for cognitive development problems. Premature infants (weighing < 2500 g or 5½ lb) are at a far higher risk for birth-related defects and infant mortality than full-term infants. Developmental abnormalities of the brain account for 30–40% of deaths during the first 12 months of life. Survivors tend to develop intellectual impairment (Hack et al., 1994; Weisberg, Strub, & Garcia, 1989). White matter abnormalities such as perinatal leukoencephalopathies (PLE) are significantly higher in preterm infants. Cerebral palsy is 30 times greater in infants weighing less than 1.5 kg (53 oz) at birth. LBW infants can develop bronchopulmonary dysplasia that can lead to neurological and cognitive impairment as well (Leviton & Paneth, 1990; Vohr et al., 1991).

Hack et al. (1994) recently tracked 68 children born 5–9 years ago weighing under 750 g (0.5% of 4×10^6 births in the United States each year). This group makes up just under 7% of the 292,000 premature infants (under 2500 g or 5½ lb) born every year in the United States. Results from this study show these children to have higher incidences of cerebral palsy, intellectual retardation, distractability/inattention, delayed speech/language problems, and learning difficulties (mathematics skills, in particular). While the researchers showed about one-third living normal lives, the majority of these children face major problems, both physical and mental, which affect their scholastic and social development.

Frontal Lobe Maturation

The slowly maturing frontal lobes play a significant role required for a young child to respond correctly to verbal instructions. Luria pointed out that in young children, the immaturity of brain structures may be such that it is physically impossible for a child not to say or do what he or she is told not to do (Luria, 1960, 1961). This situation bears close resemblance to that of adults with damage to the frontal lobes. Not until the frontal regions of the brain are well developed can a child become capable of consistently obeying certain verbal commands. It is usually not until 3½–4 years of age that children are capable of learning to carry out a complex program of actions deliberately, in accordance with unrepeated verbal instructions. The timing of myelination of the frontal lobes, starting at approximately 12 months, correlates with the development of fear response (anxiety) in infancy (Kagan, 1985; Kagan & Moss, 1983).

Stratification within the cortex proceeds according to a definite plan in terms of neuronal organization. Neurons with connections in certain parts of the brain differ from others with respect to the cerebral hemispheres. For example, in the posterior portion of the cerebral cortex, the development of the layers proceeds according to a clear-cut, typically six-layer plan with a distinct layer (IV) as the main site of termination of afferent impulses from the subcortical divisions of perceptual analyzer regions. There is a difference that exists between the structural differentiation of the anterior versus posterior divisions of the cortex in early ontogenesis. This may account for slowly developing cortical–cortical connections, essential to the later differentiation and organization of the outer three layers in middle and later childhood (Luria, 1969b; Stuss & Benson, 1986; Warren & Akert, 1964; Zimmerman et al., 1992).

Nutrition and Malnutrition

Human fetal nutrition depends largely on the size and functional capacity of the tropho-blasts in the placenta and the villous surface area through which the exchange of nutrients takes place. In the placenta, three phases of growth occur by about 34–36 weeks of gestation. Cell division ceases while weight and protein increase nearly until full term. Placentas from infants who had experienced intrauterine growth failure tend to show fewer numbers of cells and an increased RNA/DNA ratio relative to control placentas. Studies of placentas from malnour-ished populations in different parts of the world have confirmed that fewer cells are present relative to normal placentas. Maternal malnutri-tion, vascular insufficiency, and abnormal influ-ences with regard to intrauterine growth contingent on the placenta will adversely affect cell division in the placenta. During intrauterine life, all fetal organs are in a hyperplastic phase of growth and probably at no other time is the human organism more susceptible to nutritional stresses. Fetal malnutrition can result from any number of causes, e.g., reduced nutrients within the maternal circulation, faulty placental trans-port of specific nutrients, and abnormal mater-nal circulation. Deficiencies in specific nutrients are not known to affect fetal brain development. Reduction in either total calorie or total protein intake by the fetus can lead to retarded growth (Cravioto & Arrieta, 1979, 1983; DeLong, 1993).

Studies of the effects of malnutrition on human brain cell development have been limited. Infants who died as a result of failure to thrive (marasmus) during the first year of life had cor-relations of reduced protein, total RNA, total cholesterol, total phospholipid, and total DNA content. The rate of DNA synthesis was also found to be reduced. Cell division showed limita-tions, too. These factors collectively suggest that if malnutrition persists beyond 8 months postna-tally, not only the cell number but also the size becomes reduced, disproportionately. Malnutri-tion in humans tends to reduce the rate of cell division in all brain areas. Early malnutrition affects cell division, myelination, and vulnerabil-ity as to neural tissues' optimal rate of synthesis of DNA. Nutritional deprivation up to an age of 18 months causes permanent intellectual impair-ment (Dobbing, 1990).

Cerebral Oxygen Consumption and Blood Flow

In the developing brain of the newborn, oxygen consumption is relatively low but gradu-ally increases with maturation. That the neona-tal brain is able to tolerate states of anoxia is suggested by the low cerebral oxygen consump-tion at birth. This ability to tolerate anoxic con-ditions may also be related to the brain's dependence (prior to birth) on anaerobic glyco-lysis as an energy source. The level of enzymes needed for aerobic glycolysis just prior to birth shows an increase as the brain's metabolism begins to change from anaerobic to aerobic.

Cerebral blood flow (CBF) is relatively low in the newborn but increases with age to a max-imum of 105 ml/100 g per min starting at approximately 3 or 4 years of age. Disruption of CBF and oxygen consumption will affect oxi-dative phosphorylation as the brain develops. The average CBF for an adult is between 45 and 55 ml/100 g per min. In adults, a value below 20 ml/100 g per min will begin a process of metabolic degradation within neuronal mito-chondria, leading to failure in synaptic transmis-sion and EEG changes. Abnormalities that arise as a result of this degradation process are as follows: perinatal asphyxia; hypoxic–ischemic birth-related episodes; and extended decrease of CBF that is interrupted in terms of cardiac out-put (Finkelstein et al., 1980; Ingvar, Sjölund, & Ardö, 1976; Mazziotta & Phelps, 1985; Mazziotta, Phelps, & Miller, 1981; Phelps, Mazziotta, & Schelbert, 1986; Roberts, 1986).

Changes in cerebral function result in demonstrable changes in metabolism and blood flow. EEG frequency correlates with the meta-bolic rate of the brain. Total CBF correlates with oxygen consumption. Activation of specific areas of the brain associated with sensory, motor, and mental functions has been widely shown to cause increases in regional cerebral blood flow (rCBF) and metabolism. It has been proposed that neural activity results in the release of vasoac-tive substances, e.g., adenosine triphosphate (ATP), which has been implicated as a possible mediator responsible for the local coupling of blood flow and metabolism (Bruns et al., 1987).

The response to hypoxia appears to depend on the level of neural tissue oxygenation rather than arterial pressure. The role of oxygen can be

viewed in terms of *mitochondrial oxygen metabolism* which accounts for 80–90% of total cellular oxygen consumption (Lehninger, 1993). The provision of energy for the nerve cell via oxidative phosphorylation (the process in which cellular oxygen consumed produces usable energy) is the main function of oxygen. Most of the energy used by a cell comes from ATP and the electron transport chain, which yields free energy changes that occur in a series of bioenergetic steps. Inadequate delivery of oxygen to brain tissues may result from hypoxemia (inadequate arterial oxygen amount), ischemia (inadequate blood flow), or a combination of these two. Several mechanisms exist in order to protect tissue oxygenation, including local cerebral blood flow.

Mechanisms underlying brain damage in newborns are poorly understood (Cross, Gadian, Connelly, & Leonard, 1993). The first human neonatal applications of magnetic resonance spectroscopy (^{31}P-MRS) to measure relative metabolite concentrations in newborn brain tissues in vivo were described 10 years ago (Cady et al., 1983; Hope et al., 1984). Since then, the value of ^{31}P-MRS, as a research tool and investigation technique, has been widely confirmed as a useful prognostic tool in asphyxiated infants; hypoxic–ischemic states; cerebral oxidative metabolism and hemodynamics involved in perinatal brain injury; and early normal brain development (Hope & Moorecraft, 1991; Reynolds et al., 1991).

CBF has been studied using PETT investigation to address the suggestion that newborn human brains may be more resistant to ischemic injury than are adult brains. Altman et al. (1988) studied preterm and term newborns and found the range of mean CBF in preterm infants to be 4.9–23 ml/100 g per min whereas the range of CBF in term infants was 9.0–73 ml/100 g per min. This study shows that the CBF requirement for brain tissue viability in newborns is lower than in adults in contrast to normal findings on neurological examinations and Bayley Scales of 80 or greater.

Recently, ^{1}H-MRS investigation was used to examine (within the first month of life) the brains of 11 infants born at term (10 showing signs of hypoxic–ischemic encephalopathy, 1 neurologically intact). All infants had peak resonances on their spectra that could be correlated with *N*-acetylaspartate (NAA), choline compounds (Cho), and creatine/phosphocreatine (Cr and PCr). Neurodevelopmental outcome was correlated with initial spectroscopy findings as to reflecting clinical outcome (Peden et al., 1993). This study provides the latest information about five major chemical changes occurring in the brains of infants with hypoxic–ischemic encephalopathy. It demonstrates quantitatively useful in vivo MRS-based biochemical information in newborns' brains in a noninvasive manner, as to normal and abnormal metabolic brain development. This same type of study using ^{1}H-MRS has demonstrated that NAA and Cr are determined by gestational age whereas the concentration in terms of milliliters correlates best with postnatal age (Kreis et al., 1993). The central key lies in obtaining ^{1}H-MRS quantitative information regarding these chemicals, i.e., in the confirmed ability to diagnose and monitor living functional tissue as a "metabolic window" into biochemical events in normal and pathological developmental processes, since metabolic ratios are often misleading (Goplerud & Delivoria-Papadopoulos, 1993; Kreis et al., 1993; Tzika et al., 1993).

The functional activation of the human brain can be visualized with MR imaging as a method of mapping brain structure to function (Connelly et al., 1993). Neuronal activity changes through in utero and neonatal brain development causing local changes in CBF, blood oxygenation, blood volume, and oxidative phosphorylation (bioenergetic changes in the mitochondria) by using intrinsic blood–tissue contrast via functional MR imaging (FI). This technology opens a spatial–temporal window into individual brain physiology (Connelly et al., 1993; Kwong et al., 1992; Stehling et al., 1991). Because of FI and ^{1}H-MRS investigating methods, it is possible to extend metabolic and developmental brain physiology in vivo beyond immediate cellular response, e.g., asphyxia, to chronic adaptation in the newborn. Clinically applied, this now enables researchers and clinicians to quantitatively identify brain injury that is reversible, in some cases, to have sufficient time to diagnose and intervene. The prospect for future prevention and potential therapies is a clinical revolution not achieved until now (Goplerud & Delivoria-Papadopoulos, 1993; Kwong et al., 1992; Martin, Grutter, & Boesch, 1990; Peden et al., 1993; Tzika et al., 1993).

EEG Development

Human fetal EEG activity has been recorded as early as day 43 (Bernstine, Borkowski, & Price, 1955). Fetal EEG activity evolves in a rapid and specific manner. In a 5-month-old fetus, cerebral activity lacks organization, rhythmicity, and regularity. At 6 months, organization emerges; rhythmic *theta* activity (4–6 Hz) appears in flurries lasting about 2 s. In the seventh month, activity tends to become continuous at about 1 Hz with voltages ranging from approximately 100–200 μV. This slower activity is interspersed with faster frequencies around the seventh and eighth months. Differences between active and quiet sleeping states become more pronounced (Ellingson, 1964; Lindsley, 1939).

Bursts in the electrical activity pattern at 6–7 months are associated with an increase in enzymatic activity in the brain. The major difference between the immature and maturing infant's brain is the definite change in EEG between periods of wakefulness and sleep. As a generalization, the amount of quiet sleep increases with maturation. In the eighth month, during active sleep, fast waves of approximately 2–3 Hz appear with no localization and often impose on low-voltage faster waves, and become dominant. Frequency measurements of photically evoked responses recorded from the occipital area show a progressive shortening with maturation. Responses to auditory stimuli also show clear differences in waveform, amplitude, and latency of wave components with maturation (Ellingson, 1964; Hagne, 1972).

Rate of maturation of brain electrical activity decreases with age. After birth, maturity of changes occurs within the first 3 years. Fewer alterations are noted between 3 and 8 years of age. Five stages have been shown to be synchronous across regions during the first 10 ½ years of life. Thereafter, the four maturation times show independence from one another based on maturational trajectories for quantitative EEG frequencies in brain regions. This suggests a strong relationship between neuroanatomical and neurolinguistic development (Semrud-Clikeman, Hynd, Novey, & Elipulos, 1991). Because of the continually changing aspects of the EEG during childhood, problems of interpretation are more numerous than for adult recordings.

Newborns have only brief periods of wakefulness with eyes open. They sleep 16 h a day, and half of that is REM sleep. Fetuses spend most of their sleeping time in REM sleep. Two well-defined types of sleep patterns are noted in 32- to 39-week premature and in full-term neonates: active sleep and quiet sleep. Early in the newborn's life, 2- to 4-Hz waves are present, which will be replaced by those of 4–7 Hz at approximately 5 years of age. Faster activity in the occipital regions of the brain (8–12 Hz) begins to dominate, and *alpha* rhythm of the mature brain starts to emerge. Occipital alpha rhythm changes rapidly in the first year from a 3- to 4-Hz rhythm to twice that frequency by the end of the first year. Changes in frequency have been postulated to be correlated with neurohormone growth factors, brain growth, and myelination.

Changes in the EEG's alpha frequency with age have important behavioral consequences. Periods of rapid change in EEG activity can help to identify critical periods for behavioral change. One of these periods occurs at the end of the third month of life when the alpha rhythm first appears. Another important period extends from the end of the first to the completion of the second year of life when the alpha rhythm attains adult values. Alpha frequency can be construed as one key variable in brain maturation signaling critical behavioral changes.

Lindsley (Lindsley, 1939; Lindsley & Wicke, 1974) proposed that the onset of organized rhythmic occipital activity reflects a significant change in cortical organization and may mark a point at which the infant progresses from a subcortical to a cortical level of functioning. It is suspected that visual behavior in early infancy is processed by subcortical mechanisms with the cortex usually taking over in earnest at about the time rhythmic occipital EEG patterns begin to emerge.

Recent studies using quantitative complex statistical analyses of EEGs in an effort to map the physical maturational stages of the developing brain in humans from ages 1–21 have demonstrated five distinct stages of maturation (Hudspeth & Pribram, 1992). Immediate and abrupt changes were observed in specific brain regions throughout maturation in 500 studies as follows: parietooccipital (PO), temporotemporal (TT), centrocentral (CC), and frontotemporal (FT). In the first stage, all regions of the brain, including those governing somatic, visuospatial,

and visuoauditory, show signs of synchronous development up to approximately age 6. Sensory and motor systems (PO, TT, and CC) mature in concert until about age 7½. At this age, the FT region begins development in earnest. The third stage involves visuospatial functions (PO) and some visuoauditory (TT) regions. The fourth stage shows maturation of the visuoauditory, visuospatial, and somatic systems (CC) occurring from ages 13–17. The fifth stage, ages 17–21, in the FT region, governs frontal functions and shows significant maturation. The five physical brain development stages in the quantitative EEG analyses show a high degree of correlation to stages of psychological development in children, especially in light of Jean Piaget's theories (Hudspeth & Pribram, 1992).

Magnetic source imaging (MSI) is a technological advance that makes use of the physical principle that every electric signal creates a magnetic field around it. MSI tracks tiny electrical signals that are generated as the brain and muscle tissue go about their routine functions. The instrument uses superconducting quantum interference devices (SQUIDs) that enable researchers to image the function of brain tissues as well as structure. SQUIDs measure magnetic fields, which do not become distorted as they pass through the body, unlike the EEG, which cannot determine the exact location because the signals are distorted as they pass through bone and tissue (Gallen et al., 1993; Huk & Vieth, 1993; Orrison, Davis, Sullivan, Mettler, & Flynn, 1990).

Currently, researchers are using MSI to map the brain before surgery. MSI has the capability to be able to tell immediately whether brain tissue is working or not. This technique has applications for better understanding of normal versus abnormal brain activity, e.g., epilepsy, Parkinson's disease, and behavioral neurology (Gallen et al., 1993). A broader goal is to combine SQUID technology with data from MRI studies in order to create a dynamic, functional image of higher mental processes occurring in the brain (Wang, Kaufman, & Williamson, 1993).

Speech and Oral Communication Development

Speech (oral communication) is a basic tool in interpersonal relationships and serves as a key indicator of brain development in the early years of life. Interference with speech development or subsequent distortion of speech may have a profound effect on social competency and cognitive and interpersonal development in the child (Goodglass & Kaplan, 1972; Luria, 1969c; Neville, 1984). An understanding of the neuropsychological development of the speech process is needed prior to any professional advice or instruction with regard to the causes and treatment of speech-related disorders. Such diverse elements as neurological maturation, acquisition of fine muscle control, and development of symbolic formulation abilities crucial to development of cognitive processing of information can all be related to speech development. It is these neuroanatomical, neuropsychological, and neurophysiological aspects that provide the content and control from which speech is created. In later stages, especially in acquisition of words and sentences, contributions of learned behavior emerge (Darley & Fay, 1980; DeVilliers & DeVilliers, 1979; Lenneberg, 1964, 1967; Milner, 1976; Siegel, 1979).

In the early stage, any division of speech development into discrete stages can be misleading. Generally, all basic behaviors that appear at different ages function throughout childhood and into adulthood. After the prespeech stage (from birth to 3 months), speech starts with the *reflex stage*. The birth cry can be considered the beginning of speech, but any true expression is doubtful. Shortly after birth, reflex crying appears in response to discomfort or fear. Cries often vary and become differentiated from other noises, such as gurgling, sucking, cooing, and laughing. From 3 to 12 months babbling occurs. Basic changes in vocal expression are observed in the rapid increase in the number and varieties of sounds. As a child develops early awareness of vocalizations and moves into a period of vocal exploration, practice and repetition occurs in greater frequency. A child at this stage begins to modify imitations and is aware that he or she is "imitating" oneself. In many instances, early imitations of others' speech result from the repetition of sounds that the child has produced. Later, as the adult model initiates imitative responses with familiar new sounds, the basis for learning speech pattern emerges. In the earlier phase, various sounds are repeated. Sounds that approximate language are usually selected based on the most intense reinforcement derived by the child.

Another step in the development of speech emerges when the child integrates babblings and imitations into sequential patterns that sound more like true speech onset at about 12 months. Individual sounds tend to be reasonably accurate, vocal quality approaches that of voices heard, and sounds are grouped into nonsense forms and even phrases. Occasionally, what appear to be recognizable words are heard by adults, but may not represent meaningful speech at this stage.

True speech stages begin to emerge when characteristic features include motor control of breathing, phonation, and articulation. Ability to echo, complex mechanical patterning of speech, and other skills are practiced to assist in the leap to a distinctly different level of function. Complementary inter-language is a prerequisite as recognition of familiar objects in the environment requires inner language. As the child develops into later years, this type of language would be similar to what adults sometimes use when talking to oneself (Molfese, Freeman, & Palermo, 1975; Segalowitz & Chapman, 1980). The child comes to develop an awareness that certain sounds spoken by the parents stand for objects (auditory receptive language). Inner language and auditory receptive language have been suggested to precede actual production of meaningful words (Luria, 1961, 1982; Luria & Yudovich, 1959).

The *word stage* emerges from approximately 11–24 months in which true first words are usually names of concrete objects. Sentences start to appear at approximately 18–36 months. The advent of an increasing vocabulary containing a variety of representations for objects, people, and actions in the child's environment provides the opportunity for the child to discover more complex meanings and verbal reinforcement. This is a variable period for the beginning of sentences and there may be periods of little progress after sentences are first used.

Complex speech development takes place from approximately 24 months up to 7 years of age. All parts of speech increase at a rapid rate. The word "no" will cover a vast number of situations, behaviorally, and provide a distinct measure of control over individuals in the child's environment. Extrapolations of grammatical structures cause difficulty with some irregular verbs, but the process of such abstracting indicates increasing degrees of complexity of symbolic thinking. Categories are learned, e.g., male

versus female, dog versus cat. Children start to learn that matching reality to a symbol requires relative concepts as well as absolutes. This quality of assigning symbol to meaning is lacking, for example, in severely autistic children in their speech development (DeVilliers & DeVilliers, 1979; Luria, 1960; Piven et al., 1990; Siegel, 1979; Wertsch, 1979). As the expansion of potential for expression continues to develop, oral communication serves not only as an efficient tool for exploring and understanding the people and the world that surround the child, but also becomes a means for controlling and manipulating the environment. It serves to provide an extension in a variety of emotional expressions that goes beyond methods such as tensing muscles, throwing a tantrum, crying, and engaging in uncontrolled movements (Darley & Fay, 1980).

During the child's first 12–20 months, a transition occurs from visual representation to a verbalization mode in which the child's ability to participate in sequences of interpersonal exchanges via speech emerges (Mills, Coffey, & Neville, 1993). Children use language as a medium to communicate messages that become more syntactically refined over age. It is the process of assigning a memory code to a symbolic form that raises the questions of "how does a child retain what is learned?" and "how are coding errors corrected or adaptations to a changing environment effected?" (Grossberg, 1980; Vygotsky, 1980). Partial answers to these questions are seen from recent memory and auditory brain stem studies (Roncagliolo, Benitez, & Perez, 1994; Semrud-Clikeman et al., 1991; Squire & Zola-Morgan, 1991; Zola-Morgan & Squire, 1993).

It would be myopic to view speech development as an isolated process. It is integrally linked with physical, psychological, and sociological maturational processes. Disruptions or distortions in any of these areas can have serious repercussions. It is particularly important that speech be developed uninterrupted during early childhood, since there is compelling evidence suggesting that lack of developmental opportunity or severe inhibitory factors have serious and permanent effects on linguistic–symbolic–intellectual development (Jernigan, Hesselink, Sowell, & Tallal, 1991; Kulynych, Vladar, Jones, & Weinberger, 1994; Roncagliolo et al., 1994; Semrud-Clikeman et al., 1991; Wong & Wong, 1991). The child may never become a completely

functional human being in the developmental sense if speech is arrested or not developed by 7 years of age (Curtiss, 1979). Professionals and parents involved in a child's development have a significant responsibility to detect aberrant patterns during development as early as possible (Goodglass & Kaplan, 1972; Damasio, 1989).

Symptoms of possible difficulty may be noted in several ways during the first year of life. In the prespeech period, the most critical characteristic is the lack of progressive change in the nature of babbling or, conversely, deterioration of vocalization to that representing earlier stages of development. At ages when response to and imitation of sounds of others may be expected, any unusual delay may suggest difficulty in learning to talk. Failure to engage in jargon conversation is likewise an important indicator of problems. It is when more advanced behaviors have failed to materialize that one becomes concerned in terms of delay. Continuation of earlier forms of vocalizations during later months of the prespeech period is not evidence that progress is delayed. As long as speech is inclusive enough for useful communication and can be reasonably well understood by strangers by 4 years of age, concern over development of a serious problem lessens. In addition to articulation aspects, there is the possibility, during this period of development, of difficulties in fluency. For example, all children have numerous dysfluencies in speech. At certain times and under certain circumstances, these are more frequent and noticeable. The distinction between normal dysfluencies and stuttering is not always easy to make, particularly as there is variability from individual to individual. In general, however, major concern is not necessary unless there are signs of struggling behavior, tensions, anxiety, or reactions to specific dysfluencies in the child. Persistent rudimentary sentences may indicate a broader developmental delay but it must be emphasized that the total environmental background must be considered before assuming that a child has basic inadequacies.

Recognition of a speech problem versus undue concern over what are essentially individual differences in oral communication patterns can affect a child's cognitive, social, and emotional development. In this sense, appropriate evaluation can be reached by the integration of several factors: sequence and nature of speech skills; relationship of these to the child's experience and development; and the acculturation process in which others in the child's environment can influence these developments.

Acculturation Processes

Brain growth and the acculturation process are inextricably bound in human development. Neural networks are being set and affected by specific experiences related to environmental events (Szentagothai, 1978; Witelson, 1985). Acquisition of cognitive operations, which in part is influenced by a particular culture, has an effect on elaboration of neural circuitry. Neural circuits are formed during a period of acquisition and development of cognitive neural codes. Brain morphogenesis during a prolonged period of exposure to significant novel experiences can be expected to be modeled in accordance with ongoing experience (Goldman, 1975; Gottlieb, 1976a,b; McConnell, 1991; Mills et al., 1993; Plante, Swisher, Vance, & Rapcsak, 1991; Semrud-Clikeman et al., 1991; Taylor, 1969).

Data collected from studies of heredity and environment suggest that morphogenetic development of the brain's intellectual nature is attributable to both genetic and social environmental influences, the former having slightly greater effect than the latter (Oates, 1979; Plomin & Rowe, 1979; Posner, 1993). What this suggests is that several different cortical–cortical and cortical–subcortical systems are operative during the process of learning and information storage. What the infant senses, then, may be in part the result of what is neurally "set" to sense or competent to sense via a selective attending process (Dietrich, 1990; DiGuilio, Seidenberg, O'Leary, & Raz, 1994; Hudspeth & Pribram, 1992; Posner & Petersen, 1990; Pribram, 1976; Siegel, 1979).

Postnatal Perceptual, Cognitive, and Motor Development

Perception can be considered a multichannel process of visuomotor, auditory, sensorimotor, and other skills in which motor components of perceptual acts may be seen as a control process over sensory input mechanisms. Sensory input data contribute significantly to the following: perceptual processing of information; decision-making; readiness-to-act; and motor control

commands, all the way from motor reflexes to the highest neocortical levels involving planning, organizational abstract thought. The significance of these processes as to the phenomenon of control lies in the success (or failure) of the infant's development and behavioral repertoire (Petersen et al., 1994; Raichle et al., 1994).

During the earlier stage in development (the first 2 years of life), an infant changes from having little awareness of the environment, to a child who is aware of the environment via its developing sensoriperceptual systems and neurological growth processes. If development proceeds normally, the child is capable of discriminating among the various environmental stimuli. During the second stage (2–5 years), preconceptual representation as described by developmental psychologists such as Piaget and Bruner takes place in which the child develops pictorial (ideograph) images as symbols. The child also begins to advance in language competency. During the third stage (5–7 years), symbolic representation occurs in which the child becomes aware that he or she is not alone in the universe and begins to interact with several environmental forces that impinge on the child's development. The fourth stage (7–12 years) is characterized by operational thinking in which the child begins to recognize certain relationships between objects and appreciate their relative values, e.g., the concept of mass, size, distance, length, and time (Bower, 1977; Mistretta & Bradley, 1978; Siegel, 1979; Tulving, 1985).

Several attempts have been made to match developmental stages in cognition with defined structural changes in the brain (Epstein, 1978; Milner, 1976; Ploog, 1979; Vygotsky, 1974). Until recently, such efforts have met with very limited success except for recent studies (Hudspeth and Pribram, 1992; Kwong et al., 1992). Major obstacles in trying to correlate behavioral, motor, and sensorimotor development in finite stages include neural and metabolic processes involved in cellular differentiation, synaptic process formation, dendritic arborization, and myelination development discussed previously. Actual alterations or modifications can arise as a result of metabolic factors that affect function, e.g., decreased CBF; oxygen use by cerebral tissues; glucose use by cerebral tissues; cerebral vascular alterations leading to ischemic, hypoxic, or anoxic episodes; and periventricular leukomalacia (PVL). As glucose and oxygen are the primary constituents providing the metabolic energy requirements of neurons, rates at which these substrates are used can provide a quantitative assessment of the level of neuronal function in the brain (Martin et al., 1990).

Maturational changes in cerebral function in human infants have been studied by quantitative methods using 2-deoxy-2-fluoro-D-glucose (2-DFG) and positron emission tomographic technique (PETT) (Chugani & Phelps, 1986). Studies of infants at various times during development reveal significant changes in a progressive manner in local cerebral glucose metabolism. Chugani and Phelps (1986) studied 5-week-old, 3-month-old, and older infants and found glucose metabolic activity increasing in anatomical regions in agreement with behavioral, anatomical, and neurophysiological alterations that are known to occur in the first 12 months according to established patterns of infant CNS development. More recent studies have extended this growing body of information on human infants by using PETT and functional imaging (fMRI) (Chugani, 1992, 1993, 1994; Chugani & Jacobs, 1994; Kreis et al., 1993).

Although it is not yet possible to specify which brain mechanisms are specifically involved in perceptual processing, it is believed that many of the events are distributed throughout the brain. Perception represents functions drawing from systems at diverse anatomical sites, both in upper and in lower regions of the brain (Bower, 1977; Livingston, 1978; Majovski & Jacques, 1982; Posner, 1993).

Connections conceivably involved with central information processing of context-dependent and context-free events in the environment may involve cortex-to-basal ganglia and frontolimbic pathways. Sensorimotor readiness, in part, is dependent on cognitive–spatial mapping properties thought to be carried out in the hippocampal formation and neocortical structures (Izquierdo, 1975; Liben, Patterson, & Newcombe, 1981; Nauta, 1986a,b; O'Keefe, 1994; Squire & Zola-Morgan, 1991).

Memory

Memory underlies the highest functions of the brain, from multiplying two numbers to developing a sense of oneself. All memories come from the world outside of the mind.

Whereas visual images leave shadows on the retina for less than a second, sounds taper off into echoes lasting no more than 4 s. A major question arises: How does a coded memory process, specific to certain environmental events, differ from those that organize and lay down a long-term memory code? Partial answers have issued from a recent developmental study by DiGuilio et al. (1994) of procedural versus declarative memory. Structures implicated as crucial for forming new and enduring memories include the hippocampi, frontal lobes, and medial–temporal structures (Squire & Zola-Morgan, 1991). It is at this level that human thought, planning, decision-making, and organization of information involved in higher cortical functions take place, and where sensory impressions leave their "traces" in neurons. How this process works is not fully understood because only selected features are allowed to pass on to the cortex.

A child's functional memory capacity develops across years from early infancy onward. Recall performance increases reaching a plateau in adolescence (Kail & Hagen, 1977; Meudell, 1983). Procedural and declarative memory have been studied extensively in adults but research on the development of memory in childhood has been focused mainly on declarative memory from a developmental perspective. The dissociation between procedural and declarative memory systems in amnestic patients may serve as a model for a better understanding of the type of memory tasks children are capable of learning early in their cognitive development and subsequently improve with aging.

Developmental differences seen at different ages on measures of declarative memory may correspond to anatomical changes occurring in such structures as the hippocampi, diencephalon, and medial temporal lobes (Nadel & Zola-Morgan, 1984; Squire & Zola-Morgan, 1991; Zola-Morgan & Squire, 1993). Procedural memory is thought to reach maturation by middle childhood although no consensus has been reached concerning the neural mechanisms responsible. Tulving (1985) suggested that procedural memory is analogous to that of lower animals which is subserved by subcortical structures. Evidence from several animal and human studies has shown a role of the striate system, independent from corticolimbic circuit responsible for recognition and recall, involved in mediating procedural memory (Heindel, Salmon, Shults, Walicke, & Butters, 1989; Mishkin & Petri, 1984; Saint-Cyr, Taylor, & Lang, 1987).

DiGuilio et al. (1994) have demonstrated in children that the level of procedural memory performance stabilizes during a period of development when declarative memory continues to improve. A plausible explanation may come from myelination and neuronal dendritic proliferation processes that continue in the diencephalon; ongoing maturation in hippocampal formation; and associated connections involving the temporal lobe regions. The absence of age differences found in procedural memory may suggest that these brain regions are functionally and neuroanatomically mature by middle childhood.

How other information is inhibited is a mystery. How neurons are "tuned in" to the ongoing events of the environment, such that they can abruptly change in firing patterns on sensing the smell of food, the perception of fear or threat, the sight of something stimulating, is unresolved at present. Functional imaging (fMRI, MRS, MegEEG, and MSI) are quantitative methods that are providing a major gain in examining the in vivo process of how cognition takes place.

Symbolization and Early Cognitive Development

Perhaps no aspect of human development is more important than symbolic representation in its broader role in life, affecting almost everything we do. Normal healthy toddlers between ages 2½ and 3 years were studied to determine whether they could use their memory of a small room to figure out where to find a toy that was hidden in a large room (DeLoache et al., 2004a,b). Results of studies on 2½-year olds and 3-year olds showed that the 3-year olds were successful but the 2½-year olds failed. It was posited that they had no idea where to look when entering the large room but remembered the hidden toy placed in the miniature room prior to entering the large room. The 2½-year-old failure observation, it has been hypothesized, may be due to the lack of understanding "how" and "when" they acquire the ability to understand that one object can stand for another, i.e., dual-symbolic representation. *Symbol-*

mindedness is a learning process that occurs over several years throughout childhood and is not something intuitive in infants. A fundamental distinction in this age-developmental process occurs when children can view an object both as itself and representing something else, i.e., understanding that one object can stand for another. This has implications for educators and their practices in the preschool and elementary school levels in regard to young children being able to learn enormous amounts of information without directly experiencing it.

Mirror Neurons (MN)

Mirror neurons (MN) were first discovered by researchers studying individual neurons in the brains of Macaque monkeys that fired both when grabbing an object and watching another primate grab the same object (di Pellegrino et al., 1992; Sheliga, Riggio, & Rizzolatti, 1995; Rizzolatti et al., 1996). MN is a kind of nerve cell that responds when one performs an action and observing someone else performing the same action. It is postulated that MN might help explain how humans feel emotional empathy and read social cues in other humans. In the past decade, research has suggested that MN play a role in empathy in normal healthy brains, language development, and has implications for autistic children, too. However, a major problem in conducting research with humans versus monkeys is that researchers have yet to prove that humans have individual MN. Studies with the human motor cortex shows a general mirror *system*, but needs further investigation involving other brain regions Mirror neurons (MN) have reportedly been found in the (Broadman regions 44, 45) dorsal premotor cortex and Broca's area. The role of MN in humans may appear to serve wider role than in nonhuman primates. The findings of several neuroimaging studies have shown support in that observation, execution, and imitation of actions in humans involve activity in a number of regions of the brain including the premotor cortex and Broca's area. These areas are thought to be homologs to the areas in monkeys where MN have been identified, e.g., area 5.

Neurophysiological studies using EEG have been used to study "mirror neuron-like activity" in humans for over 50 years. In particular, the *mu* band which falls between 8 and 13 Hz has been studied. EEG as well as functional imaging has been used to study potential neurons in both typically developing populations and in populations of individuals with autism. Considerable interest has been focused on MN activity in individuals with autism as they frequently have deficits in imitation and MN have implicated in the development of imitation skills. A recent study using EEG provided support for the theory that mirror neuron execution/observation matching system is related to imitation abilities and specifically to the imitation impairments noted in individuals with autism (Bernier, 2006, unpublished dissertation).

At present, there is no firm evidence as to the precise function of the MN system in humans, or what alterations in neural development would cause brain–behavior dysfunction. One study with autistic people suggests that MN systems are not as active when compared to healthy normal adults (Theoret et al., 2005). Further studies are needed to address the differences in brain functioning as well as dysfunction, i.e., how healthy, normal brains versus people with autism show social reading of cues, understanding, and relating to others, i.e., *symbolmindedness* and learning which occurs in the second to third years of life.

Williams–Beuren Syndrome (WS)

Williams–Beuren syndrome (WS) is an autosomal dominant genetic disorder (Morris & Mervis, 2000) characterized by the following behavioral features: unusual friendliness; good verbal abilities and loquacious; lack of social anxiety; socially uninhibited; poor reading of social cues; and more prone to anxieties and phobias. Most WS individuals are mentally retarded, distractible, less cognitively flexible, and adaptive. Neuroimaging studies recently conducted with MRI of WS versus controls (Meyer-Lindenberg et al., 2005) have reported regarding the neural correlates of genetically abnormal social cognition in WS versus healthy subjects. They found that WS individuals show greater activity in the prefrontal cortex (PFC) and less activation in the amygdala region. Controls, however, demonstrated the opposite pattern when performing visual tasks involving face-matching, i.e., the assignment of emotional influences and

meaning to situations involving a face-matching and scene-matching tasks. Activation in the orbitofrontal region correlated mostly with the WS individuals in which damage to that region shows a relationship regarding uninhibited social behavior. The authors found that the link between the orbitofrontal cortex (OFC) and the amygdala showed disruptions in WS individuals but not the medial and prefrontal cortex (PFC) regions. This study suggests that the neural correlations in the prefrontal cortex and the amygdala regions of WS versus healthy individuals on face-matching and non-face, object tasks affect emotional influences as to inferred fearful experiences which is different from PFC functioning, i.e., decision-making, judgment, regulation activities, etc.

Representation of environmental events receives continuous updating, in part, via the thalamocortical processing of spatiotemporal events, such as formation of a spatiotemporal "envelope" of reality leading to consciousness. The thalami are the major structures and gateways for the flow of information toward the cortex and are the first point at which information can be blocked by synaptic inhibition during sleep. Lashley, Chow and Semmes (1951) asserted that the core function of the CNS lies in the spatial and temporal integration of perception and motor activity in order to provide refined adaptation of behavior. Since then, major progress has been made in investigating the role of the thalamocortical mechanism involved in arousal and sleep (Steriade et al., 1993).

Some important clues related to how brain mechanisms operate in terms of sensory processing and an infant's behavioral output come from a consideration of noncorrespondence with past experiences. The infant discovers through action that stored codes are connected after his or her behavior achieves success. Perhaps it is at that particular moment that perception itself is projected in symbolic form in a predictive manner for the desired behaviors to follow. Behavior, in this sense, is essential to the shaping process of stored sensory information and not simply its goal. Memory storage might be deposited in the neural substrates of various brain centers that are accessed according to a given context-like paging system such as is found in a library cataloging system. Delays in matching stored percepts to sensory input would then be experienced when the context is suddenly altered (Majovski & Jacques, 1982; Petersen et al., 1994; Saint-Cyr et al.,

1987; Sergent, Ohta, & MacDonald, 1992; Zola-Morgan & Squire, 1993).

Some crucial steps considered operational in this process include rapid matching stage, hypothesis formation, internal sorting from possibilities, and testing the selections made via behavioral acts. Siqueland and Lipsitt (1966) demonstrated that infants can exhibit learning during the first day of postnatal life. Head turning is a regular response in which hypothesis testing conceivably is occurring. Memory storage is taking place together with suppression of interhemispheric transfer of memory codes. The suppression phenomenon introduced here has the potential effect of expanding the capacity of the neocortex for memory storage in its early stages. The anterior commissure of the corpus callosum, which interconnects the two temporal lobes, is believed to participate in memory storage bilaterally in a yet unspecified process.

Studies that have examined the relationship between abilities of infants and subsequent cognitive functioning indicate a strong relationship between infant behaviors and cognitive and linguistic abilities in early childhood, despite rather low correlations of test scores and measurements from infant intelligence tests. It has been suggested that later cognitive development correlates more highly with early problem-solving skills, whereas language development tends to correlate more highly with a child's understanding of both object–concept and means–end relationships (Siegel, 1979). Current research on dyslexia has addressed the issue of the extent reading deficits of dyslexic children are related to processing deficits at the levels of sensory–visual, cognitive-linguistic, or both. Using evoked potential brain mapping at the P110 and N400 microstates has shown critical factors for successful identification of specific processing deficits in brain mapping studies (Brandeis, Vitacco, & Steinhausen, 1994).

Studies have also shown that cerebral functions are not necessarily localized as was previously believed based on older theories regarding left and right brain functions because children, as well as adults, involve both hemispheres. Perhaps in early development, both hemispheres serve linguistic functions, prior to left-hemisphere lateralization in the majority of right-handed individuals for language capacity (Benson & Zaidel, 1985; DeVos, Wyllie, Geckler, Kotagal, & Comair, 1995; Mills et al., 1993;

Semrud-Clikeman et al., 1991). This would suggest the possibility that greater cortical plasticity is most likely present in the earlier stages of infant language development (Molfese, 1977; Witelson, 1985). Despite the appearance of a high degree of hemispheric specialization during child maturation, the human brain can be viewed as a "single-channel system" in the earlier stages of infant development and later shifts as a result of changes in its subsequent cognitive and linguistic development (Bennes et al., 1994; Kinsbourne, 1976; Taylor, 1969; Witelson, 1977).

Some of the rather striking consistent correlations between maturation of the brain and development of behavioral processes are emerging from recent MRI, functional imaging (MR), and MRS investigations in infants (Chugani, 1992; Kreis et al., 1993; Kwong et al., 1992). The visual processing area in the brain has been studied and shows development early in the first year. Limbic areas develop later in the first year. Sensorimotor areas develop in earnest in the second year whereas auditory areas continue to develop well into the fourth year (Bronson, 1982; Bushnell, 1982; Levine, 1982; Selnes & Whitaker, 1976). The brain's highest areas (those involved in thinking, abstraction, reasoning, and problem-solving) continue to mature into the teens and perhaps into the third decade. Development of social competency can be viewed as a mixture of maturing of perceptual, sensorimotor, motor, and linguistic mechanisms in the brain, in conjunction with the social conditions of the acculturation process (Oates, 1979; Siegel, 1979).

Brain Maturation in Early and Late Cognitive Development

Maturation of cognitive abilities in relation to brain development, previously discussed, also can influence emotional and personality development in an as yet unspecified manner (Emde, Gaensbauer, & Harmon, 1976). Kagan (1985) proposed a maturational sequence of cognitive abilities as follows. First, the infant demonstrates the capacity of memory for past experiences; second, active memory formation occurs; third, there is a symbolic framework that takes shape; fourth, the infant is able to infer causality; and finally, the child is able to exhibit self-awareness. Kagan and co-workers assert that these five steps occur in sequence by 24 months in normal brain development (Kagan, 1981; Kagan, Kearsley, & Zelazo, 1978; Kagan & Moss, 1983).

Kagan's research has demonstrated that a normal developing child by 8 months has the ability to retrieve hidden objects, whereas earlier, if "out of sight," it was "out of mind." Beginning approximately at 8–9 months, incoming information is related to knowledge for the first time, giving rise to the emergence of active memory processing. At 8–10 months, cardiac acceleration occurs in relation to exposure to the visual cliff experiment. This does not occur prior to 8 months, indicating that the sympathetic nervous system is having greater influence and affects what has been commonly termed the separation anxiety phenomenon. Infants all over the world have been shown to manifest separation anxiety features between 8 and 12 months (Kagan, 1985). This may reflect the fact that myelination occurs in the frontal regions by about 12 months reaching greatest deposition of myelin by age 2 (Dietrich & Hoffman, 1992). As growth of the CNS continues, new capabilities emerge. At 17–24 months, several important behaviors emerge: appreciation of right versus wrong; appreciation that physical aggression is wrong; appearance of anxiety in relation to failure; the ability to experience empathy; and acknowledging anxiety in relation to unsolved problems.

At 1–3 years of age, children begin to recognize themselves with a sense of self-appreciation. It is thought that the maturing brain's anatomical structures and neurochemical pathways permit the concept of self-awareness to emerge, implicating structures such as the hippocampi, thalamocortical nuclei systems, corpus callosal development, and frontal lobe maturation (Aboitiz, Scheibel, Fisher, & Zaidel, 1992; Bekkers, 1993; Cowell, Allen, Kertesz, Zalatimo, & Demenberg, 1994; Mills et al., 1993; Posner & Rothbart, 1992). Kagan's (1981) studies show that in a child of approximately 2–3 years, fear is prevalent. The more a child is capable of inhibiting an unfamiliar experience, the better stabilized the child becomes. Separation anxiety is a cognitive-mediated event and the environmental context dictates the value placed on the notion of a child's "inhibitedness" (Smith & DeVito, 1984). The latter consideration may be causally related to aspects of temperament that can be influenced with experience throughout child development. The parasympathetic system quells sympathetic arousal to unfamiliar and

unregistered events in the child's repertoire of behavioral experiences. The development of temperament heavily influences a child's behavioral choices in later years in many subtle ways, e.g., children with ADD/H or behavioral adjustment difficulties show adverse effects concerning decision-making strategy.

Adolescents: Brain and Behavior Development

There are several developmental psychologists, e.g., Gesell, Ames, Kagan, Zelazo, Rebelsky, Elkind, Siegler, White, Cole & Cole who have studied healthy developing children and reported on key fundamental aspects of behavioral development and brain functioning from birth through adolescence, emphasizing the following: sensorimotor; cognitive; communication/language (including speech); gross/fine motor skills; socialization; effort/persistence (sustained attention with activities); and self-awareness/adaptive behaviors (See Arnett, 1999; Damon, Lerner, Kuhn, & Siegler, 2006; and Table 1 "Sensitive Developmental Periods:

Infancy through Adolescence" regarding key developing processes).

Disruption in any one or combination of developing processes listed in Table 1 can result in neurodevelopmental and neurobehavioral complications, selectively presented in Table 2.

There have been several prospective studies using MRI since the 1990 s which have yielded important new information about the development of the brain into adolescence. Findings indicate that there is significant heterogeneity in cortical development in normal brains. The corpus callosum, for example, demonstrates a pattern of maturing from posterior to anterior. The prefrontal cortex is one of the last areas to mature. The results of these studies indicate there is continued development of processes such as attention and memory which have both behavioral and physiological correlates. The magnitude of brain activity correlates with pattern of more diffuse activation are differences observed between children and adults (Kuhn, 2006).

Longitudinal neuroimaging research supports a pattern of increasing cognitive capacity coinciding with a gradual loss rather than formation of new synapses (Kuhn, 2006). These MRI studies have indicated that after early childhood (age 5) there is (1) lack of cerebral volume increase, (2) significant decrease in cortical gray matter after ages 12; and (3) an increase in white matter throughout childhood and young adulthood (Giedd et al. 1999; Casey, Giedd, & Thomas, 2000).

TABLE 1. Sensitive Developmental Periods in Infancy through Adolescence

Age	Developing processes in healthy brains
6 mos.–12 mos.	An infant's visual world is almost equivalent to an adult
2y	Gross and fine motor skills; sensorimotor integration (subcortical and parietal–occipital areas)
2y–6y	Language/communication (two-word stage; sentences emerge (temporal and parietal areas)
3y–4y	"Cause–result" connection made; emergence of conscience, empathy (moral development). Transition to social interaction skills from parallel play)
4y–7y	Socialization/symbol-mindedness process with assigned meaning (theory of mind, i.e., ability to empathize/understand what another person feels or desires).
8y–10y	Pre-operational/cross-modal cognitive information processing
12+	Formal reasoning/abstraction processes (insight, judgment; inferences)

TABLE 2. Problem Areas Frequently Associated with Behavioral/Psychiatric Disorders in Children and Adolescents

1. Developmental immaturity (neurological, physical, social, cognitive, language/communication, relational/attachment)
2. Abnormal motor activity
3. Sensory-motor delays
4. Impulsiveness
5. Sustained attention span/distractibility
6. Perceptual disabilities
7. Specific learning problems/disabilities
8. Emotional/mood dysregulation
9. Language/communication disorders
10. Self-regulation/inhibition ("executive functioning")

The pattern of changes is not uniform with increases in different regions of the brain, e.g., increase in dorsal prefrontal cortex but no longer in the ventral regions. The results of these changes indicate that teens are developing, fewer, but more selective, stronger, and more effective neural connections.

There has been much less work done understanding cognitive changes that may occur in adolescence relative to early childhood. Contrary to assumptions made in the past, it appears that it is not the case in adolescence that there is a uniform development toward more abstract thinking; and that there are no discontinuities between cognitive abilities observed in adolescents relative to childhood. Several lines of evidence suggest that what seems to be developing in adolescents includes significant processes such as increased inhibitory control, processing speed, and "executive" control. What seems to be evident is the use of more effective strategies in adolescents relative to school-aged children. As children enter the second decade of life it appears that not everyone continues to follow universal pathways. For example, many adults do not show any development in cognitive abilities beyond levels achieved by typical adolescents. During the second period of development significant pruning of unused connections occurs and the behavior of the adolescent and their activities play a prominent role in this process. In this way, adolescents play an active role in the shaping of their own cortical architecture. The significance of this underlies the importance of intellectual engagement by adolescence which directly influences the specialization of their brains as well as their behavior (Kuhn, 2006; Damon et al., 2006).

Autistic Spectrum and Asperger Syndrome

The population of autistic school-aged children reported in the U.S. (2006) is approximately 300,000 or 5.5 per 1,000 according to the CDC. Young children with autism tend to have larger than average head size, an increase perhaps stemming from more white matter than gray matter which affects short-distance nerve tracts versus long-distance ones. This connectivity difference may have an impact on the development of "empathy" and emotional affection in an autistic child since empathy–emotional

behavior has been shown to activate various brain regions that integrate inputs from multiple neural networks in normal, healthy brains in contrast to autistic children where the long-range inter-connectivity pattern is shown to be low (Belmonte et al., 2004a,b; Courchesne & Pierce, 2005; Ochsner et al., 2004; Welchew et al., 2005).

Autistic children between ages 18 and 35 months old showed an enlarged amygdala mass, corrected for total brain volume which continues throughout childhood but disappears during adolescence and in early adulthood showing unusually low mass (Sparks et al., 2002; Schumann et al., 2004; Rojas et al., 2004).

It remains for future research to map out and further correlate other potential morphological aspects of neural development in autistic children that show a hypermasculinized pattern versus those areas that do not. Whether there are further comparable developmental growth patterns, including biological molecular mechanisms that play a role in influencing and shaping sex differences that differ from typical healthy male brains, needs to be researched before drawing accurate correlations and differences.

Individuals with psychopathy, i.e., antisocial, conduct disorder, impulsivity, poor self-regulation and little or no concern about the effects of their actions on others or on themselves have been shown to demonstrate frontal lobe (FL) impairment and impaired performances on selected executive functioning (Raine, Buchsbaum & LaCasse, 1997; Raine, 1997, 2002). Studies of individuals with psychopathy using neuropsychological tests and fMRI have shown significant impairment on measures sensitive to frontal/medial orbitofrontal cortex (OFC) dysfunction in contrast to performances on measures preferentially sensitive to functioning of the dorsolateral prefrontal cortex (DLPC) and dysfunction in the medial/anterior cingulate cortex (ACC) (Mitchell, Colledge, Leonard, & Blair., 2002; Kiehl et al., 2001; & Veit et al., 2002).

In children with diagnosed conditions of AD/HD, behavior problems are often comorbid with executive dysfunction, i.e., conduct disorder, psychopathic risk behaviors (Biederman, Newcorn, & Sprich, 1991; Colledge & Blair, 2001). Other individuals within a psychopathy category that involves OFC dysfunction and

elevated levels of reactive aggression, frustration, and impulse dyscontrol are patients who manifest intermittent explosive disorder, childhood bipolar disorder, and borderline personality disorders (Best, Williams, & Coccaro, 2002; Gogtay, Griedd, Rapport, 2002; Gorrindo et al., 2005).

Blair et al. (2006) conducted a study of individuals with psychopathy versus comparison group using neuropsychological tests measuring executive functioning. They reported that individuals in the psychopathy group showed significant impairment on measures sensitive to OFC functioning, but the two groups did not show impairment on the neuropsychological measures sensitive to DLPF or ACC regions of functioning. The data reported according to their findings, however, do not conclusively show a functional impairment relationship to activity in the neural anatomical regions studied. All of the neuropsychological test measures used in their study required response inhibition or modulation, both of which are implicated to be impaired functioning in the individuals within this psychopathy group. The implications for neural development that can have an adverse effect on brain–behavior neural correlates with disruptive behavior disorders in children involves the sensitive limbic system regions of the septum, amygdala, and cingulate areas.

Brain Changes and Reading

The development of proficient reading skills is critical for success in academic settings as well as many life activities. The neural substrate for reading has been studied over the last 10 years using functional brain imaging techniques. The studies have used both control subjects as well as children with dyslexia. Behavioral research has indicated that phonological processing has a critical skill for the development of proficient reading. Investigations using reading and phonological paced assessments have indicated involvement of neural systems both anterior (inferior frontal gyrus) and posterior (middle temporal gyrus) (Shaywitz et al.,2004). A portion of the posterior reading system (occipital temporal area) has been shown to be critical for the development and skilled reading and appears important for quick recognition of the printed word. Brain activation in this region increases as reading skill increases. Most importantly there have been recent studies investigating the brain activation patterns in children with dyslexia who have engaged in phonological-based reading interventions. These studies support the view that the neural systems are plastic and respond to intervention positively. Encouragingly, the data from several studies indicate that intensive evidence-based reading intervention results in improvements in reading fluency and significant and long-lasting changes in brain organization. These changes in brain activation resemble those of typical readers. The results of these studies have important implications for the use of evidence-based interventions with young children who are experiencing difficulty in acquiring reading skills (Shaywitz et al., 2003, 2004; Aylward et al., 2003).

Cerebral Asymmetry and Cerebral Lateralization

To date, there is no firm conclusion as to the nature and cause of cerebral hemisphere asymmetry. However, the structure and function of each hemisphere are indeed different (Connelly et al., 1993; Mazziotta & Phelps, 1985; Sperry, Gazzaniga, & Bogen, 1969). An explanation of the functional differences solely in terms of a dichotomy of verbal or nonverbal nature of information processing also has not been adequately substantiated. Many researchers have proposed theories and models of the development of cerebral asymmetry and its function, including Buffery (1976), Corballis (1980), Kimura (1967), Kinsbourne (1974), Kinsbourne and Hiscock (1977), Krashen (1973), Lenneberg (1967), Moscovitch (1977), and Witelson (1977).

Some investigators have suggested that within the left and right cerebral hemispheres, at all ages and in both sexes, different functions are served (Benson & Zaidel, 1985; Bradshaw & Nettleson, 1983; Bryden, 1979; Corballis, 1982; Kinsbourne, 1976; Morgan, 1977; Taylor, 1969; Witelson & Pallie, 1973). It is believed that bilateral integration of information is mainly subserved by the corpus callosum. Problems arise when growth is delayed or when dysmyelination or other neural pathway dysfunctions occur in the between-hemisphere interplay during cognitive information processing (Aboitiz et al., 1992; Cowell et al., 1994; Dietrich, 1990; Dietrich &

Hoffman, 1992; Witelson, 1985). A majority of studies and theories that deal with the body of scientific evidence on cerebral asymmetry have focused on the lateralized aspects of cognitive functioning in children.

Other investigators have reported studies that have pointed away from the content-dictated, verbal–spatial dichotomies of the encoding process to a process-determined, "analytical/sequential" versus "gestalt/holistic" information processing style (Bogen, 1969; Levy, 1972; Levy-Agresti & Sperry, 1968; Luria & Simernitskaya, 1977; Sperry, 1974; Sperry et al., 1969). Kinsbourne and Hiscock (1977, 1978) have presented compelling arguments leading away from the concept of progressive lateralization with age. Kinsbourne (1982) discussed in depth the importance of the collaborative efforts of the two hemispheres of the brain. Arguing from the viewpoint of cerebral lateralization theory, Kinsbourne stated that mental activities that relate to action in the real world impose demands for integral and coordinated action of both sides of the brain.

Luria (1966, 1973a) places emphasis on each hemisphere contributing a different strategy of cognitive information-processing and does not isolate each process within a specific hemisphere of the brain. He views the human brain as hierarchically organized in order to integrate messages from its lower centers as well as across hemispheres. Luria asserts that dichotomy of functioning does not do justice to the complexity of the human brain's hemispheres. Rather, it is the manner in which the hemispheres organize or represent information versus the type of information organized that is the important distinguishing feature (Luria, 1970, 1973a,b).

Witelson's (1977) earlier review of selected developmental studies on different sensory modalities pertaining to cerebral asymmetries, handedness, sensorimotor, perceptual, and even genetic studies shows that development of cognitive functions follows a definite order. Several changes occur, some of which can be genetically determined (but influenced by the environment). Hemispheric shifts in which side of the brain handles what type of information, related to alterations in the structural development of the brain, also occur (Annett, 1978; Bakan, 1971; Satz, Strauss, Hunter, & Wada, 1994). Cerebral dominance is related not only to linguistic processes but also to underlying morphogenetic factors that are influenced by several factors including gender differences in the normal developing infant as well as pathological conditions affecting early brain development (Satz, 1993; Satz, Orsini, Saslow, & Henry, 1985; Satz et al., 1994).

The *planum temporale* (PT) has been a major focus of brain laterality research that has looked at asymmetry relative to other brain regions and neuropsychological evidence linking this structure to language development. Kulynych et al. (1994) have perhaps made this the first in vivo study reported to show evidence of gender differences in the asymmetry of PT. Left plana were significantly larger than right plana among normal males. No significant differences between left and right areas were present among females. The lack of a significant main effect of gender was interpreted to mean no difference in overall (left and right) planum size was observed, although left plana alone were significantly larger in men and women.

This finding corresponds remarkably close to Witelson and Kigar's (1992) findings concerning asymmetries of the horizontal portion of the Sylvian fissure, the posterior extent of which reflects PT length. These results also show a consistent correlation with earlier neuropsychological reports of gender differences in patterns of functional asymmetry (Kimura & Harshman, 1984). The divergence in patterns of PT laterality suggests that sex differences in the lateralization of language need major consideration in any discussion of the relationship between human psychopathology and developmental abnormal cerebral asymmetries.

Intermodal hemispheric processing of information can show differential effects when the child approaches age 8 and older, a result of the late structural maturation of the corpus callosum (Aboitiz et al., 1992; Cowell et al., 1994). This can lead to various forms of difficulties, for example, dominance problems, and learning difficulties (Satz et al., 1985; Schonhaut & Satz, 1983; Sips, Catsman-Berrevoets, Van Dongen, Van der Werff, & Brooke, 1994). Currently there are conflicting theories and hypotheses related not only to cerebral dominance and hemispheric specialization but also to the onset, development, sexual orientation, and maturation of the brain's lateralization (Geschwind & Galaburda, 1984; McCormick & Witelson, 1994; Satz et al., 1985; Witelson, 1985).

Inadequate encoding of early experience, brain insult, nutritional deficiency, anoxia at

birth, perinatal asphyxia, teratogenicity factors, and certain congenital hereditary/metabolic defects can impose severe restrictions on the developmental capacities essential for sensory processing of motor, visual, acoustic, and haptic information, e.g., neurological and neuropsychological dysfunction. Until normal brain development and the mechanisms involved in higher mental processes are more precisely measured and adequately described by newer technologies and improved experimental designs, educational, diagnostic, remedial, and therapeutic efforts will only be partially effective.

An essential first step in making scientific progress regarding normal brain maturation is to describe the events and conditions defining psychological functions before proceeding to hypotheses and constructs of brain–behavior relationships. Experimental studies of brain mechanisms and developmental issues, coupled with neurophysiological, neuropsychological, neuroimaging, and neurobiological data will yield broader generalizations and more precise knowledge leading to better understanding of the child's developing brain structures, functions, and cognitive processes involved in extracting meaning from the external environment. The next section discusses the most recent advances in brain imaging techniques and methods for mapping brain function onto structure in vivo.

New Brain Imaging Techniques for Studying Normal Brain Development and its Functions

The major new brain imaging tools in the past decade have led to advances in imaging of brain anatomy, CNS development, metabolic measurement of hemodynamics, and electrochemical physiological properties of nervous tissue that reflect a wide array of neuronal activities. With regard to cognitive human neuroscience, the major consequence of these newer technologies lies in their ability to identify, localize, and more precisely study higher cognitive processes. Methods based on noninvasive magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), functional MRI imaging (FI or EPI), magnetic source imaging (MSI or MEG), and positron emission tomographic technique (PETT) have each demonstrated their impact on

the dynamic changes occurring in the human brain. This extends beyond sensory neural systems to higher mental processes, e.g., thinking, reading, problem-solving, and how the brain attends (selects) to certain stimuli versus inhibits ("brain work" in the words of David Ingvar, M. D.).

It is now possible to apply these newer techniques to the study of healthy and abnormal brain development and certain mental functions. These new tools and their clinical impact will be briefly reviewed. Emphasis will be placed on their respective capabilities, applications in clinical and neuroscientific investigation.

Neuroimaging studies cannot, when standing alone, provide answers as to whether a function of a neural network system represents a neural substrate of that function versus a nonessential process associated with a particular function. Human brain lesions combined with neuroimaging studies have provided complimentary information when studying brain–behavior functioning (Bookheimer, 2000).

Neuroimaging and Other Research Methods

MRI

MRI (nuclear magnetic resonance) is based on proton (hydrogen) nuclei in which resonating hydrogen atoms give off radio waves (radio frequency) that reveal tissue structure, noninvasively, and can detect physical abnormalities. (For a complete discussion, see Stark & Bradley, 1992.) MRI has been applied to study human brain development as to neuroanatomical patterns of myelination and dysmyelination (Dietrich, 1990; Dietrich & Hoffman, 1992; Dietrich et al., 1988; Hittmair et al., 1994; Zimmerman et al., 1992).

There has been an explosion of studies using MRI in both diagnostic work and research. Studies of healthy brain development have revealed both age and gender differences in the pattern of brain growth (Wilke, & Holland, 2003; Matsuzawa et al., 2001; Reiss, AL., Abrams, MT., Singer, HS., Ross, JL., Denckla, MB., 1996). In healthy brains considerable variability has been found in growth of both brain structures as well as gray and white matter (Wilke & Holland, 2003). Studies of children as young as 1 month up to age 10 have revealed growth spurts of the whole brain as well as

frontal and temporal lobes. For the first two years of life the frontal lobes grew more rapidly than the temporal lobes while left-to-right asymmetry was more prominent in the temporal lobes than in the frontal lobes. The increase in gray matter was greater than that of white matter in the temporal lobes (Matzuzawa et al., 2001). Differences between boys and girls have been found in healthy children of ages 5–17. Little change in total cerebral volume after age 5 has been reported. Increases in brain volume in boys appears to be primarily due to increased cortical gray matter, while age-related changes in gray matter, white matter volumes of cerebrospinal fluid during childhood reflect the maturation and organizational changes of the central nervous system. Both boys and girls have shown the same pattern of cerebral asymmetry, i.e., prominence of cortical and subcortical gray matter on the right and prominence of cerebral spinal fluid on the left. Interestingly, IQ has been shown to be positively related with the volume of cortical gray matter in the prefrontal region of the brain. Although subcortical gray matter provides some contribution to the variance in IQ it is less than that of the cortical gray matter volume (Reiss et al., 1996). In girls, subcortical structures including the caudate, hippocampus, and pallidum are disproportionately larger, while the amygdala is disproportionately smaller relative to boys. In addition, the collective subcortical structures of the forebrain are at adult levels in female children and are greater than adult volumes in boys (Caviness, Kennedy, Richelme, Rademacher, & Filipek, 1996). Clinically, MRI studies have demonstrated differences in volume and structure size in a variety of clinical populations. For example, children born prematurely have been found to have reduced cerebral gray matters volumes which is related to lower scores on neurocognitive measures (Lodygensky et al., 2005).

Magnetic Resonance (MR) and Fluid-Attenuated Inversion Recovery (FLAIR) Imaging of the Normal, Healthy Brains

Neuroimaging studies using magnetic resonance (MR)/fluid-attenuated inversion recovery (FLAIR) imaging have been used in assessing normal, healthy brain development in terms of myelination in infants and young children. Myelination, which is one indication of brain maturation, was studied and demonstrated using comparison of techniques involving classic spin echo sequencing and on FLAIR images. These are essential components of MR imaging methods used in the dating and differentiation between healthy and pathological brain development in early childhood (Kizildag, Dusunceli, Fitoz, & Erden, 2005). Recent studies using neuroimaging techniques have provided information regarding brain development and exploration of the relationships between the development of emotion processing abilities and associated neural systems. A recent literature review was conducted of studies examining the relationship between the development of emotion expression recognition in healthy normal children and psychiatric populations involving neural systems. The results from examining behavioral and neuroimaging studies suggested that continued development of emotion expression recognition in neural regions important for this process throughout childhood and adolescence was supported, but that methodological inconsistencies and discrepant findings make any firm, fixed conclusions difficult (Herba & Phillips, 2004). Further investigation of the relationship between development of emotion expression recognition and underlying neural systems need to focus on the subcortical to prefrontal cortical structures for a broader understanding regarding the neural basis of normal versus abnormal emotional development in both children and adolescents.

In recent study using diffusion-tensor MR imaging of gray and white matter development during human brain maturation, it was demonstrated that changes in water diffusion during maturation of central gray and white matter structures can largely be explained by theoretical models incorporating simple assumptions regarding the influence of brain water content and myelination. Caution, however, is indicated since there are deviations from theory suggesting that increases as the brain matures are based on the diffusion-tensor MR imaging method when studying the process of brain development clinically and experimentally (Mukherjee et al., 2002).

EPI

Recent advances in neuroimaging technology have led to the adaptation of MRI to look not just at structure but also at function. Echo-planar imaging (EPI) was invented by Sir Peter Mansfield and colleagues (Stehling et al., 1990, 1991). It makes use of high-speed computers and mathematical algorithms to generate images of high rate frequency so that second-to-second changes in one's brain activity can be recorded. EPI lends itself to functional imaging (FI) of the CNS, depiction of blood and CSF flow dynamics, and movie imaging of the mobile fetus in utero (Stehling et al., 1990). Basic changes are viewed in the blood supply of the brain. Strong magnetic fields in an MRI scanner induce a magnetic field in hemoglobin, the basic molecule in blood that transports oxygen via heme–heme interaction. This magnetic field then distorts the signal given off by proton atoms (hydrogen) and shows up in the skin. Active areas of the brain require more blood since they thrive on glucose but they do not use more oxygen. When blood flow to an active area of the brain increases, the concentration of oxygen-poor hemoglobin leaving the area decreases noticeably. The principle works with respect to cognitive activity in that it is possible using EPI to see where thought patterns are forming since it is that region of the brain that suddenly starts to utilize more blood. Some of these areas can be quite small, but using EPI, changes are revealed in the blood supply to components of the brain as small as 1 mm in diameter. Neuronal activity causes local brain changes in the cerebral blood flow, blood volume, and blood oxygenation; by using intrinsic blood–tissue contrast, functional MRI (EPI technology) thus opens a spatiotemporal window onto individual brain physiology (Jackson et al., 1994; Kwong et al., 1992).

EPI's accuracy lies in its ability to demonstrate the differences between two brains and establish that the sites under observation do not shift over time, which is a significant advance made over the general maps of similar areas showing where specific stimuli exert their effects using PETT technology. This method of relating brain structure to function uses equipment that has become widely available in the past few years and has considerable implications for investigations of many neurologic diseases, and for understanding brain functions and dysfunctions (Connelly et al., 1993). Researchers have been using this technique in human studies of frontal cortex activation during word generation, language, and memory functioning (McCarthy, Blamire, Rothman, Gruetter, & Shulman, 1993; Shulman, Blamire, Rothman, & McCarthy, 1993). PETT studies have shown that an area of the left frontal lobe plays a role in language. However, EPI studies reveal that a part of the right-hand frontal lobe lights up as well (McCarthy et al., 1993; Shulman et al., 1993). These studies also reveal short-term memory associated with the frontal lobes. EPI as a tool assists surgeons as it has been shown that critical structures to be preserved versus excised may show slight variation from patient to patient. It is an accurate method of locating and displaying the structures while surgery is in progress. The value of functional MRI studies versus PETT is that it allows examination of brain activity in an individual in relation to his or her own brain structure in order that differences in one's brain anatomy can be studied in direct relation to mental operations (McCarthy et al., 1993). These anatomical applications allow progress to be made in considering what structures are involved in such higher cortical functions as awareness, voluntary control of information storage, motor responses under cerebral regulation, organization, and higher thought planning (decision-making).

PETT

PETT averages, among individuals, cerebral blood flow (CBF). Only one such study can be implemented at a time. Because of safety regulations, women of childbearing age cannot be scanned. CBF requirement for brain viability in newborns has been demonstrated and correlated to be lower than in adults (Altman et al., 1988). The fundamental links between blood flow and neuronal activity have remained obscure up to the recent advent of EPI. CBF measurement enables one to determine where neurons are more or less active relative to a control situation. However, increase in neuronal activity has its drawbacks. For example, it can signal either inhibitory or excitatory synaptic events. By its use in research, the task undertaken requires measurement that must be related to the efficiency of the task's performance

because blood flow lags behind in neural activity and real time (Raichle, 1987; Raichle et al., 1994).

The major advantages of the EPI technique are that it is fast, safe, yields maximum data in the least amount of time, resolution is of the highest degree, and the technique is readily available without the constraints of a cyclotron needed to make isotopes for PETT. With respect to infants, especially in terms of perfusion imaging, this is the major advance for early infant detection of hemorrhages and ischemic conditions based on the utility of the navigation technique for EPI and rapid imaging in millisecond-to-millisecond recordings (Stehling et al., 1990, 1991). The PETT method requires averaging among subjects within a normalized brain situation as opposed to functional MRI (EPI) studies, which allow examination of brain activity of *an individual* in relation to *his or her own* brain structure.

Magnetic Resonance Spectroscopy (MRS)

A new experimental in vivo technique using 13C magnetic resonance spectroscopy (MRS) has been used in studies involving neonates, children, and adults when integrated with magnetic resonance examinations of human brain functions and neurological disorders. A recent review using the 13C MRS technique in humans was reviewed based on a number of studies of 13C spectra of diagnostic utility in over 100 consecutive studies which has contributed to the understanding of human brain disorders as well as normal brain development. Novel 13C neurochemical data reported on metabolic and bioenergetic cellular processes indicated that this technique shows diagnostic promise when used in studying neonates, children, and adolescents in a clinical setting for diagnostic as well as normal brain development purposes (Ross, Lin, Harris, Bhattacharya, & Schweinsburg, 2003).

Phosphorus nuclear magnetic resonance spectroscopy (^{31}P-MRS) is a noninvasive investigation technique that measures intracellular metabolism in the brain of humans including infants. The acronym "NMR" has been replaced by "MRS" (Ross & Michaels, 1994). MRS can be used to measure relative metabolite concentrations in human tissues and organs in vivo; study energy metabolites and intracellular pH; and as a research tool and an investigative technique in cases of infant asphyxia. MRS is unique in that it provides quantitative information about a wide range of intracellular metabolites. The first neonatal applications were described in 1983 (Cady et al., 1983). The technique allows important metabolic consequences of cellular hypoxia to be detected rapidly and is being used in medical centers to investigate normal and abnormal conditions in neurodevelopment (Hope & Moorecraft, 1991). In vivo MRS provides biochemical information on living organisms in a noninvasive manner. Clinical correlations have been made regarding intractable seizures of both children and adults with long-term neurologic sequelae associated with decreased phosphocreatine; neuronal loss or damage (e.g., increased rates of Cr and Cho reflecting astrocytosis); metabolic ratios (orthophosphate); and information on morphologic and metabolic brain development (Gadian et al., 1994; Martin et al., 1990).

Recent studies have shown, preliminarily, that MRS can contribute to the evaluation of CNS abnormalities of infants and children, namely, neurodegenerative disorders that show low levels of *N*-acetylaspartate. This particular metabolite has been shown to be significantly lower in infants with a tendency to increase in teens. MRS investigations have provided new information about metabolic changes in early childhood in terms of elevation peaks on metabolites that have been attributable to myelination; in addition, membrane synthesis differences, useful for the determination of brain maturation and diagnosis of pathology as well as retardation, have been recorded by this technique (Gadian et al., 1994; Graham et al., 1994; Kreis et al., 1993; Tzika et al., 1993).

MRS imaging has permitted sequential in vivo analysis of CNS maturation in the perinatal period that is superior in anatomical resolution, and especially in the characterization of myelination, to either cranial ultrasound or radiographic CT. As a result, accurate detection and recognition of brain lesions associated with hypoxic–ischemic encephalopathy is possible, including conditions of periventricular leukoencephalopathy. This has advanced our understanding of the associated risk factors for abnormal neurodevelopment outcome with specific lesions. In this regard, MRS provides a metabolic "window" into the biochemical events during and following asphyxia. The potential application of this noninvasive technology may lie in its ability to

identify brain injury that is reversible in suffi-
cient time to intervene based on imaging studies.
The importance of combining MRI with MRS is
that MRI could improve spectroscopy interpre-
tation by identifying the observed tissue whereas
MRS may help to better clarify diagnosis of
anatomic lesions detected by MRI in newborns
(Goplerud & Delivoria-Papadopoulos, 1993;
Peden et al., 1993; Reynolds et al., 1991).

MSI

MSI is an investigative technique that
tracks electrical signals generated as the brain
and muscle tissue carry out their routine activi-
ties. MSI scans can identify the precise func-
tions of different parts of the brain. For
example, sensors placed around the skull detect
increased electrical activity where movement
originates. The system's computer can then
generate an image that pinpoints the brain
regions that control motion. The principle on
which MSI operates is based on the fact that
every electrical signal creates a magnetic field
around it. In the body, the difficulty is that such
magnetic fields are extremely small, i.e., a bil-
lionth of the earth's gravitational pull in the
case of the brain. Surface (depth) recording of
electrical or magnetic potentials via this tech-
nology allows precise measurement (millise-
conds) of changes between experimental and
controlled conditions. This is particularly advan-
tageous in tracing the circuitry of a specific men-
tal activity. Research in this field has identified
specific generators of electrical signals and has
led to developments relating to measurements of
what the brain does when neuronal systems are
involved in a given task, and how this takes place
in terms of mapping function onto structure (Gallen
et al., 1993; Huk & Vieth, 1993; Orrison et al., 1990).

Studies have investigated neuroanatomical
localization of cerebral function by magnetoen-
cephalography (MEG) combined with MRI and
CT (Orrison et al., 1990). Unlike traditional
EEG, these studies cannot determine the exact
location because electrical signals are destroyed
as they pass through bone and tissue. Because
MSI monitors electrical activity, it will be possi-
ble to tell immediately whether or not the brain
tissue is responding. This holds great promise for
diagnostic studies involving head injuries, strokes,
and psychiatric conditions. This technology, in
comparison with EPI as discussed above, which

measures the rate at which blood flows in the
brain and is only a means to an end, lends itself
to more precise measurements of the electrical
activity that is the physical manifestation of
thought. The latter is too rapid and subtle for
EPI to address at present.

MegEEG

MEG is based on the principle of magnetic
field detection of the tiniest electrical currents
that flow along nerve cells.

Research in this area has been conducted by
investigators who have been able to demonstrate
imaging of regional changes in the spontaneous
activity of the brain (Wang et al., 1993). In some
settings MEG can now be used routinely as a
clinical tool for localization in epilepsy surgery
patients, functional mapping of the cortex, and
assessment of normal and abnormal language
development (Wheless et al., 2004). MEG is
also being successfully used as a research tool
in a study of epilepsy, recovery from brain
injury, plasticity of the developing brain, as
well as disorders of language and neurocognitive
functioning in children (Otsubo & Snead, 2001).
MEG recordings have indicated that children
with autism and typically developing children
follow opposite maturational patterns in language
lateralization (Flagg, Cardy, Roberts, Roberts,
2005). In children with dyslexia, different patterns
of brain activation have been documented when
compared to normal readers, and most interest-
ingly, following intensive reading instruction the
aberrant activiation profile was normalized
(Sakari et al., 2002).

Research Designs and Methodologies

The choice of experimental designs and
research methodologies available for investiga-
tion of scientific and clinical questions in the
field of developmental neuropsychology poses
significant problems, e.g., replication, proper
statistical means of analyzing sample data,
group differences, and power as to the conclu-
sions that can be drawn from research studies.
Spreen et al. (1984) addressed some of the metho-
dological concerns regarding developmental neu-
ropsychology research and made the following
point regarding the importance of replication in
competent research:

The goals of the replication study are to answer the following questions. Can the original investigator or an independent investigator following the information provided by the original investigator replicate the results of the original study? Have social, cultural, economic, medical, etc., changes in the population made previous findings obsolete or misleading? Are the findings generalizable to a new set of subjects, test items, test settings, etc.? In sum, replication is a powerful tester for determining the relevance of an investigation and for weeding out findings that may show significance by pure chance or may have become obsolete. (pp. 88–89)

Clinical research in developmental neuropsychology is radically changing due in part to the availability of instruments that are being technologically refined for pragmatic use with different age levels of populations starting with fetal life. The key to making a systematic investigation of mapping brain function onto structure during development in order to correlate cortical processes in the functional organization of the brain lies in the combination of imaging techniques (MRI, PETT, ^{1}H-MRS) together with functional source localization (Hillyard, 1987) and neuropsychological measurement (Magnun, Hillyard, & Luck, 1993; Posner & Rothbart, 1992; Taylor et al., 1984).

The horizons that lie ahead for developmental neuropsychological research will be shaped chiefly through these technological innovations. These include imaging of in vivo brain chemistry, metabolism, and physiology by quantifying individual ($N = 1$) maturational changes in cerebral functioning via mapping brain function onto structure. A radically new database from which to make generalizations about normal brain–behavior relationships in the developing infant will come about through more refined observations and accurate measurement regarding structure, function, and metabolic requirements of the brain during development.

A current review of the literature of developmental psychology and developmental neuropsychology reveals a lack of replication in many studies. Research on normal brain–behavior relationships in infants and young children are beginning to fill in the gaps in our knowledge.

Despite the impressive existing array of technological capabilities for measurement, a major aspect is missing. Measurement of the brain's sensory, motor, and cognitive processes provides only indirect assessment of task performance. It is now possible to map brain function onto structure by bringing together neuropsychological assessment data about structural changes and correlating structural damage with change in cerebral function and altered cortical processes. Various determinants, which can be quantitatively measured and correlated, will allow more accurate description of the maturational changes in cerebral function with reasonable behavioral correlates. Cognitive tasks administered during physiological neuroimaging measurements allow for clinical and experimental investigation of specific variables affecting regional brain activity involved in cognitive information processing (Chugani & Phelps, 1986; Gur & Reivich, 1980; Posner & Petersen, 1990; Risberg & Ingvar, 1973; Roland, Eriksson, Widen, & Stone-Elander, 1989; Sergent et al., 1992). These studies have demonstrated specific behavioral effects of cognitive tasks on regional CNS activation (Wheless et al., 2004; Flagg et al., 2005; Sakari et al., 2002).

Conclusion

Relatively little is known about the normal developing brain with respect to higher cortical function development, especially during early infancy. Recent studies, NIH Brain Project (BRIN database) and neurotechnologies discussed have begun to make an impact on this situation. Significant information on the development of healthy normal brain–behavior functions is emerging from combined efforts using imaging methods with reveal structure; neuropsychological assessment techniques (which determine outcome of neurological function); neural source localization techniques (which can identify the site of those neural populations that subserve specific brain functions); and metabolic and spectral measurements (PETT and MRS) of human physiology (metabolic tissue competency) (Gallen et al., 1993; Kwong et al., 1992; McCarthy et al., 1993; Phelps et al., 1986; Shulman et al., 1993; Taylor et al., 1984; Giedd et al., 1999;Chang & Walsh, 2003; Ross et al., 2003).

Standardized quantitative in vivo correlations of structure, function, metabolism, brain electrical activity, and neuropsychological factors are leading toward a different and more accurate

data and knowledge base, enabling developmental scientists and clinicians to approach this area with a greater depth in their understanding of the development of higher cortical functions from a normal developmental perspective. The possibility now exists of linking knowledge regarding brain structure, function, and cerebral physiology with quantitative measurement techniques in a standardized fashion for gathering data so as to produce the needed correlation lacking in previous research studies concerning developing brain structures, function, and normal versus aberrant higher cortical processes in infants and children. The implications for future treatment and clinical prevention strategies are encouraging.

The role for the profession of clinical pediatric/child neuropsychology is very bright and filled with great promise of advancing the science, practice, and more importantly, the health and well-being of children; and information to assist families and caregivers involved in their lives. It is with regard to the above statement that we the authors hope this chapter will provide some use.

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Neuropsychology of Child Psychopathology

MICHAEL G. TRAMONTANA, STEPHEN R. HOOPER,
TIFFANY WATTS-ENGLISH, TYWANDA ELLISON,
AND T. CARTER BETHEA

Introduction

Our chapter in the earlier editions of the *Handbook* (Tramontana & Hooper, 1989; 1997) opened with a series of questions. We asked, What is the relationship between brain dysfunction and psychopathology in childhood? Does it depend on the extent or type of brain dysfunction? What about the age or other attributes of the child at the time of onset? How might environmental factors potentiate the child's risk? Are certain forms of psychopathology more likely to arise than others? Does the form of psychopathology change over time? There were other questions raised, namely, Is brain dysfunction more likely in certain psychiatric disorders or behavioral syndromes than others? Does its presence explain the form of psychopathology manifested? How important is it relative to other factors contributing to the child's disturbance?

These questions remain pertinent in underscoring the complexity of the topic. Clearly there are mental, emotional, and behavioral sequelae for the child who has sustained brain damage or who shows an anomalous course of brain development. In many instances, such problems may persist and significantly impede the child's overall adjustment. What is not so clear is how often this occurs and the precise factors that influence it.

Conversely, there is little disagreement that there are multiple etiologies for psychopathology in childhood and that, in many cases, brain dysfunction can play an important contributing role. How often this is the case, however, is far from clear. Estimates of prevalence have varied greatly according to the methods of analysis and samples selected for study.

The foregoing should again help to define the scope of this chapter. We will begin with a review of the key early studies in this area that provided the foundation for examining the role and prevalence of brain dysfunction in child psychopathology. Next, we will consider various models and mechanisms by which these relationships may be appreciated and conceptualized more fully. There is an updated summary of research findings pertaining to particular categories of child psychopathology from which exciting developments continue to unfold and some new areas are explored. Lastly, we will highlight what we consider to be some of the

MICHAEL G. TRAMONTANA • Departments of Psychiatry and Neurology, Vanderbilt University, Nashville, Tennessee 37240. STEPHEN R. HOOPER, TYWANDA ELLISON, AND T. CARTER BETHEA • Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27599. TIFFANY WATTS-ENGLISH • Department of Psychiatry and Behavioral Sciences, Duke University, Durham, North Carolina 27708.

major theoretical and methodological issues that will relate to further advances in this area, with respect to both research and practice.

Foundations: Review of Early Studies

Psychiatric Sequelae of Childhood Brain Dysfunction

The presence of brain dysfunction in childhood is associated with a greater risk for the development of a psychiatric disorder, far more so than with other physical handicaps (Brown, Chadwick, Shaffer, Rutter, & Traub, 1981; Rutter, Graham, & Yule, 1970; Seidel, Chadwick, & Rutter, 1975; Shaffer, 1978). Moreover, the effects can persist and impede the child's long-range adjustment in many important respects (Breslau & Marshall, 1985; Milman, 1979; Shaffer et al., 1985).

One of the best investigations on this topic came from the well-known Isle of Wight epidemiological studies of school-aged children by Rutter and his colleagues (Rutter et al., 1970). Using multiple assessment procedures, and controlling for rater bias, Rutter et al. found that about 6–7% of the general population of children studied had a psychiatric disorder consisting of some persistent emotional, behavioral, or social disability. The rate was nearly twice that (11.5%) for children having chronic handicapping physical conditions not involving the brain. This group consisted of children with disorders such as asthma, diabetes, heart disease, or orthopedic deformities, as well as diseases of the spinal cord or peripheral nervous system. In contrast, the rate of psychiatric disorder was over five times higher (34.3%) in their neuroepileptic group consisting of all children ranging from 5 to 14 years of age with cerebral palsy, epilepsy, or some other frank neurological disorder above the brain stem. Even when eliminating all cases who had an IQ of 85 or less (as low IQ, itself, was found to be associated with an increased risk for psychiatric disorder), the rate of psychiatric disorder was still twice as high in the neuroepileptic group than in the "other physical handicap" group.

Among children in the neuroepileptic group, psychiatric disorders were more likely in cases with seizures, more severe or widespread brain impairment, lower IQ, and other functional handicaps (e.g., reading deficits). An exception was in the case of children with extremely incapacitating conditions. For them the rate of psychiatric disorder was actually *less*, suggesting that protective factors may have been operating when dealing with a profound level of disability.

In a further study, Seidel et al. (1975) were better able to control for the possibility that overt stigmata, such as crippling, may have been associated with the higher rate of psychiatric disorder that Rutter et al. found in their neuroepileptic group (neither obvious crippling nor other overt stigma was common in their "other physical handicap" group). Here, they compared two groups of children with visibly crippling conditions who were alike in all respects except for the presence of brain damage. All children ranged from 5 to 15 years of age and had an IQ of 70 or higher. The two groups were matched in terms of age, sex, psychosocial factors, as well as the degree of physical disability. Again, based on both teachers' questionnaire responses and psychiatric ratings, the rate of disorder was about twice as high for children with cerebral disorders (mostly cerebral palsy) than for the group with noncerebral or peripheral conditions (including muscular dystrophy, polio, or spina bifida).

Clearly, the studies by Rutter et al. (1970) and Seidel et al. (1975) provided a strong case that an increased risk for psychiatric disorder was associated with the presence of brain damage in childhood. Neither study demonstrated a causal relationship, however. Although the neurological conditions of the brain-damaged groups typically had an early onset that probably preceded the appearance of any psychiatric disorder, one still could argue that the relationship was merely coincidental. That is, some common vulnerability (whether it be genetic, congenital, or environmental), which may have predisposed a child to cerebral damage, may also have led independently to psychiatric or behavioral disturbance. A more convincing case for the existence of a causal relationship would come from demonstrating that previously normal children with *acquired* brain injuries are more likely to develop subsequent psychiatric disorders.

Children suffering from accidental head injury represent an excellent group for examining this question. However, a complicating

factor is that they often do not constitute a random sample of the general population. These children, especially those suffering from mild as opposed to severe injuries, may show *preexisting* problems with impulsivity, aggression, and attention-seeking behavior that make them more susceptible to accidental injury (Klonoff, 1971). The families of these children, as a group, also differ from the general population in that they show more parental illness and mental disorder, more social disadvantages, and less adequate supervision of the child's play activities. Thus, the absence of adequate controls in many early studies reporting intellectual impairment and behavioral disturbance following head injury made it impossible to determine whether the psychological sequelae stemmed directly from cerebral damage rather than preexisting difficulties (Rutter, Chadwick, & Shaffer, 1983).

One of the best controlled examinations of this topic comes from the prospective studies of head-injured children by Rutter and his colleagues (Brown et al., 1981; Chadwick, Rutter, Brown, Shaffer, & Traub, 1981; Chadwick, Rutter, Shaffer, & Shrout, 1981; Rutter, Chadwick, Shaffer, & Brown, 1980). Children ranging from 5 to 14 years of age who had experienced closed head injuries of sufficient severity to result in a posttraumatic amnesia (PTA) of 7 days or more were compared with a group of children having less severe head injuries (i.e., those with a PTA of less than 7 days but at least 1 hour). In addition, these groups were compared with a matched control group of hospital-treated children also suffering severe accidents, but with orthopedic rather than cranial injuries. There were 28 children in each group. All children were studied prospectively at 4 months, 1 year, and 2½ years after their injuries. An important feature of this study was the care taken to determine the children's behavior before their accidents. This was done in an unbiased fashion by interviewing parents immediately after their child's injury, but *before* the child's postinjury psychiatric condition could have been known.

The children with milder head injuries had a higher rate of preinjury behavior problems than the other groups. The rate did not change significantly postinjury (roughly 10–18%). By contrast, children with severe head injuries did not differ from controls in their preinjury behavior, but they showed more than double the rate of psychiatric disorder at 4 months and at each subsequent follow-up period. This was true even when children with psychiatric disorders prior to their accidents were eliminated from the study, thereby focusing specifically on the comparative rate of new psychiatric disorders arising over the course of the follow-up period. Head-injured children tended to show greater impairment on timed visual–spatial and visual–motor tests than on verbal tests, but, apart from this, no pattern of cognitive deficit specific to head injury was identified. Likewise, the types of psychiatric disorder among the head-injured children were very similar to those found in controls. The only exception was in the case of grossly disinhibited social behavior, which was present only in children with very severe head injuries, and may have been linked directly to frontal lobe dysfunction.

Children with head injuries showed an increased risk for psychiatric disorder regardless of the age, sex, or social class of the child—factors that ordinarily show a striking mediating effect in the general population. Clearly, the risk was greater among those children with histories of preaccident behavior disorders as well as those experiencing various psychosocial adversities within their homes, but the effects were additive rather than interactive. Thus, although psychiatric disorders in childhood have a multifactorial etiology, the evidence from this series of studies indicated that brain injury can play an independent role.

An especially interesting finding was that Brown et al. observed a weaker and less consistent dose–response relationship between severity of head injury and behavior changes than was found in the case of intellectual impairment arising subsequent to injury. Also, the relationship between intellectual impairment and behavior disorder was weak and was limited mainly to the early postinjury period. This raised the possibility that modifying factors, such as secondary family reactions, may play a critical role in the development of persistent behavior problems.

In another landmark study, Fletcher, Ewing-Cobbs, Miner, Levin, and Eisenberg (1990) compared 45 children, aged 3–15, with mild, moderate, and severe head injuries on standardized measures of behavioral adjustment. Behavior ratings were obtained at the time of injury (based on preinjury features) and at 6 and 12 months postinjury. Cases with

preexisting neurological disorder, developmental disabilities, or behavioral disturbance were excluded. Children with severe head injuries significantly declined and differed from the other two groups over the 12-month follow-up on ratings of their adaptive behavior. They were also rated as having more school problems and as engaging in fewer social activities. Children with mild and moderate injuries did not differ from each other nor from average normative levels. No distinctive type of behavior disorder was found to be associated with head injury. Also, as was observed in the Brown et al. study, behavioral and cognitive outcome measures were related more strongly to indices of initial injury severity than to one another—again suggesting some dissociation or independence in the mechanisms for behavioral and cognitive outcomes. Subsequent studies by Levin et al. (2004) and Kirkwood et al. (2000) also reported a dissociation of cognitive and social–emotional outcomes, suggesting that this has held up as a fairly robust pattern in the findings.

Each of the preceding studies dealt with children having known or documented brain damage. A number of early studies in this area also sought to determine whether a demonstrable relationship existed between psychiatric disorder and so-called "soft" neurological signs or minimal brain dysfunction (MBD) in childhood. That question had been the subject of much debate, as some investigators regarded sensory or motor phenomena such as mirror movements, dysdiadochokinesis, dysgraphesthesia, and choreic or athetoid movements to be of little diagnostic value when elicited from patients not having a discrete neurological disorder (e.g., Ingram, 1973). Others (e.g., Rutter et al., 1970) argued that it was important to differentiate among different types of signs labeled as "soft." Some were considered soft because (1) they run a developmental course in which the signs may subside as the child grows older; (2) they are rather prevalent among otherwise normal children (with estimates ranging from 8 to 14%); and (3) they have no clear locus of origin and their neuropathological significance is obscure (Shaffer, 1978). They should not be viewed as necessarily unreliable, however, and may show consistency over time (Shapiro, Burkes, Petti, & Ranz, 1978). Other signs, such as minor reflex or tone asymmetries, would tend to be less reliable because they are more difficult to detect.

Overall, the research on neurological soft signs was found to show that (1) there is a relationship with age, IQ, and sex (with soft signs occurring more frequently among boys, younger children, and those with lower IQ); (2) they are more prevalent among children with psychiatric disorders and learning disabilities; (3) they are related to indices of emotional immaturity and dependency in childhood; and (4) the relationship with hyperactivity, aggression, and antisocial conduct is less clear, although soft signs were commonly seen among children who were described as impulsive and distractible (Shaffer, 1978; Shaffer, O'Connor, Shafer, & Prupis, 1983).

In a well-controlled prospective study, Shaffer and his colleagues (Shaffer et al., 1985) examined the comparative outcomes in adolescence of children with early soft neurological signs. Children with ($n = 83$) and without ($n = 79$) documented soft signs at age 7 received a careful follow-up assessment at age 17. Compared with controls, adolescents with early soft signs had lower IQs and were more likely to have a psychiatric disorder with symptoms of anxiety, withdrawal, and depression. These findings mainly pertained to boys, but all of the girls in this study with an anxiety–withdrawal diagnosis in adolescence showed early soft signs. The relationship was independent of IQ and, when taken together with the presence of anxious-dependent behavior at age 7, the presence of early soft signs was strongly predictive of persistent problems with anxiety and withdrawal. However, no relationship was found with attention-deficit disorder or conduct disorder.

This was a little different than the pattern that Rutter et al. (1970) found in the Isle of Wight study. Children with frank brain damage showed a heterogeneous range of psychiatric disorders without specific features. Hyperactivity and psychosis were more prevalent in their neuroepileptic group, but these appeared to be related more specifically to the presence of mental retardation. However, besides Shaffer et al. (1985), a number of other early studies found an association between brain dysfunction and the *type* of behavior problems manifested, although the exact findings varied according to factors such as age and chronicity.

In a 5-year follow-up of children and adolescents with physical disabilities secondary to brain damage, Breslau and Marshall (1985) found that problems with social isolation rather than aggression were more likely to persist. Dorman (1982) found that the relationship between neuropsychological impairment and the type of behavior problems observed varied as a function of age in a group of boys with school problems and no known neurological disorder. Whereas poor neuropsychological performance was associated with externalizing behavior problems in younger (7–8) boys, it was associated with internalizing symptoms in the older (9–14) subjects. The implication was that internalizing rather than externalizing symptoms are more distinctively tied to brain dysfunction as the child grows older and encounters repeated failure and loss in self-esteem. The relationship eventually may become blurred as other factors enter and play a more important determining role in perpetuating the youngster's poor adjustment. Moreover, this process may be accelerated in cases with early histories of more severe disorder. That was suggested in a study by Tramontana, Hooper, and Nardolillo (1988) in which the presence of neuropsychological deficits was found to be associated with more extensive behavior problems among psychiatrically hospitalized boys, regardless of factors such as IQ and SES. However, the relationship mainly applied to *younger* (8–11) as opposed to older (12–16) subjects and specifically involved *internalizing* rather than externalizing behavior problems. We will discuss more fully in a later section the question of the relationship between brain dysfunction and the form of psychopathology manifested.

Taken together, these early studies provided strong evidence that brain dysfunction in childhood is associated with an increased vulnerability for psychiatric disorder. The relationship appeared to hold both for children with frank brain damage and those with so-called soft neurological signs. The risk was noted to be greater for children with more severe neurological disorders (with the possible exception of those with extreme impairment), especially when accompanied by low IQ and other neuropsychological deficits. It may also be compounded by factors such as psychosocial adversity and any preexisting tendencies toward behavioral or emotional disturbance. The relationship is not trivial, as the evidence suggested that the effects persist and influence long-range outcomes (Breslau & Marshall, 1985; Milman, 1979; Shaffer et al., 1985). This body of research certainly underscored the importance of accurate detection of the functional deficits and behavioral liabilities in the brain-impaired child as a first step in limiting the risk for the later development or progression of a psychiatric disorder (Tramontana, 1983).

Prevalence of Brain Dysfunction Among Children with Psychiatric Disorders

Estimates of prevalence have varied greatly both as a function of the methods and criteria used in identifying brain dysfunction and in terms of differences in the subject samples selected for study. For example, the prevalence would be rather low if one simply used the presence of positive findings on a routine neurological examination as the basis for establishing neurological involvement. However, such an approach would likely be associated with an underestimation of prevalence because normal neurological examinations are common even among children with documented histories of head injury, encephalitis, or epilepsy (Rutter, 1977).

The findings from early studies that incorporated noninvasive neurodiagnostic methods, such as computed tomography (CT), were mixed. Much of the research examined children with autism or other major developmental handicaps for whom enlarged ventricles and other structural deficits were found in subgroups of the subjects examined (Campbell et al., 1982; Caparulo et al., 1981; Damasio, Maurer, Damasio, & Chui, 1980; Rosenbloom et al., 1984). Reiss et al. (1983) likewise found ventricular enlargement in a controlled comparison of CT scans for a mixed group of child psychiatric patients. The results were of questionable generalizability, however, because their subjects also tended to be among the more impaired with respect to psychiatric and developmental status, with about half of the group having a confirmed neurological disorder and a third showing mild mental retardation.

In another study, CT scans were compared across four subgroups of subjects with childhood disorders (infantile autism, attention-deficit disorder, Tourette's syndrome,

and language disorder) and a control group of medical patients without documented neurological disorder (Harcherik et al., 1985). No differences were found among the groups with respect to ventricular volume, right–left ventricular ratios, asymmetries, or brain density. The study was very well done from a technical standpoint, but the interpretation of its results were complicated by several factors. The groups were not matched in age, and the neurological status and level of functioning of subjects (including controls) were poorly specified.

The interested reader should refer to a review by Kuperman, Gaffney, Hamdan-Allen, Preston, and Venkatesh (1990), which provides an overview of the earlier findings obtained in various child psychiatric samples using other brain imaging techniques, including magnetic resonance imaging (MRI) and positron emission tomography (PET). There have also been more recent reviews by Eliez and Reiss (2000) and Hendren, De Backer, and Pandina (2000).

Prevalence rates using neuropsychological criteria have tended to be comparatively high. For example, Tramontana, Sherrets, and Golden (1980) found a high rate of neuropsychological abnormality in a mixed sample of child and adolescent psychiatric patients without known brain damage. The subjects consisted of 20 hospitalized cases ranging from 9 to 15 years of age who had neither a history of brain damage nor positive findings on a routine neurological examination. From a neuropsychological standpoint, these were "nonreferred" cases for whom brain dysfunction was not suspected. Nonetheless, about 60% of the subjects showed at least mild impairment (with 25% showing more definite impairment) according to the normative rules established by Selz and Reitan (1979) on the Halstead–Reitan Neuropsychological Battery (HRNB). Impaired performance on the HRNB was associated with lower IQ and was more prevalent among cases whose psychiatric disorders were of at least 2 years in duration and who had a lag of at least 2 years in academic achievement.

A key question had to do with the meaning of the neuropsychological abnormalities found in the Tramontana et al. study, especially as to whether they indeed reflected underlying brain anomalies that were missed in a routine neurological examination or review of history.

This was explored in a subsequent study with a similar sample of subjects in which neuropsychological results were compared with various quantified indices of brain structure examined through CT (Tramontana & Sherrets, 1985). Psychiatric cases without suspected brain damage again were found to show a high rate of neuropsychological abnormality (at least 50%) when examined on either the HRNB or the Children's Revision of the Luria–Nebraska Neuropsychological Battery (LNNB-C; Golden, 1981). Impaired performance was more likely among boys, younger subjects, and those with more chronic psychiatric histories. Interestingly, impaired performance was not associated significantly with IQ. The overall results of the two test batteries correlated quite highly, but it was the LNNB-C that corresponded more closely with CT scan results. Specifically, impairment on the LNNB-C was associated with *smaller* ventricular size and *less* density variability, suggesting the possibility of anomalous brain maturation. It was also associated with lesser regional densities, especially within the right cerebral hemisphere.

The absence of control subjects in the foregoing study did not permit one to conclude that the CT results, although associated with neuropsychological abnormality, were themselves necessarily abnormal according to any established normative standards. Nonetheless, the findings were noteworthy in that the presence of neuropsychological deficits among the psychiatric cases did correspond to variations in brain structure and were not merely the product of nonneurological factors. This was a remarkable finding, especially in view of the restricted range of the sample because of the exclusion of cases having documented neurological involvement.

Taken together, the studies reviewed in this section indicated that the question of prevalence is inextricably tied to the methods and criteria used in assessing brain dysfunction. Children with cerebral palsy, epilepsy, and other obvious neurological conditions (as evidenced on routine neurological examination) probably comprise less than 5% of the total population of children with psychiatric disorders (Rutter, 1977). The rate is uncertain, but obviously would be higher if one were to include children with clumsiness, language impairment, mental retardation, and learning

disabilities (Gualtieri, Koriath, Van Bourgon-dieu, & Saleeby, 1983; Rutter et al., 1970) for whom there is at least the *suspicion* of underlying brain damage. The rate is higher still if one further includes children for whom brain damage is not suspected, but who nonetheless may show various neuropsychological deficits when they are comprehensively assessed. Although these deficits may have a relationship with underlying structural factors (see Tramontana & Sherrets, 1985), they cannot be interpreted as reflecting brain damage per se. Rather, they should be viewed as functional impediments, some of which may be tied to abnormalities in brain structure or maturation, which may play a role in the development of child psychiatric disorders. As was noted before, the presence of neuropsychological deficits was found to be associated with more extensive behavior problems among younger boys, regardless of factors such as IQ, SES, and whether the deficits can be linked specifically with a history of brain injury (see Tramontana et al., 1988). Neuropsychological deficits are important in their own right, as they appear to comprise an important index of increased psychiatric risk.

Some outcomes in this population appear to be predicted especially well by neuropsychological assessment. This was seen in a study that examined the determinants of academic achievement within a sample of hospitalized child psychiatric cases, all of whom had been referred for neuropsychological assessment because of suspected learning impediments or other deficits (Tramontana, Hooper, Curley, & Nardolillo, 1990). Achievement test scores were examined as a function of six variables: IQ, socioeconomic status, age, sex, neuropsychological status, and severity of behavioral disturbance. Neuropsychological status proved to be the best predictor overall. It even surpassed IQ, whether examined alone or in combination with demographic and behavioral variables. This differed from what is ordinarily the case with normal school-aged children, for whom IQ and socioeconomic status are generally the most important determinants of academic performance and educational outcomes. The findings underscored the relevance of neuropsychological factors in understanding the academic deficits of children with significant mental or emotional disturbance.

Conceptual Issues

A number of mechanisms have been suggested whereby brain dysfunction may lead to psychopathology, although evidence as to their relative contribution is uncertain (Rutter, 1977, 1983). These include (1) behavioral disruption that arises directly from abnormal brain activity; (2) a heightened exposure to failure, frustration, and social stigma related to associated disabilities; (3) the possible effects of brain damage on subsequent temperament and personality development; (4) adverse family reactions ranging from overprotection to scapegoating; (5) the child's own reaction to being handicapped and its effects on his/her actual capacity to cope and compete; and (6) possible adverse effects from treatments themselves (e.g., recurrent hospitalization) that may restrict normal activities and socialization. Thus, the effects may be direct or indirect. They may also be conceptualized as transactional and dynamic.

Direct effects, for example, would be seen in the case of frontal lobe damage resulting in pronounced impulsivity and social disinhibition. Other examples include organically induced psychosis or episodic aggressiveness that may arise from certain temporal lobe disorders. In other cases, brain dysfunction may play more of an *indirect* etiological role, one that essentially sets the stage for other factors to come into play that, themselves, act to produce an emotional or behavioral disturbance and perhaps further aggravate existing functional difficulties (Tramontana, 1983).

For example, brain dysfunction may give rise to learning disabilities that, in turn, render the child more likely to encounter frustration and failure upon entry into school. This may lead to disruptive behavior problems consisting of inattention, anger, and defiance as an eventual (albeit indirect) outcome. There may also be a compounded difficulty in those areas of performance that have become anxiety-laden and aversive. Parents and teachers may come to view the child as lazy, apathetic, or otherwise difficult, and thereby generate expectations that would only serve to perpetuate the existing problems. The latter represents a *transactional* effect, namely, the differential reinforcement elicited from significant others by the brain-impaired child and his/her particular deficits. Lastly, the behavior are *dynamic* rather than static. Just as

the primary symptoms of brain dysfunction may change over time, so too they may vary in terms of their developmental significance and the reactions that they elicit from others, including the child. The pattern of behavioral disturbance itself may vary so that, for example, instead of hypersensitivity, defiance, and misconduct, the child later may show apathy, withdrawal, and resignation.

Besides the issue of how brain dysfunction may lead to psychopathology in childhood, there is also the question of what form manifest symptoms may take. Earlier thinking (e.g., Bakwin & Bakwin, 1966; Wender, 1971) suggested that the behavioral manifestations of cerebral dysfunction, whatever the cause, were uniform and comprised a rather distinctive behavioral syndrome consisting of symptoms such as hyperactivity, inattention, and impulsivity. However, there is little evidence of such a behavioral stereotype for the brain-impaired child. Symptoms such as hyperactivity, inattention, and impulsivity do not distinguish children with either frank brain damage (Brown et al., 1981; Rutter et al., 1970) or soft neurological signs (Shaffer et al., 1983, 1985). This is not to say that such symptoms are not common among brain-impaired children—they are, but they are also common features of psychiatric disorder in general, regardless of whether neurological abnormality is present (Rutter, 1977).

One may argue that the relationship between brain dysfunction and psychopathology in childhood is *nonspecific* (e.g., Boll & Barth, 1981). That is, the presence of brain dysfunction, regardless of its pattern or cause, may contribute nonspecifically to a lowered adaptive capacity and a greater likelihood of exposure to adverse experiences. In this view, brain dysfunction operates indirectly by creating the functional deficits that make successful adjustment more difficult for the child. Any of a variety of behavioral and emotional problems may result, with the distribution of specific symptoms being similar to what is seen generally among children with psychiatric disorders.

There was some support for this position. In the Isle of Wight study (Rutter et al., 1970), children with brain damage showed a heterogeneous range of psychiatric disorders with no specific features. Except for cases falling at the extreme of incapacity, the risk was greater in children with more severe injuries, seizures, and lower IQ. Also, apart from the possible relationship between frontal lobe dysfunction and gross social disinhibition, Brown et al. (1981) found no psychiatric symptoms that were specific to children with closed head injuries. From a different perspective, Tramontana and Hooper (1987) found that groups of adolescents with either conduct disorder or major depression were virtually identical in their pattern of neuropsychological functioning. Thus, although these represented two very different types of psychopathology (each falling at opposite ends of a continuum of externalizing and internalizing symptoms, respectively), there were no distinctive neuropsychological features. Kusche, Cook, and Greenberg (1993) found executive function deficits to be related to child psychopathology, in general. The latter finding relates to an important issue that will be discussed more fully after we review findings in various categories of psychopathology.

On the other hand, it was noted before that a history of soft neurological signs or the presence of neuropsychological impairment tended to be associated specifically with *internalizing* behavior problems consisting of symptoms such as anxiety, depression, and withdrawal (Shaffer et al., 1985; Tramontana et al., 1988). In addition to cognitive deficits, children with physical disabilities secondary to brain damage are likely to show persistent problems with social isolation, but problems with aggression are less likely to persist (see Breslau & Marshall, 1985). Also, results from a study of children with localized (penetrating) head injuries showed a significant association between the presence of depression and lesions specifically involving right frontal and left posterior cerebral regions; this was true regardless of the child's age, sex, and psychosocial factors (Rutter, 1983). No relationship was found between the site of injury and symptoms such as hyperactivity, inattention, aggression, or antisocial conduct. Thus, although we are not suggesting the existence of an alternative behavioral stereotype, it may be that internalizing rather than externalizing symptoms are more distinctively tied to brain dysfunction in childhood, perhaps especially in terms of longer-range outcomes. These may emerge as the child grows older, continues to struggle with chronic handicaps, and encounters repeated failure and loss of self-esteem.

A major stride in linking behavioral outcomes with a particular pattern of neurodevelopmental deficits came from the work of Rourke and associates (Rourke, 1987, 1989; Rourke & Fuerst, 1991) on the syndrome of nonverbal learning disability (NLD). This was an empirically derived model that posited a relationship, not only between nonverbal deficits and certain academic learning difficulties (especially in mechanical arithmetic), but to limitations in a broader range of psychosocial and adaptive functioning. Because of difficulties processing nonverbal cues, children with NLD may be viewed as overrelying on rote verbal memory skills in their coping. The capacity to adapt to novel situations suffers, as does the ability to relate in a flexible and appropriate fashion. Significant deficits in social perception, judgment, and interactional skills are likely. These, in turn, may lead to a tendency toward social withdrawal or isolation—i.e., *internalizing* forms of psychopathology—as age increases. The NLD syndrome may arise from various causes, although a disruption of cerebral white matter was postulated as necessarily involved. However, apart from its anatomical underpinnings, the model is significant for positing a relationship between a particular syndrome—defined neuropsychologically—and a *specific* pattern of child psychopathology.

Findings in Selected Categories of Child Psychopathology

This section provides a review of neurodiagnostic findings in major categories of child psychopathology. Included here are findings pertaining to autism, attention-deficit/hyperactivity disorder, conduct disorders, affective disorders, and anxiety disorders. We have also added a section on childhood schizophrenia based on new developments in that area. With this we will return to the question of specificity, i.e., the extent to which different patterns of brain dysfunction are associated with specific types of psychopathology.

Autistic Disorder

Autism is a behavioral syndrome characterized by impairment in reciprocal social interactions, poor communication abilities, and a pronounced restriction of interests and activities. It is distinct from mental retardation, although the majority of children with autism carry a concurrent diagnosis of mental retardation (Folstein & Rutter, 1987). It is also distinct from a number of other childhood disorders, including schizophrenia (Green et al., 1984) and developmental receptive language disorder (Lincoln, Courchesne, Kilman, Elmasian, & Allen, 1988).

A variety of etiological processes for autism have been proposed but none has gained widespread acceptance to date. However, regardless of the specific anomaly or etiology that is hypothesized, the general consensus is that some form of brain impairment is involved (Damasio & Maurer, 1978). Children with autism tend to have a significant prenatal or perinatal history and show a high rate of soft neurological signs (Jones & Prior, 1985). Garreau, Barthelemy, Sauvage, Leddet, and LeLord (1984) further noted that the presence of neurological impairment was associated with an earlier onset of autistic features. An increased incidence of seizure disorders has been found in this population, particularly with increasing age, with approximately 25–30% of children with autism developing seizures by adulthood (Deykin & MacMahon, 1979). However, this finding may be applicable mainly to cases with IQs below 70 (Bartak & Rutter, 1976).

A number of brain imaging studies have documented the presence of structural abnormalities in autism, although the precise findings have varied greatly. Some of these have identified left hemispheric and, in some cases, bilateral defects, particularly involving frontal and temporal regions (Gillberg & Svendsen, 1983; Maurer & Damasio, 1982). Findings suggestive of reversed asymmetry have been noted as well (e.g., Hier, LeMay, & Rosenberger, 1979). Other findings have included anomalies involving various subcortical structures, such as the basal ganglia (Jacobson, LeCouteur, Howlin, & Rutter, 1988), brain stem (Gaffney, Kuperman, Tsai, & Minchin, 1988), and cerebellar regions (Courchesne, Yeung-Courchesne, Press, Hesselink, & Jernigan, 1988; Gaffney, Tsai, Kuperman, & Minchin, 1987). There have also been studies in which structural abnormalities were identified but no specific localizable pattern emerged (e.g., Balottin et al., 1989; Caparulo et al., 1981). Some studies have found no

structural abnormalities of any kind (e.g., Harcherik et al., 1985; Prior, Tress, Hoffman, & Boldt, 1984).

Electroencephalographic (EEG) abnormalities have also been identified, with a prevalence of 40–50% found in one study of autistic children (Tsai, Tsai, & August, 1985). The abnormalities generally have been varied, although a pattern consisting of excessive slow-wave activity and decreased alpha bilaterally has been reported (Cantor, Thatcher, Hrybyk, & Kaye, 1986). Small (1975) suggested that, among autistic children, the presence of a normal EEG is associated with a higher IQ and a more favorable developmental course. Auditory- and visual-evoked potentials (EP) have also been observed to be impaired in autistics, with auditory processing capabilities evidently more impaired than visual processing (Courchesne, Lincoln, Kilman, & Galambos, 1985; DeMyer, Hingtgen, & Jackson, 1981). Moreover, Courchesne et al. (1985) have identified two endogenous components of EP, Nc and P3b, that appear to be associated with abnormal neural responses among autistics, responses involving attention and general cognition to important external information.

Other assorted neurobiological findings have been reported. Using positron emission tomography (PET), Rumsey, Rapoport, and Sceery (1985) found diffusely elevated glucose utilization but no clear focal abnormalities among autistic adults. Coleman, Romano, Lapham, and Simon (1985) found no consistent differences in a postmortem cell count of selected left hemispheric regions between an autistic adult and a control subject. However, Bauman and Kemper (1985) found anatomical differences involving the forebrain and cerebellum in a postmortem comparison of a 29-year-old autistic man and a 25-year-old normal. The investigators suggested that the cerebellar abnormalities were of unknown etiology but probably were acquired early in development, possibly at or before 30 weeks of gestation.

Numerous neuropsychological aspects of autism have been reported. These have included poor motor imitation abilities (Jones & Prior, 1985), disproportionate impairment in sequential processing abilities (Tanguay, 1984), poor recall of meaningless material (Ameli, Courchesne, Lincoln, Kaufman, & Grillon, 1988), and, as a group, IQ scores that are significantly lower than normals but comparatively higher than mentally retarded children (Kagan, 1981). The neurocognitive profiles of autistic children can also be rather varied when compared with children with mental retardation (Fein, Waterhouse, Lucci, & Snyder, 1985), although a pattern indicative of better visual–perceptual abilities than language abilities typically has been asserted (e.g., Lincoln et al., 1988). However, as seen below, the latter finding can vary greatly with the specific characteristics of the autistic children studied.

Many of the neuropsychological studies have been directed toward investigating the presence of lateralized deficits in autistic children. The findings have included a reversal of ear advantage for speech sounds (i.e., left ear rather than right) on dichotic listening tasks (Blackstock, 1978; James & Barry, 1983; Prior & Bradshaw, 1979); increased prevalence rates of left and mixed handedness of about 20 and 34%, respectively (Soper et al., 1986); and performance profiles on neuropsychological test batteries suggestive of predominantly left hemispheric dysfunction (Applebaum, Egel, Koegel, & Imhoff, 1979; Dawson, 1983; Hoffman & Prior, 1982). In a study by Dawson, Finley, Phillips, and Galpert (1986), there was evidence of an atypical pattern of hemispheric specialization, with about 70% of the autistic children showing right hemispheric dominance for speech. However, the investigators noted that many of the autistic children exhibited bilateral rather than unilateral dysfunction, and they also speculated that their dysfunction might involve subcortical as well as cortical levels. This interpretation is consistent with the findings in some of the brain imaging studies reported above.

Regardless of the issue of lateralization, the presence of disturbed language abilities in autism is critical. Bartak, Rutter, and Cox (1975) postulated that a language disability constitutes a necessary condition for the development of this disorder. They observed that autistic children showed more deviant language development, a severe comprehension deficit, and deficits in the social usage of language. Moreover, the degree of language impairment appears to be strongly predictive of the child's prognosis (Wing, 1971). Although related to childhood language disorders, the communication deficits in autistic children are qualitatively different from those seen in developmental dysphasia or acquired aphasia

(Arnold & Schwartz, 1983). Semantic, prosodic, and pragmatic aspects of language development (i.e., possible right hemispheric contributions) may be particularly deviant (Cohen, Caparulo, & Shaywitz, 1976; Ferrari, 1982; Prizant, 1982; Simon, 1975; Tager-Flusberg, 1981).

There have been other deficits posited as playing a key role. One of these involves the lack of a "theory of mind" among individuals with autism (Baron-Cohen, Leslie, & Frith, 1985). In this model, persons with autism are described as having significant deficiencies in their understanding of the thoughts and feelings of others. They have trouble attributing independent mental states to themselves or others and in predicting or explaining their respective actions. As a result, they experience difficulties in core areas defining the disorder (i.e., socialization, communication, imagination). Frith (1989) further hypothesized a core deficit having to do with "central coherence." In this model, individuals with autism demonstrate an imbalance in the integration of information. Whereas normal individuals will attack a problem by scanning "the big picture" (i.e., global features) before focusing on details (i.e., local features), persons with autism tend to do the opposite—focusing on the local features but missing the global ones. This can be manifested in both verbal tasks (verbal interactions, language pragmatics, story narratives) and nonverbal tasks (puzzle completion, block designs, facial recognition). It may also account for some of the strengths (i.e., areas of unusual focus) as well as weaknesses seen in this disorder.

Recent research in autism has benefited from the use or more rigorous and consistent approaches to assessment and diagnosis (Volkmar, Lord, Bailey, Schultz, & Klin, 2004). There has also been an emphasis on multiple conceptualizations of the disorder requiring study from multiple perspectives (Tonn & Obrzut, 2005) and on viewing the condition more in terms of subdivisions falling within an *autism spectrum* (Gillberg, 2002).

IQ or general level of functioning has been an important confounding factor in studies of neuropsychological deficits in autism. For example, Meyer and Minshew (2002) found little evidence of cognitive differences between cases diagnosed with High Functioning Autism (HFA) versus Asperger's syndrome (AS). Similarly, Miller and Ozonoff (2000) found no differences between cases with HFA and AS once IQ was controlled, leading them to conclude that Asperger's syndrome may be little more than "high-IQ autism."

As a group, children with HFA have provided a "cleaner" subject pool with whom to study specific neuropsychological deficits unconfounded by the general retardation characteristic of their lower functioning counterparts. Problems establishing lateral hand dominance have been found, especially in children with early language delays (Escalante-Mead, Minshew, & Sweeney, 2003), as well as weaknesses in both fine-motor and gross motor coordination (Mayes & Calhoun, 2003). Language impairment, when present, is milder and likely to involve more specific aspects of higher communication. Whereas deficits in basic phonological and syntactic processes may be absent, pragmatic impairments are nearly always present (Escalante-Mead et al., 2003; Tager-Flusberg, 1993). Findings involving visual–spatial functioning have been mixed, although a relative strength in Block Design performance has been a frequent finding regardless of IQ level (Happé, 1994). However, as suggested by the Coherence Model noted above, this may have more to do with the intensive processing of part stimuli rather than the development of a gestalt. Deficits in gestalt processing and other aspects of NLD have been linked with the cognitive profiles of children with AS (e.g., Rourke, 1989). Memory findings have also been mixed. Whereas Minshew and Goldstein (2001) found adolescents and young adults with HFA to be normal on measures of short-term memory and paired-associate learning, they did less well than controls in story recall, list learning, complex figure memory, and maze learning. Poor memory for faces has also been reported (Hauck, Fein, Maltby, Waterhouse, & Feinstein, 1998).

Recent studies have given particular attention to the study of executive functions in HFA. Deficits have been reported in problem solving, planning, flexibility/set-shifting and have been viewed as playing a major role in the disorder (e.g., Ozonoff et al., 2004). Deficits in the area of inhibition have not been observed consistently, however, suggesting that this component of executive functioning often may be spared. Kleinhans, Akshoomoff, and Delis (2005) found that children with HFA performed poorly

on a composite measure of executive functioning even after adjusting for baseline cognitive abilities. Similar findings were reported by Hooper, Poon, Marcus, and Fine (2006) comparing children with HFA to carefully matched controls on the NEPSY.

Overall, as we concluded in our earlier review (Tramontana & Hooper, 1989; 1997), the research on autism provides a variable picture with respect to neurobiological and neuropsychological features. Some autistic children show evidence of lateralized dysfunction involving the left cerebral hemisphere, although this by no means is a definitive characteristic of the syndrome (Fein, Humes, Kaplan, Lucci, & Waterhouse, 1984). The same is true with respect to a number of other neurodiagnostic findings reported. Newer research has paid more attention to diagnostic rigor and consistency while also viewing autism more as a multifaceted spectrum of disorders. There has also been greater appreciation of issues such as general level of functioning or IQ and how these can influence the nature and extent of deficits that are observed. Poor communication skills (particularly in pragmatic language), overly narrowed perceptual processes, and deficits in various aspects of executive functioning have been among the more distinctive features. However, regardless of how the underlying mechanisms are conceptualized, there probably is not another category of child psychopathology for which the evidence of a neurobiological foundation is more compelling than in the case of autism.

Attention-Deficit/Hyperactivity Disorder (ADHD)

This is another syndrome in which an organic etiology is commonly assumed. Earlier thinking linked ADHD and MBD because of the purported behavioral similarities between children with ADHD and those with documented brain damage (Strauss & Lehtinen, 1947). However, problems in documenting the presence of underlying brain dysfunction (e.g., Rutter, 1983; Taylor, 1983) led to a more descriptive approach in conceptualizing the disorder. Children with ADHD have been characterized as showing inattention, impulsivity, and overactivity (Douglas, 1980, 1983); a deficit in self-directed instruction (Kendall & Broswell, 1985); poor self-regulation of arousal, particularly in meeting environmental demands (Douglas, 1983); and deficiencies in rule-governed behavior (Barkley, 1981a,b) or inhibition Barkley, 1997).

There have been numerous debates over diagnostic criteria, issues of heterogeneity, and whether ADHD is truly distinguishable from other forms of disruptive behavior problems. Nonetheless, it has been one of the most commonly diagnosed child psychiatric disorders (Mattison et al., 1986). The current diagnostic criteria [*Diagnostic and Statistical Manual of Mental Disorders (DSM-IV),* American Psychiatric Association, 1994] recognize three subtypes of ADHD: Predominately Inattentive; Predominately Hyperactive–Impulsive; as well as a Combined subtype.

There have been a number of theories regarding the neurological basis of ADHD (Riccio, Hynd, Cohen, & Gonzalez, 1993). To date, the evidence is strongest with respect to implicating frontal lobe dysfunction in the increased distractibility and impulsive orienting reactions to irrelevant stimuli often seen in children with ADHD (Passler, Isaac, & Hynd, 1986; Stuss & Benson, 1984; Zambelli, Stamm, Maitinsky, & Loiselle, 1977). Various specific patterns of localization have been proposed, including frontal regions anterior and medial to the precentral motor cortex (Mattes, 1980), as well as frontolimbic pathways (Lou, Henriksen, & Bruhn, 1984; Newlin & Tramontana, 1980). Abnormalities in the fronto-striatal circuit have been implicated in magnetic resonance imaging (MRI) studies demonstrating volume reductions in the prefrontal cortex and striatum (Aylward et al., 1996; Castellanos et al., 2001, 2002; Durston et al., 2004) and in single photon emission computed tomography (SPECT) and positron emission tomography (PET) studies demonstrating decreased metabolism and perfusion of prefrontal areas (Kim, Lee, Shin, Cho, & Lee, 2002).

There has been a clustering of findings specifically implicating right frontal dysfunction. Voeller and Heilman (1988) found ADHD children to be markedly deficient on a task of motor persistence, a deficit ordinarily associated with right frontal lobe impairment. In a subsequent study (Voeller, Alexander, Carter, & Heilman, 1989), the motor persistence of children with ADHD improved significantly with the administration of methylphenidate. Similarly, in a

study of regional cerebral blood flow (Lou et al., 1984), children with ADHD exhibited lower perfusion rates in the region of the caudate, an anterior subcortical structure known to be involved in the motor regulatory system. Metabolic levels normalized with the administration of methylphenidate and then declined as the medication wore off. A subsequent study by Lou, Henriksen, Bruhn, Borner, and Nielsen (1989) replicated the earlier findings, but pinpointed the right striatal region as specifically deficient in children with ADHD. As before, the administration of methylphenidate resulted in a normalization of metabolic activity. From a different perspective, Hynd, Semrud-Clikeman, Lorys, Novey, and Eliopulos (1990) found that ADHD children did not demonstrate the typical right frontal asymmetry on MRI found in normal controls. The finding lacked specificity, however, in that both ADHD and dyslexic cases had significantly smaller right frontal widths relative to normal control children.

In an effort to integrate the various neurobiological findings on ADHD, Castellanos and Tannock (2002) have proposed a model which posits a specific abnormality in reward-related circuitry that leads to shortened delay gradients (and associated symptoms of inattentiveness, hyperactivity, and impulsivity), deficits in temporal processing (causing high intertrial variability), and impaired working memory. Striatal abnormalities and catecholamine dysregulation, particularly dopamine, are thought to play important contributing roles.

Studies of ADHD employing functional magnetic resonance imaging (fMRI) have further implicated altered patterns of underlying neural activation as observed under various task-dependent conditions (e.g., Bush et al., 1999; Vaidya et al., 2005). Some promising findings have emerged from recent studies exploring neurofeedback training evaluated through fMRI (Beauregard & Levesque, 2006; Fuchs et al., 2003). Improvements were observed in neural systems mediating selective attention and response inhibition, suggesting that some of the underlying abnormalities in individuals with ADHD may be amenable to nonpharmacologic interventions.

Barkley, Grodzinsky, and Du Paul (1992) reviewed a total of 22 neuropsychological studies of frontal lobe functioning in children with attention-deficit disorder, with and without hyperactivity. Tests of response inhibition were found to discriminate hyperactive cases from normals, although many measures presumed to assess frontal lobe dysfunction were not reliably sensitive to deficits in either ADD group. Numerous inconsistencies were noted, many of which were seen to reflect methodological differences across studies.

Barkley (1997) has advanced a highly influential theory of ADHD. It postulates that the primary deficit in ADHD does not directly involve attention, per se. Rather, it involves a deficit in *behavioral inhibition*, which is seen as causing impairments in four areas of executive functioning: working memory, internalization of speech, self-regulation of affect/motivation/arousal, and reconstitution. In the model, none of these areas can function properly without adequate inhibition and behavioral control. Poor attentiveness is viewed as a result rather than the cause. However, this perspective would be less applicable to ADHD cases of the Predominately Inattentive Type.

Support for Barkley's position has come from studies of ADHD confirming the presence of deficits in behavioral inhibition and various executive functions as outlined in the model (e.g., Berlin, Bohlin, Nyberg, & Janols, 2003; Stevens, Quittner, Zuckerman, & Moore, 2002). However, there have been some conflicting findings as well. Confirmatory findings were found by Scheres et al. (2004) but not after controlling for age and IQ. Geurts, Verte, Oosterlaan, Roeyers, and Sergeant (2005) found that children with ADHD (Combined Type) performed poorly on two measures of inhibition (one involving a prepotent response and another of an ongoing response) but failed to demonstrate deficits on measures of working memory, planning, or cognitive flexibility. Nor was there a difference in executive functioning when comparing ADHD children with Combined versus Predominately Inattentive symptoms. Wu, Anderson, and Castiello (2002) did find evidence of poor performance on measures of executive functioning but interpreted this as due more to deficits in speed of processing. Overall, although impairments in various aspects of executive functioning may play an important role in ADHD, deficits specifically involving inhibitory controls appear to be a more basic and consistent part of the condition.

With respect to attention factors, deficits in sustained attention rather than selective attention are more commonly reported in ADHD (Barry, Klinger, Bush, & Hawkins, 2001; Wu et al., 2002). Noting that underscores the importance of differentiating specific underlying components of attention when referring to attention deficits in ADHD and other conditions.

A major theoretical stride in the conceptualization of attention processes came from the work of Mirsky and associates and their empirically derived model of attention (Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991). Based on factor-analytic studies of tests considered to assess some aspect of attention, Mirsky et al. conceptualized attention in terms of four components or elements: (1) focus-execute, (2) sustain, (3) encode, and (4) shift. Each of these is seen as supported by distinct brain regions that, if damaged, will result in specific deficits in the particular attentional processes involved. Because so many brain regions come into play, it explains why attentional disturbances of one form or another are commonly seen in different types of brain injury or disease. This is a heuristically powerful model that permits a far more refined conceptualization of brain–behavior relationships in a functional domain that holds such a key role in childhood behavior disorders and psychopathology.

There have been a few studies examining possible neuropsychological features associated with oppositional-defiant disorder (ODD), a disruptive behavior disorder that is often comorbid with ADHD. Studies of children with ODD alone have not provided consistent evidence of deficits in inhibition or executive functioning. When examined together with ADHD, it has not been found to impart an additional impairment in executive functioning beyond that which comes from the burden of ADHD alone (Berlin et al., 2003). However, in a study of preschool boys, clinic-referred cases with ODD were more likely to generate aggressive solutions and to encode social information less accurately when compared to normal controls (Coy, Speltz, DeKlyen, & Jones, 2001).

There has also been some attention given to Tourette's syndrome (TS), another condition that has a heightened comorbidity with ADHD. Cirino, Chapieski, and Massman (2000) examined the executive functioning of 57 children having TS with and without ADHD. No significant differences were found. However, Harris et al. (1995) found that cases with only TS versus those with TS and ADHD or ADHD alone had fewer executive function problems and higher perceptual organization scores.

Conduct Disorders

Research in this broad category of child psychopathology has been beset with a number of problems. First, as a diagnosis, it pertains to a very heterogeneous range of disturbances in which the manifestation of socially unacceptable behavior is the primary common feature. Second, the bulk of research has focused on adolescents, particularly the juvenile offender. If one excludes children with ADHD, as early-onset conduct disorders seldom occur in the absence of ADHD (Pliszka, 1999), little is known with respect to the neurological and neuropsychological features of conduct disorders manifested at early ages. Third, youngsters with conduct disorders have a higher risk for accidental head injury (Lewis, Pincus, & Glaser, 1979; Lewis & Shanok, 1977; Pincus & Tucker, 1978); thus, although neurological abnormalities may be seen on examination, they may be the product—not the cause—of the initial conduct disorder. This problem obviously is compounded by the emphasis on studying older as opposed to younger conduct-disordered subjects. With these limitations in mind, the findings for this general category of psychopathology are summarized below.

A number of studies have reported abnormal neurological findings in youngsters with conduct disorders (Elliott, 1982; Korhonen & Sillanpaa, 1976; Krynicki, 1978; Woods & Eby, 1982). Electrophysiological studies (Coble et al., 1984; Elliott, 1982; Krynicki, 1978; Luchins, 1983) have found EEG sleep abnormalities, specifically in the expression of slow-wave (delta) activity (Coble et al., 1984); seizure activity that may contribute to recurrent and unprovoked rage attacks (Elliott, 1982); and in some cases, frontal lobe paroxysmal activity, particularly in conduct-disordered adolescents with a significant history of assaultive behavior (Krynicki, 1978). The latter finding bears some relationship to the work of Woods and Eby (1982) and Pontius and Ruttiger (1976) who postulated a delay in the development of normal

inhibitory mechanism (i.e., frontal lobe functions) in repetitively aggressive youngsters.

Children with conduct disorders have been reported to show a higher incidence of episodes of disturbed consciousness and, as already noted, to suffer more head injuries than other children (see Lewis & Shanok, 1977; Lewis et al., 1979; Pincus & Tucker, 1978). However, they have not been found to differ from normal controls in terms of perinatal problems, except for more frequently being small for gestational age (McGee, Silva, & Williams, 1984). These findings further serve to suggest that the neurological features in some of these children may postdate the initial onset of their conduct disorders.

Other studies of conduct disorder have found decreased glucose metabolism in frontal regions (Pliszka, 1999; Raine Stoddard, Bihrle, & Buchsbaum, 1998) and a relationship between frontal trauma and impulsive aggression (Brower & Price, 2001). Li, Mathews, Wang, Dunn, and Kronenberger (2005) found a group of adolescents with conduct disorder who demonstrated abnormalities in the arcuate fasciculus, a region extending from the frontal to temporal lobes, possibly giving rise to a "disconnection" between these cortical areas. Using fMRI, King, Blair, Mitchell, Dolan, and Burgess (2006) identified a common neural circuit that may mediate both aggressive and compassionate behaviors.

From another neurobiological perspective, a risk for conduct disorder may be associated with reduced autonomic reactivity, resulting in an underlying pathological fearlessness. For example, children with conduct disorder have been found to have a blunted startle response compared to controls (van Goozen, Snoek, Matthys, van Rossum, & van Engeland 2004). Not only did low basal salivary cortisol correlate with general conduct-disordered symptoms in children, but the relationship was found to be even stronger for aggressive symptoms (Oosterlaan Scheres & Sergeant, 2005).

Conduct-disordered youngsters have been found to have a high rate of learning disabilities (Cannon & Compton, 1980; Robbins, Beck, Pries, Jacobs, & Smith, 1983; Zinkus & Gottlieb, 1978), as well as more generalized problems with language performance (Funk & Ruppert, 1984; Stellern, Marlowe, Jacobs, & Cossairt, 1985; Wardell & Yeudall, 1980). This appears to apply to both nonincarcerated (Robbins et al., 1983) and incarcerated (Cannon & Compton, 1980) populations.

These findings suggest that the presence of cognitive impairments, perhaps particularly of a verbal nature, places the youngster at risk for acting out impulsively when placed in frustrating or provocative social situations. The degree of impulsivity per se is unrelated to either the type or the number of crimes committed by delinquent youth (Oas, 1985). Rather, it may be that the presence of faulty capacities in verbal reasoning and judgment, along with impulsivity, is a necessary ingredient in the production of chronic antisocial conduct. Thus, although unrelated to the degree of impulsivity, the presence of at least a 15-point inferiority in Verbal IQ versus Performance IQ on the Wechsler Intelligence Scale for Children—Revised (WISC-R) has been found to be predictive of recidivism in adjudicated white delinquent boys (Haynes & Bensch, 1981). Lahey et al. (1995) also found that low Verbal IQ was related to persistence of conduct disorder, especially when accompanied by a parental history of antisocial behavior.

Some studies have examined the relative effects of language and executive function deficits. Linz, Hooper, Hynd, Isaac, and Gibson (1990) selected 20 adolescents meeting DSM-III criteria for conduct disorder from a juvenile evaluation center and compared them with 20 normal adolescents on nine Lurian tasks measuring behaviors attributed to frontal lobe functioning. Differences were obtained on the verbal conflict and verbal retroactive inhibition tasks, although these disappeared when controlling for receptive vocabulary. Cole, Usher, and Cargo (1993) examined the relationship between cognitive factors and risk for disruptive behavior disorders in a sample of 82 preschoolers. Verbal, visuospatial, and executive function abilities were examined in terms of their relationship with labeling emotions and behavioral control. Difficulties in both verbal and visuospatial processes were associated with a higher risk for behavioral difficulties. Additionally, whereas verbal abilities contributed to the prediction of emotion labeling accuracy, executive functions were predictive of behavioral control. The latter was also noteworthy for the examination of behavioral risk in a younger-aged sample. Tramontana and Hooper (1987) found that 18% of a group of hospitalized adolescents with conduct disorder,

none of whom had a documented history of brain injury, were classified as impaired on the LNNB. Problems with expressive language were especially prominent.

Further investigations into the pattern of neuropsychological deficits in conduct disorders have produced mixed results. Berman and Siegal (1976) found that delinquents performed more poorly than normal controls on virtually every task of the HRNB. Whereas prominent deficits were observed in tasks requiring verbal mediation, concept formation, and perceptual organization, only minimal difficulties were found in memory and gross motor coordination. Brickman, McManus, Grapentine, and Alessi (1984) found that more violent youth tended to show more impairment on the LNNB than their nonviolent counterparts, with Expressive Speech and Memory being the distinguishing summary scales. This was true with respect to both male and female offenders. These findings were similar to the results of earlier studies by Lewis, Shanok, and Pincus (1982) and Voorhees (1981). However, in controlling for the presence of psychosis and a history of neurological disorder, Tarter, Hegedus, Alterman, and Katz-Garris (1983) failed to find differences in neuropsychological, intellectual, and psychoeducational performance across groups of adolescent offenders differing with respect to their type of offense (i.e., violent, nonviolent, sexual).

Giancola and Mezzich (2000) conducted one of the only studies to examine language functioning and conduct disorder in females. They studied adolescent girls, aged 14–18 years, with and without conduct disorder. Compared to a control group, it was found that the girls with conduct disorder demonstrated poorer language and executive functioning. Poor language competence was related to antisocial behavior, but the relationship depended on the presence of poor executive functioning as well.

The previously noted problems limit the generalizations that one can make with respect to this category of child psychopathology. It is probably fair to say that, as a group, youngsters with conduct disorders tend to have more limited verbal abilities, are more prone to impulsive reactions, and have a heightened rate of neurological signs (these, however, may arise secondarily as consequences of their behavior disorders). Newer studies have begun to identify underlying neural abnormalities and possible biopsychosocial risk factors in some cases.

Affective Disorders

Depressed children have an increased frequency of neurological soft signs relative to normal controls (MacAuslan, 1975). Conversely, as was noted earlier, adolescents with early soft signs were more likely to have a psychiatric disorder characterized by symptoms such as anxiety, withdrawal, and depression (Shaffer et al., 1985); social isolation rather than aggression was found to be more likely to persist in children with physical disabilities secondary to brain damage (see Breslau & Marshall, 1985); and internalizing rather than externalizing symptoms have been found to be more clearly tied to neuropsychological impairment in psychiatrically hospitalized boys (Tramontana et al., 1988). Also, apart from gross social disinhibition, it will be recalled that depression was the only psychiatric symptom that bore a specific relationship to lesion localization in the series of studies on head injury by Rutter and his colleagues (Rutter, 1983). Thus, depression appears to be an important feature of the brain-impaired child, perhaps especially in terms of long-range outcomes.

Much of the early neuropsychological investigation into childhood depression focused specifically on the question of lateralization of dysfunction. Research demonstrating the specialized role of the right cerebral hemisphere in the processing of human emotion and affective cues, along with reports of right hemispheric dysfunction in adults suffering from depression (Tucker, 1980), prompted inquiries into the existence of such relationships in children. A number of studies reported impaired nonverbal abilities relative to verbal abilities in children with depression. For example, Kaslow, Rehm, and Siegel (1984) found that higher scores on the Children's Depression Inventory (CDI) were associated with poor performance on the WISC-R subtests of Block Design, Coding, and Digit Span in a mixed group of children with depression. No significant relationships were found for WISC-R Vocabulary or the Trail Making Test of the HRNB. Blumberg and Izard (1985) found a similar pattern of results using the Peabody Picture Vocabulary Test and WISC-R Block Design, with the CDI again

serving as the index of depression. In both studies, girls were found to perform more poorly than boys on Block Design. However, the findings in these studies constituted very weak evidence of lateralized right hemispheric dysfunction, as the obtained pattern of results simply may have reflected the differential sensitivity of performance measures to the effects of depressed concentration and motor speed.

Some studies reported improvements on neuropsychological measures suggestive of both right hemispheric and frontal lobe dysfunction subsequent to treatment with antidepressant medication (Brumback, Staton, & Wilson, 1980; Staton, Wilson, & Brumback, 1981; Wilson & Staton, 1984). Specifically, Staton et al. found that remission of melancholic symptoms was associated with improved performance on WISC-R Similarities, Comprehension, Block Design, and Coding, as well as on the Matching Familiar Figures Test, the Category Test of the HRNB, and the Visual Reception Subtest of the Illinois Test of Psycholinguistic Abilities. Although the localizing significance of this pattern of results is uncertain, two children in the study reportedly had a mild left-sided motor deficit which also seemed to improve subsequent to antidepressant treatment.

Rochford, Weinapple, and Goldstein (1981) found greater EEG variance in the right hemisphere than in the left in a heterogeneous group of depressed adolescents. This pattern was distinct from that of normal controls, who demonstrated about equal hemispheric variance, and from adolescents with paranoid symptomatology, who exhibited greater variance in the left hemisphere. However, Knott, Waters, Lapierre, and Gray (1985) found no evidence of specific hemispheric abnormalities in a comparison of EEG patterns and auditory-evoked potentials in matched pairs of siblings discordant for affective disorder. EEG abnormalities in REM sleep latencies have also been described in depressed adolescents (Mendlewicz, Hoffman, Kerkhofs, & Linkowski, 1984).

Another perspective comes from the model of nonverbal learning disability of Rourke and associates noted earlier and its relationship to internalizing forms of psychopathology, including depression. Rather than lateralized dysfunction per se, NLD is seen as more directly related to the extent of white matter disruption present. Lateralized findings may be explained, however, by the higher ratio of white matter to gray matter in the right versus left hemisphere (Rourke, 1987).

The evidence has been mixed with respect to how well various biological markers for depression identified in adults apply to children (Birmaher et al., 1996). These include indices such as hyposecretion of growth hormone, dysregulation of the hypothalamic-pituitary-adrenal axis, abnormal serotonergic function, and sleep disturbance. Kolvin and Sadowski (2001) noted that there are probably more similarities than differences in the neuropsychological functioning of depressed children and adults. However, younger children tend to express distress and negative affect through externalizing symptoms probably because of their still immature language abilities (Cataldo, Nobile, Lorusso, Battaglia, & Molteni, 2005). Depressed children and adolescents otherwise have been found to exhibit a pattern of conservative response style, delayed response initiation, slow reaction times, as well as attention difficulties (Cataldo et al., 2005).

There have been some promising leads in the study of bipolar affective disorder (BPD) in childhood. In their review of the literature, Bearden, Hoffman, and Cannon (2001) reported on a variety of structural brain abnormalities and corresponding functional deficits in BPD. Rather than lateralized dysfunction, emphasis was given to the investigation of anterior brain regions and associated functions involving attention and memory, speeded information processing, executive functioning, and affect regulation. Neuroimaging findings have implicated the presence of decreased activity in the prefrontal cortex along with subcortical abnormalities (Castillo, Kwock, Courvoisie, & Hooper, 2000; Chang et al., 2004; Courvoisie et al., 2004). Using fMRI, Dickstein et al. (2004) found selective deficits specifically involving attention set-shifting and visuospatial memory.

Geller and DelBello (2003) reported that children with BPD have a high rate of comorbidity (89% overall), with the more frequent comorbid conditions including ADHD and learning disabilities. Lagace, Kutcher, & Robertson (2003) found that adolescents with BPD had organizational, spatial, and meta-cognitive deficits that may contribute to a specific learning disability in math. Even the children of parents with BPD have been found to have a cognitive

profile involving relatively weaker nonverbal than verbal abilities (Decina et al. 1983). Similar patterns were noted above with respect to unipolar depression, suggesting that, regardless of the issue of lateralization, deficits in nonverbal processing may constitute an important component of risk for affective disorders, in general.

Anxiety Disorders

The relationship between anxiety and neuropsychological factors is complex. Some discussions of anxiety within the context of neuropsychological functioning have dealt with the disruptive effects it may exert on formal test performance. Thus, anxiety may be viewed as a source of interference contributing to false-positive diagnosis or invalid inferences of neuropsychological deficit, especially in situations with high base rates of psychiatric disorder (Tramontana, 1983).

Alternatively, anxiety may arise as a secondary reaction in situations in which a child's deficits are challenged or brought to the fore (Tramontana & Hooper, 1989). For example, a language-impaired child may react with avoidance or withdrawal in situations requiring spoken communication. In this case, the anxiety is symptomatic of a breakdown in the child's ability to cope effectively with his/her deficits. The child's actual performance may suffer from disruptive or distracting emotional reactions. Worse yet, the underlying deficits may become compounded in time if the child's anxiety leads to a chronic avoidance of appropriate learning and stimulation experiences.

Another perspective has to do with more of a direct relationship between neuropsychological processes and particular forms of anxiety disorder. For example, right parahippocampal abnormality has been posited in the case of panic disorder (George & Ballenger, 1992). A disturbance in a network of structures involving the basal ganglia, thalamus, as well as orbitofrontal and anterior cingulate cortex has been hypothesized as a pathogenic mechanism in obsessive–compulsive disorder (Modell, Mountz, Curtis, & Gredens, 1989). Studies of obsessive–compulsive disorder (OCD) in adolescents have noted frontal and basal ganglia dysfunction (Cox, Fedio, & Rapoport, 1989; Behar et al., 1984). There were also findings suggestive of possible right hemispheric dysfunction (visual–spatial

deficits; left hemibody signs) together with larger ventricular–brain ratios on CT and a greater frequency of age-inappropriate synkinesias relative to matched controls (Rapoport et al., 1980; 1981).

Savage and Rauch (2000) suggested that the emergence of OCD in childhood may parallel the development of prefrontal functioning. Problems with cognitive flexibility may be present, although deficits on formal measures of executive functioning have not been consistently observed (Beers et al., 1999). In a review, it was further noted that memory deficits are not common in OCD unless they are dependent on organizational strategies (Greisberg & McKay, 2003).

Posttraumatic stress disorder (PTSD) has been an especially noteworthy area of emerging interest. In one of the key studies with adults, the attention and memory performance of military personnel with and without PTSD was compared (Vasterling, Roost, Brailey, Uddo, & Sutker, 1994). Those with PTSD were impaired on tasks of attention and mental control, especially where a visual component was involved. Poor organization on a constructional task and a greater susceptibility to proactive interference in verbal learning were also noted. The findings were seen as consistent with neurobiological models of PTSD emphasizing the role of hyperarousal and frontal–subcortical systems. Other findings have specifically related extreme stress with damage to the hippocampus and with associated deficits in memory function. Bremner et al. (1995) found that Vietnam combat veterans had a statistically significant 8% smaller right hippocampal volume on MRI relative to a matched comparison group. Deficits in short-term verbal memory were also noted.

Taken together, the implication from the foregoing studies was that some of the memory disturbances seen in PTSD may result from experientially induced structural changes rather than primarily reflecting the effects of defensive processes. In the previous edition of the *Handbook*, this was seen as an exciting line of inquiry that hopefully would be extended to victims of child abuse and trauma as well.

A key program of research in this area has come from De Bellis and colleagues in their study of PTSD associated with childhood maltreatment. De Bellis and Thomas (2003) postulated that traumatic stress can bring about alterations affecting endocrine,

neurotransmitter, and immune systems. Dysregulation of these three neurobiological stress systems, in turn, will influence arousal levels, stress reactions, as well as behavioral and emotional regulation, and may activate many of the symptoms experienced by children with PTSD. These alterations may also lead to abnormalities of the developing brain. Neuroimaging studies examining children and adolescents with PTSD secondary to maltreatment have found significant structural differences compared to healthy controls, including decreased volumes in prefrontal cortical and white matter regions, the right temporal lobe, and midsagittal area of the corpus callosum; decreased cortical, intracranial, and total brain volumes; along with enlarged right, left, and total lateral ventricles (De Bellis et al., 1999; 2002). Gender differences emerged, with boys exhibiting smaller volume of the corpus callosum compared to girls (De Bellis et al., 1999). Also, in a comprehensive study of neuropsychological functioning in maltreated children with PTSD, it was found that they performed more poorly than matched controls in the areas of attention, learning and memory, visual–spatial organization, as well as problem solving, abstract reasoning/executive functioning (Beers & De Bellis, 2002). This will continue to be an important and exciting area of inquiry.

Childhood Schizophrenia

Previous editions of this text did not include a section dealing with this category of child psychopathology. Although it has long been assumed that neurocognitive impairments are central features of schizophrenia in childhood (as is certainly true in the case of adults), the number of studies examining this important issue was limited (Suhulz, 1998). Below are some of the newer developments and insights that have appeared.

Early-onset schizophrenia (i.e., positive symptoms by age 12) has been found to be associated with problems involving lower IQ (Basso, Nasarallah, Olsen, & Bornstein, 1997), attention (Asarnow, Tanguay,. Bott, & Freeman, 1987; Zahn et al., 1998), motor functioning (Walker, Savoie, & Davis, 1994), smooth-pursuit eye movement (Iacono & Clementz, 1993), as well as processing speed, memory, new learning, abstract reasoning, and executive functions (Green & Nuechterlein, 1999; Heinrichs & Zakzanis, 1998;

Kenny et al., 1997). Deficits in short-term and delayed verbal recall have been implicated as being among the most prominent cognitive problems (Saykin et al., 1994; Seidman et al., 2002). In addition, there are indications that early-onset versus adult-onset schizophrenia results in greater cognitive impairment and social–emotional problems, as well as greater overall severity and resistance to treatment (Hollis, 2000).

Some of the above deficits have been found in children prior to the onset of psychotic symptoms (Cornblatt, Obuchowski, Roberts, Pollack, & Erlenmeyer-Kimling, 1999; Walker, Kestler, Bollini, & Hochman, 2004). Asarnow (1999) reported that neurodevelopmental variations can be seen in nearly 80% of children later diagnosed with schizophrenia, with particular deficits in language development and working memory. Similar neurocognitive profiles have been found in nonpsychotic first-degree relatives of those with schizophrenia (Asarnow et al., 2002; Green, Nuechterlein, & Breitmeyer, 1997), including children genetically at risk for schizophrenia versus normal controls (Davalos, Compagnon, Heinlein, & Ross, 2004).

A question as to specificity can again be raised, however. In a study by McClellan, Prezbindowski, Breiger, and McCurry (2004), children with early-onset psychotic disorders were found to exhibit deficits in IQ, attention, verbal learning/memory, and social understanding, although few group differences were apparent when they were compared to children with bipolar affective disorder. On the other hand, Oie and Rund (1999) found that adolescents with schizophrenia showed more of a generalized pattern of neuropsychological impairment when compared to adolescents with ADHD or normal controls. Those with schizophrenia versus ADHD were more impaired especially on measures of abstraction, visual memory, and motor functioning. Perhaps the distinction has something to do with the seriousness of the psychiatric conditions compared, with more widespread problems being present when one form or another of psychosis is involved.

Brain imaging studies have revealed a number of abnormalities, including progressive ventricular enlargement, reduction in total brain and thalamic volume, changes in temporal lobe structures, and reductions in frontal metabolism (Hendren et al., 2000). Adolescence appears to be an important period of differential brain

development in schizophrenia, with the progressive reduction of temporal lobe structures becoming more apparent at that time, as suggested in a study of children with early-onset schizophrenia (average onset at 10.4 years) versus healthy controls (Jacobsen, et al., 1998). In another study by this group of investigators (Giedd et al., 1999), differential nonlinear progression of brain abnormalities were seen during adolescence, with the total cerebrum and hippocampus decreasing and lateral ventricles increasing over this period for cases with childhood-onset schizophrenis versus matched normal controls. In addition, these developmental changes for the group with childhood-onset schizophrenia appeared to reach a peak by early adulthood. Thus, the findings for childhood schizophrenia point to an evolving and degenerative pattern of changes as it progresses over the period from childhood through adolescence.

Implications for Research and Practice

In the previous edition of the *Handbook*, we concluded that there was little evidence of specificity in the type or pattern of brain dysfunction associated with different categories of child psychopathology. For example, evidence suggestive of left hemispheric dysfunction was seen in disorders as dissimilar as autism and conduct disorder; frontal lobe dysfunction was reported in one study or another for almost all of the categories of disturbance considered. The same can be said with respect to deficits involving executive functioning or various aspects of attention. Given the extent of overlap, noting the presence of underlying deficits such as these does little to identify something distinctive in relation to the particular form of psychopathology involved.

As before, we can cite methodological factors as contributing here, as the picture surely was blurred by differences across studies in subject samples and the methods used in identifying brain dysfunction as well as inconsistencies in the use of diagnostic criteria. Some of the confusion can be attributed to the faulty application of neuropsychological inference in a number of studies. It is one thing to use neuropsychological test data in making inferences regarding lesion localization for cases with documented brain damage; however, even here issues such as individual differences in compensatory development can obscure specific brain–behavior relationships (e.g., Bigler & Naugle, 1985; Rourke, Bakker, Fisk, & Strang, 1983). In any event, one is certainly on rather weak ground in making such inferences on cases for whom there is no corroborating evidence as to the presence or localization of injury. A relatively low Verbal IQ is not necessarily associated with left hemispheric impairment, nor is impulsivity necessarily a sign of frontal lobe dysfunction. Although such results may have localizing significance, they can easily be attributed to nonneurological factors as well.

Another issue has to do with the level of analysis when examining psychopathology. There is a good deal of variance or heterogeneity within each of the major categories of child psychopathology even when diagnostic criteria are applied rigorously. This is not only due to differences in background variables or comorbid conditions, if any, but also in terms of differences in the pattern of primary symptoms themselves. We should not expect the neurodiagnostic findings to be any more cohesive or specific than the behavioral syndrome to which they refer. Distinguishing subtypes, as in the case of ADHD, gets at this somewhat. Perhaps even better would be an analysis at the level of individual symptoms or combinations of symptoms. For example, what underlying neural differences might there be in children presenting with inattentiveness and persistent obsessive worry versus poor attentiveness alone? Would the presence of, say, poor set-shifting capacity in the obsessive child help to make the distinction? Conversely, are there neural commonalities for children presenting with symptoms such as inattentiveness or impulsivity regardless of their general psychiatric diagnosis? Or, from yet another perspective, how can a common finding, such as a deficit in executive functioning, be further specified to allow meaningful distinctions when manifested in a child with autism versus ADHD? Uncovering more specific brain–behavior relationships in this area will depend on setting the focus at a more specific level than categorical diagnosis alone.

Promising leads have emerged in each of the areas reviewed. To no small degree, these discoveries have come about through the incorporation of more precise brain imaging techniques (see Eliez & Reiss, 2000, and Hendren et al., 2000, for reviews). As was forecasted earlier on (Tramontana, 1983), the use of such tools

within a multimethod approach has played a vital role in the growth of new knowledge in this area. The field has progressed from examining fairly gross variations in brain structure (such as left versus right damage, ventricular size, frontal lobe injury, etc.) to the point now in which integrated neural circuits spanning multiple brain regions are more the focus of inquiry (e.g., Bush et al., 1999; Castellanos & Tannock, 2002; Vaidya et al., 2005). It is predicted that future growth will come from combining this more refined technology with more of an emphasis on individual symptom patterns as suggested above.

Also highly welcome have been the theoretical advances that have appeared. This was exemplified in the work of Rourke and colleagues on the syndrome of nonverbal learning disability—especially in terms of its hypothesized relationships with particular aspects of psychosocial functioning. There has also been the exemplary work of Mirsky and associates and their model of attention components which allows for a more precise discussion of underlying deficits in conditions in which one or more aspects of attention may be disturbed. Other notable examples have included Barkley's (1997) model of ADHD as involving a deficit in behavioral inhibition, Frith's (1989) *central coherence* model as it relates to autism, and the work of De Bellis and Thomas (2003) providing a theoretical framework for understanding neuropsychological outcomes associated with PTSD. The availability of theoretical model such as these helps to bring order to what can otherwise be a confusing body of knowledge.

Issues surrounding valid neuropsychological diagnosis with this population have been discussed elsewhere (Tramontana, 1983), and thus will not be elaborated here. Briefly, the major interpretive problem involves distinguishing the effects of *deficit versus disturbance versus delay* in the neuropsychological results of psychiatrically disordered children. The standard application of neuropsychological methods is associated with a greater likelihood of false-positive errors in diagnosis with this population. This is because a psychiatric disturbance in childhood or adolescence, in the absence of brain dysfunction, may itself produce significant impairment on many neuropsychological tests. Impaired performance could result from the disruptive effects of psychogenically based problems with anxiety, depression, or frustration tolerance. Such conditions not only may disrupt present performance, but also may have impeded the past attainment of various skills that are prerequisite to age-appropriate performance in many of the areas that are assessed. It is just as undesirable to over-diagnose brain dysfunction as it is to overlook it when it does exist. This has led some to advocate the use of more conservative detection criteria when applying neuropsychological methods in a child psychiatric population (Tramontana, 1983). At the same time, as was indicated earlier in this chapter, some outcomes in this population—such as the extent of behavioral disturbance and academic performance—can be predicted especially well by neuropsychological assessment, regardless of whether the observed deficits can be linked with a history of brain injury (Tramontana et al., 1988; 1990).

The research has documented a heightened risk for psychopathology in the child with brain dysfunction. Emphasis should be given to gaining a better understanding of what factors might curtail that risk, and thereby maximize outcomes. There is a growing understanding of the natural history of behavioral disturbances secondary to brain dysfunction. There is some indication that the relationship may weaken or grow more indirect over time, as other factors perhaps come to assume a more important role in maintaining problem behaviors (Dorman, 1982; Tramontana et al., 1988). The nature of behavioral disturbances may also show some convergence over time, with symptoms such as withdrawal and depression being among the more common outcomes associated with a history of chronic handicap (Breslau & Marshall, 1985; Shaffer et al., 1985). It is important to know more precisely how this process unfolds so that it might be redirected more positively, if not prevented. The implications for clinical practice are similar. Accurate detection of the functional deficits and behavioral liabilities in the brain-impaired child is the first step in limiting the risk for the later development or exacerbation of psychopathology. The essence of the strategy is to identify, treat early, and thereby minimize the development of secondary disturbances.

Effective intervention also entails an appreciation of what may be going on at more of an experiential or phenomenological level. For

example, a child who has suffered a serious traumatic brain injury (TBI) may be seen as exhibiting "personality changes" as a result. Temper outbursts are common and can be especially alarming to parents. However, sometimes what these may really reflect are problems with irritability or frustration that flare up when the child becomes overly fatigued or stressed by having to cope with deficits brought about by the injury. Or they may reflect personality features that have been there all along, but that have now become magnified by stress. Sometimes there can even appear to be a "deterioration" in the child's behavior or emotional status as time goes on. With cognitive recovery there can be better insight and awareness of deficits, leaving the child more susceptible to feelings of anxiety, loss, or embarrassment. Or, with improvement, may come increased demands on the child and the removal of supports or exemptions that were there before. Either way, the child may be left struggling with problems not encountered previously. Add to this the anxiety or frustration that may get triggered in the parent upon witnessing such reactions, and a fairly complex set of secondary problems can arise. Mechanisms similar to these may have been involved in the prospective studies of children with severe TBI reporting a persistence or worsening of behavioral outcomes despite cognitive improvement (Brown et al., 1981; Fletcher et al., 1990). It is important to disentangle and demystify these outcomes, helping both the child and parents recognize that some of the behaviors may be fairly normal reactions to the circumstances that have unfolded. Educating the affected parties about these relationships is an essential step in promoting a positive psychosocial recovery.

The neuropsychology of child psychopathology continues to represent an important and challenging aspect of the broader field of child neuropsychology. As we noted in previous editions of the *Handbook*, it is a complex area of investigation for the researcher and the clinician alike, as there are many factors that can obscure the study of brain–behavior relationships in child psychopathology. Hopefully, our discussion has given the reader an appreciation for both the importance and the complexity of the topic. The new findings and conceptual models that have emerged have begun to take shape in coherent patterns. We predict that the picture will continue to sharpen. This again promises to be an exciting line of inquiry offering fresh insights into the neuropsychological underpinnings of child psychopathology.

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6

Neurodevelopmental Malformations: Etiology and Clinical Manifestations

GEORGE W. HYND, ALLISON E. MORGAN, AND MELANIE VAUGHN

Neuropsychologists frequently work with patients who have specified brain lesions that produce well-documented cognitive or behavioral effects. However, for those clinicians working with school-age children or adolescents who suffer developmental disorders, the pathogenesis of cognitive and behavioral deficits may be poorly understood. It should be noted, however, that considerably more is now known about neurological anomalies than in decades past. Consequently, it is more widely recognized that knowledge of neurodevelopmental processes should underscore clinical practice (Riccio & Pizzitola-Jarratt, 2005).

This chapter reviews the anomalies of neurological development that not infrequently are seen in children and adolescents with developmental disorders. Most typically the neuropsychological manifestations of these anomalies impact on widely distributed functional systems, thus producing generalized and severe impairment. However, there are exceptions, especially with regard to anomalies of neuronal migration. Some basic understanding of these effects should aid neuropsychologists in a better conceptualization of how disorders of neurological development produce different effects than do discrete lesions of the central nervous system. There is wide variability in neuroanatomical development

and, unfortunately, there is still incomplete understanding of neurodevelopmental anomalies. Our ability to define these anomalies by pathogenesis or prognosis is greater than our ability to relate them to functional or behavioral deficits. However, it is increasingly clear that a better understanding of the brain enhances the appreciation as to relations between brain functioning and the processes and behaviors we typically assess (Reynolds & French, 2005). Essentially three categories of anomalies can be specified: (1) those incompatible with life, (2) those not necessarily incompatible with life but that severely impair functioning, and (3) those of variable consequences such that they can be asymptomatic or associated with subtle cognitive and behavioral deficits.

In this chapter, five general types of neurodevelopmental anomalies, as defined by pathogenesis, will be addressed: (1) bulk brain growth abnormalities, (2) cerebral hemisphere dysplasias, (3) cerebral cortex malformations, (4) hydrocephalus and associated anomalies, and (5) neural tube abnormalities and fusion deficits.

Abnormalities in the Bulk Growth of the Brain

The usual brain-to-body weight ratio is 1:30, but there is great variability in brain bulk that can be caused by a wide range of factors. In the middle portions of the distribution, brain size

GEORGE W. HYND, ALLISON E. MORGAN,, AND MELANIE VAUGHN • Arizona State University, Tempe, A2, 85287.

is not typically correlated with functional differences. At the extreme ends of the distribution, as in the cases of micrencephaly and megalencephaly, there are associations between brain size and behavior (Hynd & Willis, 1988).

Micrencephaly

Micrencephaly is the term for small brain size with a brain-to-body weight ratio sometimes as little as 1:100. It is diagnosed when the head circumference is less than two or three standard deviations below the mean for age and gender. The term is often used interchangeably with microcephaly, which refers to a small head vault (Aicardi, 1992; Friede, 1989). Micrencephaly, however, is the preferred term because it specifies that the cause of the small head is an abnormally small brain or cerebral hemisphere (Friede, 1989).

Individuals with micrencephaly may have a small cranial vault in contrast to a near-normal face size, thickened scalp and cranial bones, and/or folded scalp. Frequently in cases of micrencephaly, the convolutional pattern of the brain is simplified with normal, or near-normal, sized gyri that are somewhat coarsened. The basal ganglia are usually of normal size and the cerebellum may appear disproportionately large (Friede, 1989). The brain tissue often has cytoarchitectonic anomalies. Males and females seem equally affected.

Micrencephaly is sometimes associated with epilepsy and moderate to severe retardation with delayed speech and motor function. Surprisingly, however, there are patients with normal intelligence (Hecht & Kelly, 1979). The deficits in autosomal-recessive transmitted cases have been reported to be more severe than those in autosomal-dominant transmitted cases (Haslam & Smith, 1979). The expected life span for individuals with micrencephaly varies, with some individuals surviving into adulthood but many others dying young because of intercurrent disease (Friede, 1975).

A variety of causal factors have been linked with micrencephaly. It can be produced experimentally by interfering with cell replication with the greatest damage seen when the interference occurs during the period of most active replication (Friede, 1989). Micrencephaly has been associated with radiation exposure. For example, Yamazaki and Schull (1990) reported that of 205 children who were exposed in utero to the Hiroshima bombing, 7 had microcephaly with mental retardation. Whereas mothers of only 4 nonmicrocephalic children were within 1200 m of the blast's center, the mothers of all 7 of these children were within this distance.

Winick and Rosso (1969) proposed a link between malnutrition and micrencephaly. In a study of individuals who died of malnutrition in their first year, the authors found that in comparison with normally nourished children, the fatalities had severe deficits in brain weight, protein, RNA, and DNA. The authors speculated that malnutrition disrupts cell division and migration and thus leads to small brains. However, other research, as reviewed by Hynd and Willis (1988), indicates that most cases of micrencephaly are probably not the result of malnutrition because (1) moderate malnutrition seems to affect the maturation of myelinated cells rather than brain size, (2) the cerebellum may be most negatively impacted by malnutrition, and (3) rat studies have indicated that malnourishment does not slow the development of the brain to a significant extent. Friede (1989) suggests that it is difficult to test the malnutrition hypothesis because of the variability in normal human brain weights at autopsy.

Other proposed etiological factors include infection by rubella, toxoplasmosis, cytomegalic disease, and herpes simplex (Baron, Youngblood, Siewers, & Medeatis, 1969; South, Tompkins, Morris, & Rawls, 1969); prenatal exposure to toxins; and metabolic disorders such as phenylketonuria (McLone, 1982; Stevenson & Huntley, 1967). There is also evidence of a genetic basis for micrencephaly. In fact Jones (1997) lists over 40 conditions in which microenchephaly frequently occurs, including a number of deletion syndromes, Angelman syndrome, fetal alcohol syndrome and trisomy 13 and 18.

Megalencephaly

Megalencephaly was first used to describe hyperplasia of the brain involving the overdevelopment of neural tissue (Fletcher, 1900). This consists of excessive neuronal and glial elements (Menkes, 1985). There is conflicting evidence as to whether or not cell size is abnormally large. The excess tissue may result from overproduction of neurons or from reduced neuronal death (Friede, 1989). In some cases, the brains weigh

twice as much as expected for age and gender (Aicardi, 1992). Friede (1989) suggests that an adult brain weighing over 1600 g, with cerebrospinal fluid (CSF) drained and increases from edema and lesions excluded, is megalencephalic. More conservatively, Escourolle and Poirier (1973) reserve that diagnosis for brain weights over 1800 g.

Megalencephaly is sometimes used to refer to abnormally large brains that result from a variety of factors including astrocytomas, tuberous sclerosis, metabolic errors, or hydrocephalus. This is an inaccurate use of the term as the large brains in these instances are symptoms of another problem rather than the result of the overproduction of cerebral parenchyma (Hynd & Willis, 1988).

In infancy, megalencephaly may be apparent when a head of originally normal size grows more rapidly than ordinary, particularly in the first 4 months (DeMyer, 1972; Lorber & Priestley, 1981). Usually there is no specific disfigurement (Friede, 1989). In most cases, all sections of the brain are proportionately enlarged, whereas in others, all are abnormally large, but certain areas are enlarged disproportionately (Friede, 1989). Sectioning of a megalencephalic brain reveals normally sized ventricles and a corpus callosum that may or may not be enlarged. The cerebral cortex is often thicker and the underlying white matter is of greater volume than in normal brains. It is these differences that cause megalencephalic brains to be so large. Cytoarchitectonic structure is usually normal (Friede, 1989; Hynd & Willis, 1988).

There have been some unilateral cases of megalencephaly reported (e.g., Laurence, 1964) but most cases are bilateral. Some have suggested that unilateral megalencephaly may represent hemihypertrophy because some of the unilateral cases were found in association with a unilaterally large face, unilateral scalp hair excess, and unilaterally large extremities (Ward & Lerner, 1947).

Clinical implications of megalencephaly vary. It can be associated with mental retardation, seizures, and other neurological abnormalities (Aicardi, 1992; DeMyer, 1972; Hynd & Willis, 1988; Lorber & Priestley, 1981). In a study by Lorber and Priestley (1981), 13% of the megalencephalic children were mentally retarded or neurologically abnormal. In contrast, megalencephaly has also been associated

with normal intelligence and even giftedness. In a study by Jakob (1927) of megalencephalic individuals with brain weights ranging from 1600 to 2850 g, 50 were gifted and 39 were mentally impaired. In fact, Deutsch and Joseph (2003) report that megalencephaly may even occur in the presence of high nonverbal abilities. Clearly there is great variability in the effect megalencephaly has on cognitive abilities. Behavioral deficits associated with megalencephaly are typically related to deficient cognitive abilities (Hynd & Willis, 1988).

In characterizing true megalencephaly, it is important to rule out other possible causal factors for a large head size because some, like hydrocephalus, require medical attention. Lorber and Priestley (1981) examined 510 children with a head circumference greater than the 98th percentile and found that only 109 had primary megalencephaly with normal pressure. DeMyer (1972) suggests that in making the differential diagnosis, the most important factor to consider is intracranial pressure.

There is evidence for familial transmission of megalencephaly by both autosomal-dominant and autosomal-recessive mechanisms (DeMyer, 1972; Friede, 1989; Lorber & Priestley, 1981). Macrocephaly is frequently found in Hunter's syndrome, Hurlers syndrome, achondroplasia, and other syndromes (Jones, 1997). The true incidence of megalencephaly is unknown, largely because asymptomatic cases are not reported (Hynd & Willis, 1988). There is a 4:1 male-to-female ratio (DeMyer, 1972; Lorber & Priestley, 1981). Table 1 summarizes the abnormalities of the bulk growth of the brain and other anomalies discussed in this chapter.

Dysplasias of the Cerebral Hemispheres

Holoprosencephaly

Holoprosencephaly results from a failure of the prosencephalon to cleave completely into two telencephalic hemispheres (Jones, 1997; Malamud & Hirano, 1974). This leaves a small forebrain containing a single ventricle (Evans, 1987). In the worst cases, the brain may weigh less than 100 g (Friede, 1989). The most severe form, alobar holoprosencephaly, is characterized by a completely undivided forebrain, little neocortex, fused thalami on the midline, and a

TABLE 1. Neurodevelopmental Malformations

Malformation	Description	Clinical manifestations
Abnormalities of bulk growth		
Micrencephaly	Subnormal brain size associated with abnormally small head (<2 SD below mean for age and gender)	Size of face near normal; folded scalp, possibly epilepsy, and most typically intellectual retardation
Megalencephaly	Abnormally large brain from overproduction of cerebral parenchyma. Males > females	Associated with mental subnormality, normality, or hypothetically giftedness. Epilepsy may occur
Dysplasias of cerebral hemispheres		
Holoprosencephaly	Two hemispheres fail to develop. A large fluid-filled cavity results. No interhemispheric fissure present. 1:13,000 live births	Faciocerebral dysplasias, cebocephaly, apnea spells, severe mental retardation, hypotelorism, and other systemic deformities. Usually incompatible with life
Agenesis of the corpus callosum	Complete or partial failure of the corpus callosum to develop. Males > females	Occasionally asymptomatic or found in association with spina bifida, facial and ocular deformities, micrencephaly, and hydrocephalus. Epilepsy and mental retardation may occur
Malformations of the cerebral cortex		
Agyria/pachygyria	Smooth lissencephalic surface of brain. Few coarse gyri may be present	Commonly found in association with agenesis of corpus callosum, micrencephaly, epilepsy, severe mental retardation, and early death
Polymicrogyria	Development of many small gyri. Microscopically they may from an overlapping folded cortex	Found in association with learning disabilities (dyslexia), severe mental retardation, and epilepsy. Also appear asymptomatically
Focal dysplasia	Focal abnormalities in the cortical architecture usually consisting of disordered cells and layering of cortex	Reported in cases of epilepsy and learning disabilities (dyslexia)
Malformation associated with congenital hydrocephalus		
Dandy–Walker malformation	Malformation of the cerebellum associated with a dilation of the fourth ventricle. Males > females	Hydrocephalus, agenesis of the corpus callosum, Klippel–Feil and DeLange syndromes, and severe psychomotor retardation
Arnold–Chiari malformation	Congenital deformation of the brain stem and cerebellum	Congenital hydrocephalus, spina bifida, and severe psychomotor retardation
Stenosis of the aqueduct of Sylvius	Obstruction of the aqueduct and CSF circulation	Often insidious onset of symptoms associated with hydrocephalus. Shunted children may suffer learning/behavioral problems. Nonverbal IQ < verbal IQ

TABLE 1. (*Continued*)

Malformation	Description	Clinical manifestations
Abnormalities of the neural tube and fusion defects		
Spina bifida occulta	Usually asymptomatic lesion discovered incidentally	Can be associated with lipoma, dermal sinuses, and dimples
Spina bifida cystica	Spinal defect that includes a cystic-like sac which may or may not contain the spinal cord	Hydrocephalus is a frequent complication. Cognitive deficits related to extent of hydrocephalus. Arnold–Chiari malformation not uncommon
Cranium bifidum and encephalocele	Fusion defects of skull referred to as cranium bifidum; myelomeningoceles or meningoceles on the skull are referred to as encephaloceles. Males < females	Many associated difficulties with hydrocephalus including ataxia, cerebral palsy, epilepsy, and mental retardation
Anencephaly	Vault of skull absent and brain represented by vascular mass. Face is grossly normal. 1 male:4 female	Condition incompatible with life
Hydranencephaly	Cerebral hemispheres replaced by cystic sacs containing CSF	Difficult initially to distinguish from hydrocephalus. Hypnoatremia, eye movement disturbances, and death
Porencephaly	Large cystic lesion develops on the brain. May occur bilaterally or unilaterally	Rarely asymptomatic but typically associated with mental retardation, epilepsy, and other malformations

well-developed brain stem and cerebellum (Aicardi, 1992). Holoprosencephaly is associated with abnormal facial features that in the most extreme cases can include cyclopia in which one or two eyeballs are contained in a partially fused orbit. Other orbitofacial anomalies include cebocephaly (nose is represented by a flattened bridge between the eyes with one or two nostrils), hypotelorism (close orbits), microphthalmia (narrowed eyelids), ethomocephaly (nose is replaced by proboscis with one or two nostrils), and cleft lip or palate (Brinholz, 1989; Evans, 1987; Friede, 1989; Hynd & Willis, 1988). There are also visceral deformities associated with holoprosencephaly including polydactyly and cardiac anomalies (Aicardi, 1992; Friede, 1975). To an extent, the severity of facial deformities is related to the extent of cerebral deformities, although the relationship is not perfect (Friede, 1989). Cases of semilobar holoprosencephaly, in which the brain is divided into hemispheres posteriorly, are associated with less severe or nonexistent facial abnormalities (Aicardi, 1992).

Holoprosencephaly has previously been called arhinencephaly under the terminology proposed by Kundrat (1882) who noted the frequent presence of aplasia of the olfactory bulbs and tracts. Since holoprosencephaly can occur with the presence of the olfactory bulb (Gilles, Leviton, & Dooling, 1983), the term arhinencephaly is now typically reserved for defects involving a primary olfactory bulb malformation (Friede, 1989). It is also possible to have olfactory aplasia in nonholoprosencephalic brains (Kobori, Herrick, & Urich, 1987).

The most severe cases of holoprosencephaly typically do not survive the neonatal period, and infants who do survive often develop seizures. The extent of neurological impairment varies, but mental retardation, usually severe, is always present (Aicardi, 1992). A semilobar patient described by Kobori et al. (1987) who lived until the age of 2 ½ years had intact vision, hearing, and reflexes but failed to thrive and did not reach any developmental milestones. Rarely, however, some individuals survive into adulthood (Aicardi, 1992).

This abnormality develops within the third to sixth week of gestation during the period of embryogenesis when the hemispheres normally differentiate. There is some evidence from animal research that holoprosencephaly may result

from exposure to neurotoxins (Hynd & Willis, 1988). Maternal diabetes may also be a risk factor (Barr et al., 1983; Kobori et al., 1987). There have been familial cases of holoprosencephaly reported in the literature suggesting the possibility of autosomal-recessive inheritance (DeMyer, Zeman, & Palmer, 1963; Jones, 1997; Hintz, Menking, & Sotos, 1968). In cases of holoprosencephaly involving multiple extracephalic malformations, it is often associated with 13–18 trisomy. It is possible, however, to diagnose trisomy 13 in cases of holoprosencephaly not accompanied by extracephalic abnormalities (Verloes et al., 1991). Additionally, holoprosencephaly can occur in the absence of chromosomal irregularities (Friede, 1989; Verloes et al., 1991).

Holoprosencephaly is estimated to occur in 1 of 13,000 births (Frutiger, 1969). The abnormality does not show gender preference (Friede, 1989; Hynd & Willis, 1988).

Agenesis of the Corpus Callosum

Agenesis of the corpus callosum is characterized by the complete or partial absence of the corpus callosum. In partial agenesis, typically the rostrum and genu are intact and the splenium and corpus are absent because of the anteroposterior direction in which the corpus callosum develops (Aicardi, 1992; Hynd & Willis, 1988). Usually the absent corpus callosum is replaced by two longitudinal bundles, called the longitudinal corpora callosa or Probst bundles (Aicardi, 1992). Usually the interhemispheric cortex is irregular in that the cingular gyrus may be missing and the gyral patterns are abnormal (Friede, 1989).

Agenesis of the corpus callosum may occur asymptomatically, and there is some evidence that a hypertrophied anterior commissure is involved in functional compensation (Fischer, Ryan, & Dobyns, 1992). It may also be found in association with other neurodevelopmental anomalies such as spina bifida, facial and ocular abnormalities, micrencephaly, megalencephaly, heterotopias, and hydrocephalus (Friede, 1989; Hynd & Willis, 1988; Jeret, Serur, Wisniewski, & Fisch, 1987). Epilepsy may be present, and mental retardation is frequently associated with callosal agenesis (Jeret et al., 1987).

In cases that appear asymptomatic, however, there are usually cognitive deficits. In an early study, Selnes (1974) demonstrated that the corpus callosum is necessary for semantic–linguistic dominance to develop in the left hemisphere. Related to this finding, Dennis (1981) reported that acallosal individuals have difficulty on tasks involving syntactic–pragmatic ability and do poorly on semantic–linguistic information-processing tasks on suppressing ipsilateral input. These deficits are common in children with learning disabilities (e.g., Hynd & Obrzut, 1981; Hynd, Obrzut, Weed, & Hynd, 1979). Koeda and Takeshita (1993) described a 15-year-old acallosal, mentally retarded female who could write dictated sentences accurately but not read them, suggesting alexia. Sanders (1989) described a 6-year-old acallosal female who had deficits in syntactic comprehension because of a difficulty in assigning appropriate semantic roles to some sentence forms. Drake (1968) reported a thinned corpus callosum in the first reported autopsy of a learning-disabled individual. These findings lend support to speculation about the role of the corpus callosum in learning disabilities.

Most recently, Hynd et al. (1995) reported that the genu of the corpus callosum was significantly smaller in dyslexics and that area measurements of various regions correlated significantly with reading ability. These findings support the view that morphological variation in the corpus callosum may be related to cognitive deficits.

Other neuropsychological deficits have also been reported. One study reported that acallosal subjects were shown to respond more slowly, although they could perform the tasks successfully, than IQ-matched normal controls on tasks requiring interhemispheric and intrahemispheric comparisons of visual and tactile stimuli (Lassonde, Sauerwein, McCabe, Laurencelle, & Geoffroy, 1988). Koeda and Takeshita (1993) reported on disconnection deficits in two patients with complete agenesis, mental retardation, and daily epileptic seizures. Specifically, they exhibited tactile naming disorder of the left hand. Importantly, the diagnostic process indicated the absence of amorphognosia and astereognosia which are gross sensory deficits rather than disconnection deficits. Although disconnection syndromes have not been commonly reported in cases of agenesis, the authors speculated that because of the severe impairments of the children, brain capacity and neural plasticity were insufficient to compensate for the absent corpus callosum.

In Chiarello's (1980) report on acallosal individuals, the 27 cases described had a mean verbal IQ of 89 (SD = 12.45). For the 25 cases for which both verbal and performance IQs were reported, the mean verbal IQ was 88.52 (SD = 12.58) and the mean performance IQ, 88.76 (SD = 15.75). These differences are not statistically significant. Hynd and Willis (1988) concluded from these studies that in cases where agenesis is incidentally discovered, general cognitive ability is approximately one standard deviation below normal. In addition, they noted that verbal scale IQ scores do not reflect the subtle neurolinguistic deficits present in these patients.

The prognosis of individuals with agenesis of the corpus callosum varies according to whether it is asymptomatic or associated with other deformities. Blum, André, Broullé, Husson, and Leheup (1990) found that of 12 infants diagnosed prenatally, 6 developed normally from age 2 to 8 years. Jeret et al. (1987) reported evidence suggesting that the life expectancy of acallosal males is greater than that of acallosal females.

Agenesis of the corpus callosum is diagnosed by neuroimaging. The disconnection of the cerebral hemispheres is also evident on CT and MRI scans. Prenatal diagnosis is possible beginning at week 20 of gestation (Aicardi, 1992).

The disruption in embryogenesis is thought to occur between weeks 12 and 22 of gestation (Hynd & Willis, 1988). There is evidence for familial transmission of agenesis of the corpus callosum (Dogan, Dogan, & Lovrencic, 1967; Menkes, Philippart, & Clark, 1964; Shapira & Cohen, 1973). There have been suggestions of autosomal-dominant inheritance (Aicardi, 1992) and X-linked transmission (Aicardi, 1992; Jeret et al., 1987; Vles et al., 1990). Agenesis of the corpus callosum is frequently found in a number of clinical syndromes including the Aicardi syndrome, Meckel–Gruber syndrome, Walker–Warburg syndrome and occasionally in a number of other syndromes including several trisomies (8, 13 and 18) (Jones, 1997). Further, agenesis has been associated with metabolic disorders of fetal (Bamforth, Bamforth, Poskitt, Applegarth, & Hall, 1988) and maternal origin (Aicardi, 1992) including fetal alcohol syndrome (Jeret et al., 1987; Wisniewski, Dambska, Sher, & Qazi, 1983).

Since agenesis of the corpus callosum is sometimes asymptomatic, the exact incidence is unknown. Although the incidence has been suggested to be 0.7%, Hynd and Willis (1988) note that the percentage of individuals with agenesis of the corpus callosum may be lower because the estimate was derived from a probably nonrepresentative population. Jeret, Serur, Wisniewski, and Fisch (1985–1986) reported an incidence of 2.3% among a developmentally disabled population. There is evidence that it is more common among males (Jeret et al., 1987).

Malformations of the Cerebral Cortex

Dysplasia, abnormal tissue growth, can occur in any region of the brain. Although it is likely that most instances of dysplasia are asymptomatic, dysplasias have been associated with behavioral and learning difficulties (Hynd & Semrud-Clikeman, 1989; Hynd & Willis, 1988). Dysplasias result from a disruption in neuronal migration. In the cases of agyria, pachygyria, and heterotopia, it has been speculated that they are variations of the same process that differ in severity (Friede, 1989). The review of radiologic and neuropathologic findings by Palmini et al. (1991) supported this theory. Similarly, a comparison of a child with generalized pachygyria, one with subcortical laminar heterotopias (or double cortex), and one with periventricular band heterotopia suggested to Palmini et al. (1993) that the pathogenesis for each of these disorders involves a disruption during the migration process, specifically neuron–glia interactions. They suggested that this disturbed interaction could lead to the halt of centrifugal neuronal movement as well as to failure of the neuron to detach from the glial guide when reaching the cortical plate. They hypothesized that the interaction of three factors—the period of migration during which injury occurred, degree of radial glial fiber involvement, and location of damage on the glial fibers—determined the severity and site of the diffuse heterotopia.

Agyria (Lissencephaly) and Pachygyria

Agyria and lissencephaly are terms that have been used interchangeably. Owen (1868) originally used the term lissencephaly as a

descriptor of brains in lower species that are smooth, flat, and unfolded. The term was later used to characterize brains that were malformed and lacked gyri. Agyria, however, is the preferable term because it refers specifically to the lack of gyri (Hynd & Willis, 1988).

Pachygyria, also called macrogyria, is used to describe brains with few gyri that are usually coarse and wide. Although agyria and pachygyria are sometimes used equivalently, it is better to distinguish between the two because they represent different levels of severity (Crome, 1956; Daube & Chou, 1966; McLone, 1982).

Children with agyria typically present with microencephaly, thickened skull (Hynd & Willis, 1988), bitemporal hollowing, and small jaw (Pavone, Gullotta, Incorpora, Grasso, & Dobyns, 1990). There are different pathological types with distinct clinical features as delineated by Aicardi (1992) and Pavone et al. (1990). Unilateral agyria has been reported (Hager et al., 1991).

In classical agyria, the cerebral cortex is thick and the white matter is reduced. Kuchelmeister, Bergmann, and Gullotta (1993) reported a 4:1 gray-to-white matter ratio. The cortex typically consists of the following four layers (from top down): (1) cell sparse, molecular layer; (2) superficial cellular layer containing a variety of cells, including large pyramidal cells usually found in layer five; (3) thin layer of white matter with no or few cells; and (4) thick bands of ectopic neurons (Aicardi, 1992; Friede, 1989).

In pachygyria, the extent of malformation is less severe and in layers two and four the expected small neurons are present (Aicardi, 1992). Both agyria and pachygyria often are accompanied by agenesis of the corpus callosum, suggesting that these anomalies occur during the first trimester of gestation (Brodsky & Lombroso, 1998; Friede, 1975). Jellinger and Rett (1976) suggest that agyria develops during weeks 11–13 of gestation and pachygyria, around week 13. Agyria is associated with postnatal microcephaly (Pavone, Rizzo, & Dobyns, 1993). A relationship between pachygyria and tuberous sclerosis has been reported (Sener, 1993).

Severe neurological problems are associated with agyria including severe mental retardation, motor retardation, diplegia, hypotonia, decerebrate posture, reduced spontaneous activity, and seizures (especially infantile spasms) (Aicardi, 1992; Friede, 1989; Hynd & Willis, 1988; Pavone et al., 1990, 1993; Tachibana, 1990). Poor growth

and feeding problems are also common (Pavone et al., 1993). Interestingly, Barkovich, Koch, and Carrol (1991) reported, based on a study of 10 patients, that the clinical manifestations did not appear to correlate with the severity of agyria. The cognitive and behavioral manifestations in pachygyria are less severe, although severe mental retardation and seizures are still common.

Most infants with agyria die before the age of 2 (Friede, 1989; Hynd & Willis, 1988; Palmini et al., 1991). These children often die of intercurrent disease. Respiratory infections, including pneumonia, are common (Pavone et al., 1993). Münchoff and Noetzel (1965), however, described a child who lived until age 6 and Kuchelmeister et al. (1993) reported on a patient who reached age 20. The expectancies for individuals with pachygyria are better. Palmini et al. (1993) described a 7-year-old female who, while developmentally delayed and epileptic, was able to attend, with difficulties, a special first grade class. Aicardi (1992) reports that he has had patients with pachygyric brains who survived into adulthood, could walk, and had limited language abilities.

As noted previously, agyria and pachygyria are the result of arrested or disrupted neuronal migration. In the schema developed by Palmini et al. (1993), diffuse pachygyria results from an early injury (before most neurons have arrived at the cortex and thus providing insufficient material to form gyral patterns) and severe and distal radial glial fiber damage. In agyria, the disruption occurs earlier.

A variety of factors have been suggested to cause the disrupted migration. Aicardi (1992) suggests that most cases of agyria are sporadic but that there have been some cases indicating dominant inheritance. Pavone et al. (1990) found evidence of autosomal-recessive inheritance and the possibility of X-linked-recessive inheritance. When agyria is part of the Miller–Dieker syndrome, it is thought to result from a chromosomal microdeletion (Brodsky & Lombroso, 1998; Ledbetter, Kirwano, Dobyns, & Ledbetter, 1992). Postconceptional factors perhaps responsible for the development of agyria or pachygyria are ischemia and viral infection (Pavone et al., 1990) including congenital cytomegalovirus (Hayward, Titelbaum, Clancy, & Zimmerman, 1991). The incidence and gender ratios for agyria and pachygyria are unknown (Hynd & Willis, 1988).

Focal Dysplasia/Heterotopia

Heterotopia is the term used to describe the presence of ectopic gray matter in the cerebral hemispheres. It is thought to be on the other end of the continuum from agyria (Palmini et al., 1993). In laminar heterotopias, the gray matter appears as symmetrical ribbons in the centrum semiovale (Friede, 1989). In pure cases of laminar heterotopia, called generalized band or "double" cortex heterotopia, the gray matter is continuous under the cortical surface and appears like a double cortex. The gray matter is most noticeable in the frontocentroparietal regions, but is typically found throughout the neocortex (Palmini et al., 1991). Although there may be slightly fewer gyri than normal, the cortex is usually not malformed. Nodular heterotopias are characterized by clustered masses of gray matter in irregularly formed nodules that are separated by thin myelinated fibers. They are usually located near the lateral ventricles (Friede, 1989; Hynd & Willis, 1988).

Laminar heterotopia is usually associated with few, if any, deficits (Hynd & Willis, 1988), but it has occasionally been associated with epilepsy and mental retardation (Miura et al., 1993; Palmini et al., 1991, 1993; Ricci, Cusmai, Fariello, Fusco, & Vigevano, 1992). One 6-year-old female with double cortex syndrome was described as slightly developmentally delayed, clumsy, easily upset, and as having poor impulse control. It was unclear whether or not she was epileptic. Her daily living appeared to be affected only slightly by her cortical anomalies (Hashimoto, Seki, Takuma, & Suzuki, 1993). Palmini et al. (1993) note that while there may be a relationship between the extent of the migration deficit and clinical manifestations, the severity of epilepsy and retardation among patients may depend on the type of epileptic syndrome that develops. The severity of mental retardation is also thought to be related to the extent the cortex over the heterotopia is disorganized (Palmini et al., 1991).

Nodular heterotopias, in small numbers, are usually asymptomatic (Aicardi, 1992; Hynd & Willis, 1988). They may be associated, however, with malformations such as agenesis of the corpus callosum and micrencephaly (Friede, 1989). Focal dysplasias have also been found in the brains of dyslexic individuals (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985). Hynd and Willis (1988) speculate that the distribution and severity of focal dysplasias may dictate whether cortical arousal, learning, or attention is negatively impacted. Life expectancy depends on associated clinical features and can be normal (Palmini et al., 1991).

Diagnosis of heterotopias is made through neuroimaging. In making the diagnosis, it is important to differentiate them from the tubers of tuberous sclerosis which they may resemble and with which they may be associated (Aicardi, 1992).

As with agyria and pachygyria, focal heterotopias are thought to develop from disrupted neuronal migration. The neurons forming a heterotopia are thought to be normal, just located in error (Clark, 2002). It has been suggested that the disruption does not completely terminate neuronal migration at a certain point. Instead, only some waves of migration are unsuccessful. In the double cortex syndrome, the superficial layers receive close to the normal number of neurons so that gyration is possible (Palmini et al., 1991). Palmini et al. (1993) propose that in heterotopia the migration is arrested late in the process and that radial glial fiber damage is mild and distal.

The etiology for the disrupted migration is uncertain. There are reports, however, of familial cases of double cortex syndrome, suggesting a possible genetic basis (Palmini et al., 1991). In the examination of ten patients with "double cortex" described by Palmini et al. (1991), it was found that maternal drug ingestion occurred in two mothers and X-ray exposure occurred in a third, leading to the conclusion that these teratogens may have been related to disrupted neuronal migration. Fever, lasting one or more days before weeks 4 and 14 of gestation, has also been implicated (Pleet, Graham, & Smith, 1981). The incidence of focal dysplasias is unknown. There is some limited evidence, however, that they may occur more frequently in males than in females (Hynd & Willis, 1988) and have been reported to exist in the brains of children with attention-deficit hyperactivity disorder (ADHD) (Nopoulus, et al., 2000).

Polymicrogyria

Polymicrogyria is characterized by crowded, small gyri, in an atypical convolutional pattern (Aicardi, 1992; Friede, 1989; Hynd & Willis, 1988). However, at gross inspection,

there does not always appear to be an excessive number of gyri. Instead it may appear to be pachygyria (Byrd, Osborn, & Radkowski, 1991) because the gyri are not separated as a result of the fusion of molecular layers (Aicardi, 1992; Friede, 1989). The extent of polymicrogyria may not be evident until sectioning (Hynd & Willis, 1988). Polymicrogyria can cover the entire cortex unilaterally or bilaterally. They are more commonly localized, however, around arterial territories, and porencephalic or hydranencephalic areas (Aicardi, 1992; Friede, 1989). Brain weight may be reduced (Friede, 1989). Polymicrogyria may co-occur with other abnormalities including cellular heterotopias, agenesis of the corpus callosum, signs of fetal infection, and cortical and vascular anomalies (Aicardi, 1992; Friede, 1989).

The clinical manifestations of polymicrogyria vary. It has been found incidentally in the autopsies of individuals without neurological impairment, and small areas are usually asymptomatic (Aicardi, 1992; Hynd & Willis, 1988). It has also been found in association with severe mental retardation (Crome, 1960; Malamud, 1964), learning disabilities (Galaburda & Kemper, 1979; Galaburda et al., 1985), seizures, and bilateral or unilateral neurological signs (Aicardi, 1992). Cohen, Campbell, and Yaghmai (1989) reported on a 7-year-old girl with developmental dysplasia who died of mononucleosis.

Diagnosing polymicrogyria is extremely difficult, if possible, even with the use of neuroimaging (Aicardi, 1992). Byrd et al. (1991) reported that 25% of the children they examined with polymicrogyria had MRI findings resembling pachygyria and that the polymicrogyria was revealed through histological studies.

The evidence suggests that rather than resulting from a disruption in neuronal migration, polymicrogyria develops postmigration and is the product of a disturbance of cortical gyration around the fifth and sixth months of gestation (Aicardi, 1992; Friede, 1989). The precipitating events may include severe trauma, carbon monoxide intoxication, maternal asphyxia, perfusion failure, and intrauterine infections (Aicardi, 1992; Hynd & Willis, 1988). There is also evidence of genetic transmission (Andermann, Palmini, Andermann, Tampieri, & Leonard, 1992). The incidence and gender ratios for polymicrogyria are unknown (Hynd & Willis, 1988).

Hydrocephalus and Associated Malformations

Hydrocephalus

Hydrocephalus results from excess CSF in the ventricles. It can develop through intraventricular or extra-ventricular obstruction of flow, excessive CSF production, or loss of brain tissue (Chervenak, 1989). Hydrocephalus can have a variety of damaging effects on the cortex and underlying white matter of the developing brain, including (1) stretching and disruption of neural tracts, particularly long fiber tracts; (2) shifting of the internal capsule, which may contribute to motor difficulties; (3) atrophy of white matter; (4) stretched or extremely thin cortex; and (5) disruption of corpus callosum myelination. Congenital malformations are causally associated with hydrocephalus, particularly the Dandy–Walker malformation, the Arnold–Chiari malformation, and stenosis of the aqueduct of Sylvius (Dyken & Miller, 1980). In one study, approximately 37% of the hydrocephalic infants had congenital deficits not related to hydrocephalus among which trachosophageal fistula and genitourinary, cardiac, and multiple anomalies were most common (Wiswell, Tuttle, Northam, & Simonds, 1990). Ocular abnormalities, motor deficits, and seizures are also often associated with hydrocephalus (Dennis et al., 1981).

Prior to the development of shunting, which transports CSF from the ventricular system or subarachnoid space to another area where it can be absorbed, the prognosis for hydrocephalus was very poor. In an early study Laurence and Coates (1962) computed survival estimates into adult life as falling between 20 and 23%. In a study by Raimondi and Soare (1974) of 200 shunted infants, only 9 died, with a mean age at death of 38 months.

In the Raimondi and Soare (1974) study, the mean IQ for 29 white infants with hydrocephalus was 84.5, SD = 25.8. This is approximately one standard deviation below average intelligence but within the normal range. For the total group of 50 hydrocephalic children (white and black), the mean IQ was 71.7, SD = 30.3. This IQ score approaches the range of mental retardation. The hydrocephalic children with associated problems, specifically

porencephaly or Dandy–Walker cyst had much lower IQs. McCullough and Balzer-Martin (1982) reported that the mean IQ of 37 shunted children was 96, SD = 22. Approximately two-thirds of the children in their study had normal or borderline IQs. Similarly, the average intelligence of children with uncomplicated hydrocephalus was reported to be 108 in another study (Shurtleff, Foltz, & Loeser, 1973). The average IQ of 78 hydrocephalic children in a study by Dennis et al. (1981) was 90.80, SD = 13.34. Some cases of superior intelligence in shunted children have been reported (Lorber, 1968). These studies indicate that in uncomplicated cases of hydrocephalus treated with shunting, mental impairment is not necessarily an associated clinical feature.

Dennis et al. (1981) reported verbal intelligence as being superior to nonverbal intelligence in hydrocephalic individuals. They suggest that nonverbal intelligence is impaired, even with the benefits of shunting, for several reasons. First, the biomechanical effects of hydrocephalus damage some regions of the brain more than others. In children with intraventricular hydrocephalus, there is an asymmetric cortex thinning in the anteroposterior direction leading to greater thinning in the vertex and occipital regions. This has a negative impact on the development of nonverbal intelligence. Additionally, they proposed that associated deficits such as disturbed visual function, motor deficits, and seizures may further impair the development of nonverbal intelligence.

Of interest, Fernell, Gillberg, and von Wendt (1991) reported that when hydrocephalus was not associated with mental retardation, hydrocephalic children did not exhibit significantly more behavior problems than control children. Hydrocephalic children with mental retardation, however, had significantly more behavior problems, particularly in attentiveness and hyperactivity, than hydrocephalic children without mental retardation and controls.

Hydrocephalus can be diagnosed prenatally through the use of sonography. Chervenak (1989) notes that the ability to measure the ventricles is particularly helpful because the ventricles often dilate before the cranium enlarges. In children below the age of 2, hydrocephalus can usually be diagnosed easily. The skull volume develops rapidly and the child may be developmentally delayed. Ocular symptoms are also associated with hydrocephalus (Aicardi, 1992).

A variety of etiological factors may lead to hydrocephalus including meningitis and arachnoid fibrosis, subdural hematoma, cysts, vascular anomalies, tumors, and major cerebral dysplasias (Milhorat, 1982). Hydrocephalus is often associated with other abnormalities, such as spina bifida, and its exact incidence is thus unknown. As a congenital disorder, its incidence has been estimated to range from 0.9 to 1.5 per 1000 births (Milhorat, 1982). In a study of 763,364 live and stillborn infants born in U.S. Army hospitals from 1971 to 1987, 370 had hydrocephalus (0.48 per 1000 births). The population characteristics of the sample were similar to the United States as a whole. There were no significant racial differences found or seasonal or yearly trends in incidence. There were significantly more males diagnosed than females and hydrocephalus was significantly more common among births in the Pacific region (South Korea and Hawaii) than in the other four regions examined (Europe, East Coast, Midwest, and West Coast) (Wiswell et al., 1990).

Hydrocephalus is frequently reported in the Walker–Warburg syndrome and is occasionally found in nearly 50 other syndromes including achondroplasia, Aplert syndrome, Crouzon syndrome, Hunter's syndrome, Hurler's syndrome, and several trisomies (9, 13, & 18) (Jones, 1997).

Dandy–Walker Malformation

Three characteristics are typical of the Dandy– Walker malformation: (1) distension of the fourth ventricle; (2) complete or partial agenesis of the vermis; and (3) enlarged posterior fossa with vertical displacement of lateral sinuses, tentorium, and torcular. The cortex may be nonfoliated. The lateral ventricles, as they converge with the sagittal sinus, form an inverted Y shape (Friede, 1989). At one time, the Dandy–Walker syndrome was thought to be the same as atresia of the cerebellum which refers to the absence or closure of the cerebellum. It became evident, however, that atresia of the cerebellum is not an essential component of the Dandy–Walker malformation (Hynd & Willis, 1988). Benda (1954) suggested the term Dandy–Walker malformation to distinguish it as a separate entity.

The occipital region in children with the Dandy–Walker malformation is prominent which helps to distinguish them from children with hydranencephaly, aqueductal stenosis, or

meningomyelocele which is associated with the Arnold–Chiari malformation (Hynd & Willis, 1988). Congenital anomalies that sometimes co-occur with the malformation include aqueductal stenosis, agenesis of the corpus callosum, craniofacial deformities, Klippel–Feil syndrome, Cornelia DeLange syndrome, polydactyly, syndactyly, and cytoarchitectonic irregularities (Evans, 1987; Friede, 1989; Hart, Malamud, & Ellis, 1972; Hynd & Willis, 1988). More than 80% of individuals with the Dandy–Walker malformation have early signs of hydrocephalus (Friede, 1989) although it is not usually present at birth (Hirsch, Pierre-Kahn, Renier, Sainte-Rose, & Hoppe-Hirsch, 1984).

Associated neurological deficits include mental retardation, slow motor development, cranial nerve palsies, nystagmus, and truncal ataxia. Mental retardation is usually pronounced (Hynd & Willis, 1988). In a study by Raimondi and Soare (1974), the mean IQ for hydrocephalic children with the Dandy–Walker malformation was 48.3. Most individuals survive past the first year without shunting and some survive into adulthood (Friede, 1989). Among 144 cases reviewed by Hirsch et al. (1984), the mortality rate was 27%. Approximately half of the survivors, however, had a normal IQ.

Diagnosis is usually not difficult if the child presents with the three classic symptoms (Friede, 1989). In approximately 80% of cases it is not diagnosed, however, until after the first birthday when hydrocephalus is evident (Aicardi, 1992).

Some have suggested that the Dandy–Walker malformation results from a developmental arrest in the hindbrain occurring sometime before the third month of gestation with persistence of the fourth ventricle's anterior membranous area. The malformation has been found among siblings (Friede, 1989) suggesting some familial–congenital mechanisms of transmission. This malformation is frequently observed in the Aircardi syndrome and the Walker–Warburg syndrome (Jones, 1997). Incidence is unknown (Hynd & Willis, 1988). Gender ratios may be equal (Friede, 1989) but some evidence suggests that males may outnumber females (Hynd & Willis, 1988).

Arnold–Chiari Malformation

The Arnold–Chiari malformation is characterized by brain stem and cerebellar deformities that crowd the hindbrain. Cleland (1883) first described this syndrome and illustrated the herniation of the vermis, the malformed medulla, and other brain stem abnormalities. Chiari (1891, 1896) further described the malformation and distinguished between three types: I, a syndrome involving herniation of the cerebellar tonsils; II, a syndrome now called the Arnold–Chiari malformation; and III, a syndrome involving cervical spina bifida with cerebellar encephalocele. Arnold (1894) reported on an infant with a ribbon like cerebellar herniation. Thus, the term Arnold–Chiari malformation was introduced by Schwalbe and Gredig (1907) in an attempt to address the brain stem abnormalities described by Chiari and the cerebellar herniation described by Arnold.

Cranial bone and cervical spine anomalies are a component of the syndrome. The brain stem and cerebellum are downwardly displaced and are tightly crowded. Cranial projection and elongation of the cranial nerves occurs because of the brain stem's caudal displacement. Cerebellar tissue herniates into the cervical spinal cord. The brain stem is deformed as the dorsal part of the medulla oblongata, the fourth ventricle, and the choroid plexus are shifted dorsally. The caudal end of the fourth ventricle and its choroid plexus are shifted into the spinal canal where they frequently form a pouch in which herniated cerebellar tissue may enter. Cases vary as to whether malformations of the vermis and medulla are equally prominent or if one type of deformity is more pronounced. There are additional malformations of posterior fossa structures (Friede, 1989).

The most consistent symptoms are increased intracranial pressure and hydrocephalus (Friede, 1989). Ford (1926) reported that of 100 cases of infantile hydrocephalus, 16 were caused by the Arnold–Chiari malformation. It is also associated with lumbrosacral spina bifida and myelomeningocele (Hynd & Willis, 1988). The Arnold–Chiari malformation can occur, however, in the absence of spina bifida, and hydrocephalus in spina bifida can be produced by other causes (Friede, 1989). Children with the Arnold–Chiari malformation frequently have severe psychomotor retardation (Hynd & Willis, 1988). It is not, however, necessarily incompatible with normal intelligence. McCullough and Balzer-Martin (1982) reported the mean IQ of

four children with Arnold–Chiari myelodysplasia to be 110.

Four classes of hypotheses exist to explain the pathogenesis of the syndrome: (1) downward traction (from the myelomeningocele anchoring the bottom portion of the spinal cord); (2) pressure from above (as the result of congenital hydrocephalus); (3) a primary dysgenesis of the brain stem; and (4) a primary malformation of the basicranium (Friede, 1989). Friede (1989) suggests that the fourth class of hypotheses is most tenable. Incidence and gender ratios are unknown (Hynd & Willis, 1988).

Stenosis of the Aqueduct of Sylvius

Stenosis of the aqueduct of Sylvius refers to the obstruction of the aqueduct and CSF circulation. The aqueduct is the most commonly blocked CSF pathway because it is the longest and most narrowest (Friede, 1989). The blockage can occur through the following four mechanisms: (1) narrowing caused by congenital factors; (2) a thin membrane lying on the aqueduct; (3) narrowing resulting from pressure by an adjacent tumor; and (4) a herniation of the cerebellum and shifting of the fourth ventricle as found in the Arnold–Chiari malformation (Hynd & Willis, 1988).

Stenosis of the aqueduct of Sylvius is a common cause of hydrocephalus. For example, Elvidge (1966) found that of 44 hydrocephalic children, 13 had aqueductal stenosis. In 100 cases of infantile hydrocephalus, Ford (1926) found that 14 had aqueduct stenosis alone.

The symptoms of stenosis are those of hydrocephalus. A study by Dennis et al. (1981) revealed that the mean Full Scale IQ of children with aqueductal stenosis was 86.73, SD = 14.99, which is slightly less than one standard deviation below average intelligence. However, these children had significantly better verbal than performance skills as indicated by a 20-point discrepancy between scale scores.

There are reports of several familial forms of aqueductal stenosis (Bickers & Adams, 1949; Drachman & Richardson, 1961; Edwards, Norman, & Roberts, 1961; Shannon & Nadler, 1968; Warren, Lu, & Ziering, 1963). Incidence and gender ratios are unknown (Hynd & Willis, 1988).

Abnormalities of the Neural Tube and Fusion Deficits

Spina Bifida

Spina bifida has long been recognized and it is thought that Hippocrates and medieval Arab physicians noted the defect (Reigel, 1982). It is a defect that occurs because of the failure of the caudal portion of the developing neural tube to fuse properly (Hynd & Willis, 1988). The lesions involve malformations of both the vertebral column and the spinal cord (Friede, 1989). Since dermal development is related to neural tube development, there may be associated malformations of the skin, vertebrae, and soft tissues (Evans, 1987).

The degree of severity of spina bifida varies with some cases being found incidentally and others being associated with so many other anomalies that it leads to early death (Hynd & Willis, 1988). The most severe form is craniorachischisis totalis in which the nervous system is completely open (Evans, 1987). Associated anomalies include skeletal, gastrointestinal, pulmonary, craniofacial, cardiovascular, and genitourinary anomalies (Hynd & Willis, 1988). Wiswell et al. (1990) reported that of 526 cases of spina bifida, 22% had additional congenital anomalies, of which gastrointestinal, genitourinary, and cardiac malformations were most common.

In spina bifida occulta, the neural structures do not herniate and are covered by skin (Aicardi, 1992). The tissue over the lesion is often normal and the defect is frequently discovered only incidentally via X-ray (Hynd & Willis, 1988). There may be one or more lesions and the defect may be associated with lipoma, dimples, and congenital dermis sinuses (Anderson, 1975; James & Lassman, 1981). It is often asymptomatic, but it may be accompanied by pain, foot deformities, abnormal gait, abnormal reflexes, shortening of one leg, and incontinence (James & Lassman, 1972). In this case, hydrocephalus is not an associated problem (Aicardi, 1992). Individuals with uncomplicated lesions have a slightly increased incidence of occult intraspinal lesions (Reigel, 1982).

Spina bifida cystica involves a vertebral defect and a visible cystic lesion on the back. In myelomeningocele, part of the spinal cord is

involved in the cyst (Friede, 1989; Hynd & Willis, 1988). Eighty to ninety percent of the lesions occur in the lumbrosacral region. The lesion may not correspond with the bone malformation (Friede, 1989). Aicardi (1992) distinguishes between myelomeningocele and myeloschisis in that in the former the lesion is bulging while in the latter the lesion is flat.

Myelomeningoceles are associated with a variety of neurological deficits particularly when located in the lumbrosacral region. Deficits may include unresponsiveness to pain and temperature, incontinence, flaccid paralysis, and weakness of the lower extremities. Foot deformities may also co-occur (Friede, 1989). The severity and location of the lesion determine the pattern of deficits (Evans, 1987). Approximately 70% of children with myelomeningoceles have the Arnold–Chiari malformation (Aicardi, 1992). Complications include meningitis, hydrocephalus, and pneumonia (Friede, 1989).

A variety of etiological factors pertaining to maternal health have been suggested. These include fevers, viruses, hormonal and ovulatory changes, folic acid and zinc deficiencies, and maternal diabetes (Friede, 1989; Hynd & Willis, 1988). Suspected teratogens include alcohol, hypervitaminosis A, and valproic acid (an anticonvulsant) (Friede, 1989; Hynd & Willis, 1988). There is also evidence that chromosomal anomalies and genetic susceptibility sometimes play an etiological role (Friede, 1989).

Screening for spina bifida can take place prenatally through analysis of α-fetoprotein (AFP) levels—preferably during weeks 16–18 of gestation. At this time, the levels in open spina bifida pregnancies are usually four times greater than in nonaffected pregnancies. Closed lesions cannot be detected biochemically. Ultrasound can be used to identify the spina bifida lesion (Wald & Cuckle, 1992).

The incidence of spina bifida varies by the type of lesion. Since spina bifida occulta is asymptomatic, it is difficult to ascertain its incidence. Reigel (1982) has estimated that it may occur in 20–30% of the population but a true incidence this high seems unlikely. In one study, 1172 routine radiological examinations of autopsied individuals revealed that 5% had spina bifida occulta (James & Lassman, 1972). This latter estimate of incidence seems more likely.

Alter (1962) reported the incidence of spina bifida cystica to be 0.7 per 1000 live births.

Wiswell et al. (1990), in their 17-year epidemiological study of U.S. Army hospital births, reported an incidence of 0.68 per 1000 when cases of spina bifida occulta and meningoceles were excluded. They noted a significant decline in the incidence of spina bifida among female infants from 1971 to 1987.

There are significant geographic variations in the incidence of spina bifida with the British Isles having the highest incidence. India, China, and parts of the Middle East are also high-risk areas. In contrast, Japan, Hong Kong, and countries in north and sub-Saharan Africa have low rates (Little & Elwood, 1992a). However, in the Wiswell et al. (1990) study, no geographic variation for spina bifida was found. Several studies have provided evidence that spina bifida is less common in blacks than in whites (Little & Elwood, 1992b). For example, Wiswell et al. (1990) reported that white infants and infants of other races were more likely to have spina bifida than black infants. It is also more common among children born of low-socioeconomic-status mothers and those at the extreme ages for childbearing (Chervenak & Isaccson, 1989). There are also sex differences in spina bifida with it being slightly more common in females. Approximately 56% of individuals with spina bifida in Canada and the United States are females (Elwood & Little, 1992).

Cranium Bifidum and Encephalocele

Cranium bifidum is a fusion defect of the skull that typically affects the midline sutures. Lesions not containing tissue are called cranial meningoceles and are rare (Aicardi, 1992; Friede, 1989). Lesions that contain cerebral tissue are referred to as encephaloceles (Friede, 1989). Approximately 10% of myelomeningoceles fit this description (Eckstein, 1983). They are most frequently found in the occipital region and are less commonly found in the frontal region. Frontal encephaloceles typically involve some frontal lobe tissues as well as olfactory tissue (Friede, 1989). Lesions in the frontal and nasopharyngeal regions are often associated with holoprosencephaly, agenesis of the corpus callosum, and ocular hypertelorism (Hynd & Willis, 1988). Encephaloceles are rare at other midline locations (Friede, 1989).

The extent of herniation is not necessarily correlated with the size of swelling (Hynd &

Willis, 1988). Encephaloceles are not usually associated with a primary skin deficit although ulcerated skin may develop. Tissue within the encephalocele connects with usually just one cerebral hemisphere through glial tissue. Encephaloceles affect the shape of the brain with the attached hemisphere usually being smaller and the contralateral hemisphere extending past the midline. This sometimes distorts cranial nerves, cerebral arteries, and the hypothalamus. Gyri radiate from the site of the encephalocele and the lateral ventricles are deformed (Friede, 1989).

Encephaloceles are sometimes associated with agenesis of the corpus callosum (Friede, 1989). Wiswell et al. (1990) reported that 40% of newborns with encephaloceles had additional congenital anomalies. Among their sample, they most frequently found multiple anomalies, cleft lip and palate, and limb defects.

Hydrocephalus sometimes develops. Clinical manifestations related to hydrocephalus include mental retardation, ataxia, cerebral palsy, epilepsy, and visual–perceptual problems (Hynd & Willis, 1988). Of 45 patients with encephaloceles and hydrocephalus described by Lorber (1967), only 4 had IQs in the normal range and only 20 survived. Surgery to remove occipital encephaloceles somewhat improves the prognosis. In one study that followed patients approximately 9 years after the operation, 25 of 40 patients were still living and had normal or near-normal intelligence (Mealey, Dzenitis, & Hockey, 1970). Wilkins, Radtke, and Burger (1993) described the case of a 36-year-old woman with an anteroinferior temporal encephalocele. She had a 23-year history of simple and complex partial seizures which were controlled after surgical treatment for the encephalocele.

Encephaloceles are considerably more rare than spina bifida. Friede (1989) cites the incidence as 0.1–0.3 per 1000 live births. In the Wiswell et al. (1990) study, the incidence for live- and stillbirths was 0.14 per 1000. They reported a significant reduction in incidence among white females during the 17-year period covered by the study. They also found that among white infants, encephaloceles were more common among females. This is consistent with reports that the sex distribution of encephaloceles is similar to that of spina bifida cystica and anencephaly (Friede, 1989).

Anencephaly

Anencephaly is a defect in which the vault of the skull is typically missing and the midbrain and forebrain consist of highly vascularized tissue containing mainly glial and scattered neurons (Friede, 1989; Hynd & Willis, 1988; Kolb & Fantie, 1997). The face is grossly normal, although the eyelids bulge and the nose is enlarged. Cranial nerves can be identified from the trigeminal down. Maxillofacial bones show some deformity. The extent of the involvement of the spine varies. Often there is abnormal vertebral segmentation. The body is disproportional in that the neck is very short while the upper extremities are large and long in comparison with the lower extremities. The term rachischisis is used to describe those severe cases in which many spinal segments are involved in an open defect at the back. This is essentially the same as spina bifida but rachischisis is the conventional term of choice.

Anencephaly is incompatible with life and is estimated to account for 29.5% of all abnormal stillbirths (Coffey & Jessop, 1957). Most infants die minutes to hours (Hynd & Willis, 1988) or weeks (Aicardi, 1992) after birth. McAbee, Sherman, Canas, and Boxer (1993), however, have described two infants with anencephaly who survived for 7 and 10 months without prolonged mechanical ventilation.

In a case reported by Dyken, an anencephalic male had spinal and brain stem reflexes, hypertrophied muscles, rigid limbs, hypothermia, and suckling and swallowing reflexes. He had no associated systemic abnormalities. He died after 6 days and structures above the diencephalon were not identified during the autopsy (Dyken & Miller, 1980). In the study by Wiswell et al. (1990), 20% of anencephalic infants had additional anomalies. The most frequent included multiple anomalies, cleft lip and palate, and other neural tube defects.

Anencephaly can be diagnosed antemortem through elevated maternal AFP levels. It results from failure of the neural tube to form at approximately the fourth week of gestation (Friede, 1989). The cause of anencephaly is not certain but several factors have been suggested. Proposed etiological factors include maternal diabetes (Gilles et al., 1983), trauma, radiation (Rugh & Grupp, 1959), and hypervitaminosis A (Brett, 1983). The recurrence rate is thought to

be 1.9% and for mothers who have previously had such a child increased consumption of folic acid should be consumed prior to conception through the first trimester (Jones, 1997).

The incidence of anencephaly is estimated to be between 0.5 and 2.0 per 1000 births in the United States and most of Europe. The incidence is higher in Britain and lower in Africa, Asia, and South America (Friede, 1989). In the Wiswell et al. (1990) study, the incidence was 0.36 per 1000 live- and stillbirths. They also reported that it was more common among females. This is consistent with other research that has revealed a 3:1–4:1 female-to-male ratio (Jones, 1997). With longer gestation periods, however, the proportion of females decreases (Friede, 1989).

Hydranencephaly

Hydranencephaly is a deficit in which cystic sacs containing CSF replace the cerebral hemispheres as a result of massive necrosis. A thin, translucent membrane containing attenuated blood vessels makes up the walls of the sac. The membrane lies adjacent to the dura mater. There is usually some preservation of the thalamus, brain stem, and basal ganglia. In some cases, portions of the temporal and occipital lobes are present (Friede, 1989).

Early in life it may be difficult to distinguish hydranencephaly from hydrocephalus. The size of the head is usually not enlarged at birth but it begins to grow at an abnormal rate during the first weeks of life (Friede, 1989). Deficits include feeding difficulties, atypical eye movements, hypnoatremia, seizures, dystonic posturing, persistence of primitive reflexes, and disturbed thermoregulation (Friede, 1989; Hynd & Willis, 1988).

Aylward, Lazzara, and Meyer (1978) described the case of a hydranencephalic male infant. As a newborn he was described as well developed, irritable, and as having a high-pitched persistent cry, primitive reflexes, and intact cranial nerves. The only abnormal physical signs were a slightly enlarged head and aberrant ocular movements. He was assessed at 41, 42, and 48 weeks. The infant was able to habituate to noise and light and was sometimes able to track a high-contrast schematic face. The infant was hyper-irritable and had difficulty attending to social stimuli. However, he displayed some socially appropriate automatisms in addition to reflex automatisms. His motor activity displayed a high number of spontaneous activities at a medium speed and at a high level of intensity. He was hypertonic and had poor head control. At 7 months, he was still alive.

In making the differential diagnosis between hydrocephalus and hydranencephaly, translumination of the head is an important clinical feature although it is not always present. EEGs may also be helpful since in most cases of hydranencephaly electrical activity is absent. Neuroimaging also contributes to the diagnostic process (Sutton, Bruce, & Schut, 1980).

The necrosis of the hemispheres has been speculated to result from infarction related to vascular occlusion. This may occur through mechanical problems such as umbilical cord strangulation or through the secondary effects of other etiological agents such as toxoplasmosis or gas intoxication (Friede, 1989; Hynd & Willis, 1988). There have been some reports of blunt trauma to the abdomen during pregnancy (Friede, 1989). In addition, some familial cases have been reported (Aicardi, 1992). Incidence and gender ratios are unknown (Hynd & Willis, 1988).

Porencephaly

Porencephaly is a deformity in which there is a circumscribed, large cystic lesion resulting from necrosis. Here we will address those of neurodevelopmental nature that occurred before the appearance of adult hemispheric characteristics. Thus, we exclude lesions occurring postnatally or during the terminal stages of pregnancy (Friede, 1989; Hynd & Willis, 1988). This usage of porencephaly is synonymous with schizencephaly, a term offered by Yakovlev and Wadsworth (1946a,b).

The term porencephaly was first used by Heschl (1859, 1868) who reported the case of a 26-year-old beggar who had symptoms similar to cerebral palsy. Autopsy revealed that he had an asymmetric skull which was thicker on the left. He also had a large perisylvian cyst which was in communication with the brain surface and the lateral ventricles.

The defect may occur unilaterally but is most often found bilaterally, typically in the insula region. The neurodevelopmental nature of the deficit is apparent because of minimal scar tissue and the anomalies in adjoining cortex.

The lesion is not space occupying so it does not increase pressure. Often the septum pellucidum is absent which allows better communication between bilateral defects. Usually the thalamus is small because of atrophy of thalamic projection nuclei, but focal lesions are typically not found in the basal ganglia, cerebellum, or brain stem (Aicardi, 1992; Friede, 1989).

Friede (1989) distinguishes between two types. In the first type, polymicrogyria is associated with the lesion. In the second type, polymicrogyria is not present but the gyral patterns are atypical, often radiating toward the defect. Often the laminar architecture is disrupted.

Behavioral manifestations vary according to factors such as the size of the lesion, location of the lesion, amount of disturbance in surrounding cortex, the extent that the cyst infiltrates the ventricular system, and whether or not the lesions are bilateral (Aicardi, 1992; Hynd & Willis, 1988). Clinical features may include mental retardation, epilepsy, cerebral diplegia, quadriplegia, macrocephaly, facial apraxia, and speech disorders (Aicardi, 1992; Hynd & Willis, 1988). Some cases may be discovered incidentally and are largely asymptomatic. Life expectancy varies according to associated complications.

The diagnosis of porencephaly is usually made through neuroimaging but it may also be detected by sonography. The diagnosis is usually easy to make but in cases involving large cysts it may be difficult to distinguish from holoprosencephaly (Aicardi, 1992).

It has been suggested that porencephaly results from an ischemic event, leading to necrosis, during the fifth fetal month. Aicardi (1992) suggests that in porencephaly, the mantle is damaged early and is inadequately repaired. In association with the damage, neuronal migration is also disrupted. It is not certain if the etiologies or time of injury for the two types of porencephaly are different (Friede, 1989). There have been a few reported cases of familial porencephaly with dominant inheritance (Aicardi, 1992). The incidence and gender ratios for this disorder are unknown (Hynd & Willis, 1988).

Conclusions

In this chapter we have reviewed in some detail the spectrum of neurodevelopmental abnormalities including those that impact on the bulk growth of the brain, dysplasias of the cerebral hemisphere, malformations of the cerebral cortex, malformations associated with congenital hydrocephalus, and abnormalities of the neural tube and fusion defects. As Crome (1960) noted, however, over four decades ago, "it seems likely that future refinements in techniques will rise to the surface other, still submerged anomalies" (p. 903). Advances in microimaging, staining, and in understanding the architecture of the neurotransmitter systems will undoubtedly improve our conceptualization of normality and its neurological deviations.

Clearly, the seminal work of Galaburda and his colleagues in articulating the neurodevelopmental pathology associated with developmental dyslexia deserves our attention (Galaburda et al., 1985; Humphreys, Kaufman, & Galaburda, 1990; Rosen, Sherman, Richman, Stone, & Galaburda, 1992). Their research demonstrates not only that cytoarchitectonic anomalies are associated with a syndrome long thought to have a neurological etiology (Hynd & Cohen, 1983), but also the vast complexity of factors that may produce some of the more subtle neurodevelopmental anomalies found in disorders of cognition.

Although this research and that of others is profoundly exciting, caution against overinterpretation must always be kept in mind. There is no one-to-one relationship between the behavioral and cognitive symptoms we may see in patients with developmental disorders and the manifestation of neuropathology seen at postmortem. In disorders such as severe or profound mental retardation there is almost always associated neuropathology (Crome, 1960; Freytag & Lindenberg, 1967); however, it is not unlikely that in cases of dyslexia or congenital dysphasia the anomalies occur only in the micro-structure, if at all. It should be kept in mind, for example, that the IQs of the patients studied at postmortem by Galaburda et al. (1985) ranged from 88 to 117. Thus, if one were to generalize, it might be said that the more severe the neurodevelopmental pathology, the more serious the impact on widely distributed functional systems (such as porencephaly), but the more focal the pathology, the more likely the effects will be negligible or more specific to the functional system disrupted.

Science is rarely without an agenda. Thus, it would serve us well to recall that it was less than

100 years ago that neuroanatomists attempted to quantify the relationship between intelligence and the estimated number of neurons in the brain (Gould, 1981). Unfortunately, some of these scholars were guided by racial preconceptions and an agenda that precluded objective inquiry. If anything is evident from our more refined understanding of how the brain grows and develops, it is that alterations occurring at specific stages of CNS development are likely to produce well-documented abnormalities. What is less clear is what causes the deviations to occur, but it seems evident that the etiology of many, if not most, of these disorders is multifactorial (e.g., genetic, environmental, vascular). Continued neurobiological research will serve to disentangle these complex relationships, and it can be presumed that neuropsychological research will equally contribute to a better conceptualization of the cognitive and behavioral effects of these neurodevelopmental anomalies.

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7

Pediatric Brain Injury: Mechanisms and Amelioration

LISA D. STANFORD AND JILL M. DORFLINGER

Little has changed regarding the mechanisms of pediatric traumatic brain injury (TBI) since the first publication of this chapter. However, increased awareness of the unique nature of pediatric TBI and greater need for intervention in this special population warrant a more contemporary consideration of this topic. Several recent outcome studies have specified a distinct course of brain injury in the young pediatric population relative to school-aged children and adults. Additionally, there has been a greater push to understand the long-term cognitive and behavioral outcome of pediatric TBI as more and more children with brain injuries enter the school environment and require more specific recommendations to address their unique educational needs. Thus, the purpose of this chapter is not to provide a comprehensive review of the neuropsychological literature in the area of pediatric brain injury, but to offer a description of the unique mechanisms of and issues pertaining to TBI in young children. These include the typical neurodevelopmental and neuropsychological sequelae associated with pediatric TBI, as well as the preexisting factors and interventions that impact the outcome of brain injury in these children. Such mechanisms are influenced by age of injury, type of injury, time since injury, and age at outcome testing (Dennis & Barnes, 1994; Taylor & Alden, 1997), as well as the epidemiologic issues that contribute to the nature of the injury and the specific characteristics of the individual who sustains that injury (individual buffers/lower thresholds). Amelioration of the injury, which has in many reviews been focused largely on rehabilitative techniques of a formal nature, is discussed in the broader context of cognitive and behavioral profile, psychological and educational interventions, and family-based activities in order to provide an overview of these issues in a practical way.

The chapter begins with a discussion of the physiological, epidemiological, and psychological mechanisms that are associated with pediatric brain injury and characterize the child who suffers the brain injury. Discussion emphasizes the unique nature of brain injury in young children as it differs from that typically occurring in brain injury of adolescents and adults. Finally, a description of the impact of pediatric TBI on neurodevelopmental and neuropsychological functioning and recommendations for how these deficits should be addressed within the home and school environment to meet the unique needs of these children and their families are offered.

Epidemiological Mechanisms

According to the Center for Disease Control estimates of TBI in the United States (2006), approximately 475,000 TBIs per year

LISA D. STANFORD • Department of Psychiatry and Neurology, University of Illinois Medical Center at Chicago, 60612. **JILL M. DORFLINGER** • Alexian Brothers Behavioral Health System, Hoffman Estates, IL 60169.

occur among children of ages 0–14 years. In children aged 0–4 years, 1120.7 per 100,000 sustain TBIs each year, and 659.3 per 100,000 TBIs occur in children aged 5–9 years. Emergency department visits account for more than 90% of the TBIs in the younger age group. It is the leading cause of death and disability in children under 25 years of age, with over 17,000 children per year sustaining permanent injuries each year (Kraus, 1995; Langlois, Rutland-Brown, & Thomas, 2005). Falls are the leading cause of TBI with rates highest for children of ages 0–4 years. Despite the high incidence of pediatric TBI, many national registers who track pediatric TBI and research populations are confounded by varying methods in determining the severity of injury. These confounds lead to less clear rates as to how many children per year suffer mild versus moderate versus severe brain injury and the outcome associated with severity of injury for those not classified as severe. Also complicating the classification of severity is that brain injury in very young children (i.e., under age4) does not necessitate loss of consciousness for severity of injury, clinical signs are unreliable at this age, asymptomatic brain injuries occur more frequently, and the incidence of skull fracture from minor impact is greater due to the growing calvarium and immature brain (Hebb, Clarke, & Tallon, 2007). Significant radiologic findings (i.e., skull fractures) are not always predictive of severity nor outcome in young children, and young children have a lower physiologic threshold for loss of consciousness than adults (Bruce et al., 1997). In the emergency department, infants and children under 2 years of age do not always show clinical signs of brain injury (e.g., vomiting, loss of consciousness), despite neuroradiologically confirmed injury (Greenes & Schutzman, 1999). Pediatric TBI has also been associated with unique injury mechanisms not routinely seen in adults, such as diffuse cerebral swelling (Levin et al., 1992; Zwienenberg & Muizelaar, 1999), as well as increased excitotoxicity and apoptotic neuronal death (Bauer & Fritz, 2004; Kochanek, 2006). Thus, classification of severity for mild and moderate injuries is difficult at a young age, and several studies have presented guidelines for assessing severity and for treatment following TBI in

the very young (Hebb et al., 2007; Schutzman et al., 2001). Children with TBI under the age of 2 years can be stratified into groups based on their risk for intracranial injury. Children in the high-risk group for intracranial injury include those presenting with depressed mental status, signs or symptoms of a depressed or basilar skull fracture, seizure, irritability, acute skull fracture (<24 h), bulging fontanel, significant or prolonged vomiting (greater than five times or lasting longer than 6 h), and loss of consciousness longer than 1 min. Head CT is indicated to expediently identify any intracranial injury, although risk for further vascular injury is greater in these young children as they require sedation for imaging.

Difficulty assessing parameters of injury severity in the young patient is also complicated by poor witness account of loss of consciousness (especially if the perpetrator is the witness), inability to assess amnesia in a child whose language is limited or is pre-language, and different expression of injury. The Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974 – Yeates book chap. 5) requires modifications to account for assessment of injury to a child who is nonverbal (i.e., nonverbal, developmentally delayed or too young to yet be speaking) such as the Child Coma Scale (CCS; Hahn et al., 1988; James, 1986), Children's Coma Scale (Raimondi & Hirschauer, 1984), or the Adelaide Pediatric Coma Scale (Reilly, Simpson, Sprod, & Thomas, 1988; Jaffe & Wesson, 1991). These scales alter the scoring for "best verbal response" in the nonverbal child to better capture the contribution of behavioral findings to severity index.

Nonverbal child	Verbal child's best verbal response (GCS)	Score
Smiles, oriented to sound, follows objects, interacts	Oriented and converses	5
Consolable when crying and interacts inappropriately	Disoriented and converses	4
Inconsistently consolable and moans; makes vocal sounds	Inappropriate words	3
Inconsolable, irritable and restless; cries	Incomprehensible sounds	2
No response	No response	1

However, even uninjured children under 5 years of age may have lower scores than adults because of reduced best verbal and motor responses (Jaffe & Wesson, 1991). Thus, typical parameters for defining severity including length of loss of consciousness, GCS score, and amount of post-traumatic amnesia are complicated in young children due to the different expression of injury, lack of language to follow commands or produce a verbal response, contribution of age at injury, premorbid skills level, and variability of event accounts.

Physiological Mechanisms

Pediatric TBI also differs from TBI in adults due to cause of injury, biological properties of the pediatric brain and skull, and levels of functional expectations. The pattern of the causes of head injuries along the lifespan parallels developmental milestones (Eisele, Kegler, Trent, & Coronado, 2006; Langlois, Rutland-Brown, & Wald, 2006; Rutland-Brown, Langlois, Thomas, & Xi, 2006). Irrespective of cause, males are more likely than females to sustain a TBI, and this ratio becomes more disparate with increasing age (Bruns & Hauser, 2003; Kraus, 1995). Most head injuries in children under age 2 are due to the actions of another person (e.g., being dropped) or to trauma during birth. As children become more independent in their mobility, there is an increase in head injuries due to falls and then to sports-related activities. There is another spike in head injuries when adolescents begin to drive motor vehicles. Violent trauma and motor vehicle accidents are other causes of head injury in children that tend to increase in incidence with age. Some studies show that African American children and those younger than 4 years have higher rates of TBI and are more likely to be hospitalized (Langlois, Rutland-Brown, & Thomas, 2005; Levin et al., 1992). Still, most pediatric TBIs tend to be mild (Atabaki, 2007; Keenan & Bratton, 2006; Kraus, 1995). When severe TBI in children does occur, it is most often associated with child abuse, gunshot, or motor vehicle accident (Kraus, 1995; Thurman, Alverson, Dunn, Guerrero, & Sniezek, 1999).

There can be focal and/or diffuse injury mechanisms with a pediatric TBI. Focal mechanisms are mostly due to penetrating head injuries that involve disruption of the skull and dura mater and cause localized brain damage at the site of penetration. Diffuse mechanisms are associated with closed head injuries, which are due to rapid acceleration, deceleration, or rotation of the head. Closed head injuries lead to widespread cerebral damage in addition to focal lesions in the anterior aspects of the brain (Levin et al., 1993, 2006). The neurological phenomena following TBI may include diffuse cerebral edema, increased cranial pressure, ischemic brain damage, hemorrhagic brain damage, or axonal stretching, tearing, or shearing. When axonal or neuronal injury occurs, there is primary axotomy (less frequent than originally proposed), delayed axotomy (affected axons become lobulated between 6 and 12 h after injury), and secondary axotomy (24–72 h after injury with Wallerian degeneration) (Povlishock, Erb, & Astruc, 1992; Trivedi et al., 2007). Later onset or secondary neurological processes of a pediatric TBI may include post-traumatic hydrocephalus or seizures, which further changes the trajectory of recovery, development, and outcome in the young child.

Since the injury mechanisms in pediatric closed head injuries are usually diffuse, the effects are global and produce a common clinical presentation. However, there is an overlaying effect of neurodevelopment, which is not a factor when evaluating adults with a TBI (Benz, Ritz, & Kiesow, 1999; Taylor, 2004; Taylor & Alden, 1997). Studies of recovery following experimentally induced lesions in monkeys led to the notion called the Kennard Principle because the younger monkeys generally recovered motor function better than the adult monkeys (Kennard, 1940, 1942). However, ensuing research has shown that the immature brain is actually more susceptible to injury because of its biomechanical properties (Bauer & Fritz, 2004; Kochanek, 2006). For example, the bones of an infant are elastic and vacuous and become progressively rigid with maturation. The bones in the skull are also initially separated by fibrous tissue leaving open fontanelles (i.e., "soft spot") and unfused sutures (Gray, 1918). The water content of the brain starts out relatively high and becomes lower as myelination increases in later childhood and adolescence (Bauer & Fritz, 2004; Durston et al., 2001), thus reducing the buffer for more sophisticated tissue.
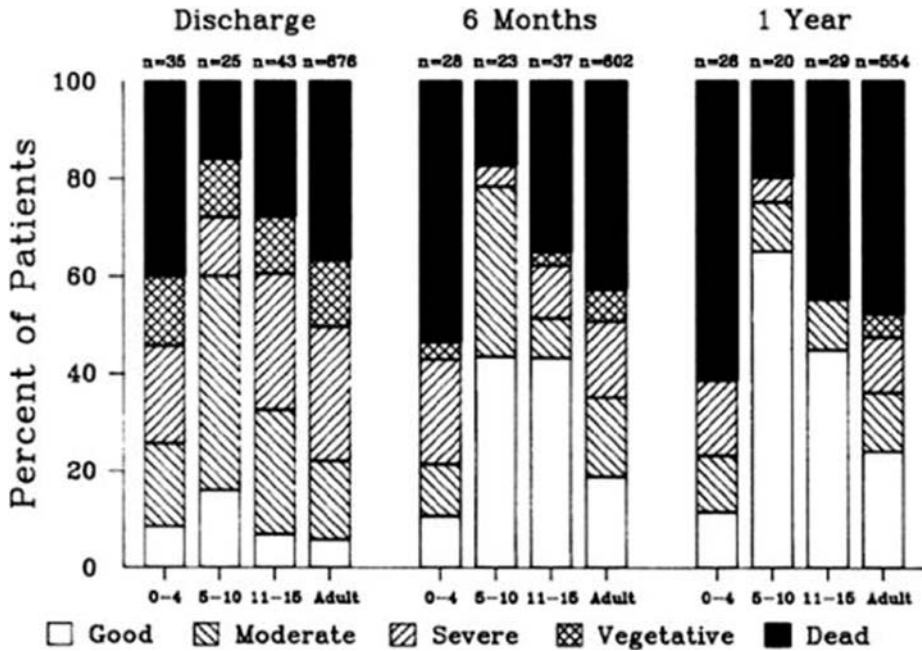
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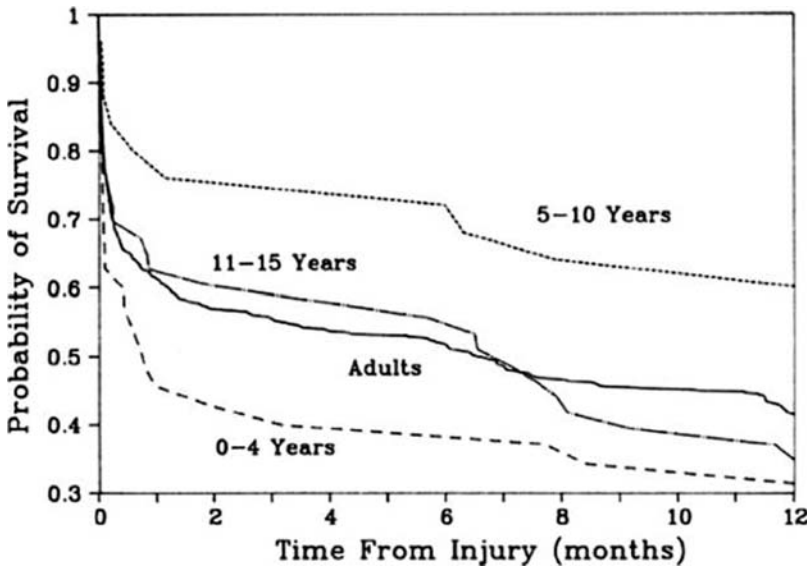
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Anatomical differences at different stages of development contribute to the variations in clinical presentation after a head injury. In contrast to the Kennard Principle, which assumes that younger brains are more apt for neuroplasticity and will therefore recover function better, Hebb (1942) proposed a hypothesis that postulated progressive and global cognitive impairments following early brain injury. Hebb's (1942) hypothesis has been supported

by years of clinical and research experience and is more parsimonious with the biomechanical, experiential, and developmental differences between children and adults. For example, research and clinical findings have demonstrated that experimental lesions in early life are associated with neural regeneration, but there is also creation of many aberrant and dysfunctional pathways (Schneider, 1979). Neuroimaging studies have offered additional information about brain volumetrics, regional morphometry, and disruption of myelination following TBI in the young child. There are also long-term neuropathological changes following pediatric TBI, such as reductions and/ or alterations in cerebral white matter (Tasker, 2006; Tasker et al., 2005; Wozniak et al., 2007) and grey matter (Wilde et al., 2005). Wilde et al. (2005) noted that whole brain volumes were significantly reduced, the majority of lesions were in the frontal regions, anterior grey and white matter volumes were smaller, cerebrospinal fluid was increased, and there was a trend toward decreased volumes in posterior regions in children with TBI compared to controls. In another study, corpus callosum lesions were greatest in the posterior body and the splenium, significant reductions in the size of the corpus callosum were seen, and total corpus callosum area size was related to GCS, and these changes were still apparent 3 years post-injury (Levin et al., 2000). As diffusion tensor imaging (DTI) is used more consistently in outcome studies, more will be learned regarding changes in the development of white matter over time in young children who have suffered TBI.

As the direct impact of early TBI on developmental trajectories is unknown, long-term studies have focused on neuropsychological outcomes including general cognitive abilities, executive functions, psychosocial outcome, and moderators of outcome. The unique characteristics of younger children (i.e., less than 7 years of age) and even more specifically those children less than 2 years of age who have sustained acquired brain injury (inflicted and accidental) have more recently been the focus of longitudinal outcome research (Anderson & Yeates, 1997; Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005). Outcome studies of early childhood TBI (i.e., injury sustained between ages 2 and 7) have indicated a relationship between injury severity and neurobehavioral functioning, with early vulnerability even when preinjury variables (e.g., age at injury, adaptive functioning, SES, family functioning) are moderated (Anderson et al., 1997). As expected, the most severe and persisting deficits were associated with those younger children who suffered the most severe injuries. A recent study examined preschoolers who had sustained TBI prior to age 2 and compared them to controls on measures of cognitive development and adaptive behavior (Keenan, Hooper, Wetherington, Nocera, & Runyan, 2007). Results indicated that a majority of the children who sustained early TBI (both inflicted and accidental) were more than one standard deviation below average on measures of cognitive ability and adaptive behavior. Additionally, those with inflicted injuries showed greater deficits in comparison to both those with accidental injuries and controls after controlling for socioeconomic status. Income level, higher GSC scores, absence of seizures, and high social capital were associated with better outcomes. Studies involving unilateral lesions in young children support adverse effects of these lesions on later developmental functioning consistent with side of lesion (Bates, Dale, & Tahl, 1995; Eisele & Aram, 1995 – refs in Taylor & Alden, 1997, JINS article), although there is evidence of considerable sparing. Other studies have indicated recovery profiles in young children who do not conform to those typically seen in older children and adults (i.e., greatest recovery of deficits in the acute period to 12 months post-injury), but are more dependent on injury severity (Ewing-Cobbs et al., 1997). Impairment that was present in younger children in the acute phase persisted at 1 year post-injury. Additionally, declines in functioning over age were interpreted to reflect both the lack of progress in skill development relative to peers and greater difficulties in higher level skills or later executive dysfunction in children who sustained brain injuries at younger ages. Development, including cognitive and academic, is more adversely affected when the child is younger at the time of injury (Taylor & Alden, 1997). Thus while there is great potential for early brain reorganization, this comes at a long-term developmental cost.

Psychological Mechanisms

The third mechanism that needs to be understood when discussing pediatric head injury is the mechanism of psychological competence. The mechanism of psychological competence includes pre- and post-brain-injury social integration, family tolerance, school performance, and neurocognitive function and dysfunction, which contribute to and directly interact with other variables that are generally described as contributing to outcome. Describing mechanism in a manner that merges the purely mechanical, the environmental, and the inter- and intrapersonal makes it clear that pediatric TBI must be understood as a continuum, in context, and as a continuous work in progress.

The finding that head injury is not random is now widely accepted, and Rutter (1981) was very probably the first to carefully spell out the implications of premorbid characteristics and behavior to post-head-injury problems. Parents burdened with the trauma of a severely injured child are understandably reluctant to grapple with their and the child's contribution to this injury, especially when this contribution appears terribly indirect. Nevertheless, Rutter found a strong relationship between children's preinjury behavior and psychiatric and other difficulties 1 year and further post-head injury. A major study on mild TBI in children (Asarnow et al., 1995 – Peg's book intro) showed that children with TBI had an increased number of behavior problems prior to injury in comparison to children with other injuries and controls. This study supported earlier hypotheses that children with more behavioral problems were at heightened risk for accidents and TBIs (Brown, Chadwick, Shaffer, Rutter, & Traub, 1981). A longitudinal study by Bijur and colleagues (1990, 1995 – Peg) also found that children with TBI showed more premorbid aggression and hyperactivity, and the mothers of children with TBI reported more symptoms of depression relative to the mothers of controls. It is therefore important that all understand that children with preinjury behavioral difficulties are at greater risk for TBI. Understanding the nature of pre-head-injury risks provides substantial prognostic information and informs the design of a treatment program that attends to appropriate variables that may not be apparent immediately following a brain injury. It is important to incorporate family functioning issues, and to understand that families of head-injured children may bring with them greater numbers of difficulties in coordinating the type of integrated effort needed to address their child's needs.

Although family-oriented research dealing specifically with adjustment to a brain-injured child is limited, several studies based on families of adults with TBI, as well as families with other chronic illness and disabilities, suggest that families go through several stages of adaptation (Blacher, 1984; Drotar, Baskiewicz, Irvin, Kennell, & Klaus, 1975; Lezak, 1986; Waaland & Kreutzer, 1991). After the initial period of shock and disbelief, the family is thankful for the patient's survival and anticipates recovery within the first year. Confusion and anxiety begin to set in as the recovery slows, and lack of motivation and uncooperativeness in the patient are viewed as impediments to recovery. As expectations for recovery diminish, feelings of depression surface, and a mourning process begins. In the final stages, the family comes to accept the permanence of the disability. It is at this time that family can benefit the most from strategies and planning for the patient's future adjustment. The availability of appropriate supportive and therapeutic resources at this time is critical to family adjustment outcome.

In the context of pediatric brain injury, children and families go through similar phases that mirror the recovery pattern. Initially, physical concerns such a motor weakness and sensory impairments are the focus of treatment. Once the more significant cognitive deficits resolve and after the initial rapid recovery period, parents may become frustrated by the slowing of progress, and residual behavioral and more subtle cognitive deficits become the focus of attention (Semrud-Clikeman, 1991). Behavioral and personality changes after brain injury are among the family's most serious concerns (Ball & Zinner, 1994; Bond, 1983; Lezak, 1986; McKinlay & Hickox, 1988) and produce the greatest amount of stress on the family (Brooks & McKinlay, 1983). Family members struggle with responding to the new behaviors of their brain-injured child while experiencing a strong sense of loss for the child they once knew. It is as if a new person has been added to the family, and their grief often resembles the bereavement associated with the actual death

of a child (Ball & Zinner, 1994). Poor fit can be as devastating as poor capacity. A child with limited abilities in an environment with limited expectations may be quite well integrated, and a child with substantially better but yet imperfect abilities may well be seen as having sustained an intolerable loss in environments where significantly more stringent demands for particular types of performance pervade. The ability of an environment to adjust to change in a child is multifactorial, and yet far more crucial to the satisfactory nature of outcome than any identifiable single intervention strategy per se. Therefore, intervention strategies aimed at increasing the malleability of the environment are far more functionally oriented than intervention strategies aimed at improving the actual capacity of the child.

Other areas of familial concern include financial hardship, lack of support from the community of health services, decreased communication and cohesiveness among extended family members, and lack of services for transitions back to school (DePompei & Zarski, 1989; Waaland & Kreutzer, 1991). The worsening of premorbid tendencies, especially those already having been found to produce difficulties, either academically, behaviorally, psychiatrically, or otherwise, is easy to predict, but all too seldom the focus of early intervention activities. Neuropsychological referrals, even less common in children than adults, should be more frequent and be part of the overall secondary and eventually tertiary preventative efforts of any head injury treatment program (Boll, 1983). Many patients with head injury are substantially more sensitive to the effects of alcohol than they were prior to their head injury. Alcohol use is substantially associated with additional head injuries, noninjuring accidents, and aggression of all sorts, not limited to the marital relationship. Therefore, individuals who have sustained a head injury in childhood are not only more at risk for other difficulties but also more susceptible to future risk factors, such as alcohol use. Furthermore, individuals with head injuries who have sustained cognitive compromise may be more inclined to experience occupational and educational difficulties, rendering them permanently in lower socioeconomic strata, further exacerbating difficulties, frustrations, and coping complications in an already compromised organism. Such an individual, then, significantly

brain injured at an early age, carries with her or him substantial and continuing risk factors that must be contended with in a variety of ways. This can only be accomplished through appropriate treatment approaches that sustain contact with this individual and her or his support system, and provides sufficient types of support to attend to these issues as they occur on a developmental basis throughout the life span.

Each of these challenges, and the demands to understand the multifaceted etiology of difficulties secondary to TBI, argue convincingly for the role of psychological treatment for the family, including siblings, and occasionally even more extended family members, as well as for the patient. The patient may not be in an adequate position to receive benefit from direct treatment because of cognitive and emotional impairments on a neurological basis. Even when the patient is perfectly capable of carrying on full involvement in psychological treatment, however, his or her symptom picture does not affect the patient alone. Rather it has substantial influence on his or her entire environment. Therefore, treatment for the family has many foci. One focus, of course, is to help in the overall treatment programing and provision of aid for the TBI survivor. To understand the nature of the condition, anticipate difficulties that will occur, make preparations, and make alterations within the family to cope with these changes are critical responsibilities that are very difficult to meet without professional help. A second focus is the stress that these demands place on family members. Stresses in marital and sibling relationships, unevenness in care demands, drains on financial and temporal resources, and changes in life pattern and style often produce significant emotional reactions in family members, even when the necessity for them is clear and the cause well understood. Being deprived of a previously well-established lifestyle, devoting resources to medical treatments rather than family vacations, turning part of the home into a rehabilitation environment instead of a recreation room, and having a sibling who is no longer fully presentable under a variety of social circumstances is something that certainly can challenge the coping capacity and reservoir of goodwill of even the most well-adjusted child and adolescent sibling, not to mention the parents. The way in which a family copes with these difficulties can, in some instances, determine the

overall outcome and satisfactory adjustment, not only of the survivor but of the entire family.

Several studies examining preinjury familial differences relative to the general population have found increased psychopathology, fewer social advantages, lower SES, and greater marital instability (Klonoff, 1971; Rutter, Chadwick, Shaffer, & Brown, 1980). Psychosocial outcomes of pediatric TBI are mediated by these same variables: family stability, parental mental health, and socioeconomic status (Brown et al., 1981). Not only the family is affected by the TBI in a child but the family environment affects the child's psychological response to and adjustment following injury. Thus, poor availability of social support, limited financial resources, and long-standing difficulty coping with family stressors may inhibit the opportunity for adjustment to a family member's brain injury and recovery of that injury on the child's later functioning.

In addition to being a direct consequence of TBI, changes in social, emotional, and behavioral functioning may create problems over time in response to increased personal awareness of deficits. Children may engage in dangerous or risk-taking behaviors as a form of denying deficits (Barin, Hanchett, Jacob, & Scott, 1985) or in response to an inability to recognize cognitive, behavioral, and physical risks and limitations. Disinhibition, impulsivity, aggressiveness, and irritability may make maintaining previous social relationships difficult or prevent a child from establishing new relationships (Barin et al., 1985). Old friends may lose patience or interest in coping with the multifaceted changes that have occurred in their friend who has suffered a TBI. This creates a sense of isolation and alienation for the child who can no longer function in the manner that her or his friends had come to expect. For adolescents, there is often a sense of dependency on caretakers at the very developmental stage when issues such as identity and autonomy become most salient (Barin et al., 1985; Lehr, 1990).

Intervention programs should help the child recognize, understand, and learn to compensate for his or her deficits. A child with brain injury may need to experience the consequences of his or her behavior several times before generalization and learning will occur (Barin et al., 1985). Modeling the appropriate behavior, maintaining consistent and explicit behavioral directives, using time-out, and reinforcing compliance behaviors combined with continuous feedback and cues are appropriate and effective techniques (Divack, Herrle, & Scott, 1985). Inclusion with other children with similar difficulties through participation in support groups for children with TBI provides opportunities for learning new behavior while decreasing the child's sense of social isolation. Finally, and of most importance, education of school personnel, family, and friends will often provide an appreciation for the child's difficulties, and allow for more adaptive responses to inappropriate behavior and disruptive social skills. This is most important because the child's outcome is dependent on the environment's ability to provide the physical, social, emotional, and educational support.

Neuropsychological/Neurodevelopmental Assessment

Many pediatric head injuries are mild and may not require a comprehensive neuropsychological evaluation. An evaluation is warranted if there are persisting deficits that are affecting the child's level of functioning. Therefore, neuropsychological evaluation is most helpful and most common in the rehabilitation and educational planning of a child who sustained a moderate to severe TBI and only occasionally in a child who sustained a mild TBI. However, it is important to consider that children may not show deficits immediately following their head injury but may develop difficulties over time as the demand for new skills emerges (Gronwall, Wrightson, & McGinn, 1997; Taylor & Alden, 1997).

The neuropsychological and behavioral sequelae of pediatric brain injury has been reviewed extensively in the literature (Arffa, 1998; Ryan, LaMarche, Barth, & Boll, 1996), and there are multiple book chapters dealing with the consequences of pediatric head injury (Yeates, 2000, chap. 5; Baron, Fennell, & Voeller, 1995). Pediatric TBI has been associated with deficits in virtually every area of neuropsychological inquiry, and a thorough review of each neuropsychological domain is beyond the scope of this chapter. It is helpful to consider the mechanisms of injury and whether the injury was inflicted or accidental (Arbogast, Margulies, &

Christian, 2005; Beers, Berger, & Adelson, 2007; Hymel, Makoroff, Laskey, Conaway, & Blackman, 2007; Keenan, Runyan, Marshall, Nocera, & Merten, 2004) when evaluating the current functioning and prognosis of a child who sustained a TBI. Since the child's level of neurodevelopment interacts with the cause, mechanism, and level of expectations, it is also imperative to include the child's preinjury level of neurodevelopment in the neuropsychological evaluation, in order to judge if the child's neuropsychological profile is consistent with a TBI. Once the child's pre-existing neurodevelopmental status and injury mechanisms have been considered, there are some general principles in the neuropsychological profile of pediatric TBI.

In concert with age and time-related factors in pediatric TBI, there is a hierarchy of neuropsychological domains that are most likely to be affected. For example, a typically developing preschool child is just learning to use language, has a limited skill set, and has limited behavioral control. A brain injury during the preschool years would interrupt the neural systems that are currently in active development. This is why intelligence, language skills, and motor skills are more likely to be negatively affected after a TBI in younger (i.e., preschool) children than in older children and adults. In addition, and in accordance with Hebb's (1942) hypothesis, an injury to an immature brain alters the development of the neural substrates that build upon those used for pre-existing skills or for brain areas that integrate information. This is why processing speed, sustained attention, and executive functioning skills are also frequently affected by a TBI. Since higher order skills emerge with development and maturation, deficits in these areas of integrated processing or executive functioning may not be observed until several years following a TBI in a preschool child. In contrast, a TBI sustained by an older child of 10 would present a different scenario. A child of 10 is not likely to have a language deficit upon neuropsychological testing unless the TBI was severe or localized to language areas in the brain. A TBI of comparable severity in a 10-year old, however, would likely show deficits in sustained attention, processing speed, and behavior regulation as prominent neurobehavioral symptoms shortly after the injury.

Taking into consideration the mechanisms of injury and the relationship of these mechanisms with neurodevelopment, the assessment of a child with TBI should be comprehensive. Since the pediatric neuropsychologist does not usually have data about the child's preinjury level of functioning, a comparison of the child's performance across and within neuropsychological domains will help guide interpretation of neuropsychological performance and the planning of treatment and educational goals. Specifically, a measure of intellectual function should be administered to assess the child's ability level in verbal and visual domains in addition to their processing speed and immediate attention abilities relative to other children their age. Academic achievement measures should be administered because a child's primary area of functioning and responsibility is his or her school work. Assessment of academic skills is necessary to create an appropriate educational plan and to ensure that the child is learning in school. Measures of attention are also very important because this may be a primary area of deficit that may be apparent with or without deficits in other domains. Learning and memory abilities for visual and verbal information should be incorporated in the assessment battery in order to evaluate how the child is best able to learn new information. Elements of language and motor skills should be assessed in order to consider the child's foundational level for multilevel and complex tasks. Executive functioning is a skill area that is most likely to relate to the child's level of functioning in day-to-day life and his or her long-term success. Executive functioning skills are difficult to assess in young children because these skills either have not developed or are not required for their typical level of functioning. This is also an area that is particularly important to monitor over time because deficits may emerge as environmental demands increase. While preschool children are not expected to plan their homework schedule, this is required to be successful in middle and high school. Emotional and behavioral changes, such as mood dysregulation, depression, irritability, poor social skills, oppositional behavior, or impulsivity are common following a TBI in adults or children and often are severe enough to warrant a diagnosis of a psychiatric disorder (Shaffer, 1995); therefore, incorporating measures of mood and behavior will help provide information about the child's ability to function in daily life and interact with his or her peers. For

younger children, the focus is on acquisition of skills (i.e., motor, language, socialization, adaptive), relationship of skills to expected development, caregiver and child interactions, and behavioral tolerance for a novel setting and for transitions between activities. While attention span and impulse control can be assessed relative to developmental level, executive functioning is much more complicated, and few measures adequately address this issue in the assessment of very young children.

School-Related Issues

With the revision of Public Law 94-142 (Individuals with Disabilities Education Act [IDEA], Federal Register, 1990 – Peg's book chap. 5), children with TBI are now classified and their education services funded under the Special Education disability category of Traumatic Brain Injury. Historically, they were served under less specific categories such as learning disabilities, orthopedically handicapped, mental retardation or other health impairment (OHI). According to the educational definition for TBI as set by the Code of Federal Regulations Part 300 (1993 – Peg #5), the acquired injury must be the result of external force, result in total or partial functional disability, and adversely affect the child's educational performance. Areas of impairment are defined as cognition, language, memory, attention, reasoning, abstract thinking, judgment, problem solving, sensory/perceptual, and/or motor abilities, psychosocial behavior, physical functions, information processing, and speech. Given the broad nature of areas that need to be addressed within the school environment, results of a comprehensive neuropsychological evaluation can inform the Individual Education Program (IEP) document, and consistent follow-up evaluations can contribute to the dynamic nature of the IEP process as the deficits change over time as a result of recovery, maturation, and increased demands.

Several factors have been established as conducive to improved transition back to school and better outcome. These include but are not limited to teacher qualities, peer interactions, and school environment (Farmer & Peterson, 1995 – Peg #5). A teacher who is accepting and flexible and who has an awareness of the variability and complexity of deficits associated with

pediatric TBI can facilitate the child's reentry into school and promote new learning. Being open to re-evaluation of his or her techniques in dealing with these unique students, varying the presentation of materials (i.e., multisensory learning), and a willingness to maintain open communication with both school-based and private therapists are critical aspects to effectively teach a child with TBI. Use of actual classroom materials in therapies will further reinforce the generalization of skills learned in the classroom. Task analysis is one of the first steps in effectively addressing the needs of student with TBI. A teacher who is able to determine which skills remain from preinjury functioning, which skills have been lost, and the difficulty associated with learning new skills and applying them to previously learned skills will greatly enhance the adjustment back to school for a child following TBI. Re-teaching underlying skills before emphasizing content is particularly important as are opportunities for hands-on and experiential learning. Facilitating healthy peer interactions, educating classmates about TBI, and participating in collaborative peer work groups allow a child to transition more easily into a peer group that may expect the child to be the same as before the injury or may not know how to react to any noticeable changes. The school environment must also be accepting, modified for the physical needs of the child with TBI, promote communication among staff members, parents, and community, and be open to learning about the special needs of children with TBI.

Children with TBI show a unique pattern of cognitive and behavioral deficits in comparison to other disability groups. They often show impairment in the ability to learn new information whereas over-learned and familiar tasks are preserved or recover more quickly. Problems with attention and concentration or increased distractibility and variability of cognitive responsiveness are also common consequences of TBI and negatively impact long-term school achievement and emotional adjustment (Dennis, Wilkinson, Koski, & Humphreys 1995 – Peg chap. 3). Memory deficits, particularly in verbal memory and learning, prevent a child with TBI from accessing information that has been previously learned and result in inefficient learning strategies (Yeates & Taylor, 1997). The course of recovery may vary, with recovery of long-term memories first, shrinking of retrograde amnesia,

and disruption of semantic versus episodic memory (Ewing-Cobbs, Fletcher, & Levin, 1985; Goodglass & Kaplan, 1979; Levin, Benton, & Grossman, 1982; Levin, Eisenberg, Wigg, & Kobayashi, 1982; Lezak, 1986). Concrete thinking, slow visual– motor dexterity, perceptual distortions, and disturbances of expressive and receptive language may also be present (Bengali, 1992; Lezak, 1994 – Peg #3). Impairment in academic achievement, specifically reading, spelling, and arithmetic, can be affected by mild, moderate, and severe brain injury, and deficits may persist 5 years post-injury (Bloom et al., 2000). Language deficits may be subtle and primarily apparent in higher level language tasks such as abstraction, problem solving, making inferences, and understanding metaphors (Dennis & Barnes, 1990 – Peg #3). All of these neuropsychological recovery patterns have an impact on the child's performance in school.

Pediatric TBI has profound and sometimes persisting effects on the developing brain that extend across physical, sensory, behavioral, cognitive, and psychosocial domains, which are all factors in school success or failure. Because of modern medical and technical advances, more children are surviving TBI and subsequently must be accommodated in the public school systems. According to Blosser and DePompei (1991), inadequate communication between rehabilitation professionals as well as school personnel's lack of preparation for working with this population are barriers that interfere with efficient and effective reentry into the school.

Certainly, brain-injured children as a group demonstrate learning difficulties similar to more traditional special education classifications, such as problems with attention, impulse control and social judgment, and learning new information (Cohen, Joyce, Rhoades, & Welks, 1985). They often, however, demonstrate greater discrepancies between abilities, more uneven patterns of progress, and often require a different academic focus in comparison to children with learning disabilities. Children with TBI may initially score poorly on tests of intellectual functioning, but the transient nature and variability of their deficits separate them from children with lifelong mental retardation or learning disability. Children with TBI may have the potential to improve cognitive and intellectual abilities, if not reestablish their premorbid IQs (Boll, 1983). Children with TBI often display behaviors that

are new or are exacerbations of premorbid behaviors. They also display original difficulties, such as impulsivity, disinhibition, and poor planning skills. They may show increased irritability, overactivity, or increased lethargy due to fatigue as a direct effect of the injury. These behaviors, however, are very different from the often explosive, maladaptive, and long-standing difficulties exhibited by children who are severely emotionally disturbed, and whose inability to learn cannot be explained by intellectual, sensory, or health factors. Children with health impairments other than TBI are often more physically limited than children with TBI, and the focus of instruction tends to emphasize adaptive skill modification. Thus, trying to meet the special needs of children with TBI by placing them in a modified classroom created for children with more circumscribed difficulties, be these physical, emotional, or intellectual, fails to recognize the need for adjusting classroom strategies to accommodate the unique, multifaceted, and often rapidly changing sequelae of deficits (Bengali, 1992). Appropriately providing education to the child with TBI requires the application of general knowledge relevant to TBI, and a specific understanding of that injury's impact on learning. Therefore, while a program may be appropriate for some TBI children with specific, demonstrable characteristics and needs that are very close to those of children in various formal special education categories, these services do not meet the varied and multifaceted needs of most children with TBI.

Popular strategies routinely recommended, such as practice and repetition, consideration of learning styles for adaptive instruction, task analysis, compensatory skill development, and minimization of distractions, are effective for children with TBI. Computer-assisted learning, systematic practice, memory photograph books, self-talk and instruction, compensatory training, academic tutoring, task structuring, and multimodality presentation are just a few of the interventions that can be utilized within the regular classroom to treat and continuously monitor a child with TBI. Appropriate educational intervention requires modifications in traditional academic instruction and gives new meaning to individualized educational planning. It is the well-trained professional who recognizes the need for utilizing instructional techniques to increase the chance for functional improvement.

The best effect approach includes enhancement of compensation strategies for physical, sensory, behavioral, emotional, and cognitive difficulties experienced by the child with TBI (Bengali, 1992). The environment must accommodate multiple needs that result from insult to physical, psychosocial, behavioral, and cognitive functioning. As stated earlier, intervention strategies should be aimed at increasing the malleability of the environment to accommodate the multifactorial needs of children who have sustained a TBI, as well as the improvement of the functional capacity of the child.

Physical Sequelae

Pediatric TBI may produce lasting or temporary physical effects that must be taken into consideration for educational and rehabilitation planning, particularly during the initial reintegration and adjustment period of returning to school following even brief but unplanned absence. As a result of TBI, many children experience problems related to endurance and fatigue, regulation of bodily functions, and motor deficits resulting from focal impairment of neurological status. A child may also experience decreased stamina and chronic fatigue as a result of prolonged inactivity, medication, or increased mental and physical effort required to complete tasks that were premorbidly routine (Lezak, 1994). Thus, it may be necessary to reduce a child's courseload or length of school day by gradually introducing the student to the school regimen on a half-day basis until a reasonable return of endurance allows for an increase in time (Rosen & Gerring, 1986), rescheduling the most difficult classes during the student's most productive time (Ball & Zinner, 1994), and building in regular rest periods at critical times throughout the day.

Hypersensitivity to noise and lower thresholds for stress as a result of TBI will make class transition and lunchtime particularly difficult periods (Boll, 1982). A "buddy system" for the child with TBI may help to reduce the stress associated with having to manage several activities at once (i.e., maneuvering through crowded halls while remembering what class is next, finding a place to sit, and deciding what to eat in a noisy cafeteria). Brain centers that control appetite regulation, body temperature, and hormone production may have also been damaged. Recognition of the overt symptoms associated with changes in body comfort regulation should be encouraged through physical consultation with family members and school personnel, and systems for either monitoring or teacher awareness of these changes should be established.

Motor deficits, such as hemiparesis, ataxia, apraxia, visual deficits, or speech disturbances, may result from TBI, depending on the injury site and extent of damage. Secondary difficulties related to motor impairment, such as maneuverability of a wheelchair, usage of augmentative devices, and transfer of handedness, are often impediments to the child's learning process that can increase frustration and fatigue. Although more likely in severe and penetrating TBI, these children are also at increased risk for developing seizures (Golden, Moses, Coffman, Miller, & Strider, 1983; Hauser, 1983; Jennett, & Teasdale, 1981, 1972). They may often be placed on anticonvulsant medication as a precaution against the occurrence of seizures. Medication side effects could include drowsiness, decreased attention, lethargy, dizziness, speech disturbance, slowed mental processing, and poor coordination, all of which decrease the child's ability to maximally benefit from traditional academic instruction.

Thus, school personnel need to be prepared to implement follow-up recommendations provided on discharge from a rehabilitation agency. These objectives should be included in the student's IEP. Close contact with rehabilitation personnel should be encouraged to maximize the child's response to appropriate therapies (i.e., occupational, physical, and speech), and to academic modifications.

Several studies have suggested that there are no distinct or unitary behavior disorders following TBI, and that behavioral recovery is strongly influenced by characteristics of the environment before and after injury (Brown et al., 1981; Fletcher, Ewing-Cobbs, & Miner, 1990; Fletcher & Levin, 1988; Levin, Benton, & Grossman, 1982). Thus, an additional burden is placed on the school to create and maintain an environment that maximizes the brain-injured child's response to and compliance with educational modifications. School personnel and family members must also learn to recognize premorbid characteristics of the environment and of the child that may contribute to or impede recovery and adjustment.

Because of the paucity of research on prescriptive academic techniques for children with TBI and the heterogeneity of this group of learners, sound teaching practices applied with an understanding of and a sensitivity to possible cognitive, psychosocial, and physical sequelae are a good instructional starting point. This can best be accomplished by early planning, education, and training of school personnel and family members. Classmates and teachers should be made aware of procedures that will facilitate adjustment in a way that is sensitive to all parties. In preparation for reentry of a child with TBI injury, coordination of efforts between hospital or rehabilitation personnel and school personnel should begin while the child is still in the hospital or under home-based care. This would include participation in the school's multidisciplinary team placement meeting or tentative IEP. The school should remain open to possible ongoing modifications in the child's educational objectives as the reentry process begins and the child is observed in the classroom setting. Because recovery from pediatric TBI is an ongoing, adaptational, dynamic process, the typical policy of retesting special educational students every 3 years may be too infrequent for a young child with TBI given the rapid changes in development that complicate determining the impact of early TBI on learning (Ball & Zinner, 1994). Instead, a child with TBI should be formally assessed at least every 12 months by a neuropsychologist trained in the subtleties of brain functioning and recovery in the context of brain maturation, with reduction in this schedule once the child has reached adolescence. Then assessment can occur at longer intervals as the older child prepares for transitions (i.e., middle school, high school, college). Of course, if an intervening event occurs (e.g., repeated injury), testing should resume a more frequent schedule.

Because not all children with TBI qualify for special education placement, regular education teachers should be included in the training process to make them aware of modifications that could be implemented throughout traditional instruction. Emphasis should be placed on functional development using process-oriented instructions. Ongoing consultations among teachers, administrators, the school nurse, school mental health professionals, and parents can be helpful in addressing day-to-day frustrations associated with the difficulties of educating a child with special needs. This may also be an effective mechanism for sharing success and progress. For the child with brain injury, gradual introduction to less predictable and more demanding situations will be needed to develop accurate environmental cues. Individual psychotherapy will help the child address issues related to increased awareness of deficits, social isolation, and adjustment changes in social dynamics at school.

Sensitivity to the variability of deficits that occur in the context of severity of TBI (i.e., mild, moderate, severe) on the part of the school is also important to address the unique educational needs of the injured child. Following very mild head injuries, small adjustments such as delaying a test for 1 week after more intensive learning to allow the child to better consolidate the material, allowing for slightly shorter attendance, offering a delay in final examinations, or providing a tutor for a matter of weeks may be required. These adjustments are not automatically attainable, however. Someone has to understand that such adjustments are necessary, know how to present the request for these adjustments, and interact with an environment that is not typically used to dealing with children who have these temporary types of changes in their mental and personal capacities.

With more severely injured children, the demands for individual educational programing, which change from time to time, and the demands of a child who does not fit neatly into categories such as learning disabled, attention deficit, or emotionally disturbed place the school under real fiscal and administrative pressures to which its teachers and administrators may respond well or badly. Even the most well-intended administrator and teacher may not understand these demands. They may seem to be driven by a higher priority for pedagogical order or fiscal limits than for consideration of an individual child's educational requirements. By the time a child has been identified and processed through a cumbersome or resistant system she or he may have fallen far, far behind. Because of this failure to promptly respond to the child's needs, much additional damage has been done. Resources required in this circumstance will be even more extensive in order to make up for the secondary harm done by inadequate immediate educational planning. It is not

at all unheard of to see a child return to school months or even weeks after a moderate or severe head injury and be in a state of modest confusion while sitting at his or her desk. To say that the child has obtained nothing from this experience understates the matter. When the child has fully recovered, it must be recognized that a period of time has elapsed during which no learning has occurred whatsoever. This period of time may be measured in months. This period may be characterized by frustration for the child and teacher. Therefore, even though the child may eventually become ready to progress adequately, the background of knowledge necessary to benefit from current lessons is missing. The circumstances of school life may also have become negative enough to further impede academic progress related to the anger, confusion, and uncertain expectations produced by the child's condition, and the school's failure to manage the situation in an informed and appropriate manner from a time even before the child returns to school. This may mean repeat of the year, summer school, or a whole variety of individual resource interventions. In order to make an adequate determination of what is necessary, deficits must be appropriately appreciated, examinations accomplished, and various meetings and planning sessions held in order to make individualized arrangements that actually fit what it is that the child needs to make adequate progress. It is never sufficient to place the child in a special class without appreciating the child's neurological state and other consequences of the head injury that have produced the need for educational changes. Even a high level of irritability and low frustration tolerance without decline in cognitive capacity can make sitting in a classroom for a grade school or junior high school student intolerable. Poor behavior is at least as unacceptable within the school as is poor academic performance. Blame, additional pressures, and exclusion from learning environments are hardly therapeutic, and yet the reaction of the teacher, particularly one who is not aware of or unprepared to deal with the child's condition, is not difficult to predict. Teachers, too, have rights, and these rights include the expectation that children will attempt to learn in their class and be in a class appropriate for the tasks at hand. If neither is possible on the part of the child, then other arrangements must be made. Simply placing them under some pious term like "inclusion," which may mean little more than ignoring the problem, is seldom if ever satisfactory. Pretending that the child will be all right if enough time passes misses the point entirely. During this period, the child may miss so much by way of academic instruction that the requirement then becomes one of reconstruction of an entire academic year. This, too, is discouraging and frustrating for the child who then may be separated from age mates of long standing either because of the severity of the head injury or because of inadequate academic management. In either case, this is an additional academic and coping challenge, and one that makes recovery from head injury all the more difficult.

Given the variability of outcome from pediatric TBI, the contribution of multiple factors of pre- and post-injury, the sensitivity to the developmental aspects of head injury, and the continuing scholarly investigation into the changing nature and outcome of pediatric TBI, the way in which young children with TBI are viewed and remediated is a work in progress. TBI sustained in young children is very different from TBI sustained in adolescents and adults, and must be addressed as such. Thus, interventions for amelioration that professionals initiate must be made in the context of current research, within a developmental framework, within a knowledge base of the relationship of the brain to behavior, and with the recognition that no two children with TBI are alike. All head injuries are not alike, and the outcome of all head injuries is not alike. Neither are children who have experienced TBI, in an overall sense, like children with other conditions. Some children with head injuries do have low IQs, some have deficits in attention, and others have specific or general learning issues, be these academic or social. In addition, others have physical limitations, including but not limited to motor and sensory deficits. Each child comes from a family rich in context, with internal buffers or individual vulnerabilities, and must function in a system that is not always designed for those who have special needs. The purpose of this chapter was to describe pediatric TBI from a developmental perspective, offer research associated with the unique issues of injury and outcome in pediatric TBI, and provide recommendations for broad interventions founded in research to address pediatric TBI in the school environment. With

heightened awareness of the developmental uniqueness of young children who have sustained TBI, more research can be directed toward better understanding the trajectory (or alteration) of development. As neuroimaging becomes a mainstay in human neurocognitive research (and hopefully, practice), the resultant understanding of neuroanatomical changes in early brain insult will further assist in developing medical and cognitive strategies to improve outcome and inform remediation of deficits when early development is altered as a consequence of TBI in young children. In addition to these causative issues, who the child is, the family from which he or she comes, the social circumstances including stability and demand level that pertain, the preinjury skills the child had, the academic flexibility of the school after injury, and the available resources, all significantly influence a child's outcome. This chapter attempts to bring those issues together and to discuss them in one place to give the practicing clinician an overview of the issues in a practical way. When an integrated set of efforts is directed toward the multifactorial issues that influence the occurrence as well as the outcome of pediatric TBI, the best interests of the child are maximally served.

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8

Neuropsychological Basis of Learning Disabilities

SAM GOLDSTEIN AND ADAM SCHWEBACH

Learning disabilities, including reading disabilities, are the most prevalent group of neurobehavioral disorders affecting children and adults. There is a strong genetic component to these disabilities. Unlike most other neuropsychological disorders, learning disabilities are not a single, relatively well-defined entity or syndrome. Rather, learning disabilities encompass an extremely heterogeneous group of problems with diverse characteristics which can result from a variety of biological influences, including genetic factors, environmental insults to the brain, and possibly, as recent research on brain development suggests, from extreme lack of early environmental stimulation. As a result, the multifaceted field of learning disabilities is complex and often contentious with many competing theories, definitions, diagnostic procedures, and suggested avenues of intervention.

Within the framework of this chapter it is not possible to adequately describe or attempt to integrate the many competing viewpoints and claims surrounding the construct of learning disabilities. This task has admirably been undertaken by other writers in the field who have approached learning disabilities from a broad, historical perspective as well as from the viewpoint of best current practices (Lerner, 1993; Mercer, 1991; Torgesen, 1991; Swanson, Harris, & Graham, 2003). This chapter will approach learning disabilities from biomedical, neuropsychological, and information-processing perspectives.

The Concept of Learning Disabilities

Learning disabilities as a category of human exceptionality evolved from observations of physicians and educators as they studied and attempted to assist brain-injured children. Alfred Strauss and Laura Lehtinen published their classic work *Psychopathology and Education of the Brain-Injured Child,* in 1947. In 1966, Clements, as head of a task force sponsored by the U.S. Department of Heath, Education and Welfare, strongly supported use of the term *minimal brain dysfunction* which became popularized as MBD (Mercer, 1991).

The terms minimal brain injury and minimal brain dysfunction were used to describe children of normal intelligence who appeared similar to some individuals with known brain injury in that they exhibited a combination of hard or soft signs of neurological deficiency concomitantly with educational and sometimes behavioral disorders. Minimal brain dysfunction was believed to be responsible for observed deficits in processes such as auditory and visual perception, symbol learning, short- and long-term memory, concept formation and reasoning,

SAM GOLDSTEIN • Department of School Psychology, George Mason University, Fairfax, Virginia 22030. **ADAM SCHWEBACH** • Neurology, Learning and Behavior Center, University of Utah, Salt Lake City, Utah 84112-9057.

fine and gross motor functions, and integrative functions, resulting in disorders of receptive and expressive language, reading, writing, mathematics, physical skill development, and interpersonal adjustment. In addition, behavioral traits such as distractibility, impulsivity, perseveration, and disinhibition were often found in children with minimal brain dysfunction syndrome (Cruickshank, Bentzen, Ratzeburg, & Tannhauser, 1961; Gardner, 1973; Johnson & Myklebust, 1967); Fletcher, Shaywitz, & Shaywitz, 1999). Thus, from the first, the field of learning disabilities centered around a medical model with the term minimal brain dysfunction being applied to an extremely heterogeneous group of individuals.

Johnson and Myklebust (1967) discussed the limitations of extant terminologies. They suggested that *minimal* was inappropriate to describe individuals whose resulting disabilities had much greater than minimal impact on their learning functions and that the words *brain injury* and *brain dysfunction* were viewed as too stigmatizing by many individuals with learning disorders and their parents.

In 1963 at a national organizing conference of concerned parents and professionals held in Chicago, Samuel Kirk proposed use of the term *learning disabilities* (LD) (Lerner, 1993). This term was quickly accepted by parents and continued to gain ascendance when federal and state governments adopted it at the time special education services were expanded to include students of average or better intelligence with otherwise unexplained academic learning disorders (U.S. Office of Education, 1977; Mercer, 1991). Kirk viewed learning disabilities from a psycholinguistic perspective which proposed that underlying specific deficiencies in central nervous system functioning result in deficits in psychoneurological learning processes which, in turn, explain observed learning disabilities. Based on the psycholinguistic-process model of Charles Osgood, Kirk described learning disabilities according to learning channels (auditory/verbal or visual/motor), learning levels (rote or conceptual), and specific processes (perception, reception, memory, integration, expression, etc.) (Kirk & Kirk, 1971). Naglieri and Das (2002), based on Luria's model of intellectual processes, described four critical processes essential for effective learning. Luria's PASS model involves planning, simultaneous processing,

attention, and successive processing. Weaknesses in various combinations of these processes have been associated with specific learning disabilities (Naglieri & Das, 2002).

While the view of learning disabilities as neurologically based process deficits remained widespread, during the 1970s a behavioral approach to the topic was promulgated. Process deficits were roundly criticized as hypothetical constructs which could not validly or reliably be diagnosed and which had little or no demonstrable relationship to effective interventions (Hammill & Larsen, 1974, 1996; Larsen, Parker, & Hammill, 1982). Proponents of this view advocated criterion-referenced or curriculum-based assessment of a multitude of specific skills and interventions based on a detailed analysis of the component parts of each skill to be taught/learned along with ecological analysis and modification of the learning environment. Well-designed and group-validated approaches to curriculum instruction were held to be appropriate and effective for all students, including slow learners, without reference to supposed internal processing deficits or disabilities. This approach, now referred to as response to intervention (RTI), has become increasingly popular and advocated for within special education programs in public schools.

While debate raged, a third approach to understanding and assisting those with learning disabilities added a new dimension. Based on research centered at the University of Virginia (Hallahan, 1980) and the University of Kansas (Schumaker, Deshler, Alley, & Warner, 1983), cognitive learning models were applied to the understanding and treatment of learning disabilities. From a cognitive framework, learners are viewed as directing their own learning by focusing on topics and skills which are personally meaningful and by developing active strategies for information acquisition. One outgrowth of cognitive theory has been the holistic or constructivist approach to teaching and learning, including whole-language methods of reading instruction. While the tenets of cognitive theory have been applied to the learning-disabled population in a number of ways, a major emphasis has been helping students to develop more reflective, accurate, and efficient approaches to learning tasks (i.e., learning how to learn). Students are taught to consciously employ self-monitoring strategies and effective learning/study strategies.

This model, which emphasizes an approach of focus on how students learn versus what a student learns, may have influenced the scientific discipline away from more deficit-based conceptualizations when explaining learning disabilities (Wong, 1987).

Prevalence of Learning Disabilities

Determining prevalence rates, or the frequency of occurrence, of learning disabilities in the population might at first glance appear to be a relatively straightforward process. However, since prevalence rates for any disease or disability are dependent on having a clear-cut definition of the disorder under consideration and since there is no consensually accepted or experimentally validated definition of learning disabilities, the process of determining the prevalence of learning disabilities is a quagmire. At the present time, incidence figures for this nondefinitive disorder or group of disorders cannot be determined precisely and are essentially broad estimates.

Important considerations regarding the determination of LD prevalence were presented by MacMillan (1993) and Lyon (1996). In a discussion of operationalizing disability definitions MacMillan described *prevalence rate* as referring to the total percentage of the population that is affected by a disorder while *detection rate* refers to the number of known or identified cases. For learning disabilities, prevalence and detection rates may, indeed likely do, differ. Depending on the stringency of identification criteria, prevalence estimates for learning disabilities have varied from as low as 1% to as high as 30% of the school-age population (Lerner, 1993). Mercer (1991) suggested that those with severe specific learning disabilities might comprise approximately 1.5% of students, while the inclusion of students with mild learning disabilities could raise that figure to about 4 or 5%. Other studies focusing on a specific classification of learning disabilities identify 5–8% of school-age children with arithmetical disabilities (Geary, 2003) and 5–17.5% with dyslexia (Shaywitz, 1998). It is still estimated that 52% of all students being served in special education have a classification of LD with an actual count exceeding 2.5 million (Kavale & Forness, 2003).

Etiology and Genetics of Learning Disabilities

From the time of the earliest medical reports which described cases of dyslexia, learning disabilities have been viewed as stemming from central nervous system dysfunction, more precisely, from dysfunction of specific portions of the cerebral cortex (Doris, 1986; Huston, 1992). This long-standing presumption is being reinforced and validated by modern cognitive neuroscience. Language-specific processing of the brain in areas surrounded by the Sylvian fissure has been associated with a variety of language functions. The temporoparietal cortex receives projections containing but not limited to visual and auditory information. The posterior superior temporal gyrus or Wernicke's area is associated with a variety of language functions, particularly involving comprehension. However, it is likely over-simplistic to describe temporoparietal areas as those responsible for the reception of language whereas frontal regions as responsible for expressive language. It is more likely that a distributed network is responsible for full coherence of the language system (Joseph, Nobel, & Eden, 2001).

PET and fMRI have been used extensively to extend an understanding of how specific components of learning map onto the brain (Rumsey et al., 1997). As these techniques have become more refined and technologically advanced, an understanding of structural differences implicated in learning disabilities has progressed. Despite their limitations, these techniques have revealed much about structures of the brain associated with visual word form (Fritch, Friston, Liddle, & Frack, 1991), orthography (Flowers, Wood, & Nailer, 1991), phonology (Rumsey et al., 1997), and semantics (Pugh, Shaywitz, Shaywitz, Constable, Skudlarski, Fulbright, Bronen, Shankweiler, Katz, Fletcher and Gore, 1996). However, a great deal of variability has been found then and between studies such that multiple sites within similar regions of the brain have been implicated in these processes (Poeppel, 1996).

Very few functional neuroimaging studies have been conducted with children, in part due to the fact that PET requires the application of radioactive material. At least one study using fMRI has mapped language dominance in children with partial epilepsy, results similar to those

observed in adults (Hertz-Pannier et al., 1997). Readers interested in an extended discussion of learning and brain imaging are referred to Berninger (2004).

Learning disabilities have traditionally been viewed as neurological deficits intrinsic to genetic and other biological factors within the individual and not of environmental origin. However, current research is documenting the intimate connection between environment and neuroanatomical development (Dawson & Fischer, 1994; Hutenlocher, 1991). The pervasive effects of early environmental programming on the formation and pruning of neural networks and the theoretical relationship of this process to the occurrence of neurologically based specific learning disabilities are an area that is only beginning to be considered.

The prenatal, perinatal, and postnatal environmental factors associated with brain development and brain injury are best viewed as potential causes of learning disability due to uncertainties and inconsistencies in the relationships between age at onset, the severity of circumstance or condition, the degree of transient or permanent brain dysfunction, and the broad range of possible effects on learning. For example, clinical studies have documented cases in which major structural deficits, even loss of an entire brain hemisphere, result in few observable signs of learning disability while many individuals with severe learning disabilities have no obvious structural deficits (Bigler, 1992; Satz, 1990). In addition, confounding variables such as socioeconomic status, parenting style, and early interventions mediate the degree to which a neurological abnormality will result in impaired learning. In many or most cases of learning disability etiology is, presumably, not a factor. However, in some cases an environmental cause is directly known or fairly certain while in other cases, the environmental contribution to etiology is cloudy, involving a subtle interplay of potential factors which may be undocumented or unknown. In the last 40 years, experimental research has provided strong support for a genetic factor in some forms of learning disability. The familial occurrence of reading, spelling, and writing disabilities has been investigated using a variety of methodologies such as study of family history and pedigree analysis, determination of concordance rates among identical and fraternal twins, comparison of linear regression in reading scores between identical and fraternal twins, and chromosomal analysis of family members.

The earliest widely cited family pedigree study of reading disorder, conducted by Hallgren in 1950 (cited in Pennington, 1991), consisted of a statistical analysis of dyslexia in 112 families. Among first-degree relatives (parents and siblings of an identified child), the risk for co-occurrence of this disorder was 41%, which is much higher than the usual prevalence estimates for the general population of 5–10%. Huston (1992), reporting on Hallgren's study, indicated that of the 112 families, in 90 families, one parent was dyslexic; in 3 families both parents were dyslexic; and in 19 families neither parent had dyslexia. While Hallgren's study has been criticized for methodological flaws, later studies carried out with greater technical precision, such as that of Finucci, Guthrie, Childs, Abbey, and Childs (1976, cited in DeFries, 1991), have found similar familial rates in the range of 35–45%. Finucci (1976) also published a critical review of the early investigations of dyslexia and genetics. Even more recent studies continue to demonstrate considerable evidence supporting that dyslexia and even dysgraphia have a developmental, genetic influence (Raskind, 2001).

The Colorado Family Reading Study, begun in 1973, compared reading abilities of 125 reading-disabled children (probands) and their family members to 125 matched control children who were not reading disabled and their family members. The total number of subjects in this study was 1,044, making it an extensive family study. Results clearly demonstrated that reading disorders are familial in nature. Scores for siblings of proband subjects were significantly lower than scores for siblings of control subjects on measures of both reading and symbol processing speed. A similar pattern of significant results was observed for the parents of probands and controls. An interesting finding was that, on average, brothers of probands were significantly more reading impaired than sisters of probands. Similarly, fathers of probands were, on average, less skilled readers than mothers of probands; however, the score difference between fathers and mothers was less than the score difference between male and female siblings (DeFries, 1991). Although reading disabilities have now conclusively been shown to be familial in nature, familial occurrence suggests but does not demonstrate genetic heritability. Empirical investigations to ascertain the genetic inheritance of learning disabilities, specifically

reading disability, have included concordance studies of twins, multiple regression studies of twins, segregation analysis studies, and chromosomal linkage studies.

Comparison of pairs of identical and fraternal twins has been used to investigate the genetic component of reading disability in the same way that other twin studies have researched the heritability of intelligence and a variety of other personal characteristics. Many twin studies have employed a comparison of concordance rates to test for genetic etiology. A pair of twins is concordant for reading disability if both twins are reading disabled; if just one twin is reading disabled, the pair is discordant. Identical twins share an identical genetic makeup while fraternal twins share about 50% of heritable variation (LaBuda & DeFries, 1990). To the extent that reading disability is genetically determined, the concordance rate for pairs of identical twins should be considerably higher than for pairs of fraternal twins when at least one member of each identical and fraternal pair has been identified as reading disabled.

Two of the earlier reports of concordance rates for reading disability in twins were those of Hermann (1959) and Zerbin-Rudin (1967). Both of these researchers pooled the findings of smaller previous studies, possibly with some overlap in their reporting of cases. The concordance rates reported by both authors were nearly identical. Based on their combined data, as reported by Huston (1992), there was, on average, 100% concordance for 29 identical twin pairs and about 34% concordance for 67 fraternal twin pairs.

Due to technical differences in the method for determining concordance rates, different authors sometimes report different concordance figures for the same study, i.e., some authors report pairwise concordance rates and others report probandwise concordance rates. The first method counts each concordant twin pair one time. The latter method considers each member of a concordant pair as a separate research subject and, therefore, counts each concordant pair twice. Using probandwise concordance increases the percentage of concordance for both identical and fraternal twin pairs (LaBuda & DeFries, 1990). For example, in the Zerbin-Rudin study, a pairwise concordance rate for fraternal twin pairs was 34% (12 of 34 cases) as reported by Huston (1992); however,

the probandwise concordance rate for those same twin pairs was 52% (24 [12 + 12] of 46 [34 + 12]) cases as reported by DeFries (1991).

Bakwin (1973, cited by LaBuda & DeFries, 1990) studied 31 pairs of identical and 31 pairs of fraternal twins, finding 84% pairwise concordance for identical twin males and 83% for identical twin females. Interestingly, the pairwise concordance rate for male fraternal twins was 42% while the rate for female fraternal twins was just 8%. Bakwin also investigated the environmental factors of birthweight and birth order as predictors of reading disability but found no significant differences between normally reading twins and reading-disabled twins on these variables.

Stevenson, Graham, Fredman, and McLoughlin (1987, cited by Thomson 1990) conducted a large-scale study of the reading and spelling abilities of 285 twins aged 13 years divided into several subgroups according to type and severity of skill deficiencies. In contrast to other concordance studies of twins, these authors reported, overall, relatively similar pairwise concordance rates for identical and fraternal twin pairs, 32 and 21%, respectively. Their findings suggest a fairly low level of heritability for reading disorder. However, with IQ controlled, Stevenson et al. found a strong genetic influence on spelling ability.

The most technologically sound large-scale twin study, the Colorado Twin Study, was begun in 1982 as part of the Colorado Reading Project. With IQ controlled (Verbal or Performance IQ = 90 or above) and other types of selection criteria in place, the Colorado Study examined reading disability in 101 pairs of identical twins and 114 pairs of fraternal twins. The pairwise concordance rate of 52% for identical twins was lower than for most earlier studies while the rate for fraternal twins was fairly typical at 33% (LaBuda & DeFries, 1990). Although there is some variation in the concordance figures generated by different studies, taken as a whole, they do provide strong evidence for a genetic factor in the etiology of reading disability.

In the search for the genetic mechanisms underlying reading disability, two primary strategies have been employed, chromosomal linkage studies and segregation analysis. Working from phenotype (clinical manifestation of disability) to genotype (underlying genetic substrate of disability), segregation analysis involves

testing all members of affected families for the presence of a learning disorder and then fitting the data to potential models of genetic transmission, e.g., autosomal dominant, autosomal recessive, codominant, or polygenetic models. Pennington et al. (1991) after performing segregation analysis on four subject samples, found support for a major gene model in which dyslexia in some families is transmitted by one or more dominant or partially dominant genes. They also found support for genetic heterogeneity, i.e., multiple genetic mechanisms in the transmission of dyslexia. Further research with more sophisticated segregation analysis has also pointed toward a major dominant gene effect which is frequently occurring (57% of the population) and which, when present, increases an individual's liability for reading problems (Gilger, Vorecki, DeFries, & Pennington, 1994). However, this putative gene is of low penetrance such that only 3% of individuals having one or two copies of the defective allele demonstrated reading deficits greater than 1.96 SD below the population mean. Nonaffected individuals (43% of the population) with two normal alleles and no copies of the defective allele had an extremely low probability ($p = .0027$) of being classified reading disabled.

Working from genotype to phenotype, linkage studies have been conducted to identify the specific chromosomes and the genetic loci on those chromosomes that are associated with dyslexia. Through cytogenic studies of families in which there are a number of persons identified as dyslexic, the search for a gene or genes that may cause dyslexia can be narrowed. Smith, Pennington, Kimberling, and Ing (1990) and DeFries and Gillis (1993) have summarized the complex principles of linkage analysis which involve investigating both the link between marker genes and the disability gene on a chromosome and the link between that chromosome and the phenotypic occurrence of reading disability.

The pioneering linkage study of Smith, Kimberling, Pennington, and Lubs (1983) found evidence in some families for a link between reading disability and a marker on chromosome 15p. A later study with a larger number of subjects provided additional support for this finding (Smith et al., 1990) and further suggested that the apparent linkage was present in approximately 15–20% of families with multiple cases of reading disability.

A second possible genetic locus for reading disability in families not linked to chromosome 15 was suggested by the observation of the co-occurrence of dyslexia and disorders of the immune system which are coded to the human leukocyte antigen (HLA) region of chromosome 6 (Geschwind & Behar, 1982; Pennington, Smith, Kimberling, Greene, & Haith, 1987; Smith, Kimberling, & Pennington, 1991). Subsequent research to test this hypothesis (Cardon et al., 1994) studied linkage in two independent samples, 126 sibling pairs and 50 fraternal twin pairs, in which at least one member of each pair was reading disabled. Analyses of the reading performance of subject pairs genotyped for DNA markers localized the reading disability trait to a small region within the HLA complex of chromosome 6.

A high incidence of reading disability is found in individuals with abnormalities in sex chromosome karyotypes, the most common of which is the 47 XXY karyotype in males (Klinefelter's syndrome), occurring in approximately 1/700–1/1,000 births (Berkow and Fletcher, 1992; Pennington, Bender, Puck, Salbenblatt, & Robinson, 1982). Although not a frequent occurrence in the learning-disabled population, the strong association between some sex chromosome anomalies and reading disorders provides additional evidence for the genetic heterogeneity of reading disability.

There is evidence that reading disability per se is not inherited but that genetic variations influence specific subskills connected to the reading process. Olson, Wise, Conners, Rack, and Fulker (1989) found significant heritability for a phonological coding task but not for an orthographic coding task. Pauls (1996) reported genetic linkage studies of dyslexic subjects and their family members assigned to one of four research groups according to the primary deficient process evident in their reading difficulty: phonological segmentation, nonword reading, rapid namings, and single word identification. Similar to previous findings, phonological segmentation showed linkage to the HLA region of chromosome 6. There was no evidence for a connection between word identification and chromosome 6; however, there was some evidence that the word identification phenotype is tied to a variation in the same portion of chromosome 15 that was first implicated by Smith et al. (1983).

In summary, family studies, concordance studies of twins, and multiple regression studies of twins have shown that reading disabilities run in families, that they are heritable, and that the heritable component is approximately 50%. Presently, segregation analyses point to genetic transmission via a partially dominant or dominant major gene effect. Genetic linkage studies have provided strong evidence that in some families and subject populations studied, reading disability is linked to chromosome 6p or chromosome 15p. Both segregation analyses and linkage analyses have led to the conclusion that phenotypic reading disability is genotypically heterogeneous, i.e., increased susceptibility to reading disability can be produced by multiple genetic profiles. Furthermore, there is preliminary evidence which suggests that within a single individual the component processes of reading may be influenced by separate genes at different loci.

Subtyping Learning Disabilities

Although public agencies have primarily chosen to define learning disability based upon a discrepancy between achievement- and IQ-based estimates of potential achievement, this statistical definition does little to facilitate an understanding of the underlying processes that contribute to successful and, in this case, unsuccessful achievement. Although it has been suggested that learning disability is a broad, nonspecific symptom for which cause must be identified, it has yet to be demonstrated that different causes lead to different types of learning disability or for that matter require different treatments.

The work of Boder (1973) and Bakker (1979), though 30-years old, exemplify efforts to classify and identify learning disability on the basis of educational criteria. Boder described three subtypes of children with learning disability: (1) a dysphonetic group lacking word analysis skills and having difficulty with phonetics; (2) a dyseidetic group experiencing impairment in visual memory and discrimination; and (3) a mixed dysphonetic, dyseidetic group. The dysphonetic group included two-thirds of those identified as learning disabled with the dyseidetic group constituting approximately 10%. Bakker's work described L- and P-type dyslexias. Children with L-type dyslexia read quickly but made errors of omission, additions, and word mutilation. The P-type group tended to work slowly and make time-consuming errors involving fragmentations and repetitions. Among the interesting and promising attempts to define learning disability are those studies involving multivariate analysis. Efforts to subgroup learning disability using such analyses find that differences between good and poor readers may reflect impairment in minor skills such as oral word rhyming, vocabulary, discrimination of reversed figures, speed of perception for visual forms, and sequential processing (Doehring, 1968). In 1979, Petrauskas and Rourke utilized a factor-analytic method to describe the difficulties of a group of deficient readers. They found these readers falling statistically into four subtypes: (1) primarily verbal problems; (2) primarily visual problems; (3) difficulty with conceptual flexibility and linguistic skills; and (4) no identified specific weakness. The first of these two groups corresponds with Boder's analysis. The third may reflect children with weaker intellectual skills while the fourth may in fact reflect the long-standing, clinical perception that there are a group of children who experience achievement problems possibly secondary to nonneurological factors (e.g., emotional disorder).

Mattis, French, and Rapin (1975) identified three distinct syndromes of learning disability based upon a factor analysis. These included (1) children struggling to read as the result of language problems; (2) children with articulation and graphomotor problems affecting academic achievement; and (3) children with visual-spatial perceptual disorder. The third group displayed better verbal than nonverbal intellectual abilities. Almost 80% of the impaired children fell in the first two groups. Denckla (1972, 1977) reported similar statistics noting that approximately 16% of learning-disabled children experienced some type of visual-spatial or perceptual motor problem.

Thus, there is a consensus among factor-analytic studies attributing a large group of children with problems related to verbal weaknesses and a smaller but significant group related to perceptual weaknesses. Joschko and Rourke (1985), based upon an analysis of the Wechsler Intelligence Scale for Children, found a clear distinction between children with learning problems

stemming from verbal weaknesses and those whose problems stem from nonverbal weaknesses.

Satz and Morris (1981) found five distinct groups of reading-disabled children, again along this verbal–nonverbal continuum. These included (1) those with language impairment; (2) those with specific language problems related to naming; (3) those with mixed global language and perceptual problems; (4) those with perceptual motor impairment only; and (5) an expected group similar to that reported by Petrauskas and Rourke (1979) in which no significant impairments were identified. Some researchers have hypothesized that this group of children simply has not experienced adequate education to develop essential achievement skills while others, as noted, suggest an emotional basis for this group of children's problems. Using cluster analysis of a neuropsychological battery, Phillips (1983) identified a fairly similar profile of five learning-disabled subtypes, including individuals with normal test scores, auditory processing problems, difficulty with receptive and expressive language, spatial weaknesses, and a global pattern of low test scores.

Rourke (1989) concluded that cluster-analytic studies have identified some association between learning delay and a wide variety of perceptual, linguistic, sequential, and cognitive skills. This finding is reinforced by the work of others over nearly a 40-year period (Benton, 1975). According to Swartz (1974) a pattern consisting of depressed scores on four Wechsler subtests, the ACID pattern (an acronym for Arithmetic, Coding, Information, and Digit Span subtest), characterizes the weaknesses of most learning-disabled children. Although this view is held by many others and has been most recently advanced by Kaufman (1997), not all learning-disabled children display this pattern. Children who do, however, are thought to have a particularly poor prognosis for academic performance in reading, spelling, and arithmetic (Ackerman, Dykman, & Peters, 1977). Some researchers have suggested that in a population of learning-disabled children demonstrating this pattern, one subgroup experiences particularly poor auditory–verbal memory and sequencing while a second group experiences poor visual-spatial abilities. This distinction is similar to that described by Joschko and Rourke in 1985. However, these authors reported a further

distinction in the ACID pattern by age between a younger group 5- to 8-years old and an older group, 9- to 15-years old. On the basis of an extensive neuropsychological battery, these authors found a distinct pattern of differences resulting in four subtypes. Joschko and Rourke (1985) noted that "although the ACID subtypes generated in this research do not differ significantly in terms of level of academic performance, the plots of the factor score profiles for each of the reliable subtests indicate that they have qualitatively different ability profiles which may have practical applications" (p. 77). However, even these authors noted that effective remediation has not been clearly tied to this manner of ability profiling.

The inclusion of learning disability among the disorders evaluated and diagnosed by the medical and mental health community has been considered an adjunct to formal psychiatric, psychological, or neuropsychological evaluation. However, as it has been recognized that learning-disabled children appear more likely than others to develop psychiatric problems, efforts have been made to refine the clinical diagnosis of learning impairments. The *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition TR (DSM-IV-TR), lists four academic skill disorders (American Psychiatric Association, 2000). These are reading disorder, mathematics disorder, disorder of written expression, and learning disorder, not otherwise specified. All four are qualified as reflecting the collection of standardized test data, indicating performance substantially below what would be expected, based upon the individual's age, intelligence, and educational experience. According to these definitive criteria, the problem must interfere with the child's academic performance or activities of daily living. The "not otherwise specified" category reflects learning disability as an isolated weakness, for example, difficulty with spelling independent of other written language problems. The DSM-IV-TR also contains a *developmental coordination disorder* diagnosis reflecting weak large or fine motor skills that may interfere with academic achievement or daily living but are not due to a specific medical condition. Readers interested in an extensive discussion of subtypes of learning disorders in childhood are referred to Silver and Hagin (1990) or Swanson et al. (2003).

A Neuropsychological Model to Assess Learning Disability

The consensus in current factor-analytic research is that there are two broad groups of skills necessary for efficient learning:

1. Auditory–verbal processes. Weaknesses in these areas result in reading disorders and other language-based learning problems.
2. Visual, perceptual, and motor processes. Weaknesses in these areas may result in reading problems but more likely affect handwriting, mathematics, and certain social skills. Tables 1 and 2 present a model for conceptualizing these skills and examples of them in a two-by-two grid.

The model conceptualizes learning skills on rote/automatic and conceptual levels, linguistically and visually.

As it has also been demonstrated that there is a significant but small group of children experiencing achievement problems in the absence of either of these sets of skill weaknesses, neuropsychologists are also urged to consider the impact of foundational skills such as an environment conducive to learning, problems with attention and impulse control, self-esteem as a learner, and other emotional (e.g., depression/anxiety) and behavioral (oppositional defiance, conduct

disorder) problems as contributing to delayed achievement (Goldstein & Mather, 1998).

As can be seen in this model, language-based learning disorders are directly related to impaired language skills, especially those related to phonological processes (Pennington, 1991; Bishop & Adams, 1990; Scarborough, 1990, 1998). Further, for many children, poor comprehension results from poor rote language skills such as inability to distinguish similar sounds which then leads to poor auditory discrimination and weak phonetics. Problems with verbal short-term memory are also common among reading-impaired individuals. Memory requires phonological skill. Poor readers may experience problems recalling letters, digits, words, or phrases in exact sequence. While the majority of children with language-based learning disabilities struggle to master basic foundational academic skills, others are capable of learning to read but when the curriculum begins to accelerate in third or fourth grade and they must read to learn, they struggle as a result of weak conceptual, linguistic skills. It is also not surprising that related language-based skills such as spelling and writing are impaired in reading-disabled children. For many, spelling is even more impaired than reading (Snowling & Hulme, 1991).

Weaknesses in visual–motor skills tend to cause problems with arithmetic and handwriting, often independent of associated reading disability. Included in problems for this group of children are difficulties involving social awareness and judgment. These problems do not appear to be primarily language-based and have been referred to collectively in the neuropsychology literature as nonverbal learning disabilities (NLD) (Pennington, 1991; Rourke, 1989). Children with this pattern have been reported to experience problems with spatial organization, attention to visual detail, procedural skills, and mathematics; problems shifting psychological set from one operation to another, graphomotor weaknesses, poor factual memory, and poor judgment and reasoning (Rourke, 1985). Neuropsychologists can reliably conclude that children with nonverbal learning disability experience greatest deficits in visual, perceptual, and organizational skills, psychomotor coordination, and complex tactile perceptual abilities (Harnadek & Rourke, 1994). Finally, it is also suspected that

TABLE 1. Categories of Academic Skills

	Auditory–verbal	Visual–motor
Conceptual	Verbal conceptual	Visual nonverbal conceptual
Rote/automatic	Auditory–motor	Letter perception
	Auditory perceptual	Spatial organization and nonverbal integration
	Rote auditory–sequential memory	Rote visual–sequential memory and retrieval
	Rote and association memory and retrieval	Motor sequencing and fine motor control

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TABLE 2. Levels of Processing Related to LD and Disability Characteristics

	Auditory–Verbal	Visual–Motor
Conceptual	Language semantics; word meaning, definition, vocabulary Listening comprehension; understanding and memory of overall ideas Specificity and variety of verbal concepts for oral or written expression Verbal reasoning and logic	Social insight and reasoning; understand strategies of games, jokes, motives of others, social conventions, tact Mathematical concepts; use of 0 in $+$, $-$, $\times$; place value; money equivalencies; missing elements, etc. Inferential reading comprehension; draw conclusions Understand relationship of historical events across time; understand scientific concepts Structure ideas hierarchically; outlining skills Generalization abilities Integrate material into a well-organized report
Rote/Automatic	Early speech; naming objects Auditory processing; clear enunciation of speech; pronouncing sounds or syllables in correct order Name colors Recall birthdate, phone number, address, etc. Say alphabet and other lists (days, months) in order Easily select and sequence words with proper grammatical structure for oral or written expression Auditory "dyslexia": discriminate sounds, esp. vowels, auditorily; blend sounds to words; distinguish words that sound alike, e.g., mine/mind Labeling and retrieval reading disorder: auditory and visual perception okay but continually mislabels letters, sounds, common syllables, sight words (b/d, her/here) Poor phonic spelling Poor listening and reading comprehension due to poor short-term memory, especially for rote facts Labeling and retrieval math disorder: trouble counting sequentially; mislabels numbers (e.g., 16/60); poor memory for facts about numbers and sequences of steps for computation (e.g., long division) Recall names, dates, and historical facts Learn and retain new scientific terminology	Assemble puzzles and build with construction toys Social perception and awareness of environment Time sense; does not ask, "Is this the last recess?" Remember and execute correct sequence for tying shoes Easily negotiate stairs; climb on play equipment; learn athletic skills; ride bike Execute daily living skills such as pouring without spilling, spreading a sandwich, dressing self correctly Use the correct sequence of strokes to form manuscript or cursive letters Eye–hand coordination for drawing, assembling art projects, and handwriting Directional stability for top/bottom and left/right tracking Copy from board accurately Visual "dyslexia" confused when viewing visual symbols; poor visual discrimination; reversals/inversions/transpositions due to poor directionality; may not recognize the shape or form of a word that has been seen many times before, i.e., "word-blind" Spelling: poor visual memory for the nonphonetic elements of words

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individuals with nonverbal learning disability experience greater internalizing problems related to depression and anxiety than those with language-based learning disability. It is unclear whether this pattern contributes to or is a consequence of the disability.

In the PASS model, Naglieri and Das (2002) note characteristic weaknesses in planning and attention processes for youth receiving diagnoses of ADHD, isolated weaknesses in planning for youth with mathematics learning disability, and isolated weaknesses in successive

processes for youth with phonics-based reading disability. Readers interested in the PASS model are referred to Chapter 32 of this volume.

Evaluating Learning Disability in the Context of a Comprehensive Neuropsychological Evaluation

A number of volumes provide thorough, in-depth models for neuropsychological assessment utilizing a myriad of tests and batteries. Interested readers are referred to Reynolds and Fletcher-Janzen (this volume) and Goldstein (1997). Due to space limitations, this section will briefly review assessment measures. The basic task facing the neuropsychologist is to answer questions concerning underlying neuropsychological skills essential to learning. Assets and liabilities must be identified. Screening of basic academic skills must also be completed. In many situations, the neuropsychologist can rely upon data collected at school to provide these basic achievement measures. The most widely used of these instruments, the Woodcock–Johnson III Tests of Achievement (Woodcock, McGrew, & Mather, 2001) is the most comprehensive. It offers by far the most thorough, well-developed assessment of academic skills. The factor-analytic model fits well with the concepts presented in this chapter concerning the underlying neuropsychological deficits contributing to learning disability. Subtest analysis often reveals patterns consistent with verbal, visual, rote, or conceptual weaknesses. Although achievement/intelligence discrepancies are most widely used to identify learning disabilities, the issue of high IQ individuals with average achievement identified as learning disabled continues to be controversial. An age/achievement discrepancy nonetheless is a good target for the neuropsychologist, with a standard deviation and a half below the age mean used as a cut-off.

In the absence of a comprehensive battery such as the Woodcock, it is recommended that neuropsychologists address collection of basic achievement data as follows:

1. *Reading*. A measure should be used to obtain single word reading reflecting phonetics skill and sight word achievement. An estimate of the ability to read within context and comprehend what is read should also be obtained. Achievement tests such as the Woodcock–Johnson III Tests of Achievement (Woodcock, McGrew, & Mather, 2001), the Gilmore (Gilmore & Gilmore, 1968), the Gray Oral Reading Test – 3rd Edition (Wiederholt & Bryant, 1992), or the Test of Reading Comprehension – 3rd Edition (Brown, Hammill, & Wiederholt, 1995), can provide clinicians with these data.
2. *Spelling*. Estimates of sight word memory for spelling and phonetic ability can be analyzed qualitatively utilizing the Wide Range Achievement Test-3 (Wilkinson, 1993).
3. *Mathematics*. The Wide Range Achievement Test-3 (Wilkinson, 1993) or the Key Math Diagnostic Inventory – Revised (Connoloy, 1988) can be utilized to generate observations of conceptual versus rote sequential mathematics skills.
4. *Written language*. Written language skills of thematic maturity, vocabulary, capacity to organize ideas, grammar, punctuation, and general execution can be observed utilizing the Story Writing subtest from the Test of Written Language – 3 (Hammill & Larsen, 1996).

Interventions for Learning Disabilities

Since views differ regarding the nature and etiology of learning disabilities, views also differ about what constitutes appropriate and effective interventions for individuals with learning disabilities. Lyon and Moats (1988) discussed critical issues in the instruction of learning-disabled students. Numerous authors, representing different theoretical orientations and instructional paradigms, have presented intervention methodologies developed or adapted for disabled learners. These include psycholinguistic process or specific abilities approach (Johnson & Myklebust, 1967; Kirk & Kirk, 1971); behavioral approaches, including direct instruction and data-based instruction (Lovitt, 1984; Marston & Tindal, 1995; White, 1986); cognitive approaches, including constructivism and instruction in learning strategies (Deshler & Lenz, 1989; Swanson, 1993; Wong, 1991); and neuropsychological approaches (Rourke, Fisk, & Strang,

1986; Hooper, Willis, & Stone, 1996). Mercer (1991) and Lerner (1993) have provided a lucid discussion of these instructional approaches and their application to individuals with learning disabilities. Mercer and Mercer (1993), Mather (1991), Mather and Jaffe (1992), and Lerner (1993) outline a broad array of specific teaching strategies and techniques which have been utilized successfully with atypical learners including those with learning disabilities.

Recent research is leading to better development of causal theories of learning disability and to promising avenues of intervention for the LD subtypes or specific information-processing weaknesses explicated by those theories. As Torgesen (1993) reports, "The two most completely developed current causal theories of learning disabilities are the nonverbal learning disabilities syndrome… and the theory of reading disabilities involving limitations in phonological processing" (p. 158).

A great deal of attention and research has been directed toward understanding phonological processing skills and their relation to the development of reading skills (Lyon, 1996; Pennington, 1991; Shaywitz, 1996; Stanovich, 1993; Stanovich & Siegel, 1994; Torgesen, Wagner, & Rashotte, 1994; Wagner & Torgesen, 1987). A number of well-designed, longitudinal studies have documented the efficacy of instruction in phonological awareness and/or phonemic analysis and synthesis for the initial development of reading skills and for improving reading in reading-deficient children (Ball & Blachman, 1988; Blachman, Ball, Black, & Tangel, 1994 cited in Lyon, 1996; Hatcher, Hulme, & Ellis, 1994; Lundberg, Frost, & Petersen, 1988).

At the conclusion of their research report, Hatcher et al. (1994) suggest that children differ in their ability to acquire phonological competence and pose the question of how to best facilitate acquisition of underlying phonological skills. In this critical area of instruction, research-based practices are emerging. In a recent contribution, Torgesen, Wagner, and Rashotte (1997) discussed approaches to the prevention and remediation of phonologically based reading disabilities. Research with the Auditory Discrimination In Depth Program (Lindemood & Lindemood, 1969) has shown that intensive instruction led to significant gains in reading and spelling skills for 281 subjects of age 5–55 (Truch, 1994). Employing a new and promising approach,

Merzenich et al. (1996) acoustically modified speech to train sound discrimination abilities in children with language-based learning impairments. Subjects engaged in highly motivating discrimination tasks with speech stimuli altered by a computer algorithm which stretched the duration or increased the volume of sound elements critical to the discrimination process. After a few weeks' instruction, children in the study markedly improved their ability to discriminate phonemes and recognize both brief and fast sequences of speech stimuli. They also showed significant improvement in language comprehension abilities. While acoustically modified speech is a logically conceived and an exciting intervention concept, experts in the field of dyslexia and learning disabilities, as reported by Travis (1996), suggested caution in regard to its potential benefits. Recent research has raised further doubts about the efficacy of this intervention (Watson et al., 2003).

Just as well-designed research can validate intervention practices and techniques for learning disabilities, it can also identify methods which are contraindicated for many LD students. In education as a whole, and in special education, there continues a great debate about the relative merits of code-oriented versus whole-language approaches to reading instruction (Foorman, 1995). Based on available research, most professionals in the field of learning disabilities have concluded that when used as the primary mode of instruction, the whole-language method is less effective than structured, explicit instruction in phonics for children with reading disabilities (Iverson & Tunmer, 1993; LDA Newsbriefs, 1995; Liberman & Liberman, 1992; Pressley & Rankin, 1994; Shapiro, 1992; Stanovich, 1994; Torgesen et al., 1994).

Summary

A neuropsychological perspective of learning disabilities provides an understanding of the underlying forces that impact rate and level of achievement across academic domains. Neuropsychological assessment has increasingly been utilized in academic settings. A neuropsychological perspective provides an understanding of the reasons why some children struggle academically. Pediatric neuropsychologists must be

well versed in academic assessment and school issues. This chapter provided an overview of the current literature concerning the history, etiology, definition, evaluation, treatment, and efforts to accelerate achievement for youth with learning disabilities. There is an increasing appreciation within educational systems for the role underlying neuropsychological processes play in rates of achievement. An increasing body of research is demonstrating that not only do brain structures and function impact learning but in a bi-directional manner achievement over time changes the brain.

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9

Measurement and Statistical Problems in Neuropsychological Assessment of Children

CECIL R. REYNOLDS AND BENJAMIN A. MASON

The field of neuropsychology as practiced clinically has been driven in large part by the development and application of standardized diagnostic procedures that are more sensitive than medical examinations to changes in behavior, in particular higher cognitive processes, as related to brain function. The techniques and methods so derived have led to major conceptual and theoretical advances in the understanding of normal and abnormal patterns of brain–behavior relationships. Despite the apparent utility of many of the neuropsychological tests discussed in this volume, their psychometric properties leave much to be desired. Much of their utility comes from the clinical acumen and experience of their users and developers, a situation that has, historically, made clinical neuropsychology more difficult to teach than should be the case. In fact, much of today's practice and yesterday's theoretical advances in clinical neuropsychology stem from intense and insightful observation of brain-damaged individuals by such astute observers as Ward Halstead, A. R. Luria, Hans Teuber, Karl Pribram, Roger Sperry, and others. These superstars of clinical neuropsychology were state-of-the-art

researchers (though the state of the art was often crude) to be sure, but their greatest inspirations came from their constant monitoring and informal interactions with the behavior of persons suffering from a variety of neurological trauma and disease. Halstead roamed the halls of Otho S. S. Sprague making notes as he observed behavior among brain-damaged individuals; Luria gained great insights into brain function with his rather informal, sometimes impromptu, bedside examination and discussions with soldiers with head injury (Glozman, 2007); Sperry and his students followed and observed a series of "splitbrain" patients going about their daily activities, even to the point of observing some as they dressed themselves and others in leisure activities.

Major advances have occurred because of the sheer clinical acumen of these individuals. Many clinical neuropsychologists continue to evaluate patients quite profitably on the basis of observation and informal assessment. Others have devoted themselves to more purely actuarial approaches to clinical work and research (e.g., see the prolific works of Reitan, Rourke, and Satz). Most clinicians engage the complementary of the two approaches, a modus operandi that has made neuropsychologists more and more accepted and contributing members to medical staff in teaching hospitals and clinics. Clearly, clinical neuropsychology has been

CECIL R. REYNOLDS AND BENJAMIN A. MASON • Department of Educational Psychology, Texas A&M University, College Station, Texas 77843.0.

successful in earning its riches in medicine and in psychology largely as a result of empirical research and clinical acumen in the field. Neuropsychological techniques have infiltrated assessment in special and remedial education for some time now (e.g., Haak, 1989; Hynd, 1981; Mattison, Hooper, & Carlson, 2006).

At the same time, many of the practices in neuropsychology, clinical and research, have been criticized extensively from inside (e.g., Ruff, 2003; Prigatano, 2003; Dodrill, 1997, 1999; Wong, 2006; Cicchetti, 1994; Reynolds, 1982a, 1986; Ris & Noll, 1994; Willson & Reynolds, 1982) and outside the discipline (e.g., Coles, 1978; Reschly & Gresham, 1989; Sandoval, 1981) for a lack of attention to certain principles of research design in the field and the failure to incorporate the many advances in psychometric methods of the past 25 years. To be sure, our research methods and statistical tools have improved greatly since Halstead's early work; yet our ability (or our inclination) to apply them uniformly or to our best advantage certainly has not kept pace with the growth in our clinical acumen and with theoretical advances in the field (Schatz, Jay, McComb, & McLaughlin, 2005). Neuropsychologists have shown an increasing interest in the educational problems of children categorized as learning disabled as well, bringing neuropsychological methods to bear on the recurring questions of neuropsychological dysfunction within this population. Clinical neuropsychological assessment of educational disorders such as learning disability offers a prime opportunity to meld theory and clinical acumen with good psychometric practice, but has not, apparently, come fully about, although improvements are clearly evident since the first edition of this work in 1989 and even more so since the second edition in 1997.

The failure to reach this coalescence in clinical neuropsychology has serious implications for the credibility and, ultimately perhaps, the survival of the clinical application of neuropsychological principles in medical and educational settings. Perhaps it is the youth of the field or its placement primarily in the medical setting, where good research design and statistical methods are too rare, that has retarded coalescence.

Problems of statistical methods and design in test development in clinical neuropsychology have been noted with frequency (e.g., Reynolds, 1982a, 1986). In reviewing the Halstead–Reitan Neuropsychological Test Battery (HRNB), Dean (1985) remarked that the "manual for the HRNB lacks the basic psychometric documentation needed in interpretation. Moreover, interpretations are more dependent on the psychologist's knowledge and clinical acumen than reported psychometric properties for the battery" (p. 645). The other major battery in the discipline, the Luria–Nebraska Neuropsychological Battery (LNNB), fares no better; as Adams (1985) remarked, "the methodological errors committed in the construction of the test [the LNNB] are both numerous and substantive" (p. 879). Other scales in common use by clinicians are equally guilty. The normative data for the Benton Test of Facial Recognition, Mirsky's Continuous Performance Test, Purdue Pegboard Test, Rey Complex Figures, Stroop Color and Word Test, National Adult Reading Test, the Wide Range Achievement Test, and numerous other measures used in neuropsychological testing are far below contemporary standards. It is a monument to the clinical acumen and tenacity of clinical neuropsychologists, and perhaps also the insensitivity of many medical practitioners to behavioral changes, that the field has survived and in fact prospered over the last 50 years.

The issues to be delineated in the following pages deal primarily with pragmatic concerns that affect the clinical practice of neuropsychology in patient care certainly, but also the study of brain–behavior relationships generally. These issues principally revolve around measurement problems evident in the neuropsychological literature, the resolution of which could enhance progress in research and practice in the field. The solutions are neither novel nor unknown nor are the problems restricted to neuropsychology. A number of difficulties in present practice are apparently the result of either a lack of psychometric sophistication among those in the field or ignoring certain well-known measurement principles or some combination of these two reasons. The following discussion will present several examples of what may be seen as a lack of sophistication or attention to measurement issues in neuropsychology and propose alternative procedures. Rather than employ a single battery or procedure as an example throughout, a variety were chosen to illustrate the widespread nature of the problem and not to appear to be "picking on" any specific application. A series of statistical issues related to diagnostic research

problems is next presented along with recommendations for improving this line of research as well.

Lest this work appear too negative, it is worth noting that neuropsychology has emerged as a major field within psychology and that the procedures critiqued herein have been and remain useful in clinical and research domains. The clinical acumen, insight, and dedication of the practitioners who use these scales are considerable and are not being questioned. Indeed, they have moved the field substantially in many ways. Nevertheless, the fact remains that our methods and techniques could be better—by following some well-known, widely accepted methods.

Normative Data and Standardization Samples

The systematic development and presentation of *normative* data has received far too little attention in neuropsychology. Perhaps this reflects the rather tedious, mundane nature of such tasks, but nevertheless, the lack of good normative data in neuropsychology is a distinct handicap to the field. Certainly one encounters reports of "normative data" in the professional literature. However, these reports either are typically based on very small samples (some even as small as $N = 10$ at yearly age intervals) or do not employ normal individuals. While many clinicians have called for larger N studies within the field with differing expectations for what is reasonable (Charter, 1999; Cicchetti, 2001), larger normative samples are necessary to ensure the reliability of parameter estimation for normatives bases for our measures. Too much of our neuropsychological data are based on impaired individuals; we simply do not know enough about how normal individuals respond to most neuropsychological tests. The latter issue is more serious clinically than most clinicians realize because in addition to the other problems it creates, it results in a lack of items with sufficient difficulty for assessment of premorbidly high-functioning individuals with less than massive neurological trauma. Most of the children with premorbid IQs of 130 or more who suffer general cerebral trauma but lose only 20–25 IQ points or less can easily go undetected in neuropsychological testing, i.e., they can appear normal and go untreated

or even lose existing services once these levels have been reached even in the case of initial massive trauma due at least in part to the correlation between FSIQ and numerous tests of neuropsychological function (Jung, Yeo, Chiulli, Sibbitt, & Brooks, 2000).

Conversely, when normative samples are drawn from neurologically intact populations, the reliance on volunteer sampling may inflate results. Russell (2005) examined all studies that included norming groups of 200 subjects or more for the Halstead–Reitan Battery and found an average full scale IQ a full standard deviation above normal. When selecting groups to represent normal performance, overly strict exclusion rules may bias results in the opposite direction (Stanczak, Stanczak, & Templer, 2000).

Without adequate normative data drawn from large-scale samplings of the population, the clinician and the researcher are also unable to assess the effects of demographic variables such as race or ethnicity, gender, and socioeconomic status on neuropsychological test performance. Demographic variables do have a significant influence on test performance on any number of tasks. Often, neuropsychologists ignore such factors during test interpretation or believe that because brain function is being evaluated, demographic variables may be irrelevant. Systematic effects of many demographic variables have been noted on numerous tasks as illustrated by even simple tasks like Coding and Digit Symbol (some of the most sensitive of all of the Wechsler tasks to neurological trauma) from the Wechsler Scales where females (both black and white) consistently outscore males (Ramsey & Reynolds, 1995). Moreover, when these differences are examined, the differences between demographic group's performances are inconsistent across studies due in part to overreliance on p values and comparisons across tests of differing psychometric strength. As an example, gender differences in tests of memory performance have been widely studied with mixed results (Lowe, Mayfield, & Reynolds, 2003). Whether using a level of performance or an ipsative profile analysis (e.g., Davis, 1959; Reynolds & Gutkin, 1980; Naglieri & Paolitto, 2005), ignorance of such robust findings could mislead the clinician. Research has considered the influence of demographic variables on more strictly neuropsychological test results, but principally this is a relatively recent phenomenon,

and most such studies deal with adults. Some of the early primary books in the field do not discuss the issue or its relationship to diagnosis at all (e.g., Golden, 1981). For such tests as the Wechsler Scales, the major studies of demographic influence on scores have occurred as a function of research involving the standardization samples of these instruments (see Reynolds & Kaufman, 1986, for a review; see also Kaufman, McLean, & Reynolds, 1988, and Reynolds, Chastain, Kaufman, & McLean, 1987), but in later editions information from these very good standardization samples has been more restrictive, and information from less adequate samples has been relied upon by clinicians who again ignore the issues of sampling adequacy in the estimation of important moments of the score distributions used to derive normative tables or to make demographic corrections to scores.

A great deal is known about potential cultural biases and other effects of demographic and other nominal variables on tests of intelligence and personality (e.g., Reynolds & Ramsay, 2003). However, there is a dearth of research on the effects of demographic factors in neuropsychological assessment, using large, representative samples. When studies have been conducted, they have found substantial variability that may compromise interpretation of results if the clinician is unaware of their existence (Kennepohl et al., 2004). This is unsurprising given even the modest correlations between full scale measures of intellectual ability and neuropsychological testing, and covarying early environmental differences was incapable of explaining these differences in a study of white and African American neurologically normal subjects by Byrd et al. (2006). Helms (1992) has argued that neuropsychological tests may be biased by cultural factors for three major reasons: (1) a lack of equivalence of testing conditions, (2) functional inequivalence across groups, and (3) linguistic inequivalence. Reynolds (1982b, 1995; Reynolds & Kaiser, 1990; Reynolds & Ramsay, 2003; Brown, Reynolds, & Whitaker, 1999) has suggested additional reasons including different latent structures of the tests across groups, differential affective responses to the examination and/or the examiner, and differences in the reliability of measurement, validity of the interpretations of performance, and in the content validity of the items and the item selection process. All of these factors may be evident to some degree for

any ethnic minority or possibly even across gender for neuropsychological tests, despite the lack of such findings for intelligence tests. The use of neuropsychological tests with Hispanic populations has attracted the most attention thus far (e.g., Ostrosky-Solis, Ramirez, & Ardila, 2004; Arnold, Montgomery, Castaneda, & Langoria, 1994) although cultural bias with regard to blacks and women has been evaluated thoroughly for the TOMAL (Test of Memory and Learning) as well as the TOMAL-2 (Test of Memory and Learning-second edition) (see Reynolds & Voress, 2007; Reynolds & Bigler, 1994) during test development with no cultural effects being detected that would bias test interpretation. Nevertheless, all neuropsychological measures must be evaluated for effects related to culture, ethnicity, gender, and other nominal variables as findings in this area do not generalize well across tests or necessarily across nominal groupings. The first and most obvious step in this direction would be for authors to report consistently on these variables in their study results. In their review of neuropsychological journals between the years of 1995 and 2000, O' Bryant, O'Jile, and McCaffrey (2004) found that authors did not report race, language, and ethnicity to the same degree that they reported age, education, and gender.

The failure to provide good, stratified samples in the development and standardization of neuropsychological tests has been a major inhibiting factor in efforts to understand demographic influences on neuropsychological test performance. Other writers have reached similar conclusions. The manual for the HRNB contains no standardization or normative data, yet age and other demographic variables are correlated with the test results. This greatly complicates test interpretation for individuals (Broshek & Barth, 2000; Dean, 1985).

By good normative data, reference is made to the application of stratified, random sampling techniques now common, and applied to such tests as the various Wechsler Scales, the KABC-II, the RIAS. Indeed, the standardization of the KABC-II (Kaufman & Kaufman, 2005) is an excellent model of the development of normative data. Good standardization samples provide a reliable standard against which to judge the performance of others and have additional benefits including at least the following: (1) communications among researchers, (2) training of clinical

neuropsychologists, and (3) the deflation and exposure of a variety of clinical myths. After a brief discussion of the first two of these benefits, we will turn to a more extensive presentation of the "myth deflation advantage."

Communication among researchers is a difficult and expensive task but a necessary one; indeed, it is in communication among us that the foundation of the "community of scholars" must lie. It would certainly enhance the clarity of research communications in the field if a good normative reference sample were available against which research samples could be contrasted (provided other appropriate demographic variables were adequately controlled). The development of scaled scores for neuropsychological tests based on such a sample would simplify matters as well. The issue of training also is ultimately one of communication. The presence of normative data makes learning easier. Although the accuracy of the statement is not known, it has often been said that when asked about how to become a good clinical neuropsychologist, Ralph Reitan replied, "Work in the field for 30 years." Although this would probably work, much of this time would be spent in developing a set of "clinical norms" in one's own mind about how normal and various groups of impaired individuals perform on such tests as the HRNB. This is necessary because of the lack of a standardization sample for such scales as the HRNB and the Boder Test of Reading–Spelling Patterns (a scale clearly intended to assess developmental phenomena), and the less than adequate sample for such popular scales as the LNNB. The transmission of the knowledge and the clinical skills of neuropsychology could be greatly enhanced by the presence of accurate, high-quality normative data.

Norms also have the advantage of allowing us to evaluate certain aspects of the "clinical mythology" of assessment. For some time, statistically significant Verbal–Performance IQ differences on the Wechsler Scales were believed (and, unfortunately, still are by many) to be indicative of brain damage, neurological dysfunction, or almost certainly a learning disability if a child were involved (Iverson, Mendrek, & Adams, 2004). From the standardization sample of the WISC-R, Kaufman (1976a) developed normative data for the frequency of occurrence of these differences. Prior to reporting these data, he took an informal poll of clinicians asking what they believed, on the basis of their clinical experience,

the typical Verbal–Performance IQ difference would be for normal children. The response indicated a belief that other than small differences were considered unusual. A 3- or 4-point difference was the typical response. Differences of 15 points have long been thought to be clinically significant and have been used (e.g., Dean, 1978) to document the presence of a learning disability.

Actual analyses of the frequency of occurrence of Verbal–Performance differences by Kaufman (1976a) with the 2200 normally functioning children in the WISC-R standardization sample revealed a very different picture. The average difference was more than 9 points, with 12-point differences (the difference required for significance at $p = 0.05$) occurring with one of three children, and 15-point differences ($p = 0.01$) occurring with one of four children. This should not have been surprising as this is essentially the same distribution of difference scores that was reported 20 years earlier for the WISC, but that had gone largely ignored until Kaufman published his analyses of the WISC-R standardization sample. Note that the availability of a proper standardization sample made the investigation possible at all. In high-ability samples, large discrepancies are even more common. In one study of children suspected of being gifted and administered the adult Wechsler Scales at age 12 in order to avoid ceiling effects, 58% of the 95 children scoring over 110 showed a discrepancy of 12 points or more between verbal and performance scores (Herskovits & Gyarmathy, 1995). Information provided in studies such as these highlight the care that must be taken when making assumptions of normality in atypical populations post brain injury.

This again points to the need to develop good normative data on which to evaluate one's clinical insights. Next I discuss another index of neurological dysfunction that was not normed until recently, serving as an example of how one goes about developing and reporting such data.

Gutkin and Reynolds's (1980) Norming of the Selz and Reitan Index of Neurological Dysfunction

Over the last several decades, hundreds of attempts have been made to develop diagnostically useful patterns based on Wechsler subtest scores (Matarazzo, 1972). In general, these

attempts have not been successful (e.g., Livingston, Jennings, Reynolds, & Gray, 2003; Ivnik, Smith, Malec, Kokmen, & Tangelos, 1994; Kaufman, 1979; Reynolds & Kamphaus, 2003, see especially review of the reliability of subtest level profiles in chapter 1; Sattler, 1974). A variety of scatter indexes have been developed and investigated as potentially useful diagnostic indicators for exceptionality. The Wechsler Scales, and especially the Wechsler Intelligence Scale for Children-Revised (WISC-R) (Wechsler, 1974), have been extensively investigated with regard to utility of scatter indexes in diagnosis. Scatter indexes from the WISC-R that have been investigated include Verbal–Performance IQ discrepancies (Kaufman, 1976a; Piotrowski, 1978; Reynolds, 1979a; Reynolds, Hartlage, & Haak, 1980), the range of subtest scores, i.e., highest minus lowest subtest score (Kaufman, 1976b; Tabachnick, 1979), and the "number of deviant signs" or number of subtests deviating significantly from the mean of all subtests (Kaufman, 1976b). Range of subtest scores in particular has attracted substantial attention as a potential technique with which normals and different pathological groups could be distinguished. Although some prior research has found statistically significant differences between diagnostic groups on this scatter index, other studies, such as Thompson (1980), have not. Even in those studies where significant differences in Wechsler subtest scatter have been found across groups of normal, brain-damaged, emotionally disturbed, and other categories of child psychopathology, the small actual differences and resulting substantial overlap of distributions have made scatter indexes such as the range of little diagnostic utility. As such results become more widely known, the search for more sensitive, sophisticated indexes of scatter has broadened and statistics such as the profile variance technique (Plake, Reynolds, & Gutkin, 1981) have been developed. The provision of full normative data has allowed such scatter indexes to be evaluated for their potential contribution (e.g., Ivnik et al., 1994). (Comparable data have not been made available for the WISC-III, despite its widespread replacement of the WISC-R in clinical practice.)

Selz and Reitan (1979) presented another Wechsler scatter index that seemed to facilitate the accurate diagnosis of neurological dysfunction when combined with other perceptual and neurological tests. Specifically, scatter was calculated by subtracting the lowest subtest score from the highest subtest score and dividing the result by the mean of all subtests (i.e., it is calculated as the range/mean). Selz and Reitan reported three levels of diagnostic criteria in their study. A scatter index calculated with this technique that equaled or exceeded 1.0 was taken as a mild indication of neurological dysfunction. A scatter index that equaled 1.4 was interpreted as being consistent with the existence of a "probable" neurological problem. A scatter index equaling or exceeding 1.76 (rounded to 1.8 for the Gutkin & Reynolds, 1980, study) was viewed as part of a symptom complex indicating definite neurological impairment.

One of the most common shortcomings in the Wechsler scatter pattern body of research has been the failure of investigators to validate the abnormality of various diagnostic incidents with a normal population. Often, seemingly abnormal levels of subtest scatter have been found to be quite common among normal individuals (Davis, 1959; Kaufman, 1976a, b, 1990; Reynolds, 1979a), prompting the Gutkin and Reynolds (1980) study, which is reviewed here as an example of how to develop and present such data.

The subjects for their investigation were the white ($N = 1868$) and black ($N = 305$) children from the WISC-R standardization sample of 2200 children. The characteristics of these children are described in great detail elsewhere (Wechsler, 1974). It is noteworthy, however, that these groups accurately reflect the 1980 U.S. census and are thus excellent, nationally representative samples of normal white and black children. The sample of 2200 was chosen to be a stratified random sample of children of the United States with sample stratification occurring by age (20 at each year between 6½ and 16½), race, sex, geographic region of residence in the United States, urban versus rural residence, and socioeconomic status (as determined by occupation of the head of household). The Wechsler series generally provides one of the best models of test standardization available, one to be emulated by developers of more distinctly neuropsychological measures.

As per the procedure separately described by Selz and Reitan (1979), a scatter index was calculated for each subject by subtracting his or

her lowest subtest score from his or her highest subtest score and dividing the result by his or her mean subtest score. This calculation was performed for both the 10 regularly administered subtests and the 12 total subtests comprising the WISC-R. A series of one-way ANOVAs was calculated to determine if subtest scatter varied as a function of the demographic and intellectual characteristics of subjects, for the stratification variables are known to be differentially related to overall performance on the various IQ scales (Reynolds & Gutkin, 1979). Socioeconomic status is typically related to level of performance on cognitive tests, whereas race has its greatest impact on pattern of performance (Reynolds, 1981a). Specifically, subjects were grouped according to age (less than 10, 10–12, greater than 12), sex (male, female), race (white, black), place of residence (urban or rural), and Full Scale IQ (FSIQ) (less than 85, 85–115, greater than 115). Because Kaufman (1976b) found significant differences in Verbal--Performance IQ scatter as a function of FSIQ, one-way ANOVAs yielding significant results were further examined with a covariance analysis with FSIQ serving as the covariate. Demographic variables that yielded significant results with covariance analysis were used to segregate the study's data.

Analysis of variance on the dimensions of place of residence, sex, FSIQ, occupation of the head of household, age, and race revealed significant differences for the latter four variables. This again points out the need for careful consideration of these variables in neuropsychological test interpretation. Using the FSIQ as a covariate resulted in nonsignificant differences for occupation of the head of household, but statistically significant differences remained for the dimensions of age and race. Because further examination revealed that the means at the different age levels never differed from each other by more than 0.04, subsequent data analyses were broken out only according to subject race and FSIQ. Means, standard deviations, and the percentage of subjects equaling or exceeding each Selz and Reitan (1979) diagnostic criterion as found by Gutkin and Reynolds (1980) are represented according to subject race and FSIQ category in Tables 1, 2, 3, 4, 5.

As indicated by the data analysis, the utility of the Selz and Reitan (1979) scatter index varies with the level of criteria employed and the

TABLE 1. Means and Standard Deviations for Scatter Index Using 10 Subtests

FSIQ	Whites	Blacks	Totals
< 85			
Mean	0.98	1.01	0.99
SD	0.36	0.38	0.37
85–115			
Mean	0.64	0.70	0.65
SD	0.23	0.23	0.23
>115			
Mean	0.51	0.62	0.51
SD	0.16	0.20	0.16
Totals			
Mean	0.65	0.84	0.68
SD	0.27	0.35	0.29

TABLE 2. Means and Standard Deviations for Scatter Index Using 12 Subtests

FSIQ	Whites	Blacks	Total
< 85			
Mean	1.07	1.10	1.09
SD	0.35	0.37	0.35
85–115			
Mean	0.71	0.78	0.72
SD	0.23	0.22	0.23
>115			
Mean	0.58	0.70	0.58
SD	0.17	0.14	0.17
Totals			
Mean	0.72	0.93	0.76
SD	0.27	0.34	0.29

TABLE 3. Percentage of Subjects Equaling or Exceeding Scatter Index of 1.0

FSIQ	10 subtests		12 subtests	
	Whites	Blacks	Whites	Blacks
< 85	49	55	62	64
85–115	9	15	14	21
>115	0	0	2	0

characteristics of the subjects examined. The most stringent criterion (i.e., scatter index equal to or greater than 1.8) appears to set a standard that is almost never reached in the normal

**TABLE 4. Percentage of Subjects Equaling
or Exceeding Scatter Index of 1.4**

FSIQ	10 subtests		12 subtest	
	Whites	Blacks	Whites	Blacks
< 85	12	18	21	23
85–115	1	1	1	0
> 115	0	0	0	0

**TABLE 5. Percentage of Subjects Equaling
or Exceeding Scatter Index of 1.8**

FSIQ	10 subtests		12 subtests	
	Whites	Blacks	Whites	Blacks
< 85	4	3	2	5
85–115	0	0	0	0
> 115	0	0	0	0

population except for 2–5% of the subjects in the lowest IQ group.

Using the second most stringent criterion (i.e., scatter index equals or exceeds 1.4) also yields satisfactory results with all but the lowest IQ group. As with the highest criterion, normal subjects with IQs of 85 and above virtually never equal or exceed the Selz and Reitan index of 1.4. It is noteworthy, however, that both black and white subjects in the lowest IQ group do exceed the 1.4 criterion at a rate that calls into question the validity of this index for this particular group, unless one assumes a rather high incidence of neurological impairment in children with IQs below 85, even though most of these children were functioning normally.

The most lenient of the Selz and Reitan criteria (i.e., scatter index equals 1.0) appears completely to lack validity with the lowest IQ group. Depending on whether one uses 10 or 12 subtests and whether the subjects were white or black, between 49 and 64% of the sample exceeded the 1.0 cutoff. Clearly, the use of this standard with this group of normal children would lead to an unacceptable number of false positives. The middle IQ group also meets or exceeds the 1.0 criterion in numbers that call

the validity of the index into serious question. Only with the highest IQ group was the 1.0 standard sufficiently infrequent.

Although the differences are not highly pronounced, statistically significant differences were evidenced on the Selz and Reitan index between blacks and whites, with the former group consistently showing higher index scores (see Tables 1 and 2) across the entire IQ range. Even smaller, but statistically significant, differences were found as a function of the children's age. No consistent pattern emerged with regard to this variable, although the youngest group most often evidenced the highest Selz and Reitan index scores.

However, the overall data from the Gutkin and Reynolds (1980) study indicate that the utility of the Selz and Reitan index varies substantially according to subject characteristics, especially FSIQ. The presentation of normative data in the detail presented here should be required for all neuropsychological measures.

Designing and conducting a normative study on such a large scale as to be useful is time-consuming and quite expensive. Few and far between are the times when money is available for the wholesale assessment of normally functioning individuals. Neuropsychologists must move actively to seek federal funding for normative studies, and test publishing houses must become convinced of the viability of neuropsychological test construction projects. Major publishing houses have been responsive to the needs of psychology in some instances resulting in large investments in test construction projects such as the Wechsler Scales. Clinical neuropsychologists must demand that neuropsychological tests meet the same psychometric standards as many other scales and move toward the development and norming of such scales. Nowhere is this more needed generally than in neuropsychology and child neuropsychology in particular. We have not done so effectively, at least to this point. In 1995, I received an ad from a major publisher of tests in the United States promoting a reading test for adults of all ages with a normative sample of less than 200 across the entire adult age range. The estimation of the characteristics of the score distributions across age with such a sample and involving some 70 years is hardly more than speculation and should be rejected heartily by the profession.

Reliability of Neuropsychological Measures

Reliability may be the single most influential of latent psychometric concepts because of its relationship to all other psychometric characteristics. It is the foundation of validity, and classical psychometric theory is known as reliability theory. The problem of reliability, particularly of internal consistency reliability such as represented in Cronbach's alpha and the various Kuder–Richardson formulas, has not been well attended in clinical neuropsychology. Observed test score variance can be divided into two components, true score variance and error variance. Only true score variance is "real," systematic, and related to true differences among individuals. Only true score variance can be shared or related between two variables; thus, we see that the criterion-related validity of any test is restricted as a function of the square root of the product of the reliabilities of the two measures [i.e., $(r_{xx}r_{yy})^{1/2}$].

Variance Definitions of Reliability and Validity

Classical test theory's variance definitions of reliability and validity are useful for understanding these two constructs and the relation between them. Briefly, a person's score on a test is a product of two things: that person's true (but unknown) score and error. Similarly, the variance in a set of scores is a function of true score variance (V_t) and error variance (V_e):

$$V = V_t + V_e$$

This relation is displayed pictorially in Figure 1. Using this definition, reliability is simply the proportion of true score variance (V_t) to total variance (V). If a test is error-laden, it is unreliable. Conversely, if scores on a test are primarily the result of the test takers' *true* scores, the test is relatively reliable.

The true score variance, a reflection of the reliability of the test, may also be subdivided. Suppose we administer several measures of reading comprehension. One measure requires children to read a passage and point to a picture that describes the passage read; the second requires the child to fill in a blank with a missing word;
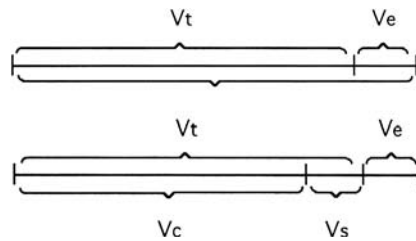
Figure 1. Variance definitions of reliability and validity. Variance in test scores may result from true score variation (V_t) or error variance (V_e). True score variation may be further divided into common variance (V_c) and specific variance (V_s), as in the bottom panel. Reliability is a function of V_t; validity is a function of V_c.

and the third requires the child to act out a sentence or passage (e.g., "Stick out your tongue"). Each method measures reading comprehension, and may do so very reliably. But each method also measures something else in addition to reading comprehension. In the first case, the child has to comprehend the passage, but also has to be able to recognize and interpret a picture depicting that passage; in the third measure, we also require the child to be able to translate the passage into action. In other words, each method measures reading comprehension, but each also measures something *specific* to that measure, although both components may be measured reliably.

Of course, the degree to which each test measures reading comprehension is the validity of that test. In Figure 1, we can further divide the V_t (reliability) into the variance each measure shares with the other (V_c, or common variance, in this example representing reading comprehension), and the variance that is specific to the test (V_s, representing pictorial understanding, etc.). As is the case with reliability, the validity of the test is simply the proportion of common variance to total variance (V_c/V). The relation of validity to reliability is clear using this definition: We may consider validity as simply a subset of reliability. This, then, is the reason for the rule learned (and often confused) by students of measurement: A test cannot be valid unless it is reliable (all valid tests are reliable; no unreliable tests may be valid; reliable tests may or may not be valid). A more extensive and informative review of these problems may be found in Thompson (2003), Cronbach (1990), Guilford (1954), and Feldt and Brennan (1989).

Calculating and Reporting Reliability

Reliability of neuropsychological measures has received attention in the literature as an area of special need (e.g., Parsons & Prigatano, 1978; Reynolds, 1982a). Reliability of neuropsychological measures is equally important to individual diagnosis and to research, as reliability will influence the likelihood that any experimental or treatment effects will be detected. In short, reliability is the foundation on which validity, the most important of measurement concepts, is built. Nonetheless, even in the research literature, reliability data are seldom presented and the most frequently used of the various batteries, the HRNB, does not even have a discussion of reliability in its manual. Reliability of the LNNB is reported but is based on highly heterogeneous groups, across a too wide age span, and is likely spuriously inflated. The Boder Test of Reading–Spelling Patterns, developed by a pediatric neurologist as a neuropsychological measure of educational deficits, provides a good example of how not to assess reliability of neuropsychological measure, although the authors must be acknowledged for at least attending to the issue.

In studying the reliability of the Boder Test, Boder and Jarrico (1982) reported on several aspects of reliability. *Test–retest* (represented as r_{12}) or stability of scores is reported for 2-month and 1-year intervals. The sample size for the 2-month study was 50 and for the long-term study, N was 14. Three aspects of the test (the Boder not actually being divided into subtests) were evaluated, those yielding scores for Reading Level, Correctly Spelled Known Words, and the number of Good Phonetic Equivalents produced by the child. Both test–retest reports of reliability are based on wide age spans; for Reading Level an r_{12} of 0.98 is reported for ages 6–9, and 0.96 for ages 10–15. These rs are inflated to an unknown degree by the correlation of Reading Level with age. The use of a wide age range with rs based on raw scores or other age-related scores such as grade equivalents and age equivalents is a common method of exaggerating the observed reliability of test scores. When corrected for the confounding with age, which is certainly correlated to some substantial degree with Reading Level, these reliabilities are far less impressive. The original r_{12} for Correctly Spelled

Known Words is but 0.64 for ages 6–9 and 0.84 for ages 10–15. For Good Phonetic Equivalents, the values are 0.89 and 0.85. After correction for spurious correlations with age, it would be surprising to find these reliabilities within any commonly accepted range for diagnosing individual cases. Also, the Ns are extremely small (ages 6–9, $N = 27$; ages 10–15, $N = 23$) for making any decision about the stability of scores on the Boder. The long-term rs were 0.81 for Reading Level, 0.62 for spelling, and 0.79 for Good Phonetic Equivalents, values that were clearly unacceptable for individual cases, but based only on $N = 14$, an unacceptable sample size in any case.

Internal consistency (corrected split-half) reliability estimates are reported for 46 cases randomly selected (by Boder and Jarrico's description) from Boder's private patient files. If truly random, the age range of these 46 children is 6–18 years. This tremendous age range greatly inflates internal consistency estimates and is unacceptable for assessing reliability. (This spurious increase in reliability estimates is the result of an artifactual, i.e., age-related, increase in item variances relative to total score variances on any test where item difficulties are correlated with age, i.e., on any test of a variable with a developmental nature). Though considerably inflated, the values were 0.97 for Reading Level, 0.82 for spelling (known words), and 0.92 for Good Phonetic Equivalents. The degree of spurious inflation is indeterminate.

The errors made in the estimation of the reliability of the Boder Test are serious but are all too common, not only in neuropsychology but in several areas of testing (e.g., see Reynolds, 1983). Lack of attention to standard psychometric methods seems all too rampant in clinical neuropsychology and is retarding developments in the field. One other piece of relevant data is reported in the Boder Test manual's reliability section—the agreement on diagnosis of one of three reading disorders for the two testings with the test–retest reliability samples. Chi-square tests were used, appropriately, to evaluate changes in classification across testings, yet even these results are interpreted improperly. According to Boder and Jarrico (1982, p. 95), when the chi-square is evaluated, "a significant result shows high agreement between the classifications at the two testings." Rather, the significant chi-squares only show a statistically significant relationship between the two classifications; that is, the two

sets of classifications were not independent. The actual number of children given the same classification on each testing was not reported and is necessary for a more proper interpretation of these results. The reliability of the Boder Test remains an open question specifically as does the reliability of the most popular of neuropsychological tests generally.

Because the validity of a test is restricted as a function of the square root of the product of the reliability coefficients of the test and the criterion [i.e., the theoretical limit placed on a test's validity coefficient is equal to $(r_{xx}r_{yy})^{1/2}$], one method of improving the validity of existing neuropsychological tests then obviously is to work toward enhancing the reliability of these scales. Too frequently, neuropsychologists rely on the "clinical" nature of certain tests and procedures to the extent that such important concepts as reliability are overlooked.

Reliability of our testing and assessment procedures is equally important to research in neuropsychology. The most direct implication of reliability for research is in the detection of experimental effects. As reliability decreases, so does the likelihood that a significant effect will be found in any experimental or clinical treatment. Marcel Kinsbourne has made reference to just this problem in consistently detecting hemispheric differences on certain tasks under a specified set of conditions (1981, personal communication). As anyone acquainted with the neuropsychology literature will be quick to recognize, the results of research employing dichotic listening procedures and tachistoscopic split-visual field presentation methods are not in great agreement. Dichotic listening and split-visual field methods are both very unreliable from a purely psychometric perspective. The reliabilities reported (albeit infrequently) in the literature are seldom better than 0.5–0.65. The reliability problems here possibly lie with the techniques themselves but a more likely problem seems to be the stimulus materials, i.e., the test that is presented through these methods. The proper application of traditional psychometric methods in the construction of tests to be presented through these methods would undoubtedly enhance the reliability of these techniques. Increases in the reliability of neuropsychological measures could increase the discriminability of the tests in studies of differential diagnosis as well. Error variance cannot contribute to the

general problem of distinguishing among clinical groups, although, as reviewed later in this chapter, error variance can contribute spuriously in single studies without internal replication. Although increasing reliability will most certainly not alleviate all of the interpretive problems existing in this literature, it is better not to base arguments over the interpretation of data on what is essentially error variance and little else. Accuracy of scoring is crucial (Reynolds, 1979b), as is the assurance of full effort from the examinee (Green, 2003).

Scaling Problems in Neuropsychological Testing

Children are in a constant state of development and change in many ways but perhaps most dramatically in their neurological and higher cortical development. Children are acquiring knowledge at the most rapid pace of their lifetime and their reasoning processes and insights into their learning grow in a dramatic manner. All are nevertheless moving at an uneven pace. Consequently, the scaling of any tests or measurement devices designed to aid the assessment of brain–behavior relations is crucial. This is true regardless of whether one takes a "key approach," looks simply at level of function, or assesses profiles of performance. The scaling of neuropsychological tests has been sporadic, with some scaled well, some poorly, and a significant number not at all. Even when scaling is handled well from a technical perspective, the quality of the standardization sample providing the estimates of population parameters from which standard scores are subsequently determined will influence the utility of the derived scores.

Raw scores, e.g., the number correct, the time to completion, or the number of errors, are problematic but common. The HRNB does not provide any transformed scores. Without standard score transformation, it is difficult to make any meaningful comparisons of scores. The dominant approaches to interpretation of the HRNB include assessing levels of performance and contrasting performance among the various tasks. Raw scores cannot be compared or assessed directly for a variety of reasons, the most potent being the lack of comparability of the raw score distributions among the tasks of

the battery and for any one task across age. As Dean (1985) noted, in reviewing the HRNB, "without standard score transformation data, it is difficult to make any meaningful comparison between scores on individual tests" (p. 645). The use of raw scores is not necessarily wrong and is typically superior to the use of inaccurate score transformations. Appropriate use of raw scores does require extensive work and numerous calculations on the part of the person interpreting the test scores. The LNNB provides standardized or scaled scores in the form of the familiar T-score (mean = 50, standard deviation = 10) although the scaling is questionable because of the shape of the distributions obtained and the sample used in their standardization. Other attempts to scale neuropsychological measures have been made but use inappropriate scales, particularly age (AEs) or grade equivalents (GEs). Neuropsychological reports, even textbook examples, often contain performance reported in GEs. The Boder Test can again provide an illustration of some of the problems with scaling as practiced in clinical neuropsychology.

The Boder Test does not actually provide any type of standard score although the test's authors treat the various scores as though they are standardized or scaled scores. The Boder Test provides a Reading Level (RL) (analogous to a GE), a Reading Quotient (RQ), and a Reading Age (RA). Without adequate normative data, which the Boder does not possess, these scores are not very meaningful. Even if carefully normed, using state-of-the-art methods, these scores have serious limitations and should be used with extreme caution if at all and never as the featured scores for any contemporary scale, neuropsychological or otherwise.

RL and RA

The RL and RA of the Boder Test of Reading–Spelling Patterns (BTRSP) have similar problems. RL has the greatest difficulties even if calculated on the basis of good normative data, so the RL (the Boder Test's analogue of a GE) will be featured here. Given the interdependence of the RL and the RA as calculated on the Boder Test, their problems are almost identical.

The GE, i.e., RL, of the BTRSP is based in the grade level at which the words from the reading lists of the Boder are estimated to be introduced into the curriculum, and assumes that half of the children master these words for reading and spelling. True GEs are based on actual student knowledge of the curriculum content as reflected in mean scores on achievement tests. When content is introduced and when it is actually mastered by 50% of the pupils may not be closely related. Actual performance must be assessed.

GEs as a score on which to base decisions about individual pupils have serious deficiencies that have been presented in detail in a variety of sources over decades, and should be well known to the profession (e.g., Hishinuma & Tadaki, 1997; Angoff, 1971); Cronbach, 1990; Petersen, Kolen, & Hoover, 1989; Reynolds, 1981a,b, 1982a; Reynolds, Livingston, & Willson, 2006; Thorndike & Hagen, 1977). Though frequently treated as a standard score, GEs are not standard scores, and attempts to standardize them (Burns, 1982) have been largely unsuccessful (Reynolds & Willson, 1983); and indeed the true meaning of the GE is often distorted if understood at all. Most of the problems with GEs can be traced to one of two factors, or both: (1) GEs are calculated independent of the dispersion or distribution of scores about the mean and (2) the regression of the age, grade, and raw score is nonlinear, and varies across subject matter within grade as well as across grade within subject matter or content areas (AEs have analogous problems). Essentially, this tells us the GEs are on an ordinal scale of measurement and not an interval scale as so frequently interpreted. This makes many common uses of GEs entirely inappropriate.

Boder and Jarrico (1982, p. 5) defined significant reading retardation as performance 2 years below grade level for age according to the Boder Test RL. Other diagnoses are dependent on the RL and its discrepancy with expected level of performance as well. The "2 years" criterion for a reading disorder has been a common ground for diagnosis for some time and only recently abandoned (see also Reynolds, 1984). The use of GE scores at a constant discrepancy level irrespective of actual grade placement produces considerable irregularity for diagnosis, however. The distortions in interpreting discrepancies between GE scores and grade placement are readily apparent in Table 6, which was developed from data available in the norms or technical manuals of the Wide Range Achievement Test (WRAT), Peabody Individual Achievement Test (PIAT), Woodcock Reading Mastery Test

TABLE 6. Standard Scores Corresponding to Performance "Two Years Below Grade Level for Age" on Four Major Reading Tests[a]

		Standard scores[b]			
Grade placement	Two years below placement	Wide Range Achievement Test	Peabody Individual Achievement Test[c]	Woodcock Reading Mastery Test[d]	Stanford Diagnostic Reading Test[c]
1.5	Pk.5	65	—	—	—
2.5	K.5	72	—	—	—
3.5	1.5	69	—	64	64
4.5	2.5	73	75	77	64
5.5	3.5	84	85	85	77
6.5	4.5	88	88	91	91
7.5	5.5	86	89	94	92
8.5	6.5	87	91	94	93
9.5	7.5	90	93	96	95
10.5	8.5	85	93	95	95
11.5	9.5	85	93	95	92
12.5	10.5	85	95	95	92

[a] Adapted from Reynolds (1981a).
[b] All standard scores have been converted for ease of comparison to a common scale having a mean of 100 and a standard deviation of 15.
[c] Reading Comprehension subtest only.
[d] Total test.

(WRMT), and the Stanford Diagnostic Reading Test (SDRT). As is typical of GE scores, some occasional interpolation was necessary to derive the exact values in Table 6. It is apparent, however, that a third-grader who reads "2 years below grade level for age" has a much more severe problem than say a seventh- or eighth-grader reading 2 years below grade level. In fact, a twelfth-grader with an IQ of 90 on a Wechsler Scale and reading 2 years below grade level for age has no reading problem at all, but rather reads at a level slightly higher than what might be expected. Standard scores are by far a more accurate representation of an individual's achievement level than GEs because they are based not only on the mean at a given level but also on the distribution of scores about the mean. Thus, in the case of deviation standard scores, such as the Wechsler IQs, the relationship between standard scores is constant across age, and there are no excuses for the failure to provide such scores. Certainly the Boder Test provides no rationale for the lack of standard scores or even the preference for GEs. Nor do most clinical neuropsychologists have an adequate rationale for continued use of AEs and GEs in reports or in their application to profile analysis.

GEs are also inappropriate for use in any other sort of discrepancy analysis of an individual's test performance or key or profile analyses for the following reasons:

1. The growth curve between age and achievement in basic academic subjects flattens out at upper grade levels. This can be observed in Table 6 where it is seen that there is very little change in standard score values corresponding to 2 years below grade level for age after about grade 7 or 8. In fact, GEs have almost no meaning at this level, for reading instruction typically stops by high school and GEs are really only representing extrapolations from earlier grades. An excellent example of the difficulty in interpreting GEs beyond about grade 10 is apparent using an analogy with AEs. Height can be expressed in AEs just as reading can be expressed in GEs. However, although it might be helpful to describe a tall first-grader as having the height of an 8½-year-old, how does one then characterize the 5' 10" 14-year-old female, for at no age does the mean height of females equal 5' 10"? Because the average reading level in the population changes very little after junior high school, GEs at these ages become virtually non-sensical, with large fluctuations in GEs

sometimes resulting from a raw score difference of 2 or 3 points on a 100-item test.
2. GEs assume that the rate of learning is constant throughout the school year and that there is no gain or loss during summer vacation.
3. As partially noted above, GEs involve an excess of extrapolation, especially at the upper and lower ends of the scale. However, because tests are not administered during each month of the school year, scores between the testing intervals (often a full year) must be interpolated on the assumption of constant growth rates. Interpolation between extrapolated values on an assumption of constant growth rates is at best a highly perilous activity. The assumption underlying score derivations on the Boder Test that each word read correctly represents 2 months of academic achievement is even more perilous, and most likely cannot be substantiated. For the Boder Test, this adds to the error and the unfounded assumption already present in *properly derived* GEs, which the RL of the Boder Test is not. Popular achievement tests in neuropsychology have similar problems. The front of the protocol for the WRAT, for example, notes that standard scores only and not the so-called grade rating (the WRAT's GE) should be used for interpretive purposes.
4. Different academic subjects are acquired at different rates and the variations in performance differ from one content area to another. As a consequence, "2 years below grade level for age" may be a much more serious deficiency in mathematics than, say, in reading comprehension. The degree of academic deficit in Reading versus Spelling, as on the Boder Test, denoted by the "2 years" marker, will differ as well. Additionally, academic subjects are often qualitatively different in the manner in which skills are acquired and used. A gifted reader in fourth grade may be able to pass a high school exit exam in reading, yet a fourth grader able to pass algebra without explicit instruction in the subject is exceedingly rare. Reading skills across grades differ in complexity, but not in operation, as seen in mathematical skills.
5. GEs exaggerate small differences in performance between individuals and for a single individual across tests. Some test authors (e.g., Jastak & Jastak, 1978) even provide a caution on test record forms that standard scores only, and not GEs, should be used for comparison purposes.

RQ

The Boder Test also provides an RQ calculated in accordance with one of three formulas offered in the Boder Manual, with the choice of derivation given to the examiner. Giving a choice of three formulas to the examiners is problematic in itself. Though some general guidelines are provided concerning when to use each formula, the choice is left to the examiner, and it is entirely probable that, faced with a similar or even identical set of scores, different examiners will arrive at different RQs; the same examiner may well fall to the same plight over time, being inconsistent in the choice of formulas given a common set of circumstances. However, this is one of the more minor problems with the Boder Test RQ. The RQ is derived from a faulty score to begin with, the RA, as noted in the previous section. The RQ, as calculated to be $(RA/CA) \times 100$ (where CA is chronological age), will not have a constant standard deviation across age and is not a standard score as thought by many. It is conceptually the antiquated notion of a ratio IQ that was abandoned many years ago in favor of more refined standard score systems. The standard deviation of the first version of the RQ will almost certainly range from at least 10 to 29, leading to the confusing (and unaccounted for in the Boder Test's diagnostic system) state wherein, depending on age, RQs of 80 and 90 represent the same overall level of performance at different ages. The actual range of standard deviations could be larger or smaller; whichever it turns out to be is less important than the fact that the standard deviation will not be constant across age and that the standard deviation at any age is unknown.

Use of either of the two alternative formulas given below for calculating the RQ is even more problematic. These formulas

$$RQ = \frac{2RA}{MA + CA} \times 100 \qquad (1)$$

$$RQ = \frac{3RA}{MA + CA + \text{grade age}} \times 100 \qquad (2)$$

are quite similar to expectancy formulas proposed by the U.S. Office of Education (1976) in their attempt to define severe discrepancies between aptitude and achievement. Commentary on such formulas has shown them to be grossly inadequate for use in any kind of normative reporting or discrepancy analysis and far more sophisticated approaches are needed (Dombrowski, Kamphaus, & Reynolds, 2004; Reynolds, 1984). The standard deviation of the scores derived from these formulas will also vary and is unknown. The same number of children will not be identified at each IQ level *or each age level* using the BTRSP classification rules. There is no established validity for either formula; they are only intuitive in their appeal.

Given the problems of age- and grade-based equivalency scores and the amount of severe criticism they have received in the literature, it is difficult to imagine a justification for their use in place of standard scores. Certainly, standard scores should be provided at a minimum with AEs and GEs and related derived scores (e.g., RQ) provided as supplementary if at all. Because AEs and GEs are representing only ordinal scale data (and thus cannot be averaged or otherwise manipulated with any confidence except under special conditions), it is particularly important that these scores not be used for comparative purposes. Standard scores could not be reported for the Boder Test because there are no normative data on which to base these calculations.

Ratios and Quotients

Probably the best known of all scores to the layperson is the ratio IQ, originated for use with the Binet Scales early in the century. As every introductory psychology course student knows, IQ = (mental age/chronological age) × 100. This forms the ratio or quotient from which the designation IQ was derived. Such ratios or quotients have numerous psychometric problems and are no longer used by the major test publishers but do persist in certain areas of neuropsychology, even to the point of developing ratios of "hold" to "don't hold" subtests for estimating

premorbid functioning. Such ratios are nonsensical for most interpretive purposes, however, and lead primarily to confusion. Although they may be used to rank individuals who take a common test, no comparisons beyond rank on the common measure are possible—including profile analysis or any comparisons across tests. The so-called ratio IQ is a ratio of numbers with radically different underlying distributions and mathematical properties. Chronological age is a ratio scale of measurement. Mental age is on an ordinal scale of measurement. Creating a ratio of two such disparate scales is a conceptual nightmare of some proportion. The standard deviation of the distribution of such ratios will also vary across age. The 1937 Stanford–Binet Intelligence Scale, which yielded such a ratio IQ, showed a standard deviation that ranged from about 9–32 depending on the age of the individual assessed. The familiar standard deviation of 16 used then by the Binet Scales was the average standard deviation across ages 2 to about 16. Gross inaccuracies of interpretation were facilitated by such scales and they were not standard or scaled scores in any sense of contemporary uses of these terms. Various ratio scores and quotients such as the early IQ remain in use in neuropsychological assessment but do not possess the properties of standard scores that make the latter so useful in all areas of testing and assessment (for further discussion of the history of the Stanford Binet, see Kamphaus & Kroncke, 2004).

Standard or Scaled Scores

The primary advantage of standardized or scaled scores lies in the comparability of score interpretation across age. By standard scores is meant scores of the Wechsler Deviation IQ genre, referred to more properly as age-corrected deviation scaled scores. This designation is used because the mean and the standard deviation of the scaled score distribution are reset or rescaled periodically, typically every 2–4 months at preschool ages and every 4–6 months thereafter until the adult years when much larger age groupings may be used. Standard scores of the deviation IQ type have the same percentile rank across age, for they are based not only on the mean but the variability in scores about the mean at each age level. For example, a score that falls two-thirds of a grade level below the

average grade level has a different percentile rank at every age.

Standard scores are more accurate and precise. When constructing tables for the conversion of raw scores into standard scores, interpolation of scores to arrive at an exact score point is typically not necessary, whereas the opposite is true of GEs. Extrapolation is also typically not necessary for scores within three standard deviations of the mean, which accounts for more than 99%; of all scores encountered.

Standard scores are on an equal interval scale in many cases (see Gordon, 1984), making profile analysis possible across subtests of a common scale (for a review of concerns regarding profile analysis, see Borsuk, Watkins, & Carnivez, 2006). Ipsative analysis of performance only makes mathematic sense with an interval or higher scale of measurement. Score comparisons among different batteries or subparts of different measuring devices are also possible provided the reliability of each measure is known, and, for some purposes, the correlation between the various pairs of scores must also be known. If the reliability coefficients are comparable, the score distributions are normal, and the percentile rank of scores is known, Table 7 can be used to place scores on a commonly expressed metric, i.e., a scale having the same mean and standard deviation. The choice of standard score scales is often arbitrary but is sometimes dictated by the standard deviation of the raw score distribution, such that the score

TABLE 7. Conversion of Standard Scores Based on Several Scales to a Commonly Expressed Metric

$\bar{X} = 0$	$\bar{X} = 100$	$\bar{X} = 100$	$\bar{X} = 100$	$\bar{X} = 500$	$\bar{X} = 50$	$\bar{X} = 50$	$\bar{X} = 36$	$\bar{X} = 10$	Percentile rank
SD = 1	SD = 15	SD = 16	SD = 20	SD = 100	SD = 10	SD = 15	SD = 6	SD = 3	
2.6	139	142	152	760	76	89	52	18	>99
2.4	136	138	148	740	74	86	51	17	99
2.2	133	135	144	720	72	83	49	17	99
2.0	130	132	140	700	70	80	48	16	98
1.8	127	129	136	680	68	77	47	15	96
1.6	124	126	132	660	66	74	46	15	95
1.4	121	122	128	640	64	71	44	14	92
1.2	118	119	124	620	62	68	43	14	88
1.0	115	116	120	600	60	65	42	13	84
0.8	112	113	116	580	58	62	41	12	79
0.6	109	110	112	560	56	59	40	12	73
0.4	106	106	108	540	54	56	38	11	66
0.2	103	103	104	520	52	53	37	11	58
0.0	100	100	100	500	50	50	36	10	50
−0.2	97	97	96	480	48	47	35	9	42
−0.4	94	94	92	460	46	44	34	9	34
−0.6	91	90	88	440	44	41	33	8	27
−0.8	88	87	84	420	42	38	31	8	21
−1.0	85	84	80	400	40	35	30	7	16
−1.2	82	81	76	380	38	32	29	6	12
−1.4	79	78	72	360	36	29	28	6	8
−1.6	76	74	68	340	34	26	26	5	5
−1.8	73	71	64	320	32	23	25	5	4
−2.0	70	68	60	300	30	20	24	4	2
−2.2	67	65	56	280	28	17	23	3	1
−2.4	64	62	52	260	26	14	21	3	1
−2.6	61	58	48	240	24	11	20	2	>1

points should not be artificially spread over too many standard score points nor should too many raw score points be collapsed into a single scaled score point. Such problems are usually avoided by the choice of an appropriate scale and finding a suitable scale is easy enough that it is seldom a serious problem in the application of scaled scores to most practical problems of assessment. There are few instances when other score systems are superior to scaled scores, and methods are now available for the use of scaled scores even at the most extreme points in the distributions of intelligence, achievement, and other special abilities (e.g., see Reynolds & Clark, 1985, 1986).

Differential Diagnosis: Determining Membership in Clinical Populations

One of the major problems for psychologists in professional practice has historically been that of differential diagnosis of mental disorders. In the area of clinical neuropsychology, differential diagnosis has been of particular importance. The major area of research in clinical neuropsychology has had as its purpose the development of clinical tests and procedures to differentiate reliably between brain-injured and neurologically intact individuals and to separate brain-injured groups into subsamples according to location, cause, time of onset, and, in some cases, prognosis. Many neuropsychologists still earn a considerable portion of their "keep" differentiating organic from nonorganic psychiatric referrals and evaluating the nature and extent of lesions for the neurology service. This does bring out another major area of methodological and statistical problems in clinical neuropsychology—one that, oddly enough, is nearly the opposite of the preceding discussions. In differential diagnosis, rather than being naive about the underlying psychometrics or scaling, the tendency has been to perform analyses that are too sophisticated for the data.

To their credit, researchers have, over the last two decades, brought to bear the most sophisticated statistical methodologies directly on the problem of diagnosis and classification of mental disorders in the form of various multivariate analytical techniques. In the quest to provide accurate diagnosis of neurological disturbances, a large set of behaviors is typically assessed. Rourke (1975), in discussing more than two decades of research on differential diagnosis, indicated that children referred to his laboratory are typically administered

the WISC, the Peabody Picture Vocabulary Test, the Halstead Neuropsychological Test Battery for Children, the Reitan Indiana Neuropsychological Test Battery, the Wide Range Achievement Test, an examination for sensory–perceptual disturbances, the Klove–Mathews Motor Steadiness Battery, and a number of other tests for receptive and expressive language abilities. (p. 912)

This continues to be a common practice in the field. Multivariate classification techniques are very powerful in the determination of group membership.

Unfortunately, with such a large set of variables, small numbers of subjects can all be grouped and classified purely on the basis of random or chance variation that takes maximum advantage of correlated error variances. Thus, the need for large numbers of subjects in such research is a crucial one.

In the study of clinical disorders, however, one is frequently limited to relatively small samples of design. Although most researchers acknowledge this difficulty, few realize the devastating effect of subject/variable ratios approaching 1 on the generalizability of studies of differential diagnosis. This is not to say that excellent studies have not been done. Studies of discriminability by Satz and his colleagues (e.g., Satz, Taylor, Friel, & Fletcher, 1978) use large numbers of variables but have considerable subject populations. Large-N studies of clinical populations continue to be the exception rather than the rule. Willson and Reynolds (1982) evaluated the effects of small samples on the validity of research attempting to discriminate among clinical disorders on the basis of neuropsychological test performance and have reported on many of the statistical problems that seem to plague the area.

Some Statistical Considerations

In predicting group membership from a set of variables (e.g., neuropsychological test scores) there are several considerations. First, procedures that use *samples* of the target populations involve sampling error in the estimation of the relationships being examined.

This means that results are expected to fluctuate from sample to sample as a result of the random differences inherent in the samples. The usual measure of prediction is the squared multiple correlation (R^2). In applying results of a particular sample to a second sample, R^2 is expected to decrease because correlation is a maximizing operation—R^2 was made as big as possible for the first sample capitalizing on correlated error variances whenever possible. It is unlikely the same fit of the data will occur in a second sample. Thus, rules for classification derived from a particular sample cannot necessarily be expected to generalize to any other sample without a cross-validation effort to demonstrate such an effect.

A second consideration in prediction occurs when the prediction used a strategy for selecting a small number of variables from a much larger initial set of variables (e.g., Purisch, Golden, & Hammeke, 1979). In the same, some correlations underestimate the population value and others overestimate it. In stepwise regression or discriminant procedures and related multivariate methods, the overestimates are always chosen. When a large number of predictors is available, stepwise procedures maximize the chance of selecting anomalous variables (Hogarty, Kromrey, Ferron, & Hines, 2004). These are variables that do not predict well in the population but by chance correlate highly with the outcome in the particular sample being used.

The degree of decrease in R^2 from sample to population can be estimated. The most commonly used estimate is from Wherry (1932; see also Lord & Novick, 1968, p. 286) and is

$$R_{\mathrm{p}}^2 = 1 - (1 - R^2)(N-1)/(N-K-1) \quad (3)$$

where N is the number of observations, K the number of predictors, R^2 the observed squared multiple correlation between outcome and predictors, and R_{p}^2 the population squared multiple correlation. This formula holds for either multiple regression or discriminant analysis.

Formula (3) has been widely cited. A review by Cattin (1980) suggested that for small N and K, another approximation should be used:

$$\hat{R}^2 = \frac{(N-K-3)p^4 + p^2}{(N-2K-2)p^2 + K} \quad (4)$$

where

$$p^2 = 1 - \frac{N-3}{N-K-1}(1-R^2)$$

$$\left[1 + \frac{2(1-R^2)}{N-K-1} + \frac{8(1-R^2)^2}{(N-K+1)(N-K+3)}\right]$$

Although $\hat{R}^2$ is biased, the amount of bias is on the order of 0.01–0.02 for $N = 60$ and $K = 50$.

Of special interest is the case where there are more predictors than people. In equation (4), the shrunken $\hat{R}^2$ may become negative or greater than 1.0. What this really means is that mathematically with more predictors than observations of the outcome, there is no unique solution to a best prediction. In discriminant analysis this may result in perfect classification entirely at random by the predictors. Mathematically, this results from having more parameters to estimate than data points. Either one is forced to make enough side conditions to constrain the solution or one accepts a solution that results from a particular order of entering predictors. As it is mathematically impossible to estimate all regression coefficients, there will be

$$\frac{K}{N} = \frac{K!}{N!(N-N!)}$$

different solutions that would provide perfect classification but would not generalize to any other sample. In particular, it may be quite likely to find a solution that maximizes R^2 based entirely on chance correlations if there are enough correlations from which to choose.

Even when there are fewer predictors than subjects, the shrunken R^2 estimate will rapidly approach zero as the number of predictors becomes a significant proportion of the number of subjects. When small samples of subjects are involved, as with many neuropsychological studies, the use of a large number of tests as predictors frequently fulfills this condition.

Multiple regression and discriminant analysis have been discussed interchangeably to this point, but some distinctions need to be made about them. Formally, they are identical in two-group prediction, e.g., brain-damaged versus non-brain-damaged. For more than two groups, discriminant analysis must be used. There have been a number of different

classification rules proposed using discriminant analysis. These pertain to assumptions about prior probabilities for population composition and about homogeneity of within-group covariances. In any case the R of relationship between predictor and between group distance is computed. It is a canonical correlation (see Cooley & Lohnes, 1971, p. 249). Because there may be more than one discriminant function, there will be a canonical R for each. Their squares do not necessarily add together to get a total R^2, as there may be redundancy between functions (Cooley & Lohnes, 1971, p. 170), but their squared sum is the maximum possible R^2. This may be useful as a liberal estimate because if it can be shown that $\hat{R}_p^2$ is near zero, there is no need to estimate the study's R^2, as it will produce an even smaller estimate of $\hat{R}_p^2$.

For two groups, multiple regression and discriminant analysis yield the same results. For more than two groups, the canonical R^2 is still useful as an approximation to a multiple regression R^2. This interpretation can be a useful one but is rare in clinical neuropsychology, as multiple group discriminant analysis is so seldom applied by clinical researchers. The omission is significant in that although researchers in neuropsychology may not be familiar with or do not apply this technique for other reasons, it may be quite useful in discriminating among several populations.

The Willson and Reynolds Examples of Classification Problems

To illustrate the problems that can be created by these statistical considerations, Willson and Reynolds (1982) examined all articles in three journals (*Psychology in the Schools, Journal of Consulting and Clinical Psychology*, and *Clinical Neuropsychology*) for the years 1979–1981. They selected studies that used test batteries, socioeconomic or demographic variables, or a combination of these variables to predict clinical group membership and that could help illustrate the difficulties of such work. Nine studies were found. Such studies are not unique to this era and the problems noted below continue (e.g., Bernard, Houston, & Natoli, 1993; Boone, Ghaffarian, Lesser, & Hill–Gutierrez, 1993; Miles & Stelmack, 1994;

Thienemann & Koran, 1995) although well-accomplished works are becoming more frequent and continue to come from the laboratories of Rourke and of Satz as noted earlier as well as other research centers (e.g., Guilmette & Rasile, 1995; Ivnik et al., 1994).

The studies are listed in Table 8 (from Willson & Reynolds, 1982). Also listed are sample sizes (N), total number of predictors used in stepwise procedures (K_T), and number of predictors used in the final or discriminant equation (K_F). In one case, R_F was determined indirectly through a 2×2 classification table that was reported in the studies. The tetrachoric correlation was computed and squared (see Glass, 1978, and Pedhazur & Schmelkin, 1991, for a discussion of estimating correlation effects).

Table 8 lists several other statistics that represent estimated values of R_p^2 and their significance via their associated F-statistic. The statistic $\hat{R}_T^2$ represents the estimated R shrunken by equation (3) to account for all predictors originally considered. Because in no study was the overall R_T^2 reported for all predictors, it was necessary to use the R_F^2 based on the final regression. Thus, $\hat{R}_T^2$ underestimated the shrunken R_p^2 to some degree. Its upper bound is given by $\hat{R}_F^2$, the shrunken estimate based on the number of predictors actually used. This is an *overestimate* of the actual shrunken R_p^2.

A second set of statistics was calculated from the nine studies to estimate loss of classification power resulting from shrinkage and is presented in Table 9. For the reported R_F^2 and the $\hat{R}_T^2$ the t-statistic equivalent was computed according to

$$t = \left[\frac{R^2/K}{(1 - R^2)/(N - K - 1)} \right]^{1/2} \tag{5}$$

Although most studies had only two groups, in Selz and Reitan (1979), the t-statistic was based on a reduction of three groups to two (normal versus abnormal). Then, an effect size was computed:

$$\in = t(1/n_1 + 1/n_2)^{1/2} \tag{6}$$

as defined by Glass (1978). This statistic is the number of standard deviations separating the two groups. Finally, the percentile point under

TABLE 8. Summaries of Prediction Studies from Three Special Population Journals

Study		Sample size	Total number of predictors	Number of predictors used	R_F^2 (reported)	$\hat{R}_T^2$	$\hat{R}_F^2$
Dean (1978)		120	14	4	0.25[*]	0.09	0.21[*]
Selz & (Reitan 1979)[a]		75	37	37	0.57	0.57	0.57
Wallbrown, Vance, & Pritchard (1979)		200	8	3	0.19[*]	0.13	0.17[*]
Purisch, Golden, & Hammeke (1979)	(a)	100	282	40	1.00[*]	0[b]	0[b]
	(b)	100	14	14	0.88[*]	0.84[*]	0.84[*]
Taylor & Imivey (1980)	(a)	30	16	5	0.44[*]	0.00	0.26
	(b)	30	3	1	0.08	0.00	0.05
	(c)	30	16	5	0.30	0.00	0.10
	(d)	30	3	1	0.14[*]	0.02	0.12
	(e)	30	16	2	0.25[*]	0.00	0.22[*]
	(f)	30	2	1	0.11	0.03	0.09
Dunleavy, Hansen, & Baade (1981)		24	37	3	0.82[*]	0[b]	0.79[*]
Fuller & Goh (1981)		80	22	12	0.38[*]	0.05	0.19
Golden, Moses, Graber, & Berg (1981)	(a)	60	11	2	0.55[*]	0.37[*]	0.54[*]
	(b)	120	11	2	0.68[*]	0.62[*]	0.68[*]
Malloy & Webster (1981)[c]	(a)	36	14	14	0.57	0.57	0.57
	(b)	36	14	14	0.94[* d]	0.94[*]	0.94[*]

[a] Trinomial classification table was reported; it was converted to a binomial (normal versus brain-damaged or LD) and the tetrachoric correlation computed, which was squared to obtain R_F^2. Because it was based on a prediction equation from another study, no shrinkage was expected.
[b] An R^2 of 0.00 is expected in an overdetermined system, in which there are more predictors than subjects. Perfect classification is always possible.
[c] Binomial classification was reported. The tetrachoric correlation was computed as in footnote a.
[d] The R^2 values were estimated from a misclassification rate of 20% with 36 subjects. Although the actual study was trinomial, the R^2 represents the equivalent for binomial classification for ease of computing.
[*] $p < 0.05$.

the normal curve for *half* the effect is presented. This is the point that minimizes misclassification assuming equal cost for either false-positive or false-negative errors, and the equal population base rates.

Of the 17 R_F^2 obtainable from the studies, 12 were initially significant. After correcting the shrinkage, only four were significant as $\hat{R}_T^2$, and eight as $\hat{R}_F^2$. Thus, half the results reported in these studies are attributable to chance alone. Under the most optimistic of circumstances, the upper limit of shrinkage R^2 estimate shows a mean R^2 of 0.37 versus a mean obtained R^2 value of 0.48 for all studies considered. The lower bound estimate of the shrunken R^2 yields even more pessimistic results, demonstrating a mean value of but 0.25. The chance variation that can appear on the surface to be reliable

discrimination with powerful multivariate techniques is thus rather considerable. The importance of large subject/variable ratios and proper cross-validation becomes immediately obvious in considering the results summarized in Tables 8 and 9. Interested professionals must consider with special care the prediction rules generated from those studies when R dropped to nonsignificance.

In examining the misclassification rates (see Table 9), there is a change from about one-third expected in the original studies (35%) to almost half (44%) using the corrected values, the chance rates under no knowledge, and very unimpressive when contrasted against base rates in referral populations. This is not surprising given the considerable decline in effect sizes shown in Table 9.

TABLE 9. Expected Misclassifications from Nine Studies

		t-equivalent for		Estimated effect[a] size for two populations for		Two-population % misclassification for	
		$\hat{R}_F^2$	$\hat{R}_T^2$	$\hat{R}_F^2$	$\hat{R}_T^2$	$\hat{R}_F^2(\%)$	$\hat{R}_T^2(\%)$
Dean (1978)		2.76	0.86	0.50	0.16	39	47
Purisch, Golden, & Hammeke (1979)	(a)	0	0	0	0	50	50
	(b)	6.27	6.27	1.25	1.25	27	27
Selz & Reitan (1979)[b]		1.15	1.15	0.27	0.27	45	45
Wallbrown, Vance, & Pritchard (1979)		3.12	1.89	0.44	0.27	41	45
Taylor & Imivey (1980)	(a)	1.69[c]	0.00	0.62	0.00	38	50
	(b)	1.21[c]	0.00	0.44	0.00	41	50
	(c)	0.73[c]	0.00	0.27	0.00	45	50
	(d)	1.95[c]	0.42	0.71	0.15	36	47
	(e)	2.84[c]	0.00	0.73	0.00	36	50
	(f)	1.76[c]	0.65	0.64	0.24	37	45
Dunleavy, Hansen, & Baade (1981)		5.01	0	2.05	0	16	50
Fuller & Goh (1981)		1.14	0.37	0.25	0.06	45	49
Golden, Moses, Graber, & Berg (1981)	(a)	5.78	1.61	1.49	0.42	23	42
	(b)	11.15	4.00	2.04	0.73	15	36
Malloy & Webster (1981)[b]	(a)	1.19	1.19	0.40	0.40	42	42
	(b)	5.04	5.04	1.68	1.68	20	20
Mean		3.11	1.38	0.81	0.33	35	44

[a] Effect $= t(1/n_1 + 1/n_2)^{1/2}$ (Glass, 1978).
[b] No shrinkage occurred.
[c] Single group statistics; effects were computed as if for two groups. Single group results are smaller than reported here.

It must be reiterated that the shrinkage occurs in research in which correlation maximizing procedures have been used: stepwise multiple regression, stepwise discriminant analysis, and canonical correlation. The R^2 does not shrink in a fixed variable study in which all variables are included and in which order is unimportant (balanced ANOVA design) or in which order is predetermined (path analysis design, causal model design). Diagnosis seeks to find the best empirical discriminators, but it is most subject to chance.

The shrunken estimate of R^2 and the expected misclassification rate are part of the technique of cross-validation. Cross-validation requires two independent samples. Ideally both are drawn independently from the same population. Often a single sample is split into two halves. In either case the regression is computed on one sample and the weights applied to the scores of the second population to predict the outcome or group membership as appropriate. The R^2 is a one-sample estimate of the R^2 in the nonvalidation sample, but it is not nearly so convincing. First, it is a statistic itself that may vary; second,

it uses information from one sample, not nearly as good as that available from two samples. In clinical samples the N is typically so small that splitting it is not a good idea. The regression weights and R^2 will become even more changeable as the subject/variable ratio is halved. This leaves two-sample cross-validation. Samples should be drawn from the same population initially. There may also be considerable value in determining the generalizability of the results to other populations in an effort to improve the clinical utility of the classification rules. These are separate problems; the sampling procedure in the first case is obvious and has been discussed. Sampling in the second case will be dictated by the specific design of the study.

Should prediction studies be cross-validated prior to publication? Is it the responsibility of the researcher to provide this evidence? If actuarial rules for diagnosis are used, the obvious answer is yes. Even in more purely clinical decision-making, the repeatability of one's results from a referral pool cannot be ignored. The Selz and Reitan (1979) research is an

example where this procedure was followed, with quite credible results. The application of such a prediction rule to new populations requires new cross-validation, however. To those who argue it is difficult to obtain subjects in rare disorder categories, hold the results until a second population is sampled. There will be no real loss to the discipline. On the contrary, there will be a new gain, for only the cross-validated results will achieve publication. Given the sometimes harsh attacks on the application of clinical neuropsychological techniques (e.g., Coles, 1978; Reschly & Gresham, 1989; Sandoval, 1981) to the rehabilitation of learning and related problems, it certainly behooves researchers to be careful in deciding when research is ready to report. The external validity of one's "findings" must be clear.

Cross-validation, when it is presented as evidence for the consistency of results in one population, does not provide evidence for generalizability to other populations. This can be done by additional studies. There is no reason to believe that the regression weights that discriminate two groups will discriminate either from a third. This point is not restrictive to prediction studies but occurs in all behavioral research.

A related issue should be obvious and of great significance to the practicing clinician in neuropsychology and other subdisciplines involved in differential diagnosis. When actuarial rules for the diagnosis of psychological and neuropsychological disorders appear in refereed professional journals, those in applied settings, especially those keeping closest to current developments in the field, may feel very confident in applying such rules in diagnosis and in the development of treatment plans. Clearly, the Willson and Reynolds (1982) results show that in the absence of proper cross-validation, many diagnoses or classifications may be made on the basis of random relationships. This constitutes an unacceptable situation for all involved, but especially for the patient and her or his physician.

Profile Reliability

A related problem when multiple scores are being used in classification or individual diagnoses and decision-making is the reliability of the set of scores for each individual considered. Perhaps stability is a better conceptualization, as the question is whether (or how much) the profile of scores, taken as a whole, would change and whether this change would affect clinical decision-making. Stability of subtest level and battery level profiles over at least very short periods of time (largely depending on the clinical disorder under investigation) needs investigation and yet has gone largely ignored for neuropsychological tests. The problems of such research, which may at first seem simple, are difficult ones, but can be solved.

One difficult problem is that of differential practice effects among the various scales that go into making up the score profile. These effects may impact scores on some tests even when alternate forms are introduced for subsequent testing (Beglinger et al., 2005). This introduces methodological artifacts that require statistical control through estimation of regression effects for each part of the battery prior to comparing the two profiles obtained—in such a case, only the second profile should be corrected. Following this set of corrections, profile stability or reliability can then be assessed. Profile reliability is essentially a multivariate problem and thus requires a multivariate solution. A variety of statistical approaches may be used and the specific purpose of the study may dictate different approaches. Roffe and Bryant (1979), in a study of profile reliability for the McCarthy Scales, used the Pearson correlation. This approach is problematic from several perspectives. If the Pearson correlation is employed, profiles must first be "standardized" as described by Nunnally (1978). However, even under these circumstances, the Pearson correlation is likely to be inaccurate, for it does not consider level, dispersion, shape, and accentuation of the various profiles. Several very powerful techniques have been developed that accurately determine the similarity of profiles, including D^2 (Cronbach & Gleser, 1953; Osgood & Suci, 1952) and the coefficient of pattern similarity, r_p (Cattell, 1966). These two approaches in particular are accurate, sophisticated measures of profile similarity and should be employed whenever possible (see also Nesselroade & Cattell, 1988). It is best to use multiple measures of multivariate profile similarity as demonstrated by Livingston, Jennings, Reynolds, and Gray (2003).

Research on the stability of intelligence tests' subtest level profiles generally indicates a high degree of instability over a period of 2–3 years (e. g., see Livingston et al., 2003; and

Reynolds & Kamphaus, 2003, for a review of this issue in their Chapter 1), and most empirical research now argues against subtest level interpretation of intelligence tests such as the various Wechsler Scales (also see Gluting, Watkins, Konold, & McDermott, 2006). On intelligence tests, this may be associated with the relatively high g-loadings of the subtests as well as generally low subtest scores' internal consistency reliability relative to composite or index scores. Thus, this research may not generalize to neuropsychological batteries that have greater levels of subtest specificity, lower g-loadings, and often stronger score reliability at the subtest level (since many, but certainly not all, neuropsychological batteries are actually composed of independent or complete tests that can be used independently of the so-called battery). Research on the relative stability of neuropsychological test score profiles for both normal and central nervous system compromised samples is direly needed to address this significant gap in the neuropsychological literature.

Sensitivity, Specificity, Diagnostic Accuracy, and Positive/Negative Predictive Value

Neuropsychologists and other clinical researchers are, as I have noted, often interested in how well a disorder is detected or how well it is diagnosed. Too often, researchers fail to consider and report on the sensitivity, specificity, and diagnostic accuracy of their procedures, retarding the clinician's ability to understand the utility of a diagnostic procedure.

In any diagnostic question, there are four outcomes. The clinician can be: (1) right about the presence of a disorder (a true positive), (2) wrong about the presence of disorder (a false positive), (3) right about the absence of a disorder (a true negative), or (4) wrong about the absence of a disorder (a false negative). These conditions are illustrated in Figure 2, and seldom are reported in research on diagnosis.

Sensitivity in diagnosis refers to the ability to detect a disorder when it is present. Sensitivity thus refers to the probability that a disorder will be diagnosed when a patient has the disorder. Of course, if we diagnose every child-patient we see as having a learning disability, we will "miss" none who do, making our diagnostic decision highly sensitive—but we would lack specificity.

Specificity refers to the ability to differentiate among conditions or, in essence, to detect the absence of a disorder. In the above example, we guard against false-negative diagnostic errors at the expense of creating a large number of false-positive errors.

FIGURE 2. Illustration of possible classification of diagnostic decisions. Square 1 = true positives, square 2 = false positives, square 3 = false negatives, square 4 = true negatives.

Often we must seek a balance between specificity and sensitivity in diagnosis. It is a given in neuropsychology that we will not be 100% accurate in diagnosis. All four conditions in Figure 2 are likely to occur in any set of diagnostic decisions. Through our research, we seek to enhance both sensitivity and specificity through maximizing squares 1 and 4, thereby minimizing squares 2 and 3 (see Figure 2). Often, however, by increasing one we often decrease the other. Researchers should always report a table such as represented by Figure 2 (e.g., see Guilmette & Rasile, 1995, Tables 4, 5, 6) so that specificity, sensitivity, and diagnostic accuracy can be assessed and preferably using multiple cutoff scores of classification rules. Sensitivity is represented by the ratio of square 1 to the sum of squares 1 and 3 while specificity is represented by the ratio of square 4 to the sum of squares 2 and 4. As this ratio approaches 1.00, sensitivity and specificity improve.

Diagnostic accuracy is a related concept that is determined to be the ratio of square 1 plus square 4 to the sum of all four squares. As this value approaches 1.00, diagnostic accuracy improves. These values are relatively easy to determine and will vary by diagnostic rule. Clinicians need to assess these concepts in deciding whether to apply a given diagnostic rule.

Positive predictive value (PPV) is often mistakenly equated with sensitivity by clinicians (Labarge, McCaffrey, & Brown, 2003). Whereas sensitivity refers to the likelihood of a positive sign given the true presence of a diagnosis, PPV is the inverse: the likelihood of the examinee having the diagnosis given the presence of a specific sign.

Negative predictive value (NPV) is the chance a given disorder is absent given the absence of a specific sign. The clinical confusion noted above is present due to the importance of base rates in the PPV and NPV, an unnecessary component in the calculation of sensitivity or specificity. However, the awareness of base rates is important for clinical accuracy and should be incorporated in order to avoid the unthinkable: diagnostic accuracy worse than sheer chance alone (Kennedy, Willis, & Faust, 1997; Glutting et al., 1997)!

Is it better to make the error of a false-positive diagnosis or a false-negative diagnosis? This is a very complex question (see also Reynolds, 1984) that will vary in correct response as a function of the disorder and the consequences of each type of error. Errors will be made, however, and clinicians should be informed about the sensitivity, specificity, and diagnostic accuracy of their techniques so that a truly informed decision can be made about adopting a new test or a new interpretive rule.

Summary

It has become customary over the years to end reports of research with cautionary statements and call for further research. If diagnostic or classification studies with small samples and large numbers of variables employing powerful, sophisticated multivariate classification techniques are to continue to appear without concurrent cross-validation, and multivariate profiles are to be considered, much stronger cautions are needed to avoid the inadvertent leading of the diagnostician into potential malpractice. The most obvious, and the most sound solution is not to publish such small-*N* studies without concurrent replication and not to rely on profiles with unknown stability in differential diagnosis research or clinical practice. Meta-analysis of these studies may also be conducted, but with the understanding that such analyses are not without their own set of limitations (Demakis, 2006).

Last, use of flexible versus fixed batteries has become a contentious issue in recent years. It is important to this debate that practitioners and researchers alike understand the greater potential for false positives when administering a large number of individual tests that do not have equivalent scaling or norms, particularly when the relationship between those tests are examined for interpretive purposes (Russell, Russell, & Hill, 2005). Each individual test carries its own specific chance of false positive or false negative result and in large numbers, these cumulative percentages may lead to erroneous conclusions if correction measures are not employed.

Many problems related to measurement and statistics in clinical neuropsychological research and in clinical diagnosis have been reviewed here. Many other problems exist but a substantial portion of these difficulties can be resolved by avoiding the problems noted in this chapter. By so doing, other, now fuzzy, issues, methodological, statistical, and clinical, should

be brought into a sharper focus and new problems can be identified. The failure to resolve basic measurement issues in clinical neuropsychological research can do nothing except restrain progress in the field at a time when sophisticated technology is experiencing explosive growth all around us. Specificity, sensitivity, and diagnostic accuracy are all information to be gathered and reported as new techniques (and old) are evaluated and reevaluated.

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10

Models of Inference in Evaluating Brain–Behavior Relationships in Children

EILEEN B. FENNELL AND RUSSELL M. BAUER

Introduction

Neuropsychologists generally measure behavior as a means for making inferences about brain function. Regardless of whether such measurement takes place in the clinic or the laboratory, the basic process is the same: Behavioral and cognitive performances that are readily observable "stand in," as it were, for the less observable "brain states" they are thought to reflect. Once measurement is completed, the quantitative and qualitative relationships among such performances are assembled according to certain rules in order to make probabilistic statements about brain function. The rules that are applied in the given case depend on the inferential model that one uses in relating behavioral performance to brain function. This basic process characterizes all of neuropsychology, transcends theoretical persuasion or tests employed, and, in fact, is a fundamental aspect of the clinical-inferential method in general.

Making inferences about brain functioning from behavioral data is a fundamental aspect of the neuropsychological approach to assessment. However, because such inferences are so routinely made, it is important not only to articulate the various levels at which they play a part in our thinking but also to understand the specific theoretical assumptions on which they are based. The goal of this chapter is to describe major inferential models that relate behavior to brain function in child neuropsychology. In working toward this goal, we will first describe basic issues in clinical inference as they relate to child neuropsychology. In doing so, we will outline a hypothesis-testing approach to neuropsychological assessment that borrows from classical methods of inductive inference. We will articulate some of the basic models of inference of particular relevance to child neuropsychological assessment. Finally, we will briefly discuss several misconceptions in child neuropsychology that, if utilized by an examiner, may lead to faulty conclusions about the meaning of clinical test data.

Basic Issues of Clinical Inference

Clinical-Inferential Methods

Inference refers to the process of arriving at a conclusion by reasoning from evidence. Inferences generally take place according to organized systems of rules that stipulate (1) the kind of evidence on which conclusions can be drawn, (2) the kinds of conclusions that are possible given certain evidence, and (3) a set of logical connections between evidence and conclusions. In child neuropsychology, the performance of the child on cognitive or neuropsychological

EILEEN B. FENNELL AND RUSSELL M. BAUER • Department of Clinical and Health Psychology, University of Florida, Gainesville, Florida 32610.

tests is the evidence on which inferences about brain functioning are based. It is assumed that the conclusions of interest are couched in terms of some aspect of brain function that is not directly observable by the neuropsychologist. In general, we do not observe or measure functions; we see only the behavioral indicators of spared and impaired brain functions. Thus, for example, we make inferences about language *function* on the basis of performance on tests of language *ability*, or we may infer that there is some disturbance in brain-based attentional mechanisms when the child cannot stay on task, repeat digits, or shows inconsistent performance across a set of homogeneous test items. As Taylor and Schatschneider (1992) note, interpretations of child neuropsychological findings are based on two assumptions regarding the utility of the tests employed: (1) that these tests have neurological validity (i.e., reflect the state of the central nervous system) and (2) that these tests also have psychological validity (i.e., reflect meaningfully some aspect of childhood functioning).

In what follows, we presume that there are complex differences between children and adults in terms of how brain pathology leads to neuropsychological and behavioral deficits. Thus, the meaning or utility of a behavioral "sign" that has been well validated with adults may be different when that sign is applied to child neuropsychology cases (Fletcher & Taylor, 1984; Rourke, 1983). Similarly, the predictive value of knowing that a patient has had a specific brain insult may critically depend on the age at which the damage was incurred (Rasmussen & Milner, 1977; Woods & Teuber, 1973).

Despite the fact that the behavioral effects of the brain disease are complexly dependent on such factors as age and stage of development, we believe that one fruitful approach to understanding childhood neuropsychological data is the classical inferential method commonly used in adult neurology (Adams & Victor, 1977). This method involves the collection of clinical data in terms of signs (e.g., neuropsychological impairments) and symptoms (clinical complaints). These findings are then correlated with similar signs and symptoms occurring in neurological disorders in which the underlying anatomy is known. By making analogy with these better-known disorders, and by reasoning from anatomic data, the findings in an individual case

can be interpreted in terms of some pathophysiological mechanism. With children, however, the additional knowledge regarding normal developmental change must also be factored into the inferential process in order to take into account the changing nature of skills and abilities that occur with maturation.

The classical inferential method can be applied to the individual case or can form the framework for a general conceptualization of a childhood disorder that is as yet poorly understood. An excellent example is that of a neurobehavioral model of autism (Damasio & Maurer, 1978; Maurer & Damasio, 1982). These authors observed various abnormalities in a group of autistic children, including disturbances of motility (stereotyped movements, abnormal posturing and gait), attention (unpredictable response to sensory stimuli, gaze aversion), communication (mutism, use and comprehension of nonverbal signs), and social behavior (poor cooperative play, failure to initiate social interaction). They related each of these signs and symptoms to findings in specific acquired neurological diseases (e.g., basal ganglia disease, acquired mutism from mesial frontal lobe lesions) in which the pathogenesis and localization were more firmly established. On the basis of this analysis, they proposed a specific neuroanatomy for autism that included the mesolimbic cortex (mesial temporal and frontal lobes), the neostriatum, and the anterior and medial thalamic nuclei. For our purposes, the specific merits of this hypothesis, and its ability to explain core features of autism, are not at issue. What is important, however, is that the hypothesis was derived by starting with observable signs and symptoms and by inferring from them a possible functional anatomy.

Levels of Inference

Thus far, we have discussed clinical inference as if it were a simple process of reasoning from neuropsychological test performance to brain function. In fact, there are several types of inference involved here, each of which exists at a different level of analysis. For purposes of discussion, consider a 5-year-old male child who has received a closed head injury in a vehicular accident. He is given a battery of neuropsychological tests including assessment of intellectual ability, memory, language, visual and auditory

perception, attentional ability, sensorimotor skill, and achievement. Results indicate low average intellectual ability, attentional and recent memory problems, and poor beginning reading skills. We are asked to relate the child's current status to the recent head injury and to assist in educational planning. There are three basic levels of analysis involved in utilizing our test data to answer such questions. At the first level, we are concerned with the degree to which the behavior elicited by the test battery is representative of the domain of behavior that would have been elicited given unlimited testing time (Cronbach, Rajaratnam, & Gleser, 1963). The basic issue here is whether our test findings are generalizable to other settings or conditions. At the second level of analysis, we are interested in the specific meaning of each of the test findings. Each test finding might have a formal statistical (see Wiggins, 1973) relationship with a specific form of brain impairment or may suggest a qualitative feature seen in other known brain disease (Adams & Victor, 1977). In either event, we are inferring what the outcome of each test means in terms of some nontest behavior or variable. This is a process that Holt (1968) termed primary inference. Thus, we make inferences regarding the status of verbal memory ability (and its constituent variables) by individually noting performance on tests to which this ability contributes. At the third level, we are concerned with integrating the diverse test findings to arrive at a general interpretation or conceptualization of their meaning. We are concerned here with the degree to which the pattern of spared and impaired abilities suggests a specific neuropsychological mechanism that can best account for the test findings and the clinical complaints. Holt (1968) indicated that this level

> demands a knowledge of the range of expectable syndromes, what their constituent variables are, and some means of measuring the strength of each variable. By drawing on this knowledge and on his [sic] knowledge of theory, the diagnostician puts together his primary inferences and in an act of secondary inference locates the subject with reference to diagnostic syndromes. (p. 15)

It is important to note that the specific inferences the clinician makes at each of these three levels will differ depending on the purpose of assessment and will at least in part be related to the assumptions the clinician makes about the relationship between test behavior and brain function. Such differences are most apparent at the second and third levels. For example, clinicians who favor an actuarial or statistical approach to test interpretation will be most concerned with the formal quantitative relationships between test findings and specific forms of neuropsychological impairment. Those who favor qualitative approaches might be more interested in demonstrating the presence of one or more "pathognomic signs" that are considered crucial indicators of functional impairment. In either case, an attempt is made to relate the pattern of test findings to previously available data on children with head injuries. With quantitative data, the clinician might focus efforts on determining the degree to which this child is similar to other head-injured children in terms of specific neurobehavioral mechanisms that can best account for their neuropsychological deficit pattern. In actual practice, the responsible clinician frequently uses a mixture of actuarial and clinical methods in making inferences from test data (Lezak, 1995; Meehl, 1957). The final goal of the assessment, to assist in educational planning, assumes that the inferences about brain functioning are valid and can be utilized to provide specific recommendations to remediate behavioral difficulties resulting from the observed test deficits (Taylor & Fletcher, 1990).

Fundamentals of Hypothesis Formation: The Logic of Strong Inference

In the previous section, we briefly considered three levels at which inferences about brain function may be made from test performances. The specific nature and content of such inferences will depend in large part on the assumption the clinician makes about the relationship between test behavior and brain function. That is, inferential processes in neuropsychological assessment are inextricably related to the theoretical or conceptual basis of one's assessment approach. Regardless of whether one adopts a quantitative or a qualitative approach, or some mixture of the two, an important concern is the manner in which clinical data contribute to hypotheses about the nature of the child's neuropsychological status.

In this section, we outline a general approach to forming and testing hypotheses

derived from neuropsychological test data that seems equally well suited to both quantitative and qualitative models. This approach is based on our belief that there is no fundamental distinction between scientific and clinical hypotheses. That is, we believe that the same inferential processes one uses in the research laboratory for distinguishing between viable and invalid scientific hypotheses can be used in deriving and testing clinical hypotheses (see also Landy, 1986, who takes a hypothesis-testing approach to the process of test validation). Our approach is based on a model of inductive inference outlined by Platt (1964), a model that abounds in the physical sciences, particularly molecular biology and high-energy physics. Platt called his approach *strong inference* because its systematic application seems related to rapid scientific advance in the fields that utilize its strengths. It is based primarily on disconfirmatory logic (Popper, 1959) and consists mainly of the sequential evaluation of hypotheses that survive disconfirmation in experimental (clinical) test. Strong inference consists of the systematic application of the following steps:

1. Devising alternative hypotheses
2. Devising "crucial experiments", with alternative possible outcomes, each of which will exclude one of the alternative hypotheses
3. Carrying out the experiments "cleanly"
4. Recycling the procedure with surviving hypotheses.

These four steps are recognizable to all neuropsychologists as the basic elements of inductive inference. The difference, however, is in the systematic, formal applications of all of these steps to every clinical problem.

We will illustrate the utility of this approach by describing a series of simple "experiments" designed to determine more precisely the nature of a specific neuropsychological deficit. As an example, assume we have a child who performs poorly on WISC-III Block Design and assume that we have reason to believe from the medical history that a significant neuropsychological factor is involved. Because Block Design measures more than one ability, a question of some relevance might be to determine more specifically the nature of the child's failure. On an a priori basis, the Block Design test can be thought of as tapping motor, visuoperceptual, visuomotor, constructional, and problem-solving abilities. A strong inference approach to isolating the reason(s) for a deficit in Block Design performance would proceed first by devising a series of tests that systematically eliminate one or more of these constituent abilities and then observing the resulting effects on the child's performance. Assuming relatively good control over difficulty level, performance on Block Design could be contrasted with performance on visuoperceptual tasks without motor demands (e.g., tests of form discrimination, visual synthesis). The relative role of visuomotor versus motor abilities could be assessed by contrasting performance on motor tests not requiring visual tracking (e.g., finger tapping, fine finger movements) with tasks with high visuomotor demands (e.g., drawing, visual reaching, grooved pegboard) and so on. Alternatively, the role of motor abilities could be excluded by requiring the child to perform on a match-to-sample task which emphasized the perceptual demands rather than motor components of the Block Design assembly task. By such a systematic approach to ruling out alternative hypotheses for the deficient Block Design performance, attention is gradually directed toward surviving hypotheses. For example, a pattern of good performance on visual, problem-solving, and motor tasks would tend to rule these abilities out as explanations, leaving the hypothesis that it was the visuomotor or constructional aspect of Block Design that specifically contributed to the child's difficulties on this task. It is our view that almost any complex test behavior can be broken down into its constituent features in this way in order to develop more precise hypotheses about performance deficits.

The strong inference approach, with its emphasis on disconfirmation, is quite different from the logic typically used in traditional approaches to neuropsychological testing. Traditional approaches typically utilize a pattern of test performance (e.g., lateralized motor or sensory findings, poor nonverbal memory performance) as confirmatory evidence for a particular hypothesis. This is the fundamental assumption underlying the so-called sign approach. Our view is that although this approach may result in correct inferences, it does so inefficiently and at the risk that alternative explanations for a test sign or performance have not been entirely ruled out. The qualitative approach also depends

heavily on the ability of any given "sign" to discretely predict to a specific brain system or locus. A good example of the weakness of this sign approach is the so-called Gerstmann syndrome. This combination of clinical signs (acalculia, agraphia, left–right confusion, and finger agnosia) frequently points to dominant parietal lesions in adults but is less reliably diagnostic among children with developmental disorders (Kinsbourne & Warrington, 1963; Spellacy & Peter, 1978).

Clinical Judgment in Neuropsychology

We have implied in the previous section that the theoretical model the clinician espouses will be an important factor governing the kinds of inferences made about neuropsychological test data. Although this makes the clinician an additional source of variation in test interpretation, which some (e.g., Rourke, Bakker, Fisk, & Strang, 1983) find somewhat undesirable, we believe that the "cognitive activity of the clinician" is an integral and inevitable aspect of neuropsychological test interpretation. This issue has received little systematic attention within neuropsychology, though some guidance is available from the contemporary application of the Brunswick Lens Model (Brunswick, 1956) to the practice of psychodiagnosis (Hammond, Hursch, & Todd, 1964; Hursch, Hammond, & Hursch, 1964; Meehl, 1960; Wiggins, 1973).

The basic idea is that inference in neuropsychology is dependent not only on the specific relationship among test signs and brain function (so-called criterion-oriented validity) but also on the manner in which the neuropsychologist uses such test signs in arriving at interpretive statements. There are two basic issues involved here. First is the degree to which the clinician accurately uses the test results to arrive at a clinical diagnosis. This issue can be understood if one assumes that the separate test performances function as variables that, separately and in combination, predict to some criterion (e.g., brain function). The intercorrelations among test performances, and their individual relationships to the criterion, determine the relative importance (weighting) each performance has in predicting the criterion. In an ideal setting, the neuropsychologist utilizes the various test performances in a manner that accurately reflects the separate and combined relationship such performances actually have with the criterion. In this ideal world, the clinician's inferences directly reflect the empirical validities of the various test performances vis-à-vis the criterion; the test performances that bear stronger relationships with the criterion are given more weight than are those that correlate less highly. However, in actual clinical practice, the clinician may not have precise knowledge of the predictive relationship between test performance and criterion. What might result from this situation is a method of combining test performances that does not accurately reflect their predictive validity with respect to the criterion. In this case, it becomes important to distinguish empirical validity (the statistical relationship that exists between predictor variables and criterion) and cue utilization (the relationship between test performance and the inferences made by the clinician) (see Wiggins, 1973, p. 157).

A second issue is the manner in which test results are combined to arrive at a clinical conclusion. Do neuropsychologists combine test findings in the linear fashion implied by multiple regression accounts of empirical validity, or do they adopt a more complex, nonlinear method of combining data in which certain test scores are viewed as a priori more important than others? An example of a nonlinear approach to test score interpretation is the use of the "pathognomonic sign" approach in neuropsychology. Pathognomonic signs are performances that are seen rarely, if ever, in persons with normal brain function. When they do appear, therefore, they more than likely suggest some brain impairment. For example, the appearance of aphasia is regarded as a pathognomonic sign of left hemisphere impairment; significant discrepancies in right- and left-handed finger tapping speed are pathognomonic of lateralized motor system impairment. In terms of this discussion, pathognomonic signs could be weighted very heavily and could form the basis of the clinical judgment even in the absence of other supportive clinical evidence. In this situation, the clinician could elect, perhaps unwisely, to ignore the relationships among other test performances and the criteria if pathognomonic signs are present.

Summary of Basic Issues

In discussing these basic issues, our purpose has not been to argue for one or another approach to interpretation, but rather to articulate the processes entering into the inferential process in child neuropsychology. Our view is that it is important to be explicitly aware of the crucial role such processes play in making sense out of neuropsychological test data. In large part, the concepts that are invoked to explain neuropsychological test performances (e.g., attention, memory capacity) are unobservable and must be inferred from overt behavior. Whether one elects to deal at the individual test level or at the level of pattern analysis, the same basic inferential processes are involved. In this section, we have purposely emphasized the context, rather than the content, of inductive inference in the clinical setting. As we have stated, this is important because the inferential method is such a fundamental aspect of the neuropsychological approach. We have outlined a strong inference model that, for us, is a useful way of conceptualizing the process of hypothesis formation and hypothesis testing in child neuropsychology. Finally, we have attempted to point out some of the general issues involved when a clinician attempts to derive meaningful interpretations of multiple test performances. With these broad issues as a background, the specific nature and content of the inferences made by the neuropsychologist will in large part depend on the level of data analysis and on the conceptual model that governs the assessment approach. We now turn to a discussion of the major inferential models of relevance to the child neuropsychologist.

Models of Inference in Child Neuropsychology

As Tarter and Edwards (1986) noted, clinical neuropsychological assessment is descriptive, correlational, and inferential rather than explanatory, causal, and direct. Neuropsychological procedures provide descriptive information regarding behavior in both normal and neurologically impaired children. This description of behavior on standardized and formal observations (tests) is then correlated with suspected or known pathological lesions derived from other tests (concurrent validity) in order to enable the neuropsychologist to (1) infer the presence or absence of brain pathology from test signs (*primary* inference) or (2) classify the individual child according to test and historical variables into some classification group (e.g., brain injured, learning disabled, attention deficit disordered) by a process of *secondary* inference. Although the inferential *process* may be similar in adult and child neuropsychology, major differences exist in the *context* of that process.

The Inferential Context of Child Neuropsychology

Several recent texts devoted to child or developmental neuropsychology emphasize the critical differences in the neuropsychological organization and functioning of children relative to adults (Baron, Fennell, & Voeller, 1995; Hartlage & Telzrow, 1986; Rourke et al., 1983; Spreen, Risser, & Edgell, 1995). Furthermore, as the analytic focus for the child neuropsychologist is on the developing brain, inferential processes regarding brain function must rest on models that account for differences in development at different ages (Dean, 1986; Fletcher & Taylor, 1984; Segalowitz & Gruber, 1977; Van der Vlugt, 1979) rather than rely on the models of adult brain functions and acquired pathologies (Heilman & Valenstein, 1993; Lezak, 1995). In addition, basic descriptions of the neuropsychological effects of developmental and acquired pathologies of childhood are still emerging (Baron et al., 1995; Berg & Linton, 1989; Boll, 1983; Boll & Barth, 1981; Menkes, 1990; Netley & Rovet, 1983; Pirozzolo, Campanella, Christensen, & Lawson-Kerr, 1981; Rutter, 1983; Spreen et al., 1995). Our understanding of the influence of individual differences in development and how these may affect the descriptive and inferential processes in child neuropsychology (Bakker, 1984; Bolter & Long, 1985; Clark, 1984; Dean, 1986; Rourke & Adams, 1984) is still incomplete. Finally, only recently has an emphasis been placed on the discriminative validity of various test signs and historical indicators of certain subgroups of childhood disorders, such as learning disabilities (Lyon, 1994; Morris, Blashfield, & Satz, 1986; Rourke, Fisk, & Strang, 1986), developmental language disorders (van Santen, Black, Wilson, & Risucci, 1994), minimal brain dysfunctions (Chadwick & Rutter, 1983; Denckla, 1979; Ross & Ross,

1992; Satz & Fletcher, 1980), nonverbal learning disabilities (Rourke, 1995), or attention deficit disorder (Barkley, 1994). Specific information regarding the neuropsychological profiles of children with a variety of psychiatric disorders has recently emerged (Bornstein, King, & Carroll, 1983; Tramontana & Hooper, 1989). To the extent that the content of neuropsychological knowledge of the developing brain is still emerging, primary and secondary inferences in child neuropsychology are affected by maturational and experiential variables to a more significant degree than is typically assumed in adult neuropsychology. At the same time, methods of assessing neuropsychological functioning in children were historically rooted in the work on adult assessment (Incagnoli, Goldstein, & Golden, 1986). It is not surprising, therefore, to find that there are many clinicians who have approached child neuropsychology with techniques of assessment that were modified from adult batteries or that use "scaled-down" versions of adult tests, the results of which form the data for their clinical inferences (Golden, 1989).

Assessment Methods in Child Neuropsychology

Broadly speaking, assessment approaches in child neuropsychology can be classified into three major types: a fixed battery approach, a flexible battery approach, and an individualized or patient-centered approach. In the fixed battery approach, the same set of tests, designed to tap a very broad spectrum of functions and abilities, is administered to each child regardless of the referral question. This approach may be either empirically or theoretically based. In the former instance, the test battery is selected according to its ability to separate groups and is typified by the work of Reitan and his associates. Theoretically based batteries, in contrast, are founded on a theory of development as it relates to rather broad or narrow dimensions of behavior and is typified by the Florida Longitudinal Project Battery (Satz & Morris, 1981). Fixed batteries may also include formal decision rules for clinical interpretation (Reynolds, 1989; Rourke et al., 1986). The advantages of a fixed battery approach include the breadth and depth of functions assessed, the normative databases frequently provided, and the ease with which a systematic database for clinical interpretation of large numbers of clinical groups can be gathered

(Hartlage & Telzrow, 1986; Tarter & Edwards, 1986). However, a fixed battery approach, particularly one that is empirically rather than theoretically based, may not be designed to describe age-related differences in problem-solving behaviors because the emphasis is often on quantitative discrimination between diagnostic groups. Frequently, educational and other experiential variables are not treated in the content of the battery itself. Often the battery may not be designed to address specific referral questions such as prescription of remediation programs for a developmental impairment. Finally, many fixed batteries suffer from dependence on the match between the validation and cross-validation samples and the base rate of clinical problems for the sample to which it is applied. Thus, for example, batteries developed at a hospital-based referral clinic may or may not be as capable of detecting cognitive disorders in a school-based or psychiatry inpatient setting (Tramontana & Hooper, 1987).

In the flexible battery approach, a core set of standardized tests are administered to which are added a selected set of additional tests designed to enhance examination for specific referral questions (Rourke et al., 1986) or to examine problem behaviors that are detected on the core battery (Bauer, 1994; Hartlage & Telzrow, 1986). Like the fixed battery, such an approach may be empirically derived or theoretically based or some mixture of the two. For example, a screening battery, empirically derived, may be followed by a theoretically based complement of tests designed to test the best fit to a syndrome type. The advantage of such a flexible battery is that the neuropsychologist is able to employ both a nomothetic and an ideographic approach to child assessment. Thus, this approach permits the evaluation of broad classes of behaviors as well as subcomponents of a specific ability or symptom related to a particular referral question.

In the individualized or patient-centered approach to assessment (Goodglass, 1986), the set of test procedures employed is driven by two interacting factors: the referral question that includes the child's history and presenting symptoms and the child's test performance (successes and failures) (Christensen, 1975; Luria, 1973). More than any other approach, the patient-centered assessment requires that the clinician have substantial clinical knowledge of the specific as well as nonspecific effects of

brain lesions on brain development and neuropsychological functioning. The patient-centered approach has, as a primary goal, the isolation of a specific neurobehavioral mechanism to account for the pattern of test findings. In this sense, the logic underlying this approach is most easily adapted for use in the strong inference model outlined earlier.

A number of lesion-related factors have been shown to have a differential impact on the developing brain, including age at time of insult (e.g., prenatal versus adolescence), type of lesion (e.g., vascular versus infectious), site of lesion (e.g., primary versus association cortex), and etiology (e.g., anoxia versus trauma). As yet, however, detailed descriptions of the neuropsychological functions and organization of behaviors in many children with development or acquired neuropathologies are not available (Baron et al., 1995). As a result, the clinical-inferential approach of the patient-centered battery is less frequently seen in practice (Fennell, 1994).

Quantitative Inferences in Child Neuropsychology

There are four major inferential approaches that focus on quantitative aspects of performance in child neuropsychological assessment. These interpretive approaches derive primarily from the fixed battery methods in clinical assessment outlined by Reitan and others and focus on (1) level of performance, (2) differential score patterns, (3) comparisons between sides of the body, and (4) comparisons of performance across time (Boll, 1983; Rourke et al., 1986).

In the level of performance approach, the child's performance on a variety of measures is individually compared with normative data available for age-matched normal subjects or for selected clinical comparison subgroups (Satz & Morris, 1981; Spreen et al., 1995). One risk of this approach is a high number of false-positive errors resulting from the large number of factors (e.g., psychiatric disturbance) besides brain dysfunction that can lead to poor performance.

The differential score or pattern approach evaluates an individual's set of performances on a battery of tests and may compare relative strengths or weaknesses in the total performance or may attempt to match a pattern or profile of

scores to a clinical subtype. This is frequently done in the learning disabilities literature. This latter inferential approach is often difficult because of the fact that all measures do not equally allow for a comparison between the idealized referent group and the individual case (Morris et al., 1986) or because of the absence of a well-defined ideal subtype to which the individual case is compared (Boll, 1983).

Comparisons between sides of the body may be made on the basis of speed of performance (e.g., finger tapping rate), skill of performance (e.g., manual dexterity), preferred performance (e.g., handedness), or accuracy of performance on sensory or motor tasks (e.g., tactile form discrimination). Transfer of learning from one side to the other may also be compared (e.g., dominant versus nondominant hand time to complete Tactual Performance Test; Reitan & Davison, 1974). In this analysis, differential performance between the sides of the body or in transfer of learning is the basis for inferring differential functional integrity at the level of the brain (Reitan & Davison, 1974).

The fourth approach, the longitudinal approach, compares performance on a battery of tests over time. In this approach, pretest versus posttest comparisons can be made of the effects of a known acquired lesion (e.g., surgical excision of an epileptic lesion), of the effects of recovery or restoration of function following an acquired lesion (e.g., recovery of memory functions subsequent to head trauma), or of the effects of a treatment intervention (e.g., pharmacological therapy for attention deficit disorder with hyperactivity).

In all of these quantitative approaches, the reliability and validity of the interpretation made rest on the database available. Although normative data continue to be developed, there is still a paucity of data about the neuropsychological performance of various childhood neurologic disorders as well as a paucity of longitudinal studies of these clinical groups against which normal versus abnormal inferences can be derived.

Qualitative Inferences in Child Neuropsychology

Reflecting the emphasis of U.S. psychology on a psychometric approach, it is an unfortunate truth that only recently have developmental neurologists begun to collect data on the qualitative

aspects of performance in both normal and abnormal development and attempted to relate these findings to neurologic models of brain development and to cognitive development (Fletcher & Taylor, 1984; Taylor & Schatschneider, 1992; Waber & Holmes, 1985). The focus of a qualitative approach is the emphasis on the qualitative features of performance (how a test is performed) rather than solely on the quantitative features of performance (what is achieved). By examining these qualitative features of performance, inferences are derived about the processes involved in executing a given behavioral task. These processes are then related to the differential functions of the right or left cerebral hemispheres or to other subcortical functional processes (Van der Vlugt, 1979). To some degree, this approach has also been applied to an analysis of errors in performance, for example, among different subgroups of learning-disabled children (Hynd, Obrzut, Hayes, & Becker, 1986) and to understanding the neurobehavioral deficits of autistic children (Damasio & Maurer, 1978). Similarly, this qualitative approach also underlies the pathognomonic sign approach in models of developmental delay versus deficit (Hartlage & Telzrow, 1986), in the analysis of "soft" versus "hard" neurologic signs among learning-disabled children (Denckla, 1979; Shafer, Shaffer, O'Connor, & Stokman, 1983; Shaffer, O'Connor, Shafer, & Prupis, 1983), and in the search for behavioral signs of "organicity" such as rotations in drawings (Boll, 1983). In this latter context, the neuropsychologist infers that the presence of the "sign" indicates the presence of brain damage or brain dysfunction. As Rourke et al. (1983) pointed out, however, the risk of relying on this approach is the likelihood of increasing false-negative errors, for the absence of sign is interpreted to reflect the absence of pathology. In fact, it is now recognized that behavioral signs of brain pathology are age related and may appear, disappear, and reappear at different stages of development reflecting the late versus early effects of a lesion as well as the capacity of the developing brain to adapt and to compensate for brain pathology (Boll, 1983; Spreen et al., 1995; Stein, Rosen, & Butters, 1974). As noted with regard to quantitative inference, qualitative inference also depends on carefully documented empirical data relating qualitative aspects of performance to normal and abnormal development, which are still not widely available to clinical practitioners (Spreen et al., 1995). Finally, both quantitative and qualitative approaches depend on the fundamental validity of the measures employed (Taylor & Schatschneider, 1992) as well as the accuracy with which quantitative techniques (e.g., multivariate clustering) or clinical techniques (e.g., clinical subtyping) are applied to the assessment data (Reynolds, 1989).

Inferential Fallacies in Child Neuropsychology

Fletcher and Taylor (1984) pointed out a number of inferential fallacies about the relationship between a child's test performance and the integrity of that child's brain. These fallacies include (1) the differential-sensitivity fallacy, (2) the similar-skills fallacy, (3) the special-sign fallacy, and (4) the brain–behavior isomorphism fallacy.

In the differential-sensitivity fallacy, it is assumed that neuropsychological test findings associated with brain lesions in adults will be useful signs of brain disease in children. Instead, Fletcher and Taylor (1984) argued that one must document that a particular measure is a sensitive neurobehavioral measure in children whether or not it is helpful in the description of brain pathology in adults. Although it has been argued that the type and locus of childhood brain pathologies often do not lead to a picture of focal deficits (Boll, 1983; Boll & Barth, 1981), wherever possible, appropriate neurological and neurodiagnostic criteria must be utilized to assess the sensitivity of behavioral tests to brain pathology.

The similar-skills fallacy focuses on the belief that tests developed and normed on adult subjects measure the same abilities in children. Thus, for example, age norms that step down from adult age groups to younger children have been published for such widely used adult measures as the Wechsler Memory Scale (Ivinskis, Allen, & Shaw, 1971). In this example, it is assumed that children process these task demands in a fashion similar to adult subjects, despite clear evidence of age-based differences in the capacity and processes of verbal memory in children (Kail, 1984). Other major differences between children and adults are widely recognized in such important behavioral domains as language (Segalowitz, 1983); right-hemisphere

functions (Witelson, 1977); and early versus later acquired reading skills and the role of the right versus the left hemisphere (Bakker, 1984).

The special sign fallacy occurs when neuropsychologists utilize specific test behaviors (e.g., rotations in drawings) as signs of brain pathology or infer from the presence of minor, accompanying or correlated signs that the major pathology from which these signs derive is present. A variant of this same fallacy occurs through the overreliance on analogies between signs of CNS pathology in adults and the assumption that such signs must also mean CNS pathology in children. As Boll (1983) and Fletcher and Taylor (1984) noted, there is very little evidence that similar behavioral pathologies seen in adults and children reflect similar etiologies. We do not want to imply that lessons learned from adult neurology should not be applied to children—only that they must be applied with caution. The major advantage of such application would be to generate new hypotheses capable of being put to subsequent disconfirmatory trials.

Finally, the brain–behavior isomorphism fallacy consists of mistaking dysfunction on behavioral tests as prima facie evidence of brain dysfunction. Instead, there is a need to document that behavioral dysfunction observed on a test is related to brain pathologies and not to other sources of variability such as experiential, socioeducational, or emotional factors. As Fletcher and Taylor (1984) noted, there is no simple relationship between the degree or extent of brain involvement and the degree of behavioral disorder among children with brain pathology. This fallacy is often embedded in the language employed by the child neuropsychologist such that descriptions of behavioral dysfunctions are equated inferentially to etiology (developmental delay) or to diagnosis (brain damage) (Hartlage & Telzrow, 1986).

Boll (1983) cautioned against several other persistent misconceptions in the field of child neuropsychology. One misconception suggests that there are certain predictable characteristics of brain-damaged children rather than recognizing that the overriding effect of brain damage on psychological functioning is to increase the variability of behavior. A second misconception asserts that brain damage in children causes characteristic hyperactive motor behavior rather than recognizing that changes in simple, complex, and integrated motor skills may occur in many but not all neurologic disorders, including psychiatric/behavioral disorders without evidence of neurologic abnormality (Tramontana & Hooper, 1989).

Still another misconception asserts that perceptual dysfunctions are the major difficulties produced by brain damage in children. This misconception fails to recognize that no single pattern of neuropsychological deficits is characteristic of brain damage in children. A final misconception is that brain damage causes serious emotional disturbance. This misconception ignores the complex interplay between intrapersonal factors (age, type of lesion), interpersonal factors (family, school environment), and adaptational abilities that can lead to the same spectrum of emotional and conduct disorders seen in non-brain-damaged children (Taylor & Fletcher, 1990). Although many of these misconceptions were based in the use of single-test behavioral indices of brain pathology, they continue to persist in part because of the need for more comprehensive data on the developmental effects of brain lesions in children.

Since the publication of the previous edition of this volume, many new test batteries designed to assess various dimensions of children's cognitions have been released. Many of these measures, for example, the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) and the Wide Range Assessment of Memory and Learning-2 (WRAML-2) (Adams & Sdaslow, 2003), have included normative data across age spans from early childhood to later adulthood. Interest in so-called "executive functioning" has led to the development of both comprehensive test batteries such as the Delis Kaplan Executive Functions System (DKEFS) (Delis, Kaplan & Kramer, 2001) and parent questionnaires designed to capture behavioral indices of executive dysfunctions in children such as the Behavior Rating Inventory of Executive Function (BRIEF). A compendium of test data and norms among selective clinical groups of children has also been released (Baron, 2004). There is now increasing interest in the measurement of effort and malingering in children undergoing neuropsychological assessment in the context of legal proceedings (Constantinou & McCaffrey, 2003; Donders, 2005). In addition, recent revisions in normative data and scaling to a widely used measure of adaptive abilities is now available (Vineland Adaptive Abilities

Scale-2) (Sparrow & Cichetti, 2006). Despite these needed additions to the information and procedures available to the professional who examines children for suspected neuropsychological dysfunction, recognition of the potential inferential problems that can occur in an examination is critical to optimal interpretation of data and communication of the findings to the child, the family, and the referring professional.

Summary

In its present state, the typical approach to assessment of children for the presence of neuropsychological dysfunction involves the collation of data from developmental/clinical history with data derived from a battery of neuropsychological tests. On the basis of a quantitative analysis of the test data and to a lesser extent an analysis of the fit between qualitative aspects of test performance with known clinical subtypes as well as with historical data and presenting symptoms, the child neuropsychologist then can proceed by a process of primary inference to relate test data to brain function and further, by secondary inference, assign the individual child to a classification group.

The context of the primary or secondary inferential process in child neuropsychology is influenced by several critical factors that include the lack of a consistently employed neurologic model of brain development to relate to behavioral data; the differential effects of lesions according to age at insult; type and etiology of lesion on a developing brain; the need for better descriptive data on a wide variety of clinical populations in developmental neuropathologies; and the need for better specification of quantitative as well as qualitative aspects of normal and abnormal behavior. In the absence of substantive knowledge of the influence of such critical factors, inferential models in child neuropsychology are still primarily descriptive in nature. The beginning emergence of an integration of description and adequate neuropsychological tests (Freides, 1985; Rourke, 1995) with classification schemes should facilitate prescriptions for remediation and better understanding of the effects of intervention on the remediation of neurobehavioral deficits resulting from neurologic pathologies in infancy, childhood, and adolescence.

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II

Neuropsychological Diagnosis

11

Halstead–Reitan Neuropsychological Test Batteries for Children

NANCY L. NUSSBAUM AND MELISSA R. BUNNER

The purpose of this chapter is to review the children's version of the Halstead–Reitan neuropsychological test batteries for children. The Children's Halstead–Reitan Neuropsychological Test Battery (CHRNB) for children 9–14 years of age (Reitan & Davison, 1974; Reitan & Wolfson, 1992) and the Reitan– Indiana Test Battery (RINB) for children ages 5–8 (Reitan, 1969; Reitan & Davison, 1974) are two children's batteries based on the adult version of the Halstead–Reitan (Halstead, 1947; Reitan & Wolfson, 1985). These two batteries will be discussed in terms of their development and validity. This discussion will be followed by a description of the measures, their administration, scoring, and the functional domains they are purported to measure. Finally, the interpretation of test results obtained and the clinical applications of these batteries will be discussed.

The Halstead–Reitan Neuropsychological Test Battery for Older Children (9–14) and the Reitan–Indiana Neuropsychological Test Battery for Younger Children (5–8) were originally designed for use in a fixed battery (Reitan & Wolfson, 1985). The children's batteries include modifications and a downward extension of the adult Halstead–Reitan, as well as the addition of some supplementary measures not included in the adult version (see Table 1).

The reason for the development of the Halstead– Reitan and the Reitan–Indiana was to standardize a battery of measures to identify the presence of brain damage in children by proposing that behavior has an organic basis. Thus, performance on behavioral measures could be used to assess brain functioning. Early in the development of the HRNB (and CHRNB), Halstead realized that brain damage resulted in numerous deficits, and that a variety of measures would be necessary to evaluate brain integrity, leading to the development of a battery of tests to evaluate brain functioning rather than a single test (Reitan & Wolfson, 2004). In order to assess brain functioning based on behavioral measures, it was necessary to validate these measures on children with known brain damage.

Validation Studies

Although the HRNB manual does not provide detailed information regarding reliability and validity (Davis, Johnson, & D'Amato, 2005), numerous later studies have provided further information about psychometric properties. In fact, the HNRB is one of the most researched neuropsychological batteries developed (Horton, 1997). The validation of the CHRNB was first reported by Reed, Reitan, and Klove (1965) for 9- to 15-year-old children with known brain damage, and by Klonoff, Robinson, and Thompson (1969) for 5- to 8-year-old children.

NANCY L. NUSSBAUM AND MELISSA R. BUNNER • Austin Neurological Clinic, Austin, Texas 78705.

TABLE 1. Subtests of the Halstead–Reitan Neuropsychological Test Batteries for Children

Halstead battery (9–14 years)	Reitan–Indiana battery (5–8 years)
Category Test	Category Test
Tactual Performance Test	Tactual Performance test
Finger Tapping Test	Finger Tapping Test
Speech Sounds Perception Test	–
Seashore Rhythm Test	–
Trail-Making Test, A and B	Marching Test
Strength of Grip Test	Strength of Grip Test
Sensory–Perceptual Exam	Sensory–Perceptual Exam
Tactile Finger Localization Test	Tactile Finger Localization Test
Fingertip Number Writing Test	Fingertip Symbol Writing Test
Tactile Form Recognition Test	Tactile Form Recognition Test
Aphasia Screening Test	Aphasia Screening Test
	Color Form Test
	Progressive Figures Test
	Matching Pictures Test
	Target Test
	Matching Figures and Matching V's Test
	Drawing of Star and Concentric Squares

These studies demonstrated the validity of using neuropsychological variables from the CHRNB to differentiate brain-damaged from nonbrain-damaged children. Subsequently, numerous studies have shown the discriminant validity of the CHRNB and the RINB in separating children with known brain damage from nonbrain-damaged children (Boll, 1974; Reitan, 1974; Selz, 1981; Selz & Reitan, 1979a, 1979b). For example, Boll (1974) matched 27 brain-damaged children with 27 normal children on the basis of age, sex, race, and handedness. Significantly poorer performance by the brain-damaged group was reported for finger oscillation (dominant and nondominant), the Tactual Performance Test (dominant, nondominant, and both hands), finger recognition (dominant), fingertip number writing (dominant and nondominant), Seashore Rhythm Test, and Speech Sounds Perception Test. Similar results were found by Reitan (1974) in a study with children aged 5–8, matched for age and sex. Furthermore, in a study of children with questionable rather than definite neurological impairment, it was found that a neuropsychological test battery correctly identified the presence or absence of impairment, even when the initial subjective clinical impressions did not suggest deficits (Tsushima & Towne, 1977). Also, in a somewhat more recent study (Nici & Reitan, 1986) using intellectual, achievement, and neuropsychological measures, it was found that measures of motor functioning and general neuropsychological abilities were the best discriminators of 9- to 14-year-old brain-damaged children versus nonbrain-damaged children.

The HRNB has been found to be useful in the diagnosis of learning disabilities (LD) and in defining strengths and weakness within the LD population. For example, the HRNB has been used as an adjunct to traditional psychoeducational measures, such as the Wechsler intelligence scales. In a study examining the incremental validity of the HRNB to the WISC-R in an LD sample, it was found that HRNB increased the variability accounted for in academic measures from 16 to 30% (Strom, Gray, Dean, & Fischer, 1987). This suggests that there was a significant amount of unique variance contributed by the HRNB. Similarly, Shurtleff, Fay, Abbott, and Berninger 1988) found that cognitive and HRNB variables were not redundant and that inclusion of both improved educational assessment. Also, in terms of predictive validity, it was found that the Seashore Rhythm Test appeared to be a useful tool in detecting young children who showed early signs of reading impairment (McGivern, Berka, Languis, & Chapman, 1991).

As the applications of the CHRNB and RINB have changed over time, research has begun to focus on specific subtests of these batteries. For example, the Halstead Category Test (HCT) was found to have acceptable internal consistency and concurrent validity (Reeder & Boll, 1992). In addition, the HCT has been shown to correlate moderately with Full Scale IQ (Berger, 1998; Golden, Kushner, Lee, & McMorrow, 1998;). However, this test has only 11–13% shared variance with Performance IQ (Donders, 1996; Titus, Retzlaff, & Dean, 2002), indicating that the HCT is not merely a measure of visual spatial processing. Other subtests have also been examined including Finger Tapping,

Trails A and B, Seashore Rhythm Test, and the Tactual Performance Test.

In summary, the RINB and the CHRNB have been validated and have useful clinical applications. These test batteries can provide unique information in the behavioral assessment of children with known brain damage, as well as in the evaluation of the functional abilities of the child without known brain damage. In the next section, types of behaviors measured and the administration and scoring of the HRNB and the RINB will be discussed in greater detail.

Subtests from the Halstead–Reitan Neuropsychological Test Battery for Children Ages 9–14

Below is a description of each task in the CHRNB, scoring procedures, and a description of abilities required for each task.

Category Test

Description. This test includes 168 items presented visually to the child. The stimuli are different than stimuli in the adult version of this test. The child must respond by selecting a number (1, 2, 3, or 4) that corresponds with the visual stimulus. Feedback is given on each item regarding the correctness or incorrectness of the response.

Scoring. The child's raw score is the total errors made.

Domain measured. The Category Test is a measure of concept formation. The child must abstract principles related to number concepts, spatial position, and unusualness of the stimuli. The child must develop and test hypotheses and then adapt behavior based on both positive and negative feedbacks. Reitan and Wolfson (2004) considered this test the best measure of abstraction and reasoning which leads to organization of behavior. There also is a memory component involved in the last subtest. This test is thought to measure general cortical functioning rather than localized brain function (Reitan & Wolfson, 2004). Factor analysis of subtests revealed a multifactor solution (Donders, 1996), and use of a single error score may, in fact, limit its clinical usefulness (Nesbit-Greene & Donders, 2002).

Tactual Performance Test

Description. On this test, the child is required to complete a six-figure form board while blindfolded, rather than the 10-figure board in the adult version. The test is carried out first with the dominant hand, then the non-dominant hand, and finally with both hands. Next, the board is removed and the child is asked to draw from memory the shapes and their correct locations.

Scoring. The child's raw score is the amount of time taken with the dominant, nondominant, and both hands. The total time is the sum of the trials with the dominant, nondominant, and both hands. Also, the memory raw score is the total number of blocks recalled, and the location raw score is the number of blocks reproduced in their correct locations.

Domain measured. The Tactual Performance Test is a measure of tactile, motor, spatial, and memory functioning. It is considered a measure of functional efficiency of each hemisphere, as well as overall efficiency – measured by improved performance with practice on each of the successive trials. Given the complex motor and sensory requirements, performance on this test depends on the central part of both hemispheres – sensory, motor, and association areas. The left hemisphere is primarily measured when completing the task with the right hand, the right hemisphere is measured when completing the task with the left hand, and global efficiency of the entire cortex and bilateral transfer is measured when using both hands (Reitan & Wolfson, 1985). In adults, total time to complete the task was a good predictor of cognitive impairment (Strauss, Sherman, & Spreen, 2006). The TPT has also been shown to predict brain damage in blind patients (Bigler & Tucker, 1981). People with learning disabilities have been shown to have impaired scores on Memory and Localization subtests (McIntosh, Dunham, & Dean, 1995).

Finger Tapping Test

Description. This test requires a child to tap a mounted key as quickly as possible with the index finger of the dominant and nondominant hand. Five trials are given for each hand.

Scoring. The child's raw score is the average of the five scores from the dominant and

nondominant hand, although a variety of administration techniques are described in the literature (See Baron, 2004, for review).

Domain measured. This task is a measure of fine motor speed and coordination. Finger tapping is purported to measure the integrity of posterior frontal (motor) areas of each hemisphere (Reitan & Wolfson, 2004). However, a variety of conditions have led to impairment on these measures including head injury (e.g., Prigitano & Borgano, 2003), alcoholism, and multiple sclerosis, suggesting that other cognitive functions are also involved including attention, processing speed, and task initiation (Strauss et al., 2006).

Speech Sounds Perception Test

Description. On this test, the child must discriminate nonsense words presented on a tape recorder. The child is given four choices from which to select and must underline the correct stimulus.

Scoring. The child's raw score is the total number of items correct out of 30.

Domain measured. Auditory perception and discrimination, sound–symbol matching, and attentional abilities are assessed on this task. Performance on this task has been purported to measure left-hemisphere functioning, but research suggests that this measure is sensitive to brain damage, regardless of location (Reitan & Wolfson, 1990).

Seashore Rhythm Test

Description. The child is presented 30 pairs of rhythms on a tape recorder and must discriminate whether they are the same or different.

Scoring. The child's raw score is the total number of items correct out of 30.

Domain measured. This test is a measure of alertness to nonverbal auditory stimuli as well as perception of the stimuli, attention, and concentration. This task has been hypothesized to measure right-hemisphere function, but is a better indicator of generalized cortical function and does not differentiate lateralized lesions (Reitan & Wolfson, 1985).

Trails A and B

Description. On Trails A, the child must connect circles containing the numbers 1–15 as quickly as possible. On Trails B, the child is required to connect alternating letters (A–G) and numbers (1–8).

Scoring. The child's raw score is the number of seconds taken to complete each task and the number of errors made.

Domain measured. This task includes components measuring visual perception, scanning ability, motor speed, sequencing skills, and symbol recognition. Trails B also is a measure of simultaneous processing and cognitive flexibility. Performance on this measure is generally related to global cortical function rather than localized abilities. Ability to recognize and deal with numerical and language symbols is sustained by the left hemisphere, while visual scanning is sustained by the right hemisphere, and speed relates to the general efficiency of both hemispheres. Given the integration of both of these demands, Trails A and B is considered a good measure of general brain function (Reitan, 1955, 1958). Trails A and B have been found to indicate impairment in a variety of etiological causes of cognitive impairment including Fragile X, lead exposure, and academic problems (Lezak 1995; Moore et al., 2004; Reitan & Wolfson, 2004; Stewart et al., 1990).

Strength of Grip Test

Description. The child's grip strength is measured using a dynamometer adjusted for hand size. Three alternating trials are allowed for the dominant and nondominant hand.

Scoring. A mean raw score is obtained for each hand.

Domain measured. Differential hand strength is assessed by this measure, and performance informs integrity of posterior frontal areas of the hemispheres through relative performance between hands as well as in terms of overall performance (Reitan & Wolfson, 2004).

Sensory–Perceptual Exam

Tactile, auditory, and visual perception are measured by this task. These tasks were developed from behavioral neurology tasks, in which both normal and people with brain damage often did well, but impairments were considered pathognomonic signs of damage to the brain (Reitan & Wolfson, 1985).

Tactile perception. The child is asked to close the eyes and to report whether the right hand, left hand, right face, or left face is being lightly touched. Following unilateral trials to determine whether the child can perceive unilateral stimulation, bilateral trials are randomly interspersed with unilateral trials. Bilateral trials include the stimulation of both hands and the contralateral stimulation of the hand and face, the so-called double simultaneous stimulation (DSS) procedure. By ages 3–5 years, children can complete this task (Maiuro, Townes, Vitaliano, & Trupin, 1984).

Scoring. A raw score for each body side is calculated by summing the total number of errors made on unilateral and bilateral trials.

Domain measured. Differential tactile perception is measured by this task.

Auditory perception. The examiner lightly rubs his or her fingers together by the child's right ear, left ear, or both ears. The child is asked to close his or her eyes and report where the sound is coming from. Following unilateral trials to determine whether the child can perceive unilateral stimuli, bilateral trials are randomly interspersed with unilateral trials. Bilateral stimulation constitutes the DSS procedure for auditory stimulation.

Scoring. A raw score for each ear is calculated by summing the total number of errors made on unilateral and bilateral trials.

Visual perception. The child's visual fields are tested by quadrant. Then the child is asked to report peripheral, unilateral, and bilateral single movements by the examiner at eye level, above eye level, and below eye level. Bilateral stimulation constitutes the DSS procedure for visual stimulation.

Scoring. A raw score for the right and left visual fields is calculated by summing the total number of errors made on unilateral and bilateral trials.

Domain measured. Differential visual perception in the right and left visual fields is measured by this task.

Finger Localization Test

Description. With the child observing, the examiner numbers the child's fingers. The child must then close his or her eyes and report the number of the finger being stimulated.

Scoring. The raw score is the sum of the errors made on each hand.

Domain measured. This test is a measure of tactile perception, tactile localization, and attention for each body side. This test measures the integrity of the contralateral parietal lobes (Reitan & Wolfson, 2004).

Fingertip Number Writing Test

Description. The child watches while the examiner traces the numbers 3, 4, 5, and 6 on the palm of the child's hand. The child is then asked to close his or her eyes and report the number written in a set order on the fingertips of the right and left hands.

Scoring. The raw score is the sum of the errors made on each hand.

Domain measured. Aspects of complex tactile perception and concentration are assessed by this task for each body side. As with finger localization, integrity of contralateral parietal areas is assessed.

Tactile Form Recognition Test

Description. The child places a hand through an opening in a board, and the examiner places either a small cross, triangle, square, or circle in the child's hand without the child seeing what object has been placed there. The child must then point to the correct object on the board with the other hand. The task is carried out twice with each hand.

Scoring. The raw score is the sum of errors made with each hand, and the number of seconds taken to identify the object with the right and the left hand.

Domain measured. This test is a measure of attention, tactile perception, and reaction time for each body side. Again, contralateral parietal area functioning is evaluated with this measure (Reitan & Wolfson, 2004).

Aphasia Screening Test

Description. This test includes 32 items requiring naming, copying, spelling, reading, writing, repeating, verbal comprehension, and right/left discrimination.

Scoring. Originally, qualitative descriptions of errors were used, but Selz and Reitan (1979b)

developed a scoring system for the items from the Aphasia Screening Test.

Domain measured. The Aphasia Screening Test is a useful screening measure for dyspraxia (both spelling and constructional), dysnomia, dysgraphia, dyslexia, dyscalculia, ideational dyspraxia, expressive aphasia, receptive aphasia, dysarthria, visual dysgnosia, auditory dysgnosia, and right/left disorientation. This test requires perception of auditory or visual stimuli, central processing, comprehension, and formulation of a response (verbal, written, or drawing).

Ordering Information

The Halstead–Reitan Test Battery for Older Children can be ordered from the Reitan Neuropsychology Laboratory at www.reitanlabs.com for approximately $2,375.00. In addition, books are available by Reitan and Wolfson (1992, 1993) which serve as manuals and provide information on rationale for the batteries and their uses, administration, and scoring. Davis et al. (2005) recommended that only psychologists trained in neuropsychological testing and child development should use these instruments.

Subtests from the Reitan–Indiana Neuropsychological Test Battery for Children 5–8

The Reitan–Indiana (Reitan, 1969) is a downward extension of the Halstead–Reitan Neuropsychological Test Battery for Older Children (see Reitan & Wolfson, 1985) developed for children 5–8 years of age. The modifications discussed below were necessary because of the developmental differences found between younger and older children (Boll, 1981; Reitan & Davison, 1974).

Category Test

Description. The number of test items was reduced to 80 items in five categories. On the first subtest, the child is required to identify colors by selecting a corresponding lever. The following four subtests involve principles of size, shape, color, or memory.

Scoring. See the previous description of scoring for the Category Test.

Domain measured. Nonverbal reasoning, learning, memory, and concept formation are assessed by this task (Reitan & Wolfson, 1995).

Tactual Performance Test

Description. The same six-figure form board employed in the older children's battery is used on this test, but the board is presented horizontally. (See the previous discussion of the Tactual Performance Test for a more detailed description of the task, the scoring, and the abilities measured.)

Finger Tapping Test

Description. The same procedure is used with younger children, as was described for older children, except that an electric finger tapping device is used to compensate for the younger child's poorer fine motor coordination. (The scoring and domain measured are the same as described previously.)

Speech Sounds Perception Test, Seashore Rhythm Test, Trails A and B

These tests are not components of the younger children's battery.

Marching Test

Description. On this test, the child is required to follow a sequence of circles connected by lines up a page, by touching each circle as quickly as possible.

Scoring. The raw score is the number of errors and time taken to complete the task.

Domain measured. This test is a measure of upper extremity gross motor functioning, speed, and coordination.

Strength of Grip

This test remains unchanged from the older children's battery.

Sensory–Perceptual Exam (SPE)

The tactile and auditory tasks of the SPE remain unchanged from the CHRNB. Only a minor modification of the visual task has been

made requiring that visual stimulation be presented at eye level only. In addition, if the young child has difficulty verbally reporting the body part touched or the side of stimulation (i.e., right, left), he or she is allowed to point to or raise the hand on the side of stimulation.

Tactile Finger Localization. The procedure for this task remains unchanged from the older children's battery.

Fingertip Symbol Writing. This task is similar to the Fingertip Number Writing Test from the older children's battery. The child is required to close his or her eyes and report which symbols (Xs and Os) are written on the child's fingertips. (See the older children's battery for a description of the scoring procedure and the domain measured.)

Tactile Form Recognition. The procedure for this task remains unchanged from the older children's battery.

Aphasia Screening Test

Description. Some items were deleted or simplified for the younger children. Items included in this test require the child to write, copy simple geometric figures, identify pictures, read letters and simple words, carry out simple mathematical functions, identify body parts, and identify right/left body side.

Scoring. Knights and Norwood (1979) developed a scoring system for the younger children's version of the Aphasia Screening Test.

Domain measured. This is a screening instrument for constructional dyspraxia, dysgraphia, dyslexia, dyscalculia, right/left disorientation, receptive aphasia, expressive aphasia, visual dysgnosia, and body dysgnosia.

Color Form Test

Description. A board is presented with different colored geometric shapes. The child must alternate between touching shapes and colors selectively attending to one aspect of the stimulus (e.g., color), while ignoring the other (e.g., shape).

Scoring. The child's raw score is the total number of errors made and the amount of time taken to complete the task.

Domain measured. This test is a measure of attention, ability to inhibit, visual scanning, cognitive flexibility (Sattler & D'Amato,

2002), as well as upper extremity gross motor coordination.

Progressive Figures Test

Description. The child is presented a sheet of paper on which are printed eight large geometric shapes (e.g., circle), with a smaller shape (e.g., square) inside. The child must use the small inside figure as a cue for moving to the outside shape of the next figure.

Scoring. The child's raw score is the total number of errors made and the amount of time taken to complete the task.

Domain measured. This test measures visual perception, motor speed, cognitive flexibility, attention, and concentration.

Matching Pictures Test

Description. The child must match pictures beginning with identical pictures and progressing to matching pictures from more general categories.

Scoring. The raw score is the total correct out of a possible 19.

Domain measured. This test is a measure of visual discrimination, reasoning, and categorizing skills.

Target Test

Description. The child is shown an 18-in. card with nine dots printed on it and is given a sheet with the same dot configuration. The examiner taps out a design on the stimulus card and the child must draw the design on the response test.

Scoring. The raw score is the number of items correct.

Domain measured. Visual/spatial memory and sequencing ability are measured by this task.

Matching Figures and Matching V's Test

Description. On the Matching Figures Test, the child must match figures printed on blocks with figures printed on a card. The figures become progressively more complex. The matching V's task requires the child to match V's that vary in the width of the angle.

Scoring. The raw score is the number of errors and time taken to complete the task.

Domain measured. This test is a measure of visual perception and reaction time.

Drawing of Star and Concentric Squares

Description. The child must copy figures of varying complexity.

Scoring. The raw score is the number of errors and time taken to complete the task.

Domain measured. This test is a measure of visual perception, fine motor coordination, and constructional praxis.

Ordering Information

The Reitan–Indiana Test Battery for Younger Children can be ordered from the Reitan Neuropsychology Laboratory at www.reitanlabs.com for approximately $2,490.00. As with the CHRNB, a book is available for purchase as a manual.

Normative Analysis of Halstead–Reitan Neuropsychological Test for Children

Normative data on the CHRNB have been gathered since approximately the 1960s (Reed et al., 1965; Crockett, Klonoff, & Bjerring, 1969; Spreen & Gaddes, 1969) through more recent time (Cramond & Jones, 2005). Using normative data, the clinician can examine a child's performance on a given test in comparison with other children of similar age. This approach is different from Reitan's initial one, which was a "cutoff" approach (Reitan, 1974). The "cutoff" approach viewed brain dysfunction more as a dichotomy – either present or absent. However, more contemporary views of brain dysfunction are from a perspective of a continuum.

Unfortunately, there are some significant concerns regarding much of the normative data that have been reported over the years. Very few of the studies reporting normative data included all subtests from the CHRNB and RINB batteries (Reitan, 1987; Maiuro et al., 1984; Knights & Norwood, 1980; Boll, 1974; Crockett et al., 1969; Spreen & Gaddes, 1969), and most of the reported data includes small sample sizes and/or often-inconsistent test data. Small sample size and non-representative samples are consistently a problem with much of the normative data reported in the literature.

Small sample size can often create a skewed distribution of scores and very large standard deviations. For example, in normative data for 8 year olds reported by Knights and Norwood (1980), the standard deviation (6.00) for the Tactual Performance Test-dominant hand is larger than the mean (5.71).

In addition to limited sample sizes, other problematic issues are noted in much of the available normative data. The data are often based on limited geographical representation, and information regarding the gender and ethnic composition of the samples is often not reported. Also, the issue of above average intelligence in normative samples has been discussed in the adult and child HRNB literature (Russell, 2005; Findeis & Weight, 1993). For example, the selection criteria for a number of samples of normal or control subjects for the CHRNB excluded children with a history of neurological abnormalities (i.e., tumor, seizure disorder, head injuries, mental retardation), and it appears that some also excluded children with a history of learning disabilities. Not surprisingly, this has led to above average ability scores in these samples. This is illustrated by the normative data reported by Maiuro et al. (1984), which was based on a large ($n = 451$) normative sample of 5- to 8-year-old school children. In this suburban Seattle, Washington, sample, the mean Full Scale IQ was found to be 115.

In order to address the issue of normative data derived from small sample sizes, Findeis and Weight (1993) developed metanorms for several of the child neuropsychological tests from the Halstead–Reitan batteries. As noted by these authors, these metanorms do not truly substitute for more comprehensive norms developed on an intact, single representative normative sample, but they do allow for the use of existing data to create the largest possible sample of normal or control subjects. Using these normative data, presented in Table 2, the clinician can examine a child's performance on a given test in comparison with other children of similar age, thereby determining whether the child's performance is coherent with or discrepant from those standards documented. Also, see Tables 3 and 4 for an example of a raw score conversion table, in which raw scores are converted to standard scores ($M = 100$, SD $= 15$) using normative data. For the clinician, these tables and that follow may be quite useful.

TABLE 2. Metanorms for Neuropsychological Test Performance by Age: Metameans (Meta-SD)

Metanorms for Reitan–Indiana and Halstead–Reitan Neuropsychological Test Batteries: Ages 5–14

Subtest	5	6	7	8	9	10	11	12	13	14
Category Test errors	27.40	26.00	20.56	12.35	53.56	46.58	40.88	35.12	36.29	30.81
Ages 5–8 (80 items),	(9.1)	(12.7)	(8.9)	(6.7)	(17.4)	(18.6)	(16.3)	(16.0)	(16.4)	(12.0)
Ages 9–14 (168 items)										
Finger Tapping, DH	29.39	29.87	33.67	36.40	34.01	37.52	40.72	41.36	44.64	44.38
(taps per 10 s)	(4.2)	(3.3)	(4.6)	(4.6)	(4.1)	(5.4)	(4.8)	(5.4)	(5.2)	(6.8)
Finger Tapping, NDH	26.32	27.22	30.01	32.03	30.31	34.04	35.06	36.66	39.64	40.67
(taps per 10 s)	(4.6)	(3.3)	(3.9)	(3.8)	(3.3)	(4.8)	(4.8)	(4.1)	(4.7)	(6.1)
Grip Strength, DH (kg)	8.27	9.13	11.60	12.48	14.74	17.14	19.45	22.92	26.65	36.50
	(1.9)	(2.2)	(2.3)	(2.6)	(1.9)	(2.7)	(3.4)	(3.5)	(4.7)	(3.0)
Grip Strength, NDH (kg)	7.53	8.41	10.56	11.47	14.12	16.09	18.86	21.65	25.40	32.48
	(1.9)	(2.2)	(2.1)	(2.3)	(1.9)	(2.3)	(3.2)	(4.3)	(4.9)	(4.6)
Tactual Performance Test	6.47	5.93	5.17	4.15	4.36	3.67	3.15	3.20	2.44	NA
DH (min)	(3.1)	(3.1)	(2.7)	(2.2)	(2.4)	(1.7)	(1.4)	(1.6)	(0.8)	
Ages 5–8 (6 blocks)										
Ages 9–14 (10 blocks)										
Tactual Performance Test	5.24	4.74	3.66	3.13	3.08	2.73	2.17	2.20	1.61	NA
NDH (min)	(3.1)	(2.8)	(1.9)	(3.1)	(1.7)	(1.6)	(0.9)	(1.4)	(0.9)	
Tactual Performance Test	3.80	3.11	1.98	1.68	1.28	1.27	1.13	1.03	0.80	
Both hands (min)	(2.6)	(2.1)	(1.2)	(1.1)	(0.7)	(0.7)	(0.6)	(0.5)	(0.3)	
Tactual Performance Test	15.50	13.83	10.98	8.79	8.80	7.66	6.36	6.13	4.90	NA
Total time, (min)	(5.6)	(6.8)	(4.5)	(3.8)	(4.1)	(3.3)	(2.3)	(2.6)	(1.5)	
Tactual Performance Test	2.47	3.06	4.15	4.44	4.40	4.48	4.53	4.77	5.04	NA
Memory (correct)	(1.8)	(1.5)	(1.2)	(1.2)	(1.2)	(1.2)	(1.1)	(0.8)	(0.9)	
Tactual Performance Test	1.10	1.80	2.69	3.22	3.00	3.07	3.07	3.75	3.00	NA
Location (correct)	(1.1)	(1.5)	(1.7)	(1.7)	(1.6)	(1.5)	(1.6)	(1.5)	(1.3)	

Metanorms for the Halstead–Reitan Neuropsychological Battery for Older Children (ages 9–14)

Subtest	9	10	11	12	13	14
Trail-Making Test, Part A (s)	25.09(9.4)	21.04(5.9)	18.87(6.2)	17.19(5.8)	16.00(5.7)	NA
Trail-Making Test, Part B (s)	54.77(20.0)	49.80(20.0)	41.20 (15.6)	37.14(14.1)	32.73(10.9)	NA
Trail-Making Test Total time (s)	79.85(28.9)	70.84(30.4)	60.07(20.3)	54.33(22.6)	48.73(10.3)	NA
Speech Sounds Perception (errors)	7.23(4.7)	6.58(3.3)	5.36(2.6)	5.50(2.9)	5.04(1.3)	NA
Seashore Rhythm Test (correct)	14.23(5.5)	18.85(6.3)	19.10(6.3)	19.66(5.3)	20.85(4.9)	19.43(5.4)

Metanorms for the Reitan–Indiana Neuropsychological Test Battery for Younger Children (ages 5–8)
(individual performance tests)

Subtest	5	6	7	8
Matching Figures (s)	41.30(13.7)	30.70(9.7)	23.82(9.0)	21.07(7.8)
Matching Figures (errors)	0.48(0.9)	0.40(0.8)	0.21(0.6)	0.15(0.5)
Matching V's (s)	52.39(26.5)	40.22(16.9)	32.31(12.6)	28.72(11.5)
Matching V's (errors)	2.58(1.9)	1.91(1.7)	1.29(1.6)	1.08(1.3)

TABLE 2. (*Continued*)

Metanorms for the Reitan–Indiana Neuropsychological Test Battery for Younger Children (ages 5–8)
(individual performance tests)

Subtest	5	6	7	8
Star (correct)	3.72(3.1)	6.03(2.6)	7.17(1.4)	7.82(1.4)
Star (s)	29.63(23.1)	23.43(17.1)	19.71(17.4)	17.65(9.4)
Concentric Squares (s)	37.48(21.4)	33.24(14.8)	32.29(18.1)	30.22(15.6)
Concentric Squares (Correct)	2.21(2.2)	2.75(2.3)	4.26(2.8)	5.10(2.5)
Progressive Figures (s)	96.12(57.4)	73.43(50.4)	51.74(31.0)	41.50(21.4)

Note: Normative data including means and standard deviations in parentheses from Findeis and Weight (1993).

TABLE 3. Fingertapping – Dominant Hand

	Electric tapper			Manual tapper			
Age[a]	6	7	8	9	10	11	12
M	27.2	30.01	32.03	30.31	34.04	35.06	36.66
SD	3.3	3.9	3.8	3.3	4.8	4.8	4.1
Raw score							
20	67	61	*	*	56	*	*
21	71	65	56	57	59	56	*
22	76	69	60	62	62	59	*
23	80	73	64	66	65	62	*
24	85	76	68	71	68	65	*
25	90	80	72	75	71	68	57
26	94	84	76	80	74	71	61
27	99	88	80	84	78	74	64
28	103	92	84	89	81	77	68
29	108	96	88	94	84	81	71
30	112	99	91	98	87	84	75
31	117	103	95	103	90	87	79
32	121	107	99	107	93	90	82
33	126	111	103	112	96	93	86
34	130	115	107	116	99	96	90
35	135	119	111	121	103	99	93
36	140	123	115	125	106	102	97
37	144	126	119	130	109	106	101
38	**	130	123	134	112	109	104
39	**	134	127	139	115	112	108
40	**	138	131	144	118	115	112
41	**	142	135	**	121	118	115
42	**	**	139	**	124	121	119
43	**	**	143	**	128	124	123
44	**	**	**	**	131	126	126
45	**	**	**	**	134	131	130
46	**	**	**	**	137	134	134

TABLE 3. (*Continued*)

	Electric tapper			Manual tapper			
Age[a]	6	7	8	9	10	11	12
M	27.2	30.01	32.03	30.31	34.04	35.06	36.66
SD	3.3	3.9	3.8	3.3	4.8	4.8	4.1
47	**	**	**	**	140	137	137
48	**	**	**	**	143	140	141
49	**	**	**	**	**	143	**
50	**	**	**	**	**	**	**

Note: Standard scores ($M = 100$, $SD = 15$) were calculated based on the metanorms developed by Findeis and Weight (1993).
[a] 6- to 8-year-old norms are for the electric fingertapper; 9- to 12-year-old.
norms are for the manual fingertapper.
* Standard scores greater than three standard deviations below the mean.
** Standard score greater than three standard deviations above the mean.

TABLE 4. Fingertip Symbol/Number Writing – Right Hand

	Fingertip symbol writing				Fingertip number writing					
Age	5	6	7	8	9	10	11	12	13	14
M errors	6.00	3.50	2.70	2.05	4.36	3.25	2.75	2.00	0.50	0.50
SD	3.00	2.50	2.00	1.50	3.73	3.01	2.00	1.00	0.55	0.40
Raw score										
0	130	121	120	121	117	116	121	130	113	119
1	125	115	113	111	113	111	113	115	86	81
2	120	109	105	101	109	106	106	100	59	*
3	115	103	98	91	105	101	98	85	*	*
4	110	97	90	81	101	96	91	70	*	*
5	105	91	83	71	97	91	83	55	*	*
6	100	85	75	61	93	86	76	*	*	*
7	95	79	68	*	90	81	68	*	*	*
8	90	73	60	*	86	76	61	*	*	*
9	85	67	*	*	82	71	*	*	*	*
10	80	61	*	*	78	66	*	*	*	*
11	75	55	*	*	74	61	*	*	*	*
12	70	*	*	*	70	56	*	*	*	*
13	65	*	*	*	66	*	*	*	*	*
14	60	*	*	*	62	*	*	*	*	*
15	55	*	*	*	58	*	*	*	*	*

* Standard scores greater than three standard deviations below the mean.
Note: Standard scores ($M = 100$, $SD = 15$) were calculated based on the normative data developed by Spreen and Gaddes (1969).

Interpretation of Children's Performance on Neuropsychological Batteries

In the past, a number of approaches have been applied to the interpretation of children's performance on neuropsychological tasks (Fletcher & Taylor, 1984; Taylor & Fletcher, 1990; Fletcher, Taylor, Levin, & Satz, 1995; Reitan & Davison, 1974; Rourke, Bakker, Fisk, & Strang, 1983; Selz, 1981; Teeter, 1986; Baron, 2004). These various approaches and their limitations will be discussed below.

Level of Performance

In this approach, the child's level of performance on neuropsychological measures is compared with normative data, such as the norms developed by Spreen and Gaddes (1969), Knights and Norwood (1980), and Findeis and Weight (1993). If the child's performance falls significantly below (e.g., two standard deviations below the mean) what would be expected for her or his age, then a deficit is diagnosed in the particular area measured by the neuropsychological task. For example, on the Finger Tapping Test, the mean performance for a 9-year-old boy is 40.4 (SD = 4.87) (Cramond & Jones, 2005) for the dominant hand. Using the level-of-performance approach, if a 9-year-old boy obtained a score of 30, fine motor speed with the dominant hand would be interpreted as impaired.

There are a number of disadvantages to relying solely on this method for the interpretation of children's neuropsychological test performance. First, because of the large variability in normal children's performance on neuropsychological measures, it is often difficult to interpret the individual child's scores. For example, the mean performance for an 8-year-old on the Tactual Performance Test (dominant hand) is 5.71 min, but the standard deviation of 6 min is greater than the mean (Knights & Norwood, 1980)! If a two-standard-deviation cut-off is adhered to for interpreting a deficient level of performance on this task, the child would be required to continue for over 17 min in order to diagnose impaired performance. Even if the Findeis and Weight (1993) metanorms are used (see Table 2) an 8-year-old would be required to continue for over 8 min to reach a two-standard-deviation cutoff. As any experienced examiner knows, it is often quite difficult to keep a blindfold on an impulsive 8-year-old for that length of time.

Another problem that is encountered when using only the level of performance to interpret children's neuropsychological performance is the tendency to yield a large number of false positives. This is largely because so many factors other than impairment can negatively influence a child's performance (e.g., motivation, attention, frustration tolerance) (Rourke et al., 1983; Baron, 2004).

Pathognomonic Signs

The pathognomonic signs (e.g., hemiplegia, aphasia, hemisensory deficit) approach refers to the identification of specific deficits that are not commonly seen in normal individuals. For example, articulation errors on the Aphasia Screening Test could be interpreted as an aphasic "sign." Again, one of the limitations of this approach would be the large variability seen in the normal population. For example, because of the wide variation in the development of language abilities in children, it is often quite difficult to interpret specific errors made by the individual child. There may be a tendency to interpret as abnormal an isolated error made by the child.

Conversely, it has also been found that the sole use of the pathognomonic signs approach has a tendency to yield a large number of false negatives. For example, Boll (1974) found that 26 of 35 children with known brain damage were misclassified as normal when this approach was used to classify subjects. One reason for this is the variability in outcome that can be associated with neurological insult in the developing child (Spreen, Risser & Edgell, 1995). For example, such conditions as infantile hemiplegia may show considerable plasticity and recovery of function (see Bigler & Naugle, 1985), and their neuropsychological test performance may not conform with what would be expected with a more recently acquired brain lesion. In contrast, the effect of an early insult, such as a frontal lobe injury, may remain functionally occult or hidden until a later time in the child's development (Kolb, 1989).

Patterns of Performance

In this approach, the relationship among performance on neuropsychological measures is examined. If large discrepancies are noted, then strengths and weaknesses are interpreted. For example, a child who does very well on the Speech Sounds Perception Test and the verbal items from the Aphasia Screening Test, but who performs poorly on the constructional tasks of the Aphasia Screening Test and poorly on the Tactual Performance Test Memory and Locations subtests, may be interpreted as having adequate auditory processing but deficits in the area of nonverbal, visual/spatial functioning.

This approach is of limited use in the interpretation of neuropsychological performance of very young children and children with severe disabilities (Rourke et al., 1983). However, it has been used quite extensively in the subgrouping of children with LD (Nussbaum & Bigler, 1986; Rourke, 1984; Korhonen, 1991).

Comparison of Right and Left Body Sides

This approach compares the relative performance of one body side to the other on motor and sensory–perceptual tasks. For example, a large discrepancy between the right (dominant) and the left (nondominant) hand on the Finger Tapping Test, with the right-hand score less than the left-hand score, may indicate impairment in left-hemisphere functioning. However, once again, because of the wide variability in the performance of normal children, discrepancies between performance on the right and left body sides may often be difficult to interpret for the individual child. This is especially true of the younger child.

Multiple Inferential Approach

Boll (1974, 1981) proposed a multiple inferential approach to the interpretation of children's neuropsychological performance because of the limitations of the isolated use of the approaches discussed previously. In the multiple inferential method, the complementary use of level of performance, pathognomonic signs, pattern analysis, and right/left comparisons is employed in the interpretation of neuropsychological performance. This approach minimizes the limitations that are encountered when these methods are used in isolation.

Rules Approach

The rules approach developed by Selz and Reitan (1979b) also combines a number of inferential methods in the interpretation of children's neuropsychological performance. The rules are based on the four methods of inference discussed earlier: level of performance, pathognomonic signs, pattern analysis, and right/left differences.

The rules were initially developed and validated as an objective system for classifying children aged 9–14 years as normal, learning disabled, or brain damaged. The rules were derived using neuropsychological data from three samples of 19 children and subsequently validated on three samples of 25 children. The rules system consists of a four-point scoring method in which 37 aspects of neuropsychological performance are rated on a scale from 0 (normal to excellent performance) to 3 (very abnormal performance). For example, a child who made nine or more errors on the Tactile Finger Recognition task would receive a score of 3 (impaired) using the rules system. In summary, the rules approach is an attempt at providing an objective system to measure the degree of impairment in the neuropsychological performance of children.

Neuropsychological Deficit Scale

Similar to the multiple inferential approach and the rules approach, the methodology used with the Neuropsychological Deficit Scale (NDS) involves the combination of level of performance, right–left comparisons, and the consideration of dysphasia and other deficits. The NDS developed by Reitan and Wolfson (1992) employs cutoff scores to gauge the examinee's neuropsychological functioning. The examinee's performance is compared to individuals with brain damage to determine overall performance via the NDS. Also, Reitan and Wolfson have recommended that the examinee's NDS score be compared to the brain damage sample for the following domains: Motor functions, sensory–perceptual functions, attention and concentration, immediate memory and recapitulation, visual spatial skills, abstraction and reasoning, and dysphasia. Finally, it is recommended by Reitan and Wolfson that the data gathered from the NDS scores be used as a framework for the interpretation of other data, in particular, measures of cognitive ability, academic achievement, and personality.

Biobehavioral Approach

The biobehavioral approach is another method that has been proposed for the interpretation of children's neuropsychological performance (Taylor & Fletcher, 1990). In this model, there are four basic factors that differentiate child neuropsychological assessment from other types of child assessment.

First, neuropsychological evaluation involves the assessment of four types of variables: (1) the manifest form of the disability or *presenting complaint* [e.g., the impulsive behavior of the child suspected of having attention deficit/hyperactivity disorder (ADHD)]; (2) the *cognitive* and *psychosocial* characteristics (data from formal measures of attention, emotional functioning, and so on) of the child; (3) the *environmental, sociocultural, and historical* variables (e.g., classroom setting, home setting); (4) the *biological and genetic* variables (e.g., parental history of ADHD, maternal prenatal alcohol use).

Second, it is recognized that although the manifest disability is at least partially based on weaknesses in basic neurocognitive functioning, these interact with other child characteristics and environmental influences. The extent to which these cognitive weaknesses result in the manifest disability is influenced by these other factors, which may either intensify or diminish the disability.

Third, although there is often a high degree of covariation among skills, an increased amount of variability is often characteristic of many children with disabilities. Thus, it is important to analyze the child's assessment profile in terms of strengths and weaknesses in order to understand how they are expressed in the manifest form of the disability. For example, a child who has ADHD and an auditory processing disorder may have even greater attention problems in a noisy environment.

Fourth, although there are some childhood disorders and manifest disabilities that have very strong neurological influences (e.g., learning difficulties in a child with hydrocephalus), one also must take into account environmental factors. When interpreting neuropsychological data, the relevance of the central nervous system can only be determined by taking into account both biological limitations and environmental variables.

This model avoids the tenuous inference involved in the interpretation of direct brain–behavior relationships in children using behavioral data. Rather, the biological or neurological substrate is seen as influencing the manifest disability by imposing limits on the basic behavioral competencies of the child. Additional moderator variables, such as the family system and the educational setting, are also taken into consideration.

Furthermore, the relationship between performance on neuropsychological measures and the manifest disability is not seen as causal but instead as correlational. Thus, performance on neuropsychological measures is used to clarify various functional aspects of the child's manifest disability. For example, the ADHD child's performance on neuropsychological measures can help to determine the degree of cognitive impulsivity present in the disorder. In this example, the functional aspects of the child's performance would be stressed in the interpretation of the neuropsychological data. Also the importance of interpreting neuropsychological data in a developmental context is emphasized in this model.

Pragmatic Approach

More recently, a pragmatic model has been discussed as a method for approaching neuropsychological assessment in children (Baron, 2004). The pragmatic approach, as described by Baron, is a fluid non-battery approach, where tests are chosen to explore various aspects of functioning based on the child's history, presenting problem, and performance during the assessment. In this model, it is recognized that the utilization of a fixed battery may include measures that have limited clinical utility and/or may be lacking in measures to assess relevant aspects of functioning for the particular child.

In the pragmatic approach, as in the biobehavioral approach, an emphasis is placed on understanding the child's strengths in order to understand any observed weaknesses. The pragmatic approach is similar to dynamic models, where identifying the child's capabilities as well as weaknesses is stressed. By developing this type of understanding, it allows for the effective use of strengths to address any particular weaknesses noted.

In addition, through the dynamic sampling of behavior using various measures, the neuropsychologist is able to be sensitive to the needs of special populations, developmental levels, and cross-cultural assessment issues. According to this model, the evaluation is tailored to the child, so that interpretative conclusions are supported by relevant test data.

For example, a 10-year-old child is referred for general problems with learning in school. She is noted to have a history of mildly delayed early

language development. Her performance on measures from the CHRNB reveals adequate spatial abilities on the Tactual Performance but poor performance on the Speech Sounds Perception Test and aspects of the Reitan Aphasia Screening Test. In interacting with the child, the neuropsychologist notes that she often needs questions and directions repeated and rephrased.

The child's performance on the CHRNB and clinical observation leads the neuropsychologist to employ additional measures to explore hypotheses regarding possible underlying memory deficits that may be contributing to the child's poor learning. The neuropsychologist finds that the child performs excellently on the memory portion of the Rey-Osterreith Complex Figure Design (Denman, 1984) and the Abstract Visual Memory Subtest from the Test of Memory and Learning, Second Edition (TOMAL–2) (Reynolds & Bigler, 2007), but she demonstrates poor performance on the California Verbal Learning Test – Children's Version (Dellis, Kramer, Kaplan, & Ober, 1994) and the Memory for Stories subtest from the TOMAL. Additional testing in receptive and expressive language functioning and specific aspects of academic functioning also would likely be carried out.

The information regarding the child's strengths and weaknesses gathered from this type of pragmatic approach would serve as guide to more targeted intervention. For example, understanding the child's strength in spatial abilities and visual memory would suggest learning strategies involving the use of charts, hands-on demonstrations, and visual mapping of verbal material.

Applications

The CHRNB has been used extensively in research and clinical settings. Although the RINB and CHRNB were originally developed to assess brain damage in children, they also have been used extensively to better understand various functional abilities. As such, in general clinical practice, the assessment of specific strengths and weaknesses may be the most widely used application of these measures. Through the use of the RINB and the CHRNB, information can be obtained concerning certain aspects of sensory functioning, motor abilities, auditory processing, attention, spatial abilities, visuospatial abilities, visuomotor abilities, conceptual processing, sequential processing, and language functioning. Therefore, although the RINB and the CHRNB are often used in the evaluation of organic dysfunction in children, they also have a great deal of clinical utility as measures of behavioral competencies in children. In regard to this use of the RINB and the CHRNB to assess behavioral functioning, Fletcher and Taylor (1984) proposed that the greatest clinical utility of these instruments is in their usefulness in defining the ability structure of the child. They argued that the widest clinical application of the children's neuropsychological batteries is related to the clinical sensitivity of these measures to the child's behavioral strengths and weaknesses.

An issue that must be addressed thoughtfully when discussing the use of the CHRNB is the issue of its use in toto as a fixed battery or its inclusion in a flexible or dynamic battery. The CHRNB and RINB were developed as fixed batteries to include a formalized selection of tests and assessment techniques that were originally conormed, although much of the subsequent normative data was not collected on the complete battery (Findeis & Weight, 1993).

There are a number of advantages to prepackaged or fixed batteries, such as the CHRNB, the Wechsler Intelligence Scale for Children – IV (Wechsler, 2003), the Kaufman Assessment Battery for Children–II (Kaufman & Kaufman, 2004), or the NEPSY–II (Korkman, Kirk, & Kemp, 2007) to name a few. There is the familiarity with the battery that lends itself to fluency in test administration and scoring. Also, the neuropsychological interpretation of test results is facilitated when subtests within a fixed battery have been standardized, conormed, and validated as a battery (Russell, Russell, & Hill, 2005). This allows for a more straightforward understanding of how subtests relate to one another. In addition, the prepackaged batteries may have an advantage in the forensic realm, in that it has been argued that they may be more likely to withstand a "Daubert" challenge (Daubert v. Merrell Dow Pharmaceuticals, 1993), because of numerous articles reporting on the reliability or validity of the fixed battery (Lezak, 2002).

Unfortunately, the prepackaged battery can have serious limitations in many clinical situations. These types of fixed or set batteries

are often limited in the type of information they provide for certain clinical conditions or aspects of neuropsychological functioning, such as certain components of perceptual, communication, and executive functioning (Benton, 2000; Crawford, 1992; Lezak, 1995).

As noted previously, child neuropsychology grew out of adult neuropsychology, where the field was first concerned with understanding the effects of specific neurological insults, such as missile wounds, tumor, and cardiovascular accidents. Similarly, the first child neuropsychology studies involved the validation of the HRNB for children (CHRNB) with known neurological insults. Subjects were divided into a dichotomous category of Brain Damaged or Normal.

There may be some research and forensic situations where the salient question is Brain Damage versus Not Brain Damaged, but frequently, even in forensic situations, the functional implication of brain damage is a very relevant issue after injury has been established by other means (e.g., scanning procedures). In order to thoroughly answer these types of questions, more in-depth measures of neurocognitive functioning are required.

As the field has progressed, clinical neuropsychological assessment has been applied to a wider variety of pathological conditions and assessment situations. The clinical neuropsychologist may be asked to assess a child for reasons ranging from the evaluation of baseline functioning prior to the onset of intracranial radiation, to the effect of a traumatic brain injury, to delineating strengths and weaknesses associated with a developmental learning disability. The setting for the assessment may range from inpatient hospital to outpatient clinic to the school setting.

Often the clinical neuropsychologist is asked to provide in-depth information regarding a specific domain of neurocognitive functioning, such as attention or memory. Similarly, the child neuropsychologist may be asked to evaluate a child with a specific medical condition that requires more in-depth assessment of a specific area of functioning. For example, it would be important to thoroughly assess new learning and memory in a child referred with a traumatic brain injury.

The CHRNB has serious limitations as a stand-alone battery in regard to this type of in-depth assessment. For example, in the memory domain, while many of the CHRNB subtests require aspects of memory, none of them address it directly. Basically, there are no in-depth measures of narrative recall, recognition memory, verbal learning, or visuospatial memory (Baron, 2004). The 9- to 14-year-old battery has a very limited auditory memory component involved in the SSPT and the SRT. Perhaps, a remote memory component could be found in the naming tasks from the Reitan Aphasia Screening Test, and in the alphabet and numbered aspects of Trails, Finger Localization, and Fingertip Graphesthesia. Also, Subtest VI from the Category Test involves recall of the correct principal employed in the previous five subtests. These subtests require several other functional skills; disruption of any one causes poor performance. Hence, there is a trade-off between sensitivity (e.g., brain damage versus not brain damage) and specificity (e.g., Memory, Executive Function, Sensory Processing).

This issue is also illustrated in the adult literature. Baron (2004) cites a factor analysis of the HRNB, Wechsler Adult Intelligence Scale (WAIS), and the Wechsler Memory Scale-Revised (WMS-R), where it was found that the HRNB tests loaded with WAIS factors of Perceptual Organization and Processing Speed, and with a WAIS/WMS-R attention factor, but no support was found for an HRNB memory component.

Similarly, the Therapeutic and Technology Assessment Subcommittee of the American Academy of Neurology discussed the use of the HRNB to assess neurologic function in the journal Neurology (1996). It was noted that more recent measures in combination with traditional tests could be useful in providing insight into neurocognitive functioning associated with different disease states.

The type of referral question asked will serve as a guide for the assessment procedures required in the evaluation of the patient. If the assessment question pertains to whether or not a child has underlying brain dysfunction or not, then the CHRNB or RINB demonstrates good sensitivity for addressing this specific type of question. A fixed battery approach using the CHRNB or RINB would be quite appropriate.

In certain situations, our need to understand the complexity of the behavioral manifestation of brain function may fall beyond the capacity of single standardized battery to fully

cover important components of neuropsychological functioning (Baron, 2004). Important areas of functioning may require the addition of more specialized examination techniques or tests (Larrabee, 2005). For example, if a referral involves the question of a child with a traumatic brain injury, and their learning, academic, and psychosocial needs upon returning to school, then it would be appropriate to construct a flexible battery including measures with good specificity regarding those needs. It is more likely that critical areas of competency and dysfunction would be better understood by incorporating relevant component tests from a prepackaged battery, such as the CHRNB into a core or flexible battery, and then adding selected tests to more thoroughly explore these specific concerns (Bauer, 1994; Stringer, 1996; Yedid, 2000).

In addition, practical time considerations may be an important factor in choosing to incorporate relevant subtests from the CHRNB into a flexible battery. In a survey study conducted by Camara, Nathan, and Puente (2000), the mean time reported for administration, scoring, and interpretation of the adult HRNB was 6.66 h. Similarly, it has been estimated that the CHRNB and RINB may take anywhere from 5 to 10 h for a trained examiner to administer (Strub & Black, 1988). If additional measures, such as intelligence, academic, continuous performance tests, are required, then the assessment may become unrealistically lengthy. Thus, in practical terms, it may be necessary to create a flexible battery incorporating relevant parts of the CHRNB and other measures that are tailored to the referral questions and presenting problem.

In the forensic realm, some have contended that a fixed battery is the only acceptable validated procedure (Hom, 2003; Russell et al., 2005). However, this does not seem to be the standard of practice as evidenced by findings based on a survey of forensic evaluations by 100 examiners identified as experts in neuropsychology from 20 states and the province of Ontario, Canada (Lees-Haley, Smith, Williams, & Dunn, 1995). Many neuropsychologists were not using the HRNB in a traditional fixed manner. For example, the study reported that in 48% of the evaluations, Trails A was employed, the Tactual Performance Test was used in 26%, Grip Strength was used in 17% and the Reitan Aphasia Screening Test was employed in 12%.

Obviously, many of these evaluations did not include the complete HRNB. Similarly, only 10% used the Luria Nebraska Neuropsychological Battery (Golden, Purisch, & Hammeke, 1985).

Furthermore, the superiority of the HRNB in a fixed battery over other neuropsychological measures is not supported in empirical studies. For example, it was found that the WAIS-R and the HRNB were equivalent in sensitivity to the presence of brain damage (Sherer, Scott, Parsons, & Adams, 1994). Similarly, Rohling, Meyers, and Millis (2003) found that a flexible battery showed the same association with head injury severity found by Dikmen, Michamer, Winn, and Temkin (1995) using an HRNB augmented by the WAIS and memory procedures such as the Verbal Selective Reminding test.

As part of a flexible battery, the CHRNB may be included as a whole and combined with other measures, or only parts of the CHRNB may be combined with other assessment procedures. Based on a survey conducted by Sweet, Moberg, and Suchy (2000), it appears that the majority of neuropsychologists use the adult HRNB in more of a flexible battery approach. Unfortunately, data were not available on the use pattern of the CHRNB, although it is likely that a similar pattern would be seen.

Summary

In summary, the CHRNB and the RINB were developed by Reitan (Reitan & Davison, 1974) based on the adult version of the Halstead–Reitan Neuropsychological Test Battery (Reitan & Wolfson, 1985). The development of these batteries represented a significant contribution to the understanding of children's neuropsychological functioning. Since that time continued progress has been made in this field, particularly in the advancement of assessment models that promote a more in-depth understanding of the child's strengths and weakness, as related to underlying brain function.

In terms of future directions for the CHRNB and RINB, if the CHRNB is to remain relevant and employed as a battery, then it should be updated with broader and more in-depth measures, particularly in areas such as memory and attention. The demands of clinical practice require a more sophisticated battery that is able to respond to more complex

questions of neuropsychological functioning, brain/behavior relationship, and treatment. Also current psychometric standards in the field require better developed norms with a large representative sample incorporating consideration for gender, geography, ethnicity, and SES (Strauss et al., 2006).

Where would we be if there had not been keen clinicians, academicians, and theorists such as Piaget, Luria, Reitan, and Kaplan, whose foundational observations and assessment experimentation laid the groundwork for modern neuropsychological assessment techniques and interpretation? We must continue to promote this type of innovative thinking in evaluation techniques if we are to avoid the "petrification of assessment procedure" referred to by Lezak (2002). The CHRNB and RINB have been very useful assessment techniques that could continue to be essential to the field. However, it will be important to breathe new life into these batteries and interpretive models associated with them, if they are to avoid fossilization and irrelevancy over time.

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12

The Nebraska Neuropsychological Children's Battery

CHARLES J. GOLDEN

Beginning in the mid-1970 s, there was increasing interest in the application of the theories and assessment procedures developed by the Russian neurologist A. R. Luria. Luria's theories integrated sophisticated analysis of the way in which the brain is organized in the individual client along with a series of assessment procedures and rehabilitation techniques that were attractive to the newly developing area of clinical neuropsychology. Among these interests was the adaptation of Luria's testing procedures for U.S. audience.

Adaptation of Luria's work was hampered by the need to translate Luria's open-ended, qualitative evaluations into a more standardized format consistent with U.S. approaches to psychological assessment (as contrasted to neurological assessment techniques). For children, this was first attempted by Lawrence Majovski in an unpublished manuscript. Majovski had studied with Luria shortly before Luria's death and so was intimately familiar with his approach.

The Luria–Nebraska Children's Battery was an amalgamation of some of Majovski's work along with terms and procedures selected from the adult version of the Luria–Nebraska. Following completion of this first test for 8- to 12-year olds, Golden and his associates embarked on a decade-long study to develop a second form, initially the LNNB-3, which integrated the adult and child versions to produce a more comprehensive single battery applicable from ages 5 through adulthood.

The present chapter will focus on the development of these tests and most directly on the issues around neuropsychological assessment and interpretation in children using these tests. Specifically, it will look at several issues: (1) the process of development of the original battery; (2) a description of the original battery with a brief review of current research; (3) methods of interpreting the original test battery; and (4) current research studies (on the LNNB-3) aimed at improving the test battery and extending its usefulness to lower ages.

Development of the Battery

The original development of the battery was begun by administering the adult LNNB to children from ages 5 to 12. It was discovered that children of age 8 and up could do a majority of the procedures used in the adult battery. It was also found that those items in general corresponded to those that one would expect from Luria's theories on brain development. It was also found that below age 8, drastic changes were needed in the battery content to have a useful test. Thus, it was initially decided to develop a test down to age 8.

Similarly, it was found that 13- and 14-year olds could perform adequately on the adult

CHARLES J. GOLDEN • Center for Psychological Services, Nova Southeastern University, Fort Lauderdale, Florida 33314.

battery (which was originally intended to extend down to age 15). At the 12-year-old level, children began to show difficulties with the adult battery (although above-average 12-year olds can also perform normally). Thus, it was decided that the adult battery could be used down to age 13 and that the new children's battery should aim at ages 8–12. A battery for younger children was postponed until completion of this work and is described in the last section of this chapter.

Items were deleted from the adult battery that appeared to be too difficult for initial normative youngsters in this age range. When possible, similar but easier items were substituted. We were also privileged to consult with Dr. Lawrence Majovski who was working on developing a qualitative approach to the assessment of children based on his studies with Luria. We were able to adapt and add several additional items and areas of examination to the test from his suggestions. This initial work consisted of three successive versions of the test that were evaluated on groups of normal and impaired children until the fourth and published version was completed.

Description of the Battery

The final version of the children's battery consisted of 11 basic scales (as for the adult battery) and 149 procedures. However, most of these procedures consist of numerous items so that the actual number of items exceeds 500. Administration takes about 1½ to 3 hours depending on levels of cooperation and levels of impairment.

This version was given to 125 children. The group consisted of 25 normal children at each of five age levels: 8, 9, 10, 11, and 12. Performance norms were developed on each procedure and scale based on the performance of this group. The first task was the development of scale scores for each item. It was decided to have different scale scores for each age group on each item so that scores for a given individual could be directly compared. For each procedure, a score of 0 was set to mean a performance within one standard deviation of the mean score for the age group. A score of 1 represented a performance between one and two standard deviations below the mean, and a score of

2 represented scores more than two standard deviations below the mean.

Each item of the test was assigned to 1 of the 11 basic scales. Originally, this was done on the basis of our experience with the adult battery and on our theoretical belief of where items should load. From this assignment, scale raw scores were calculated by adding up the scaled score on each procedure to yield a total raw score. Procedures were then correlated with each of the raw scores to ensure that procedures correlated highest with the scale they were assigned to, so that items could be recognized when necessary.

After final scale assignments were determined, scale T scores were generated by first calculating the means and standard deviations of each of the original 125 normal subjects. An ANOVA for each scale score by age indicated no significant differences between the scale mean scores for each age group, and F tests indicated no significant differences among group variances. As a result, the conversion of scale raw scores to T scores was done on the basis of all 125 subjects rather than for each age group alone.

Each of the 11 scales is multifactorial in structure. This was done for several reasons. First, each scale was conceived not as covering a specific skill but rather as a domain of skills in a given area (such as motor function). Second, this allowed the test to yield stable test scores (which are related to the number of items on the scale as well as the individual stabilities of the items) with fewer items in each skill area. This has the positive effect of allowing for a broader coverage of skills in a reasonable period of time. This has the drawback, however, of not covering any one area in as much detail as possible. This is remedied by simply following the LNNB with specifically selected testing in areas in which more information is needed after examining the LNNB performance, and by using qualitative observations to enrich the data generated by quantitative analysis alone.

The original test scales (which are described in detail later) were labeled Motor, Rhythm, Tactile, Visual, Receptive, Expressive, Reading, Writing, Arithmetic, Memory, and Intelligence. In addition to the basic scales, the 149 items were factor analyzed in a population of 719 brain-damaged and normal children. The resulting factors were impressive in that few of the factor scales used items from multiple scales, suggesting

that item placement was essentially correct. Some factor scales simply repeated what the regular scales already yielded, and some failed to achieve reasonable stability. Those scales that were both stable and yielded new information were kept for further study.

A second analysis involved the factor analysis of each scale alone. Many of the resultant factors duplicated factors found in the first analysis and were discarded, as were factors that were insufficiently stable. At the end of this process, 11 additional scales were derived, 2 of which were cross-scale factors and 9 of which were intrascale. For each of these 11 scales, T scores were derived on the basis of the performance of 240 normal children in the overall sample.

The 11 factors were briefly described as: (1) academic achievement, the largest cross-scale factor including reading, writing, arithmetic, and expressive items; (2) spatial organization, the second major cross-scale factor; (3) purposeful unspeeded movement; (4) motor speed; (5) drawing quality; (6) drawing time; (7) rhythm perception and reproduction; (8) basic tactile function; (9) basic receptive language skills; (10) repetition; and (11) abstract verbal skills.

For those readers interested in the details of general research on the battery, the test manual (Golden, 1986) offers the most complete and detailed account of this work. Other reviews may be found in Plaisted, Gustavson, Wilkening, and Golden (1983). In general, research has examined the ability of the test to discriminate between brain-damaged and normal subjects (with hit rates of about 86%), and other studies have examined correlations between the LNNB and such tests as the PIAT and the WISC-R. As reported in the test manual, this work has generally confirmed the validity of the LNNB scales. Other work has evaluated the effectiveness of the test with such groups as children who are learning disabled or who have epilepsy.

Interpretation

Of prime importance with any test battery are the methods of interpreting the battery. This is especially important with the LNNB-C for many because the process is often different from the procedures used with other tests. In interpreting the LNNB-C, little confidence is placed in formal interpretations of elevations on individual scales, a major reason being that these are clearly not homogeneous scales with many items intended to measure not just one ability but rather a domain of abilities. As a result, a single interpretation of an elevation on any particular scale would be ludicrous and possibly lead to obscure diagnostic errors. Thus, pattern analysis of the scales and items, combined with a qualitative analysis of the test performance, is the major approach to interpreting scale profiles.

Levels of Interpretation

When interpreting the LNNB-C, or other similar batteries, it is important to be aware that the many levels on which the battery can be interpreted depend on the needs, as well as the skill and knowledge, of the user. While the LNNB-C has clear rules for classifying children derived from research and clinical practice, the major goal of the battery is an analysis of the way in which the child functions cognitively and the implications for rehabilitation or educational planning.

As a consequence, the first two levels of analysis are considered preliminary to a full analysis consisting of all of the steps outlined below. The first level is primarily concerned with ascertaining whether significant brain injury exists in a given child. The test can determine the probability of such a classification, although the concept of "brain injury" in children is complicated by the difficulty of differentiating genetic and early developmental disorders from brain damage. Luria's theories emphasize that the organization of the brain in the child is as sensitive to environment as it is to the structure of the brain. Thus, environmental factors, especially when extreme, can lead to conditions that appear very similar to brain injury. When there is a high likelihood of brain damage, children must be referred for a more sophisticated evaluation of the data. On the other hand, because most children are seen initially by nonneuropsychologists, this level of practice is quite important to determine which children should be referred for further evaluation.

The second level of interpretation involves simple description of what the child can and cannot do, without drawing any conclusions or reaching any integrative statements. This level is enhanced by the qualitative analysis of the data.

The qualitative or process analysis requires an identification of the basic reasons why an individual erred in a given item as well as any unusual ways in which the person got specific items right. The LNNB-C includes 66 qualitative categories that are used to classify specific performance on each item as well as extratest behavior. The latter application is especially important as the battery is designed to generate a large number of conditions for the child to react to, which can yield abundant behavior and insights far beyond the basic quantitative score. Thus, the examiner is encouraged not only to score the items but to observe and test for why items were missed.

This step is enhanced by the test standardization that allows flexibility in administration in many areas. This flexibility is limited within each scale by the specific quantitative purpose of the scale (e.g., receptive language items cannot be repeated when misunderstood, expressive speech items can be repeated). This procedure allows the examiner to search for methods that maximize the child's accuracy and effectiveness. By noting these methods within the qualitative scoring and in general observation, the process of giving the test can yield valuable rehabilitative cues.

The third level of interpretation takes the second level to the next logical step: identification of the probable underlying causes of the child's overall behavior. This step requires extensive understanding of the various brain–behavior relationships. The interpretation process generally evolves from a theoretical orientation of how the brain functions and the ways in which information is processed through the central nervous system.

Finally, the fourth level of interpretation involves the integration of all findings and conclusions into a description of how the brain of the individual is functioning. This is a difficult task in most cases, because the result of brain damage is affected by a variety of factors. In many cases, this last level of interpretation concerns the understanding of basic underlying deficits rather than simply determining location. Our goal is not to understand location per se, but rather the functional localization of a disorder, i.e., how does it affect the ability of the brain to function in a normal manner? By an analysis of the functional localization we develop a map of the child's strengths and weaknesses.

In general, there has been too much emphasis in neuropsychology on localization of lesions to the exclusion of understanding the individual being tested. Physical localization of a lesion can be generated from detailed functional analysis, but in most cases this is an academic rather than a useful exercise (the exceptions to this lie primarily in the forensic arena and occasionally in identifying an unsuspected acute lesion). Actual physical localization in children is complicated by the fact that early lesions can dramatically change the normal organization of the brain so that the normal relationships between function and location are severely disrupted.

The study of function allows us to generate testable hypotheses about the child's cognitive behavior as a whole. By testing these hypotheses we gradually develop a fully integrated analysis of how the individual child functions neuropsychologically, which allows us to understand the child as an individual. This information *must* be integrated with personality, family, environmental, and social data before a complete and fully formed picture can emerge. In too many cases, unfortunately, the analysis is never completed to this level, which lessens the value of the neuropsychological data.

Identifying Brain Damage

Use of the Critical Level

Adjusting for Age. The first step in identifying when a profile is statistically abnormal and likely to be indicative of brain damage is based on establishing a valid critical level for the child. The critical level represents the highest LNNB-C score that can be considered normal for the battery. In contrast to some other tests, this cutoff level is variable with the LNNB-C, and is adjusted for age.

Identifying Deviant Scores. Once the critical level has been established using the appropriate formulas, determining the probability of brain damage is relatively simple. The number of scales on the battery that exceed the critical level is counted, yielding the number of abnormal scores. The scores that are considered at this point are the basic clinical scales (C1–C11). *In general, three or more scores above the critical level are thought to be indicative of brain damage, whereas zero or only one elevated scale suggests*

the probable absence of brain damage. If the critical level has been chosen correctly, the accuracy of this decision is about 75–85% of all cases. The likelihood increases as the number of elevations increase. Other rules may be applied to further refine the assessment at this level, especially in borderline cases.

Interpreting Scale Patterns

Factors Affecting Scale Interpretation

It is important to recognize that injuries in any part of the brain can potentially affect the scores on any of the scales of the battery. This reflects the relatively homogeneous content of the scales with respect to secondary skills that are measured in conjunction with the primary skill as denoted by the scale label. Despite this caution, hypotheses may be generated from individual scales and overall patterns of scores if proper caution is used in recognizing the wide ranges of factors that affect the neuropsychological performance on a given scale. For example, a child may have such severe expressive language problems that any item that requires any verbal response, no matter how simple, may be missed. Similarly, severe receptive language problems may make it impossible to adequately communicate instructions to the child. Although the administrative procedures attempt to minimize the effects of these disorders, in some cases it is not possible to eliminate these factors. Similarly, children with severe peripheral deficits or brain stem injuries may appear to have more severe cognitive injuries than are actually present. These problems are unfortunately common to all standardized tests. To an extent, the identification of these factors through the qualitative scoring is possible, although interpretation of these indices is not as well established as for the quantitative scores.

Other factors that cause changes in scale elevations as well as overall patterns include a wide variety of neurological factors. One of the most important factors is the duration of the brain disorder, and whether or not it is still present. In general, the acute disorders, i.e., those that are continuing, will affect LNNB-C scores much more significantly than will disorders from which the child has had 3–6 months or more to recover.

The size of the lesion must be considered along with the question of chronicity. In individuals with disorders that resolve themselves without structural damage to the brain, LNNB-C scores will return essentially to normal, reflecting the child's recovery of all major skills. The examiner should nevertheless be alert to specific items, even on normal scales, that the child may fail to adequately perform and that may reflect residual damage. It is important to notice these factors, as they are often useful in explaining specific problems the child may be having that were not noticed before the damage occurred, as well as in designing specific rehabilitation training.

Another important aspect is the location of the damage. Brain damage in each hemisphere is expressed very differently on the pattern of scores, as is brain damage in different locations within a single hemisphere. In general, the LNNB-C is more sensitive to the disruptive effects of left hemisphere lesions.

The cause of the brain dysfunction also represents a major problem with respect to the battery's results. Brain dysfunction may be caused by a wide range of problems: from overt structural damage to metabolic disorders and idiopathic problems that have no clear genesis. In general, those disorders that destroy brain tissue cause much more damage to the brain and therefore cause more highly significant deviations on the LNNB-C battery. Disorders such as idiopathic epilepsy, which may not have a clear structural focus or clear cause, may produce relatively little damage.

A final consideration is the premorbid level of the individual. Specifically, an individual with higher skills prior to a given brain injury will have higher skills afterward than would a person with overall lower initial cognitive skills; the person with higher cognitive skills can more easily reorganize brain function to adapt to the loss in specific areas. An individual who is extremely intelligent prior to an injury may show only motor and sensory signs with relatively few cognitive deficits in the abnormal range even after a significant injury, because the person's skills have simply been reduced from above average to average. In these cases, one must be sensitive again to the pattern of items missed by the child that may indicate brain dysfunction. One obvious problem with

children is that we may not have an idea of what the "premorbid" level was.

For the reasons discussed above, interpretation of the LNNB-C typically focuses more on scale patterns and on intrascale variability than on interpretation of scale elevations per se. Scale patterns have the advantage of allowing the user to make deductions about the reason a given scale was impaired. For example, in profiles in which C5 (Receptive Speech) is the highest score, one can hypothesize that deficits on other scales may be attributed to the loss in receptive skills. As with any other procedure, this leads only to hypotheses, but can offer valuable insights in attempting to understand the child's basic underlying deficits. The major patterns on the LNNB-C are discussed below in the context of the highest scale among the basic clinical scales.

Developmental Issues in Interpretation

Another substantial problem in interpretation is the role of developmental issues. There are several major problems that must be recognized when the test is interpreted. All of these problems stem from the fact that children's brains are not fully developed until midway in their teenage years. Thus, there is a difference in what brain skills can be affected at given ages and in the long-term impact of such injuries when the injury occurs at different developmental stages. It is not the purpose of this chapter to review theories of brain development, but such issues must be considered in the interpretation of any child neuropsychology battery. Even with these limitations, one can examine scale patterns to generate hypotheses. Each hypothesis that is generated must be tested against the actual patterns of items in the scales and the qualitative data on how the items were performed. The scale pattern serves only to generate hypotheses that must be checked against more detailed analysis of the child's performance on the individual items.

Clinical Scales

C1 (Motor Functions). The C1 scale is one of the most complex scales on the LNNB-CR. A wide variety of motor skills reflect both right and left hemisphere performance. The first three items involve simple movements of the hands. These items are especially sensitive to disorders in or near the posterior frontal lobe. In many cases, evidence of lateralized motor disorders may be detected by examining the raw scores on these items.

Items 21–32 assess construction dyspraxia. Items that are performed very poorly often reflect severe spatial disorganization characteristic of injuries to the right hemisphere or to the left parietal area. Drawings that are accurate but done slowly may simply reflect motor dysfunction of the dominant hand and the opposite cerebral hemisphere (or, sometimes, compulsiveness).

Because of the nature of the items on the C1 scale, it tends to be sensitive to many different types of brain dysfunction. Primary sensitivity is to sections of the posterior frontal lobe, but lesions of the temporal and parietal lobes, as well as the anterior frontal lobe, will also cause significant elevations in the score. However, extreme elevations (scores exceeding 80T) will usually only be caused by lesions in the motor system.

Elevations on the C1 scale are best interpreted relative to elevations on C3 (Tactile Functions). When C1 is elevated but C3 is not, this is suggestive of difficulties with motor tasks. This comparison can be very useful in initially localizing a deficit in the anterior–posterior dimension. Clients displaying pure parietal lobe dysfunction will rarely achieve a C1 score above 60T, although specific items involving kinesthetic feedback will be most frequently missed. On examination, the items on the battery will usually show a clear pattern in these posterior injuries that is highly effective in localizing a given disorder.

When both of these scales (C1 and C3) are highly elevated, generalized impairment of motor and sensory areas is suggested, but this is often in the context of diffuse deficits. If only these four scales are affected, then peripheral disorders affecting motor and sensory skills need to be considered, as well as the possibility of subcortical diseases.

C2 (Rhythm). The C2 scale is much more simply organized than the C1 scale. Item 35 involves the analyses of groups of tones. The child must compare two groups of tones, saying whether one is higher or lower. Items 36–38 require the child to reproduce tones. Whereas the initial items involve the perception of tonal

qualities, these latter items involve the expression of tonal relationships.

Items 39 and 40 involve the evaluation of acoustic signals. The child must identify the number of beeps in groups of sounds. The last two items in the C2 scale deal with the perception and reproduction of rhythm. Item 41 measures the ability of the child to reproduce rhythmic patterns. This item requires both the perception of rhythmic patterns and the reproduction of sounds, usually using the dominant hand. The item can be missed by individuals with deficits in either hemisphere. Item 42 asks the child to make a series of rhythms from verbal commands. The combination of verbal and rhythmic content on this item also makes it sensitive to injuries in either hemisphere.

Of all of the basic clinical scales, C2 is the most sensitive to disorders of attention and concentration. When giving these items to such individuals, it is often useful for the examiner to stop the administration between the stimuli in each item and not go on to the next item until the individual's attention has been secured. Because there are usually only two choices in each item, items cannot be repeated. Consequently, it is important to ensure that the first administration is carried out as accurately as possible.

When elevations of the C2 scale are the highest in the profile, they are most often associated with right hemisphere injuries that are usually more anterior than posterior. This is especially true when the highest scales are some combination of C2, C9 (Arithmetic), and C10 (Memory). However, this same pattern may be seen in left anterior lesions as well, although in those cases it is accompanied by at least subtle, if not gross, deficits in some form of verbal skills. When the C2 deficit is combined with C4 (Visual Functions) scale elevation, then the lesion may be either anterior or posterior, with a more posterior lesion being more likely with higher elevations on C4.

C3 (Tactile Functions). Items 43–56 involve different levels of cutaneous sensation. Individuals must identify where they are touched, how hard they are touched, and so forth. Injuries to the anterior parietal area will cause significant elevations on this scale as will injuries to the middle parietal areas that Luria (1973) designated as the "secondary area" of the parietal lobe. Individuals with damage in and around the angular gyrus may have particular problems

with verbal/tactile items. The last two items on the C3 scale involve the stereognostic perception. Individuals with old injuries to the parietal lobe on either side may have difficulty meeting the time requirements.

Profiles with highest scores on the C3 scale are interpreted in conjunction with the relative standings on the C1 scale. If C3 is greatly elevated over C1, then this points to a posterior lesion. This generally remains true even when the C1 scale equals the C3 scale, especially if the C1 deficits arise from construction difficulty and sequencing rather than motor paralysis.

Deficits may be related to an inability to concentrate, which should also result in inconsistent behavior, or to an inability to integrate and identify all stimuli. In the latter case, the deficit will have a similar effect but will also show up as a rule in other naming and identification tasks while causing less difficulty in purely spatial tasks. When the deficit is purely spatial, such as in profiles with C3 and C4 (Visual Functions) elevations, the injury is likely to be right parietal–occipital, although this pattern may also reflect subcortical involvement of one or both hemispheres. When naming is strongly involved, left parietal deficits should be considered. All such hypothesized localizations assume a normally dominant left hemisphere. Such patterns can be changed significantly by mixed or right hemisphere dominance for speech.

C4 (Visual Functions). The C4 scale evaluates a range of visual functions. Items 59 and 60 ask the child to identify objects by viewing either an object itself or a picture of an object. The person need not identify the object by name but rather can describe function or indicate recognition in other ways. Despite this, naming must be considered a component of these items. If the child is not able to do these items, later items on the battery that are more sensitive to right hemisphere function may be missed simply because of left hemisphere involvement. Thus, interpretation of the scale must depend on the child's performance on the simple, initial items.

Later items require a great deal more visual–spatial perception than do these first two items, although naming is still required. Item 61 presents pictures that are difficult to perceive. Item 62 presents objects that overlap one another and that the child with poor visual–spatial skills has difficulty identifying. Item 63 examines the ability to determine that two

figures are mirror-image versions of one another. Item 64 is a modification of items from the Raven Progressive Matrices (Raven, 1960). It is also a strong measure of visual–spatial organization and right hemisphere function. Item 65 involves spatial rotation without any speech components. Individuals may point to the correct answer or circle it as necessary (or say it if this is not possible). Poor performance on this task is suggestive of impairment of visual–spatial skills.

Profiles in which the C4 scale is highest, in combination with any secondary scale, generally reflect impairment in the right hemisphere or the occipital areas of the left hemisphere. The C4 scale can be elevated in other left hemisphere injuries, but rarely will it be the highest scale overall. In right hemisphere injuries, deficits on only more complex visual tasks suggest either a mild parietal involvement or injury to anterior areas. These lesions are usually accompanied by elevation on the C1 scale suggestive of right hemisphere lesions. Subcortical lesions that interfere with visual processing can also cause patterns suggestive of right hemisphere injury, as can severe peripheral visual problems.

C5 (Receptive Speech). C5 items evaluate the ability of the child to understand receptive speech, from simple phonemic analysis to the understanding of complex sentences with inverted English grammar. Items 66–71 concern the understanding of simple phonemes. For items 66–70, the individual hears simple phonemes and must then repeat or write them. It is important to note if individuals are able to either say or write phonemes but not to do both.

Item 71 tests the ability to understand phonemes spoken at different levels of pitch. It is not unusual for individuals with significant damage in the right temporal area to miss this item. Items 72–77 involve the understanding of simple words and sentences. The child must do relatively simple tasks of naming, pointing, and identifying, and must define simple words. The intent of these items is simply to ensure that the child is hearing correctly and interpreting correctly what is said to her or him.

Beginning with item 78 and continuing through the end of this scale to item 83, the individual is given increasingly more difficult instructions. These items assess the child's ability to understand and to perform or answer as requested. All of these items can be affected by damage to the left hemisphere, but several items can also be affected by right hemisphere dysfunction. For example, item 79 requires some spatial orientation on the part of the child. If the child appears to understand the sentence but disrupts the spatial requests made, the possibility of right hemisphere dysfunction must be suspected.

When this scale is highest, as well as significantly elevated above the critical level by at least 15 points, deficits are usually associated with left hemisphere injury. Lesser elevations, caused by difficulty with the more complex items, can occur as the highest scale in right anterior injuries. This can be especially true in mild elevation combinations of C5 and C10 (Memory), C5 and C2 (Rhythm), C5 and C4 (Visual Functions), C5, C11 (Intellectual Processes), and C9 (Arithmetic). In the most significant elevations, however, left hemisphere involvement is generally indicated.

An important caveat in evaluating speech in children without a history of normal language achievement is differentiating between problems related to environment and nonneurological physical factors and those related to brain-based deficits. One common problem is the child with hearing difficulties resulting from multiple infections requiring tubes or infections that caused partial or complete deafness. In these children, language abnormalities may simply reflect an inadequate chance to develop the relevant skills. Similar problems arise from backgrounds with inadequate verbal stimulation. It is very difficult to differentiate between deficits related to a poor premorbid history and those related solely to brain damage.

C6 (Expressive Speech). The C6 scale evaluates the individual's ability to repeat simple phonemes and words and to generate automatic as well as more complex speech forms. Initial items simply require the repetition of sounds or words spoken by the examiner. Beginning with item 89, the child must repeat the same list of words and sounds by reading them rather than hearing them. If an individual is able to pass either one of these sections, significant expressive speech deficits are not present. For example, the individual who is able to read but not to receive auditory information will be able to do the second section. Inversely, the child who is unable to read will be able to do only the first section. Therefore, one must carefully examine

the pattern of answers to see if the errors are confined to one modality or the other.

Beginning with item 93, the child must repeat increasingly more difficult sentences. Item 94 examines the ability to name from a description rather than from a visual presentation of the object. Items 95–98 ask individuals to count and say the days of the week, first forward and then backward, all a form of automatic speech. Items 99–104 evaluate the ability to produce speech spontaneously under three conditions: after looking at a picture, after hearing a story, and after being given a topic to discuss. If other items on this scale are performed without difficulty, and yet the child experiences problems with these items, there is the possibility of low intelligence. The final section involves complex systems of grammatical expression; the child must fill in words that are missing in a sentence or make up a sentence from words that are given to him/her.

In general, C6 scores are sensitive to injuries in the left hemisphere only. It is rare to see a high C6 score in individuals with unilateral right hemisphere injuries. Exceptions to this are individuals who had difficulty reading prior to their injury, or whose disorders have somehow interfered with auditory perception or have had generalized effects (e.g., pressure effects from a tumor). However, examination of the patterns of the items on the battery can easily eliminate these possibilities. In the absence of these types of conditions, elevation on the C6 scale, especially above a score of 70T, is almost always indicative of a left hemisphere injury.

Very mild C6 elevations may be associated with right hemisphere lesions, with the major errors occurring in the last items of the scale (spontaneous speech, sequencing, and fill-in terms). One assumption underlying interpretation of all of the language scales is that the child was originally fluent in English, as all of the current research is based on native-born speakers.

C7 (Writing). The C7 scale evaluates the ability to analyze words phonetically in English and then to do copying of increasing difficulty. Initially, children are asked to copy simple letters, then combinations of letters and words, and then write their first and last names. They are then asked to write sounds, words, and phrases from dictation.

In general, disorders of writing localize to the temporal–parietal–occipital area, especially in and around the angular gyrus of the left hemisphere. However, specific disorders may indicate problems in other areas. For example, the ability to write from written material but not from auditory material suggests a specific lesion in the temporal lobe. Conversely, the ability to write from dictation but not from written material suggests a lesion in the occipital or occipital–parietal areas of the cerebral cortex.

If the child is, in general, able to write but has difficulty forming letters and changing from one letter to another, there could be a problem in kinesthetic feedback in which the child mixes up letters that are formed by similar motor movements. If the child is unable to write at all because of paralysis, this, of course, is suggestive of a lesion in the motor strip area of the posterior frontal lobe. Finally, if the child writes at an angle to the page, suggesting some spatial problems, and has no other writing disorders, this can be related to right hemisphere dysfunction. Lack of the ability to read or write one's name is often indicative of a general dementia or, in some cases, a disorder of automatic writing that may occur with injuries in both hemispheres.

Motor writing errors are generally associated with the hemisphere opposite the child's normal writing hand, although care must be taken in injuries that cause the child to change writing hands. In these cases, writing may remain poor but reflects an injury in the ipsilateral hemisphere. Motor writing problems may arise simply as a result of motor problems reflecting the functions of the motor areas of the brain, but may also arise in injuries involving kinesthetic and tactile feedback. Motor writing deficits in which the writing itself is motorically intact but spatially disrupted (at large angles to the horizontal, or where words are written over one another) may reflect injuries to the right (or spatially dominant) hemisphere.

C8 (Reading). The C8 scale closely parallels the C7 scale. The child is asked to generate sounds from letters that the examiner reads aloud. This generally measures the ability of the child to show integration of letters and auditory analysis functions of the temporal and parietal areas of the left hemisphere. The child is then asked to name simple letters, read simple sounds, and read simple words and letter combinations that have meaning. Finally, the child must read entire sentences as well as paragraphs. If the child is able to read simple words but not

entire sentences or paragraphs, possible injuries include disorders of visual scanning that make it impossible for the child to grasp more than one word at a time.

Generally, deficits on the C8 scale, in a child who could read prior to an injury, are almost always associated with a left hemisphere injury, usually posterior. The exceptions to this are deficits that occur because of spatial disruption (inability to follow a line, which shows most clearly in the paragraph reading) or neglect of the left side (which should be corrected by the examiner if the test is administered correctly). Both suggest right hemisphere dysfunction. However, we are not justified in making such conclusions in an individual who never was able to read unless there is other evidence to confirm a given injury.

C9 (Arithmetic). The C9 scale is the most sensitive of all of the LNNB-C scales to educational deficits. Even in normally educated individuals, this is the scale most likely to appear in a severely pathological range when there is, in fact, no damage.

This scale starts with the child simply writing down numbers from dictation in both Arabic and Roman numerals. Several items have been employed to identify the spatial dysfunctions that are possible. The child is asked to write 17 and 71, 69 and 96. Thereafter, the scale requires the person to write down numbers of increasing complexity. As numbers become more complex, it is possible to see if the child places the numbers in the correct sequence, again looking for possible spatial deficits that can be caused by right hemisphere or left occipital–parietal dysfunction. In the next section, the child is asked to compare numbers, an operation that is basic to the left occipital–parietal area. In items 124 and 125, the child is asked to do simple arithmetic problems. These are problems that most individuals can probably do from memory. The last item is the presentation of serial 3s.

The C9 scale appears to be potentially sensitive to lesions in all parts of the brain, as well as to preexisting deficits common to about 20% or more of the normal population whose performance is well below grade level expectations.

C10 (Memory). The C10 scale is basically involved with short-term memory functions. The first items on C10 look at the ability of the child to memorize a list of seven simple words and to predict his or her performance. Items 129–131

involve immediate sensory trace recall. The items test word memory and visual memory.

Items 132 and 133 involve simple verbal memory under two conditions of interference. Several difficulties in short-term memory are seen in these items. Finally, item 135 is a measure of the individual's ability to associate the verbal stimulus with a picture. This item can be interfered with by either left or right hemisphere dysfunction and is sensitive to high-level disturbances in memory skills.

Overall, the C10 scale is most sensitive to verbal dysfunction because of its importance in a majority of the items. However, nonverbal dysfunction caused by right hemisphere lesions will show up in a moderately elevated C10 score of about 60T, with a pattern of missing the nonverbal items. It is always important to look at the pattern of the items missed before venturing the hypothesis of a possible etiology.

C11 (Intellectual Processes). The items in C11 should be differentiated from items in a standard intelligence test. All of the items on this scale have been selected because they are able to discriminate between brain-damaged and normal subjects. Thus, rather than giving a level of intelligence that can be associated with a child's learning history, the items tend to give a functional intellectual level.

Initial items in the scale involve the understanding of thematic pictures. The first item asks the child to interpret a picture in her or his own words; items 137 and 138 ask the individual to put pictures into a series that makes sense, similar to the items in Picture Arrangement. Item 139 asks the child to tell what is comical or absurd about certain pictures. Deficits of visual scanning can also be seen in individuals who are not able to appreciate the complexity of a picture and who, thus, tend to focus on one area. Item 140 requires the child to interpret a story. Items 141 and 142 ask for similarities. Item 141 involves simple concept formations and definitions; items 142 and 143 call for comparisons and differences between objects in much the same way as do items on the Similarities subtest of the Wechsler Adult Intelligence Scale (WAIS). Performance in this area is further evaluated by items 144–146, in which the child must find the logical relationships between specific objects and the groups to which they belong. The last items on the scale, items 147–149,

involve simple arithmetic problems very similar to those seen on the WISC-R Arithmetic subtest.

Overall, the C11 scale is highly sensitive to disorders in both hemispheres but is most sensitive to disorders in the left hemisphere. Injuries in the parietal lobes will cause maximum dysfunction. The determination of laterality, however, must be made by investigating specific items to judge whether those initial items that are right hemisphere oriented suggest adequate visual interpretation skills. If these skills appear to be intact, then the scale is likely to be reflecting a left hemisphere dysfunction alone. If these are the only items missed on the scale, the possibility of isolated right frontal dysfunction must be seriously considered.

The C11 scale score correlates about 0.7 with WISC-R Full Scale IQ. However, this scale, because of its flexibility in administration, may yield higher IQ estimates in individuals with impairment in expressive or receptive speech skills. Although the scale can reflect impairment in either hemisphere, a high elevation combined with C2 (Rhythm), C4 (Visual Functions), C10 (Memory), and C9 (Arithmetic) generally points to right hemisphere dysfunction, whereas elevations combined with C6 (Expressive Speech), C8 (Reading), and C7 (Writing) indicate left hemisphere damage.

Qualitative Analysis

The LNNB-C lends itself to a qualitative analysis along with the quantitative analysis discussed in this chapter. The consideration of the qualitative factors becomes the next step in the diagnostic process. Here, the interest is not in whether a child got a certain score on a certain item but rather *how* that score was achieved. One of the great advantages of this battery is that the same test procedures lend themselves to both quantitative and qualitative analyses. Although it is possible to interpret the battery from only one method or the other, the use of only one technique does not take full advantage of the possibilities within the battery nor does it yield the maximum amount of useful information in any given case.

In scoring qualitative errors, there is a wide range of possibilities aimed at gaining a better understanding of the "why" behind a child's error. Qualitative analysis can also aid in the evaluations of responses that are correct in terms of the quantitative scoring but still unusual, such as the child who reads a word on the C8 scale but stutters in pronouncing it, or the child who can describe an object and its uses on the C4 scale but is unable to give its name.

The disadvantage of qualitative inferences is the lack of formal scoring criteria and reliability across examiners. At present, there is no way in which such problems can be completely eliminated, but there are ways in which such problems can be minimized. The Qualitative Scoring Summary allows the user to score over 60 categories of qualitative observations that can be made during administration of the battery. The presence of such a scoring system emphasizes the need for intelligent observation on the part of the user. The effectiveness of the system is directly related to the effectiveness of the observer/tester as well as her or his active participation in the testing procedure. Interpretation of this information requires a detailed understanding of the ways in which the brain functions.

It is very important that the clinician learn to observe and record the child's approach to the items, especially if that approach differs from those seen in the normal child. (The examiner must have adequate experience with normals to make this comparison.) This should be done even if the examiner does not understand the meaning of the behavior or its significance. Sometimes the significance becomes clear after the quantitative analysis is completed, or it may become clear on consultation with one's supervisor or a consultant. By doing this on a systematic basis, the user will begin to appreciate the meaning of the child's behavior and to develop the ability to perform such analyses independently.

After a qualitative analysis has been made, it should be integrated with the quantitative analysis. It is our strong belief that neither form of data is inherently "superior" in any given case. In some cases, the qualitative data help to explain inconsistencies that cannot be resolved in the quantitative results. In other cases, the quantitative data suggest an alternate approach to an observation that clears up in the interpretation of a qualitative aspect of behavior. Only when the two sets of data have been integrated has a fully effective initial evaluation been completed.

Personality

Another important aspect of the analysis is to identify the personality factors playing a role

in the child's behavior. Personality, as much as cognition, is derived from the brain. Indeed, those functions we label as personality may be the only things impaired in a given disorder. Evidence is increasing that personality is as much a function of biology as it is of environment, although both are absolutely necessary. Evaluation of personality comes from testing (e.g., Rorschach, CAT, PIC), observation, as well as clinical interaction.

Prior History

Even at this point, there still remains another step in the diagnostic process, namely, the reconciliation of the conclusions of the above techniques with the history. This can be done in two ways: (1) knowing the history when the case begins and considering it throughout the diagnostic process or (2) analyzing the case with a minimum of information and checking the detailed history afterward. (Doing any case completely blind is not recommended.) Both techniques have their drawbacks. If too much history is known, one may be so biased that the inconsistencies between the history and data are overlooked or deemed unimportant.

History includes information about not only medical status but also social information, family information, school proceedings, social situation, and environmental inputs. In current language, this is a holistic approach that recognizes that everything we are and experience interact to produce our behaviors, successes, and failures. Only such a holistic approach is adequate for maximum understanding.

Historical information and the conclusions made available by others prior to the neuropsychological assessment may be right or wrong. A lesion may exist as reported, or may not. The child's developmental history may be accurate or may contain serious errors. The relative accuracy of information does depend on the source of that information as well as its nature. In all cases, however, it is important to double-check all such information.

Consequently, our bias suggests working from a basic history for important aspects that concern the validity of testing. In the evaluating process, we treat conclusions from the data as simply hypotheses to be confirmed or discarded. This leaves the clinician more flexibility to take his or her data seriously and to learn from those data all that is possible. If, at the end, discrepancies are found between history and neuropsychological findings, the clinician should investigate the history and the findings for errors that may cause this discrepancy, and look for conditions outside neuropsychology that may have affected one or the other source of data. It should also be recognized that conclusions are working conclusions, open to revision at any time when events suggest that the conclusions are inadequate. This allows us to work closer toward "perfection" although it is unlikely we will ever achieve that.

Updated Approach to Qualitative Scoring

In order to focus better on the qualitative aspects of the test performance, new work has developed 66 qualitative categories that are scored throughout the test administration. These categories are grouped into ten major areas:

1. Dysarthria. These represent the scores that measure basic speech dysfluency. These include articulation, paraphasias, simplification and substitutions, slurring, and stuttering. All of these categories represent mispronunciation of words, except for some paraphasias which may represent substitutions of words for one another (such as hat for dress).

2. Expressive Language. These categories are generally disorders of oral speech, although they may have cognitive rather than motor etiologies. These categories include circumlocution, dropping of articles, impoverished speech, jargon, naming disorder, oral language absence, prosody, spelling, stiff speech, and vocal quality. In each case, errors on speech items or general cognitive items can be more precisely defined by using these categories or others as appropriate.

3. Motor. These categories measure disorders of motor functions (other than motor speech). These include associated movements, involuntary movements, macrographia, micrographia, midline failure, motor awkwardness, motor writing, paralysis, stiff motor movements, torque, and tremors.

4. Peripheral Impairment. These categories identify when peripheral injuries to the limbs, face, or spinal cord cause defects on the tests which may not be related to "brain" function per se. For example, we need to identify when errors on visual items are caused by inability to see the items clearly.

5. Receptive Language. These items identify when problems in the understanding of language interfere with test performance (which potentially includes all items since all have some form of instructions). The categories include auditory discrimination, failure to comprehend instructions, grapheme recognition, and letter–number recognition.

6. Self-cueing. These categories evaluate when the client uses some external aid to help solve a problem. These include gestural and visual cueing, postural cueing, repetition, and verbal cueing. These all identify circumstances where clients cannot work things out "in their head."

7. Self-monitoring. These are very important categories where there may be profound functional effects but only mild concrete cognitive effects. These categories include additional responses (where they give a right answer plus additional information), anticipation, automatic phrases, confusion, context confabulation, description, elaboration, emotional responses, impulsivity, irrelevant associations, perseveration, self-correction, and sequence errors. All of these categories represent instances where clients cannot monitor or control their behavior so as to conform to the requests of the item even though they may still get a correct answer in some cases. It is entirely possible that a brain injury may be restricted to these and related categories alone with minimal objective findings.

8. Speed. These categories identify problems related to response latency (taking too long to begin) and time delay (getting the right answer but in an excessive time period).

9. Sustained Performance. These are important indicators about how well the client can maintain a level of function over time. These clients may be characterized as individuals who do well for a period of time and then do poorly. Their performance depends less on the item content than on when the item is presented in the course of the test. It is important to discriminate between those clients who do poorly because of cognitive dysfunction and those who do poorly for problems in sustained attention: Both may be injured but the necessary rehabilitation is quite different. These categories include attention difficulties, fatigue, and impersistence.

10. Visual–Spatial. These include a variety of disorders related to basic spatial orientation, e.g., counting errors, echopraxia, number spatial impairment, omission, reversal, right–left disorientation, rotations, unilateral neglect, and visual focusing.

These general categories and the 66 individual categories allow the clinician a great deal of flexibility in identifying the underlying cause of a client's problems. Consistent with Luria's own testing and theoretical approach, this extends the information that can be gathered from simply doing a basic objective scoring of items. By using them within a quantitative context, we can generate both types of information enhancing the value and strength of the overall evaluation.

Interpretation

Interpretation is basically similar to the earlier versions of the test, with an emphasis on a multilevel, integrationist, holistic approach to both testing and interpretation. Although diagnoses can be generated from the test, the biggest emphasis is on understanding the individual's underlying issues and problems and how these affect day-to-day function. The new version of the test enhances the range of information gathered and thus permits both recreation of the information generated by the earlier tests as well as new information to better understand the underlying neuropsychological performance.

Conclusions

The Luria–Nebraska Children's Battery is a test that evaluates a wide range of skills aimed at assessing the neuropsychological competence of children between the ages of 8 and 12. The battery offers a variety of quantitative and qualitative scores by which to detail the performance of children and to integrate that performance with historical data. The battery has been shown to be highly successful in diagnosis, but does need to be supplemented by other tests when detailed analysis of single areas is necessary or preferable. The battery lends itself to interpretation on a variety of levels. Thus, it can be useful to people with varying backgrounds provided caveats on use are followed carefully. The test is in the process of being updated and extended down to ages 5 through adult. The new test offers a large number of advantages and extensions to the previous battery in a variety of areas.

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13

Applications of the Kaufman Assessment Battery for Children, 2nd Edition in Neuropsychological Assessment

KRISTEN L. MAYS, RANDY W. KAMPHAUS,
AND CECIL R. REYNOLDS

The *Kaufman Assessment Battery for Children, 2nd Edition* (KABC-II) (Kaufman & Kaufman, 2004a) is an individually administered clinical test of intelligence designed specifically for use with children from the ages of 3–18. The KABC-II represents a major revision from the original *Kaufman Assessment Battery for Children* (K-ABC) (Kaufman & Kaufman, 1983) in both its theoretical conception and structure. This chapter will provide a brief historical, conceptual, and theoretical background of the KABC-II. It will also provide an overview of the test, an evaluation of its strengths and weaknesses as a cognitive assessment tool, and its implications for neuropsychological assessment.

Overview

History

At its conception, the original K-ABC represented a marked departure from other commonly used cognitive assessments. Based on a combination of theoretical underpinnings from cerebral specialization research, Luria–Das successive-simultaneous processing, and work in cognitive psychology, the K-ABC was one of the first intelligence tests to be principally derived from a strong theoretical basis and was the first major intelligence test to be based on neuropsychological theory (Reynolds & Kamphaus, 1997). Furthermore, the K-ABC achieved notoriety by yielding smaller average score differences (about 1/2 SD) than were typical between African-American and European-American ethnic groups.

Similar to any instrument that substantially deviates from its predecessors, the advent of the K-ABC raised a great deal of controversy across

KRISTEN L. MAYS AND RANDY W. KAMPHAUS • Department of Educational Psychology, University of Georgia, Athens, Georgia 30602 and Department of Counseling and Psychological Services, Georgia State University, Atlanta, Georgia 30302. **CECIL R. REYNOLDS** • Department of Educational Psychology, Texas A&M University, College Station, Texas 778430.

the field of cognitive assessment. A selection of this debate was captured in a special issue of the *Journal of Special Education* (1984) entirely devoted to reviews of the K-ABC. While some professionals praised the K-ABC for its strong theoretical basis and clinical utility, others questioned its claims of strong internal and external validity and reduced cultural bias. Despite the test's criticisms, the K-ABC became an accepted and widely used measure of intelligence.

In light of the concerns raised by psychologists and educators regarding the original K-ABC, current clinical needs of tests administrators, and the advancement of assessment knowledge in general, the Kaufmans articulated several new objectives for the test's revision. The central goals for the revised test included (Kaufman, Lichtenberger, Fletcher-Janzen, & Kaufman, 2005) the following:

- Strengthening the test's theoretical foundations
- Increasing the number of constructs measured
- Enhancing the test's clinical utility
- Developing a test that fairly assesses children from minority groups
- Enhancing the fair assessment of preschoolers.

Theoretical Framework

The KABC-II differs from the K-ABC in both its conceptual framework and test structure. Unlike the K-ABC, which is grounded in a simultaneous/sequential processing approach, the KABC-II incorporates two distinct theoretical models: the Luria and Cattell–Horn–Carroll (CHC) models. According to the authors, the dual-theoretical model allows the examiner the flexibility to utilize one of two separate assessment orientations depending on the child's background and reason for referral (Kaufman & Kaufman, 2004a).

Luria Model. Similar to the original K-ABC, examiners have the option to interpret a child's scores according to Luria's neuropsychological theory. Luria (1980) conceptualized the brain's basic functioning as represented by three main blocks. According to this theory, Block 1 is responsible for arousal and attention; Block 2 is responsible for the ability to analyze, code, sort, and synthesize information; and Block 3 is

responsible for the application of executive functions for formulating plans and programing behavior. Rather than measuring each specific block, the authors assert that the KABC-II measures the mental processes that stem from the integration and interaction between these blocks. For a more thorough illustration of the theory and its relationship to neurological structures, see figure 2.1 in the *KABC-II Manual* (Kaufman & Kaufman, 2004a).

CHC Model. Alternatively, examiners have the choice to interpret a child's scores based on Cattell-Horn-Carroll (CHC) theory. CHC theory refers to the integration of the G*f*–G*c* theory developed by Cattell (1941) and later refined by Horn (1965), with Carroll's three-stratum hierarchal theory (1993). According to Carroll's theory, mental abilities exist across a hierarchical structure composed of three strata. The first stratum consists of approximately 70 discrete cognitive abilities. The second stratum consists of eight broad abilities (fluid intelligence, crystallized intelligence, general memory and learning, broad visual perception, broad auditory perception, broad retrieval ability, broad cognitive speediness, and processing speed), which are composed of combinations of first stratum traits. Finally, the third stratum represents the global construct of general intelligence. Kamphaus (in preparation) argues that the integration of these two theories is awkward, given their different underlying assumptions. For example, Horn did not subscribe to the construct of general intelligence and thus, would not have endorsed the existence of Carroll's third stratum. In practice, the term CHC theory typically refers to the similarities in the stratum-two intellectual abilities posited independently by these two intelligence research traditions.

The authors recommend that examiners primarily use the CHC model, except when the examiner believes that the inclusion of a measure of knowledge (crystallized ability) may compromise the validity of the global test score. Cases in which the authors suggest that the Luria model would be appropriate include (Kaufman & Kaufman, 2004a) the following:

- Children from bilingual backgrounds
- Children with non-mainstream cultural backgrounds that may affect a child's

knowledge acquisition or verbal development

- Children with language disorders
- Children with autism
- Children with hearing impairments.

Although current neuropsychological research with the KABC-II is limited, prior research with the K-ABC supports the utility of the KABC-II as a neuropsychological assessment tool for children with a variety neurological impairments. A selection of previous neurological research with the K-ABC is described in the next section.

Research with Pediatric Samples

The pediatric literature contains several studies that utilized the K-ABC to differentiate among the cognitive effects of various types of neurologically related pathology. In one study, Brown, Buchanan, et al. (1993) examined the effects of the various types of sickle-cell disease (SCD) on cognitive ability compared with a control group of their healthy siblings. SCD is a chronic, hereditary disease that is most commonly found in African-Americans in the United States, with an incidence rate of 1 in about 400 or 500 (Brown, Armstrong, & Eckman, 1993). Three types of SCD exist: homozygous HbSS, also known as sickle-cell anemia, in which the child has both abnormal genes for hemoglobin S; heterozygous HbSC, in which the child has one gene for hemoglobin S and hemoglobin C; and heterozygous HbS- thalassemia, in which the child has one gene for hemoglobin S and one gene for thalassemia. In all of these cases, the child actually presents the symptoms of SCD, although in HbSS type the symptoms are more severe, more frequent, and have an earlier onset (Brown, Armstrong, et al., 1993). Children who are carriers of the sickle-cell trait, but may not show symptoms of the disease, have the genotype of HbSA. Children who do not carry the gene for SCD have the genotype HbAA (Brown, Buchanan, et al., 1993).

Brown, Buchanan, et al. (1993) hypothesized that children with sickle-cell disease would perform worse on cognitive and achievement measures than their healthy siblings who were matched on race, SES, sex, and as closely as possible on age. They also predicted that children with the homozygous condition (HbSS) would perform worse than those with the heterozygous conditions, considering that all other symptoms showed a similar pattern. Children selected for the SCD group had been diagnosed with SCD, but had no prior history of neurological disease. Additionally, none of the children were taking narcotic analgesics, which had been shown to affect reaction time.

The researchers chose to use the K-ABC as a measure of cognitive ability because it provides minimal use of verbal content and because it was less dependent on prior learning than the Wechsler series. Because previous research had indicated that children from low-SES backgrounds are at a disadvantage on tests that tap verbal ability, utilizing a test that features minimal verbal content was important since the majority of the children in the sample came from low-SES backgrounds (Brown, Buchanan, et al., 1993). The K-ABC Reading Decoding and Arithmetic Achievement subtests were also included so that the researchers could see the application of the child's processing skills to complex learning tasks, assess the child's functional academic level, and estimate the child's long-term memory ability. The results revealed that the SCD type displayed no significant effects on cognitive ability or academic achievement. Brown, Buchanan, et al. found no effect for SCD type on cognitive ability or academic achievement. In contrast, hemoglobin level was shown to be a significant predictor of both cognitive ability ($R^2 = 0.10$, $p < 0.03$) and achievement ($R^2 = 0.12$, $p < 0.04$). As expected, the SCD children displayed normal overall cognitive ability, but with specific deficits in sustained attention, concentration, and reading decoding that were not observed in their healthy siblings (Brown, Buchanan, et al., 1993). This study suggested that the K-ABC was a useful tool for identifying cognitive processing problems that were not identified by other neurological assessment techniques.

In another study, Coles, Brown, & Smith (1991) used the K-ABC as the criterion measure to assess the cognitive ability and achievement of children with prenatal exposure to alcohol. The authors chose to use the K-ABC because its subtests tap several specific cognitive functions in which children with neurological impairment are likely to be deficient. The K-ABC also

provided local norms for low-SES children, which comprised the majority of the sample (Coles et al., 1991). The study compared three groups: those whose mothers drank heavily throughout pregnancy, despite an educational intervention during the second trimester; those whose mothers drank heavily throughout the second trimester, but then stopped for the remainder of the pregnancy; and those whose mothers had abstained from alcohol for the entire pregnancy and did not drink afterward. The results of this study indicated that both alcohol-exposed groups had significantly lower scores than those who were not exposed, with the "continued to drink" group scoring lowest on all but one subtest. Both alcohol-exposed groups displayed significant deficits in sequential processing, achievement, and the Mental Processing Composite (MPC) especially when the patterns of current drinking were controlled. Overall, Sequential processing was affected more than Simultaneous processing; however, the children in the "stopped drinking" group performed similar to the children in the "never drank" group on sequential processing. The findings of this study suggested that children whose mothers continued to drink throughout pregnancy suffered from deficits in short-term memory and the ability to encode visual or auditory information. The crucial brain structure involved in learning and memory, the hippocampus, has been shown to be especially susceptible to the effects of alcohol (e.g., Korsakoff's syndrome, which is a memory deficiency common in people who consume excessive amounts of alcohol). Therefore, third-trimester exposure to alcohol may affect hippocampal development, which may in turn lead to deficits in the ability to encode visual or auditory information. The K-ABC achievement tests also indicated that children in both alcohol-exposed groups displayed significant deficits in math skills and in reading decoding of words and letters. Coles et al. (1991) hypothesized that though prenatal alcohol exposure was associated with deficits in cognitive development and academic achievement, the children whose mothers stopped drinking in the third trimester may have experienced a cognitive "recovery" during that time of fetal development. Both of these studies indicate the utility of the K-ABC for use in identifying processing problems in various pediatric samples.

With the advent of the KABC-II, there is a need for additional research to evaluate its utility as a tool in neuropsychological assessment.

In contrast to the two studies mentioned above, a study by Donders (1992) suggested caution when using the K-ABC as a measure of cerebral impairment. The subjects of this study included 43 consecutive patients at a regional rehabilitation hospital. The children ranged in age from 6 to 12 years and none had suffered from previous CNS dysfunction or displayed evidence of psychopathology. The sample included 32 males and 11 females. All children were administered both the K-ABC and WISC-R within a year after their initial injury. The children's initial status in the emergency room was classified as severe (using the Glasgow Coma Scale) in 27 cases and mild in 16 cases. In all cases, the children scored slightly higher on the K-ABC (MPC; $M = 92.33$) compared to the WISC-R (Full Scale IQ; $M = 89.33$). Based on these findings, Donders (1992) concluded that "the K-ABC appears to be no more sensitive to diffuse cerebral impairment than the WISC-R" (p. 228).

In light of its relationship to the KABC, these studies suggest that the KABC-II may be a promising tool for assessing intelligence and cognitive impairments within a neuropsychological framework and thus, warrants future research evaluate the KABC-II's applicability to neuropsychological assessment.

Test Overview

The KABC-II is composed of 18 core and supplementary subtests, which are grouped into four to five scales, depending on the child's age and the interpretive model the examiner has chosen to utilize. The Luria model organizes the subtests into four scales: Sequential Processing, Simultaneous Processing, Learning Ability, and Planning Ability. The CHC model simply renames these scales: Short-Term Memory (Gsm), Visual Processing (Gv), Long-Term Storage and Retrieval (Glr), Fluid Reasoning (Gf), and includes an additional scale of Crystallized Ability (Gc). Descriptions of the theoretical conceptualization of both sets of scales are included in Table 1.

Although the number of core and supplementary subtests vary depending on the age of the child and the theoretical model, the same

TABLE 1. Luria and CHC Conceptualizations of KABC-II Scales

KABC-II scale	Luria conceptualization	CHC conceptualization
Learning/G*lr*	Learning Ability	Long-Term Storage and Retrieval (G*lr*)
	Measures the integration of the processes associated with all three of Luria's Blocks to encode, retain, and retrieve new information efficiently. Although this ability primarily capitalizes on the attention and concentration processes encompassed within Block 1, it also requires Block 2's sequential and simultaneous processes and Block 3's planning and strategy generation processes	Measures the ability to store and efficiently retrieve newly or previously learned information
Sequential/G*sm*	Sequential Processing	Short-Term Memory (G*sm*)
	Measures the "successive" coding processes associated with Luria's Block 2, which involves arranging linearly- or temporally-related units of information in sequential or serial order	Measures the ability to perceive, retain, retrieve, and apply information within a few seconds
Simultaneous/G*v*	Simultaneous Processing	Visual Processing (G*v*)
	Measures the "simultaneous" coding processes associated with Luria's Block 2, which involves holistically synthesizing and integrating information	Measures the ability to perceive, store, and manipulate visual stimuli
Knowledge/G*c*	(This scale is not included in the Luria model)	Crystallized Ability (G*c*)
		Measures the breadth of knowledge acquired from one's developmental context including schooling and culture

Table adapted from Kaufman et al. (2005a, p. 14).

core subtests are administered for each scale regardless of their interpretation. In application, the principle difference between the two models is that the CHC model includes a measure of Crystallized Ability, whereas the Luria model excludes this scale. Comparable to other commonly used cognitive assessments, subtest standard scores are scaled to a mean of 10 (SD = 3) and index scores are normed to mean of 100 (SD = 5).

The KABC-II yields two general intelligence composite scores: the Mental Processing Index (MPI) according to the Luria model and the Fluid-Crystallized Index (FCI) according to the CHC model. In addition to the MPI and FCI and the five stratum-two scales, the KABC-II also produces a Nonverbal Scale (NVI), which is composed of subtests that can be administered in pantomime and do not require verbal responses. This scale encompasses a mixture of core and supplementary subtests for all age groups and permits the assessment of those children who possess hearing, speech, or language impairments, limited English proficiency, or any disability that would make the core battery unsuitable for administration.

Psychometric Properties

In this section, we provide an overview of the measurement characteristics for the KABC-II based solely on information provided in the manual. Future psychometric studies are undoubtedly in the publication process;

however, we are limited by a lack of independently published research at the present time.

Standardization

The standardization of the KABC-II was based on a sample of 3,025 examinees, aged 3–18 years, all of whom spoke English, were non-institutionalized in special care or therapeutic settings, and did not possess physical or perceptual impairments that would prohibit them from completing the assessment tasks. A target sample size was selected for each age group, which included an equal number of males and females. The sample was then stratified by geographic region; race/ethnic group; parental education attainment (used as a measure of socioeconomic status); parental education within ethnic groups; and at age 18, educational status (in secondary school, in post-secondary school, or not in school) to reflect U.S. population samples based on 2001 Census data. Representative proportions of children with learning disabilities, mental retardation, gifted and talented placement, and other special populations were also included in the sample according to data provided by the U.S. National Center for Education Statistics. In addition, the KABC-II was co-normed with the *Kaufman Test of Educational Achievement, Comprehensive Form, second edition* (KTEA-II; Kaufman & Kaufman, 2004b) to provide co-normed tests of intelligence and achievement. Whereas the original K-ABC was criticized by Bracken (1985) for including a disproportionately high number of upper socioeconomic (SES) minorities and under sampling low-SES minorities, the KABC-II norming sample distribution more closely reflects the SES distribution of the U.S. population.

Reliability

Test–Retest Reliability. Given that the KABC-II aims to measure relatively stable cognitive abilities, knowledge of the instrument's test–retest reliability is extremely important. The test authors based their reliability computations on the test performance of 205 children who were divided into three age groups (ages 3–5, 7–12, and 13–18). Each group was administered the test twice over an average period of approximately 4 weeks. Test–retest reliability data are presented in Table 2.

All reliability coefficients were corrected for the variability of the sample using Cohen's variability correction and were based on the standard deviation obtained from the first testing. Retest reliabilities of the global scales ranged from 0.72 to 0.94, with retest stability increasing with age. The mean stability coefficients for each of the five scales ranged from 0.74 to 0.95, with the Simultaneous/Gv scale showing the least stability and Knowledge/Gc scale showing the most stability. The individual subtests scores showed a greater amount of variability with stability coefficients ranging from 0.50 (Hand Movements) to 0.90 (Expressive Vocabulary).

Practice effects for the FCI and MPI were approximately 5–6 points (ages 3–5) and 10–12 points (ages 7–18). Across all ages, the largest scale score gains were observed for the Learning/Glr, Planning/Gf, and Simultaneous/Gv scales, whereas the Sequential/Gsm and Knowledge/Gc scales displayed relatively small practice effects. The authors attribute the magnitude of the practice effects for the Planning/Gf and Simultaneous/Gv scales to the "novelty" of the subtests. That is, because the test items were designed to be innovative and engaging, they may be more memorable upon re-testing. Furthermore, the Kaufmans suggest that the practice effects observed for the Learning/Glr scale provide support for the scale's construct validity. In summary, although the test–retest reliability coefficients suggest that performance on the KABC-II remains fairly stable over time, examiners should be cognizant of the substantial practice effects, especially for children ages 7–18 when re-administering the test within a brief time period.

Internal Consistency. Internal consistency was assessed using the split-half technique with Spearman–Brown formula correction within age groups. The average internal consistency for each of the two age groups (ages 3–6 and 7–18) was computed using Fisher's z-transformation for each subtest. The median reliability for core subtests was reported as 0.85 (ages 3–6) and 0.87 (ages 7–18). The reliability of supplementary subtests was lower than that of the core subtests.

Internal consistency coefficients of the scales and global indexes were computed using Nunnally's formula for determining the reliability of a composite score. The mean coefficients for the MPI, FCI, and the NVI were quite high

TABLE 2. Temporal Reliability for Scale and Global Scores Across Age

		N	Test 1 M (SD)	Test 2 M (SD)	Gain	Correlation adj	Test Interval (Days) M (SD)
3–5 years	Seq/Gsm	47	100.7 (16.5)	102.9 (15.4)	2.2	0.79	24.2 (9.8)
	Sim/Gv	48	101.2 (17.1)	106.2 (20.8)	5	0.74	
	Lrn/Glr	48	98.5 (14.6)	104.4 (15.0)	5.9	0.79	
	Pln/Gf	–	–	–	–	–	
	Know/Gc	48	98.9 (16.0)	102.7 (17.7)	3.90	0.93	
	MPI	60	100.7 (15.5)	106.6 (16.3)	5.9	0.86	
	FCI	60	100.1 (15.6)	105.4 (16.7)	5.3	0.90	
	NVI	62	99.8 (17.4)	104.6 (19.2)	4.8	0.72	
7–12 years	Seq/Gsm	82	103.2 (15.0)	102.4 (15.5)	–0.8	0.80	28.9 (9.6)
	Sim/Gr	82	99.7 (15.6)	108.9 (17.0)	9.2	0.76	
	Lrn/Glr	82	99.1 (17.7)	113.7 (17.7)	14.6	0.76	
	Pln/Gf	82	98.5 (14.5)	108.9 (18.3)	10.4	0.82	
	Know/Gc	82	99.0 (14.8)	102.3 (16.7)	3.3	0.88	
	MPI	82	99.8 (16.2)	111.7 (18.7)	11.9	0.89	
	FCI	82	99.6 (16.0)	109.9 (18.5)	10.3	0.91	
	NVI	82	99.2 (15.7)	107.1 (17.7)	7.9	0.87	
13–18 years	Seq/Gsm	61	102.2 (13.7)	103.3 (14.5)	1.1	0.80	28.2 (11.7)
	Sim/Gr	61	100.5 (15.0)	107.1 (17.1)	6.6	0.78	
	Lrn/Glr	61	101.2 (14.8)	115.1 (18.4)	13.9	0.81	
	Pln/Gf	61	101.3 (15.0)	112.1 (17.8)	10.8	0.80	
	Know/Gc	61	100.3 (13.8)	103.7 (14.0)	3.4	0.95	
	MPI	61	101.8 (13.7)	113.1 (18.4)	11.3	0.91	
	FCI	61	101.3 (13.7)	111.6 (17.8)	10.3	0.94	
	NVI	61	100.7 (15.4)	108.5 (17.3)	7.8	0.87	

Adapted from Table 8.3 in Kaufman and Kaufman (2004a, p. 90).

ranging from the low to upper 0.90 s across all ages, meeting the conventional criterion of 0.90 for measures used to make important decisions about a client (e.g., offering a diagnosis) (Kamphaus, in preparation). The average internal consistency of scale indexes was slightly lower than the global scales, although still adequate, with mean coefficients ranging from 0.90 to 0.92 (ages 3–6), and from 0.88 to 0.93 (ages 7–18). All subtest reliabilities were 0.75 or above with the exception of Hand Movements and Gestalt Closure, neither of which is specified as a core subtest. The mean standard errors of measurement of standard scores for the global scores were approximately 3.5 points (MPI), 3 points (FCI), and 5 points (NVI).

The KABC-II manual does not include an inter-examiner reliability study. Given the importance of examiner proficiency in standardized test administration, future studies of inter-examiner reliability are needed to examine the stability of a child's scores across different examiners.

Validity

The test authors reported using confirmatory factor analytic (CFA) procedures in an exploratory fashion to determine the factor structure of the KABC-II. The main CFA statistics that were used to evaluate "goodness of fit" were the comparative fit index (CFI) and the root mean square error of approximation (RMSEA). Both the CFI and RMSEA were evaluated across narrow age ranges (1–3 years). The analyses supported varying factor structures across separate age levels.

Age 3. At age 3, CFA results supported a distinction between the Sequential/Gsm subtests and the remainder of the battery. However, the

authors chose to base the battery at age 3 on a single factor model.

Age 4. For the 4-year-old age group, the analyses supported distinct Sequential/G*sm* and Learning/G*lr* factors. Although the analyses did not support differentiation between the Knowledge/G*c* and Simultaneous/G*v* factors, the authors chose to separate these two groups of subtests into different scales based on item content.

Ages 5–6. For the 5–6-year-old age group, the analyses did not differentiate between the Simultaneous/G*v* and Planning/G*f* subscales. Accordingly, the authors chose not to separate these factors and decided to retain a four-factor model.

Ages 7–18. Finally, CFA results for ages 7–18 years supported a five-factor model including Sequential/G*sm*, Simultaneous/G*v*, Learning/G*lr*, Planning/G*f*, and Knowledge/G*c* scales.

The overall CFI values were reported as above 0.99 for all age groups. The RMSEA results also supported the overall factor structure across age groups with RMSEA values ranging from 0.033 to 0.055 for the test batteries that only included the core subtests. Both of these findings meet accepted standards in the structural equation modeling literature (Hu & Bentler, 1999).

In a recent article evaluating the factor structures of commonly used intelligence tests, Frazier and Youngstrom (2007) provided evidence of exponential increases in the factorization of intelligence tests over time. Based on the results of their analyses, where Kaiser, CFA, and a variety of criteria for identifying the number of factors were used, the authors concluded that commonly used confirmatory factor analytic methods could lead to an over-factorization of tests. In other words, CFA methods are liberal methods of factor extraction that tend to confirm the a priori structure of intelligence tests and do not clearly point researchers toward alternative models. Their use of other factor selection criteria suggested that most modern "multifactor" tests are probably measuring far fewer latent traits (probably 2 or 3) than indicated by a priori theory or CFA models that are often reported in test manuals.

Although the KABC-II was not evaluated for the purposes of these analyses, it is possible that the five-factor structural model would not be supported using more conservative factor analyses. In light of these new findings, parsimony appears to be the wisest course of action to take in interpretive practice (Frazier & Youngstrom, 2007). In other words, recent findings suggest that interpretation of most intelligence tests should focus on the general intelligence composite and the two or three largest factors available (i.e., those that account for the largest portion of variance explained, typically the verbal and spatial factors) (Kamphaus, in preparation).

Correlations with Other Measures of Intelligence

Correlation coefficients, mean differences, and standard deviations were calculated between the KABC-II scores and several concurrent intelligence measures: the original K-ABC, the *Wechsler Intelligence Scales for Children, third and four editions* (WISC-III; Wechsler, 1991; WISC-IV; Wechsler, 2003), the *Wechsler Preschool and Primary Scale of Intelligence, third edition* (WPPSI-III; Wechsler, 2002), the *Kaufman Adolescent and Adult Intelligence Test* (KAIT; Kaufman & Kaufman, 1993), and the *Woodcock-Johnson III, Tests of Cognitive Abilities* (WJ-III-Cog; Woodcock, McGrew, & Mather, 2001). Overall, the comparisons between the KABC-II and these cognitive measures showed consistently high correlations between the FCI and MPI and the other global intelligence scores. For example, the global score correlations with the FCI ranged from 0.77 for the WISC-III and 0.89 for the WISC-IV.

The KABC-II scale scores tended to be correlated highest with test scales that measure similar abilities. For instance, the Knowledge/G*c* scale correlated highly with other scales of verbal ability (e.g., 0.86 with the WISC-IV Verbal Comprehension Index), while the Planning/G*f* scale correlated with other reasoning or nonverbal composites (e.g., 0.69 with the WISC-IV Perceptual Reasoning Index). The KABC-II scales correlated only slightly higher with WJ-III-Cog scales with the same name than with other dissimilar scales. While it is beyond the scope of this chapter to explain this finding, we think that differences in item content should be investigated in future studies comparing these measures.

Correlational studies between the KABC-II and measures of academic achievement were

also conducted. The *Peabody Individual Achievement Test, Revised* (PIAT-R; Markwardt, 1989, 1998), the KTEA-II, the *Woodcock-Johnson III, Tests of Achievement* (WJ-III-ACH; Woodcock et al., 2001), and the *Wechsler Individual Achievement Test, second edition* (WIAT-II; Wechsler, 2001) all produced moderate to high correlations with the KABC-II. For example, the correlations between the FCI and the WIAT-II total score were 0.72 for grades 2–5 and 0.87 for grades 7–10.

Demographic Group Differences

Gender. For ages 3–6, girls outperformed boys across the Sequential/G*sm*, Simultaneous/G*v*, and Learning/G*lr* scales with scores differing between 2.5 and 3.3 standard score points. No gender differences were identified for the Knowledge/G*c* scale. Global scores also showed significant differences with girls outperforming boys between 3.5 and 4 score points. For ages 7–18, girls significantly outperformed boys on the Learning/G*lr* and Planning/G*f* scales, whereas boys outperformed girls on the Simultaneous/G*v* scale. No statistically significant differences were noted in the Sequential/G*sm* and Knowledge/G*c* scales or for any of the global scores. These findings are generally consistent with prior research in terms of their direction and small magnitude of about 1/5 SD or less (Kamphaus, in preparation).

Parental Education. The means across all scale scores and global scores displayed an expected trend of increase in scores with increase in parental education. Parental education accounted for a greater amount of the test score variance for ages 3–6 than ages 7–18. These differences were moderate at less than 1/3 SD making it difficult to generalize about the size and consistency of developmental trends in the data. The greatest amount of variance was detected in the Knowledge/G*c* scales for both groups. For the Knowledge/G*c* scales the differences between parental education groups was as large as $1\frac{1}{3}$ –$1\frac{1}{2}$ SD (See table 8.6 of the *KABC-II Manual*).

Ethnicity. After controlling for child sex and mother's education, child ethnicity still accounted for a significant portion of the variance for all scale and global scores except for the Learning/G*lr* scale and the MPI for ages 3–6. For ages 7–18, ethnicity accounted for a significant portion of the variance across all scale and global scores. Typical bias mitigation procedures were used during the test development process including expert panel reviews, statistical item bias detection methods, and adequate inclusion of U.S. minority group populations in the sampling process. These procedures along with other design features reduced the magnitude of typical score differences between U.S. ethnic, linguistic, and cultural groups. For example, the White and African-American groups differed by approximately 1/3 standard deviation for the MPI and 1/2 deviation for the FCI. These differences are smaller than the score differences that have been reported for global scales in many other cognitive assessments (Kamphaus, in preparation).

Performance of Clinical Groups

The KABC-II was administered to children previously classified as possessing one of the following diagnoses: Mental Retardation, Learning Disabilities (reading, math, and written expression), Attention-Deficit Hyperactivity Disorders, Autistic Disorder, Emotional Disturbance, Gifted, and Hearing Loss. The means and standard deviations across the clinical samples are reported in Table 3. Given the small sample sizes for many of these clinical groups, the results from these pilot studies should be interpreted with caution. Additional studies with larger sample sizes should be conducted to provide greater confidence in the validity of KABC-II inferences for these samples.

Learning Disabilities. Diagnosis of learning disabilities was based on a severe discrepancy between the performance on an achievement measure in the area of disability and a measure of intellectual ability. The KABC-II was administered to 141 students from the ages of 6:10–18:9 ($M = 13:2$) for the reading disability sample, 96 students from the ages of 6:10–18:9 ($M = 13.7$) for the mathematics sample, and 122 students from the ages of 6:10–18:9 ($M = 13.3$) for the written expression sample. All three clinical groups displayed significant differences from the non-clinical reference group across scale and global scale scores, ranging from 13 to 18 points.

Mental Retardation. The KABC-II was administered to 42 students (ages 3:10–18:10; $M = 11.2$) previously classified as having mild

TABLE 3. *M* (SD) of the KABC-II Factor and IQ Scores for Exceptional Individuals

	Mental retardation	Hearing loss	LD reading	LD written exp.	LD math	ADHD	Gifted	Autism	Emotional disorders
Sequential/G*sm*	69.4 (13.9)	83.2 (13.1)	85.4 (14.8)	84.6 (14.2)	83.7 (15.1)	93.4 (15.5)	113.5 (13.8)	72.3 (16.4)	88.7 (13.5)
Simultaneous/G*v*	64.5 (13.4)	94.6 (13.5)	88.1 (15.5)	87.7 (15.7)	84.6 (14.4)	92.5 (17.9)	114.1 (13.9)	68.3 (15.8)	92.3 (18.2)
Learning/G*lr*	72.4 (15.5)	101.6 (15.4)	84.3 (14.1)	83.9 (14.1)	83.7 (16.0)	95.9 (17.6)	113.3 (12.3)	76.1 (20.6)	95.5 (17.1)
Planning/G*f*	65.3 (13.3)	97.6 (18.3)	86.8 (14.8)	86.8 (15.6)	82.7 (13.1)	94.1 (16.0)	113.4 (12.0)	70.7 (20.2)	94.1 (17.1)
Knowledge/G*c*	69.1 (15.0)	80.9 (15.3)	84.8 (14.0)	85.2 (15.3)	82.0 (13.7)	95.9 (16.8)	118.4 (13.1)	66.1 (21.3)	94.2 (15.3)
MPI	64.8 (13.1)	94.3 (14.7)	82.6 (13.4)	82.1 (13.5)	79.8 (13.2)	92.5 (17.2)	118.7 (11.9)	68.1 (17.7)	90.9 (16.1)
FCI	64.5 (13.6)	90.6 (14.9)	82.2 (13.6)	82.0 (14.0)	79.3 (13.2)	93.0 (17.3)	120.1 (11.8)	66.9 (18.7)	91.1 (15.9)
NVI	65.6 (15.1)	95.7 (17.1)	85.3 (13.5)	84.9 (13.8)	81.7 (11.8)	93.1 (17.7)	116.8 (12.9)	68.6 (18.8)	91.9 (15.9)

Adapted from Tables 8.31–8.39 in Kaufman and Kaufman (2004a, pp. 126–131).

mental retardation. All individuals possessed a full-scale score on a previous intelligence measure ranging from about 50–70 with concurrent deficits in adaptive behavior. As expected, all individuals performed much lower when compared to the non-clinical group, scoring in the mid-60s across all three global scales. In contrast to the original K-ABC, the KABC-II possesses a larger range of obtained scores allowing for greater separation between levels of mental retardation.

Autistic Disorder. The clinical sample of children with autism was composed of 38 children (ages 4:3–18:10; $M = 13:3$) who were independently diagnosed according to the criteria set by the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision* (DSM-IV-TR; American Psychiatric Association, 2000). The global scale scores were reported as 66.9 (FCI), 68.1 (MPI), and 68.6 (NVI). Although the test manual recommended using the Luria model when administering the test to children with autism, the FCI score for this clinical sample only differed from the MPI score by approximately 1 point.

Attention-Deficit/Hyperactivity Disorder (ADHD). The ADHD clinical sample was composed of 56 children (ages 5:11–18:9; $M = 12:9$) who were independently classified according to the criteria set by the DSM-IV-TR. Although this subgroup scored within the average range, the global scales were 9–10 points lower than the non-clinical sample.

Emotional Disturbance. The KABC-II was administered to 37 children (ages 5:11–18:11; $M = 14:1$) with emotional disturbance. Individuals in this category were defined as possessing "an emotional condition that, over a long period of time and to a marked degree, consistently interfered with the learning process" (Kaufman & Kaufman, 2004a, p. 130). Members of this sample displayed significant differences from the non-clinical sample on all scales except for the Learning/G*lr* scale. The most pronounced deficit (11.7 points) was observed for the Sequential/G*sm* scale. These findings are in contrast to investigations of the original K-ABC, which found individuals with behavioral or emotional disturbance performed better on the Sequential Processing scale compared to the Simultaneous Processing scale items (Kamphaus, 2003). The global scales were lower than

those observed for the non-clinical sample by 8–9 points.

Gifted. For the study of children identified as gifted, 95 students who were independently identified by their schools as high performing or talented in one or more academic, artistic, or leadership categories were administered the KABC-II. The mean FCI of 120.1 was far lower than the expected cutoff of approximately two standard deviations above the mean. These score differences could be contributed to many factors including the Flynn effect or statistical artifacts such as restriction of range, selection bias, and/or regression to the mean (Kamphaus, in preparation).

Hearing Loss. The KABC-II was administered to 28 students (ages 6:8–17:7, $M = 12.5$) who possessed moderate to severe hearing loss, which had adversely affected their educational performance. Individuals in this subgroup performed significantly different from the non-clinical sample across all scale scores except for the Learning/G*lr* scale. The largest performance deficit occurred in the Knowledge/G*c* scale (26.7 points) domain, which is consistent given the verbal emphasis in the Knowledge/G*c* subtests. The mean NVI (95.7) and MPI (94.3) global scores were 4 and 5 points higher than the FCI score. These data support the clinical utility of administering the Luria or NVI batteries to children with hearing impairments.

Administration

The KABC-II manual indicates that administering the core subtests takes approximately 30–60 min (Luria Model) and 40–70 min (CHC) depending on the age of the examinee. The expanded battery of all core and supplementary subtests, depending on age, takes approximately 1 h (ages 3–4), 90 min (ages 5–6), or 100 min (ages 7–18).

In the test manual, specific details are given regarding administration procedures such as which subtests to administer depending on age and interpretation system; start, basal, and discontinue rules; guidelines for querying; and when to invoke special administration alternatives that can be used when testing bilingual, motor impaired, hard of hearing children, and/ or children who may score much higher or lower than other children of the same age. Some of the

unique administration alternatives are described in more detail in the following sections.

Teaching Items. All subtests, with the exception of those on the Knowledge/G*c* scale and the delayed recall tasks, include test items that the Kaufmans have termed "teaching items." Teaching items were originally introduced in the original K-ABC and have now become ubiquitous across most cognitive measures. Two of these items are administered at the beginning of the subtests, and allow the examiner to provide feedback if the child does not understand the task. If the child does not answer the second teaching item correctly, the examiner may use his/her own words to explain how to perform the tasks by providing additional examples, using easier language, or writing the instructions on a sheet of paper. Although the subtest questions must be delivered in English, the teaching items can be delivered in any language.

Out of Level Testing. Another innovation of the original K-ABC, which was retained in the KABC-II, is an option that allows examiners to administer an out-of-level testing battery for children ages 3–7. This administration alternative provides a way to examine high or low functioning children whose age level battery may not contain adequate ceilings or floors. All subtest scores are based on norms for the child's own age.

Non-English Responses. Another asset of the original test and the KABC-II is that for questions that require verbal responses, the examiner may accept a response in any language, sign-language, or sub-cultural slang. Moreover, the KABC-II record form provides sample answers to verbal-response-based questions in both English and Spanish.

Timed Items. Several subtests (i.e., Triangles, Pattern Reasoning, and Story Completion) provide bonus points for rapid responding. Although the practice of awarding bonus points can help distinguish between high performing adolescents, it penalizes children whose response time is reduced due to motor impairments (e.g., children with cerebral palsy) rather than cognitive speed. Fortunately, the KABC-II allows the examiner to compute a child's score without time-based bonus points. Examiners should keep this option in mind when administering the test battery to children with physical impairments that may influence their response time.

Qualitative Indicators. The KABC-II allows examiners to monitor a child's test-taking behavior through the use of Qualitative Indicators. For each subtest, the response form includes a checklist of common test-taking behaviors that may exert a positive or negative influence on a child's test performance (i.e., "perseveres," "fails to sustain attention," "reluctant to respond when uncertain"). While documenting these behaviors does not directly tell the examiner about the test construct being assessed, documenting these observations is useful for qualitatively assessing the way a child approaches a cognitive task.

Interpretation

The interpretation of an examinee's unique performance on an intelligence test can be difficult. Detailed information on how to interpret these measures is beyond the scope of this chapter, however a brief overview of an interpretation process is offered by the Kaufmans in the *KABC-II Manual*. The Kaufmans' interpretative analysis consists of four main steps. The initial step involves interpreting the global scale index (FCI, MPI, or NVI). The KABC-II manual provides tables to obtain the percentile rank, confidence interval, and descriptive category for an individual's global score. The descriptive categories include Upper Extreme, Above Average, Average Range, Below Average, and Lower Extreme and are based on a standard deviation of 15 points to define each category. For instance, the Average category ranges from 85 to 115 which correspond to +/− 1 SD from the mean, the Above Average category ranges from 1 to 2 SD above the mean, and so forth. If the Nonverbal scale is administered or if the child is age 3, the examiner should not proceed to any other interpretive steps.

The next step involves interpreting the individual's profile of scale indexes to identify both the individual's personal (relative to the child's overall ability) and normative (compared to children about the same age) strengths and weakness. The third step involves evaluating planned comparisons between Initial Learning versus Delayed Recall and Learning Ability versus Acquired Knowledge. Finally, the last step involves the interpretation of the results from supplementary subtests. Some of these interpretive steps, such as ipsative interpretation, have

been rigorously debated. A full review of this debate is beyond the scope of this chapter, but interested readers should pursue other sources of information regarding models of test interpretation (i.e., Kamphaus, in preparation).

Reynolds, Kamphaus, and Rosenthal (1989) proposed a neuropsychological framework, using Vygotsky's conceptualization of the Zone of Proximal Development, for interpreting the original K-ABC, which could be extended for use with the current version.

Vygotsky espoused what continues to be a widely held "truth" regarding children's learning: "A well known and empirically established fact is that learning should be matched in some manner with the child's developmental level" (Vygotsky, 1978, p. 85). Hunt (1961), in his now-classic volume, concurred with this sentiment and conceptualized this concept in part as the "problem of the match." Although true for normally developing children, such a match may be absolutely crucial for promoting the development of children with an immature or traumatized central nervous system.

In formulating the concept of the Zone of Proximal Development (ZPD), Vygotsky rejected what he considered to be the three primary alternative developmental theories of learning (learning broadly defined and not restricted to school learning). The first rejected theory centers on the assumption that processes of child development are independent of learning, which is considered an external process, not an activity involved in development. Vygotsky classified Piagetian theory under this theoretical rubric. The second rejected approach includes theories assuming that learning *is* development. These theories reduce development to a simple accumulation of all possible responses by the child. The third rejected theoretical proposition is based on a combination of the two prior positions, in which development is based on two different but related processes, maturation, which depends on the development of the central nervous system, and learning, also considered here as a developmental process. In this apparently reciprocal relationship, maturation makes new learning possible which then stimulates and pushes forward the maturation process. The latter is the approach that led educators in the past to conclude that the study of certain subjects (e.g., Latin) was of great value for mental development. Vygotsky framed the concept of ZPD to

provide a more adequate view of the relationship between learning and development. This concept can lead practioners to develop improved cognitive retraining and rehabilitation programs for children who have resisted more traditional approaches.

In determining and using ZPDs, two developmental levels must first be established. The first is the child's current, *actual level of development*. Vygotsky viewed this level as reflecting existing developmental achievements as assessed by rigidly administered, standardized measures of intelligence and achievement. It is the level determined by cognitive tasks that children can currently complete on their own. The second level of development to determine is the level the child can achieve if an adult or more advanced, accomplished peer provides help through demonstration, asking leading questions, or actual collaboration leading the child to discover the answer. ZPD is "the distance between the actual developmental level as determined by independent problem solving and the level of potential development as determined through problem solving under adult guidance or in collaboration" (Vygotsky, 1978, p. 86). The upper limit of the ZPD today becomes the actual developmental level of tomorrow.

In neuropsychological work in particular, it can be helpful to apply this principle in rehabilitation efforts. The KABC-II is structured in such a way as to give a readily available assessment of the ZPD because it can provide a measure of both developmental levels. Typically, the ZPD is determined by contrasting scores on the same test under standardized versus nonstandardized limit-testing procedures. Unfortunately, the use of two different tests is confounded by differences in normative samples and other technical differences between the scales (e.g., see Reynolds, 1984, 1986, for discussions of these problems). The structure of the KABC-II offers a good solution to these problems.

The first developmental level, independent problem solving, can be determined from administration of the KABC-II Knowledge/G*c* scale. The second level of development can be ascertained perhaps more accurately with the KABC-II MPI under Luria's model. To assess the second developmental level, an examiner should administer the KABC-II MPI subtests using the following procedures:

1. Administer these subtests under standardized procedures.
2. After the sample and teaching items, however, continue to use the teaching procedures whenever a child misses an item when administered under standardized conditions. Give credit for an item whenever you can lead the child to the correct response, but do not assign credit when you must demonstrate or recite the correct response.
3. Continue administration of each MPI subtest until the child fails to obtain credit on two consecutive items (a ceiling we have estimated to be appropriate based on the growth curves of the various mental processing subtests and the length of time available for testing) *when assistance has been provided by the examiner*.
4. Compute the raw and scaled scores for the mental processing subtests and the MPI just as though a standardized administration had been conducted.

The difference between the MPI and the Knowledge scale approximates the child's ZPD. This quantification of the ZPD, which can be particularly useful for research purposes, provides relatively clear guidance in developing short-term and intermediate goals for cognitive rehabilitation programs. The next step in the developmental process is revealed through assessment of the ZPD. In cognitive retraining it is important to know which skills are most likely to be responsive to rehabilitation efforts at specific points during the retraining process.

This assessment can be repeated periodically as well. By this conceptualization, we are constantly seeking to move children forward to a level that is within their reach by constantly reassessing the child's reach so that we continue the "match" (i.e. Hunt, 1961) between development and learning. This approach can be a useful guide for children with disabilities as well and certainly is not restricted to children with neuropsychological problems.

Conclusions

The Kaufmans and their colleagues have built upon the foundation set by the K-ABC to create a new version that addresses past inadequacies and meets modern standards of test design. The KABC-II, like most modern comprehensive intelligence tests, measures similar intelligence constructs with similar evidence of reliability and validity. Kamphaus (in preparation) makes the point that intelligence testing is now so well developed that these tests have become "commodities." In other words, choosing an intelligence test for use is now based primarily on practical considerations rather than superior psychometric characteristics. As Kamphaus (in preparation) points out, intelligence testing technology is now so good that it is not unlike Magnetic Resonance Imaging machines where the hospital makes the decision to purchase a particular machine based on practical matters such as size and cost, rather than for superior measurement characteristics, since the basic functionality of the machine is not that different for General Electric, Phillips, or other manufacturers.

The KABC-II, similar to most modern cognitive assessments measures general intelligence, crystallized abilities, and spatial abilities quite well. However, given concerns of over-factorization (Frazier & Youngstrom, 2007), its measurement of additional constructs is likely to continue to be a focus of debate across the intelligence testing literature. Thus, we suggest caution when attempting to interpret beyond these core factors. In the concluding section we offer our perceptions of the strengths and weaknesses of the KABC-II as an assessment tool.

Strengths

- The test results demonstrate minimal differences between demographic groups (i.e., less than 4 points across gender, corresponding increases of scores with increases in parent education, and less than 7 points across ethnic groups)
- Teaching items help ensure that the examinee understands the task and can be performed in any language
- Qualitative indicators encourage behavioral monitoring during the test session for factors that may impact a child's performance
- The test provides adequate score ranges to differentiate between students who score well above or below average

- Test materials include a list of correct responses in both English and Spanish.
- Test materials are bright, interactive, and fun for children
- The authors made laudatory efforts to make it possible to develop valid inferences about an individual's intelligence, while at the same time reducing subgroup mean differences.

Weaknesses

- The authors state that mental processes and cognitive abilities are distinct, but do not explain how a single test can measure two distinct theoretical constructs
- The factor structure of the test is not completely supported at all age levels
- Some subtests place emphasis on processing speed (bonus points for time responses) to support differentiation for older or very intelligent examinees; however, the test does permit calculation of standard scores without time-related bonus points
- Differing core and supplementary subtests across age levels can make test administration confusing for the examiner
- Differing start and discontinue rules for each subtest can also create difficulties for the examiner.

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14

Clinical Neuropsychological Assessment with the Test of Memory and Learning, Second Edition

CECIL R. REYNOLDS AND JUDITH K. VORESS

Memory complaints seem ubiquitous in the clinical practice of neuropsychology. Nearly every central nervous system (CNS) disorder associated with disturbances of higher cognitive functions has memory disturbance in some form noted as a common complaint (see, for example, reviews of disorders and their assessment in Baron, Fennell, & Voeller, 1995; Fletcher-Janzen & Reynolds, 2003; Gillberg, 1995; Knight, 1992; Lezak, Howieson, Loring, Hannay, & Fischer, 2004). In cases of traumatic brain injury (TBI), memory disturbances are the most common of all patient complaints (Corrigan, Whiteneck, & Mellick, 2004; D'Amato, Fletcher-Janzen, & Reynolds, 2005; Tyler & Mira, 1999). Three age groups account for a majority of cases of TBI – birth to 5 years, 15–24 years, and over 75 years, with males outnumbering females by about 2 to 1. Motor vehicle accidents are the most common cause of TBI; falls and violence are second and third, respectively (Langlois, Rutland-Brown, & Thomas, 2006). TBI produces the least predictable forms of memory loss with the exception of increased forgetting curves. However, as research becomes more sophisticated, disturbances of memory and learning are being discovered elsewhere as well. In many medical disorders as well as in a variety of neuropsychiatric disturbances, retrieval of information is often compromised along with acquisition of new material. Table 1 lists some of the more frequently occurring disorders in which memory and learning are likely to be compromised and should thus be assessed.

Memory is almost always one focus of cognitive rehabilitation or retraining (Skeel & Edwards, 2001). However, recovery of memory functions post-TBI is less predictable than improvements in more general aspects of intellectual function, likely, at least in part, because of the disturbances of attention and concentration that typically accompany TBI. Problems with memory are some of the most persistent sequelae of TBI (Skeel & Edwards, 2001). While some forms of memory tasks (e.g., immediate recall) are suppressed in functional and organic disorders, other memory tasks (e.g., delayed recall or forgetting) provide very good discrimination between psychiatric disorders such as depression and TBI and other CNS insult.

Given the ubiquitous nature of memory in daily affairs, particularly during the school-age years, and the importance of memory in evaluating the functional and the physiological integrity of the brain, it is surprising that comprehensive

CECIL R. REYNOLDS • Department of Educational Psychology, Texas A&M University, College Station, Texas 778430. JUDITH K. VORESS • Donald D. Hammill Institute on Disabilities, Austin, Texas 78757.

TABLE 1. Frequent Disorders in Which Memory and Learning Are Likely to be Compromised

Alzheimer's disease
Anoxia
Attention deficit-hyperactivity disorder
Autism and other developmental disorders
Cancer (especially brain tumors, lung cancer, parathyroid tumors, leukemia, and lymphoma)
Cerebral palsy
Down syndrome
Endocrine disorders
Extremely low birth weight
Fragile X
Huntington's chorea
Hydrocephalus
Hypoxic-ischemic injury
Iatrogenic memory disorders (e.g., secondary to chemotherapy, ECT)
Inborn errors of metabolism (e.g., PKU, galactosemia)
In utero toxic exposure (e.g., prenatal exposure to cocaine, fetal alcohol syndrome)
Kidney disease/transplant
Learning disability
Lesch-Nyhan disease
Liver disease/transplant
Major depressive disorder
Meningitis
Mental retardation
Myotonic dystrophy
Neurodevelopmental abnormalities affecting brain development (e.g., anencephaly, microcephaly, callosal dysgenesis)
Neurofibromatosis Prader–Willi syndrome
Parkinson's disease
Pick's disease
Rett's syndrome
Schizophrenia
Seizure disorders
Tourette's syndrome
Toxic exposure (e.g., lead, mercury, CO)
Traumatic brain disorder
Turner's syndrome
Wernicke–Korsakoff's syndrome
Williams syndrome
XXY syndrome
XYY syndrome

assessment of memory in children and adolescents is a recent phenomenon. This seems particularly odd, given the plethora of such tasks available for adults dating from at least the 1930s.

To some extent, memory assessment with children and adolescents must have been viewed as important since the earliest of modern intelligence tests (the 1907 Binet) and even the venerable Wechsler Scales, in their various children's versions, all included one or two brief assessments of immediate recall. Still, the major texts on child neuropsychology of the 1970 s and 1980 s (e.g., Bakker, Fisk, & Strang, 1985; Hynd & Obrzut, 1981) do not discuss assessment of memory despite the finding that 80% of a sample of various clinicians who perform testing noted memory as an important aspect of the assessment of cognitive and intellectual functions (Snyderman & Rothman, 1987). By 1995, assessment of memory function in children is discussed in key textbooks (e.g., Rourke, Bakker, Fisk, & Strang, 1983) and its relation to various medical (e.g., Baron et al., 1995) and neuropsychiatric disorders (e.g., Gillberg, 1995) routinely included in major works on child neuropsychology.

Dorothea McCarthy, the noted psycholinguist, was aware of the importance of memory and included a memory index on the then-innovative McCarthy Scales of Children's Abilities (McCarthy, 1972). Koppitz (1977), another pioneer in assessment of children, noted the need for a more detailed evaluation of children's memory functions and devised the four-subtest Visual–Aural Digit Span Test (VADS; Koppitz, 1977). The VADS quickly became popular with school psychologists, among whom Koppitz was well known because of her work in childhood assessment with the Bender–Gestalt Test (and recently updated, Reynolds, 2007) and human figure drawings, but was not adopted among neuropsychologists. The VADS is relatively narrow, assessing only sequential memory for digits but altering modality of input and output. No real attempt at developing a comprehensive assessment of children's memory appears until the introduction of the Wide Range Assessment of Memory and Learning (WRAML) for ages 5 through 17 by Sheslow and Adams (1990).

The WRAML was born of the frustration and dissatisfaction of its authors in not having a sound, comprehensive measure of memory functioning in children (Sheslow & Adams, 1990). The WRAML consists of nine subtests divided equally into three scales – Verbal Memory, Visual Memory, and Learning – followed by a brief delayed recall to assess rapidity of decay of

memory (i.e., forgetting). The WRAML was a substantial improvement over existing measures of memory for children but still provided a limited sample of memory and learning tasks. To increase the breadth and depth of analysis of memory function from the preschool years through the high school years (ages 5–20), Reynolds and Bigler (1994a, b) developed the Test of Memory and Learning (TOMAL). The second edition of the TOMAL, the TOMAL-2 (Reynolds & Voress, 2007a), continues to provide professionals with a standardized measure of different memory functions for children and adolescents.

After a brief review of the basic neurobiology of memory, this chapter turns to a description of the TOMAL-2 and its clinical interpretation. The TOMAL-2 is featured for assessment of memory because this measure is the most comprehensive of its kind. The variety of well-normed, reliable subtests available on the TOMAL-2 provides examiners with the maximum flexibility in evaluating various referral questions with the choice of the most comprehensive of assessments available as well, with good reliability and specificity of measurement for individual subtests.

Basic Neurobiology of Memory

Attention leaves tracks or traces within the brain that become memory. Memory, as commonly thought of, is the ability to recall some event or information of various types and forms. Biologically, memory functions at two broad levels, one at the level of the individual cell and the other at a systemic level. With the creation of memories, changes occur in individual cells (e.g., see Cohen, 1993; Diamond, 1990; Scheibel, 1990), including alterations in cell membranes and synaptic physiology.

At a systems level, there exists a division of sorts in the formation of memory and memory storage. There is considerable evidence for distributed storage of associative memory throughout the cortex, and which may even occur in a statistical function (Cohen, 1993). At the same time, there is evidence for more localized storage of certain memories and localized centers for the formation of memory and in classical and operant conditioning.

The medial aspect of the temporal lobe, particularly the hippocampus and its connecting fibers within the other limbic and paralimbic structures, is particularly important in the development of associative memory. The limbic system (with emphasis on the posterior hippocampal regions) also mediates the development of conditioned responses, and some patients with posterior hippocampal lesions may not respond to operant paradigms absent one-to-one reinforcement schedules. Damage to the medial temporal lobe and its connecting fibers or to the midline structures of the diencephalon typically results in difficulties in the formation of new memories (anterograde amnesia), but may also disrupt recently formed memories preceding the time of injury (retrograde amnesia). Various regions within the limbic and paralimbic structures have stronger roles in the formation of certain types of memory, and simple conditioned memories may occur at a subcortical level. Through all of the interactions of these systems, related mechanisms of attention, particularly in the brain stem and the frontal lobes, are brought to bear and will influence memory formation directly and indirectly. Memory is a complex function of the interaction of brain systems (with unequal contributions) and damage to one or more of many structures may impair the ability to form new memories.

In right-handed individuals, there is a tendency for damage to the left temporal lobe and adjacent structures to affect verbal and sequential memory most strongly. Damage to the cognate areas of the right hemisphere affects visual and spatial memory more adversely.

Through distributive storage of memory, the entire brain participates in memory functioning. The recall of well-established memories tends to be one of the most robust of neural functions, while the formation of new memories, sustained attention, and concentration tend to be the most fragile of neural functions. Neurological dysfunction of most types is associated with a nonspecific lessening of memory performance along with disruptions of attention and concentration, but with greater consequence when temporolimbic, brain stem, or frontal lobe involvement occurs. However, a variety of psychiatric disturbances, especially depression, may also suppress fragile anterograde memory systems, and a careful analysis of memory, forgetting, affective states, history,

and comprehensive neuropsychological testing may be necessary before one can conclude that memory disturbances are organic in origin.

TOMAL-2

The TOMAL-2 is a comprehensive battery of 14 memory and learning tasks (eight core subtests and six supplementary subtests) normed for use from ages 5 years 0 months 0 days through 59 years 11 months 30 days. The eight core subtests are divided into the content domains of verbal memory and nonverbal memory that can be combined to derive a Composite

TABLE 2. Core and Supplementary Subtests and Indexes Available for the TOMAL-2

Core subtests	M	SD
Verbal		
Memory for Stories	10	3
Word Selective Reminding	10	3
Object Recall	10	3
Paired Recall	10	3
Nonverbal		
Facial Memory	10	3
Abstract Visual Memory	10	3
Visual Sequential Memory	10	3
Memory for Location	10	3
Supplementary subtests		
Verbal		
Digits Forward	10	3
Letters Forward	10	3
Digits Backward	10	3
Letters Backward	10	3
Nonverbal		
Visual Selective Reminding	10	3
Manual Imitation	10	3
Summary Scores		
Core indexes		
Verbal Memory Index (VMI)	100	15
Nonverbal Memory Index (NMI)	100	15
Composite Memory Index (CMI)	100	15
Supplementary indexes		
Verbal Delayed Recall Index (VDRI)	100	15
Attention/Concentration Index (ACI)	100	15
Sequential Recall Index (SRI)	100	15
Free Recall Index (FRI)	100	15
Associative Recall Index (ARI)	100	15
Learning Index (LI)	100	15

Memory Index. A Verbal Delayed Recall Index that requires recall of two of the verbal subtests' stimuli 30 min after their first administration is also available.

As noted above, memory may behave in unusual ways in an impaired brain and traditional content approaches to memory may not be useful. The TOMAL-2 thus provides alternative groupings of the subtests into the Supplementary Indexes of Sequential Recall, Free Recall, Associative Recall, Learning, and Attention and Concentration.

Table 2 summarizes the names of the subtests and summary scores, along with their metric. The TOMAL-2 subtests are scaled to the familiar metric of mean equaling 10 and a standard deviation of 3 (range 1–20). Composite or summary scores are scaled to a mean of 100 and standard deviation of 15. All scaling was done using the Roid's (1989) continuous norming procedure and is described in detail in Reynolds and Voress (2007b).

TOMAL-2 Subtests

The eight core, six supplementary, and delayed recall TOMAL-2 subtests require about 45 min for a skilled examiner. The subtests were chosen to provide a comprehensive view of memory functions and, when used in toto, provide the most thorough assessment of memory available. The subtests are named and briefly described in Table 3.

The TOMAL-2 subtests systematically vary the mode of presentation and response so as to sample verbal, visual, motoric, and combinations of these modalities in presentation and in response formats. Multiple trials to a criterion are provided on several subtests, including selective reminding, so that learning or acquisition curves may be derived. Multiple trials (at least five are necessary according to Kaplan, 1996) are provided on the selective reminding subtests to allow an analysis of the depth of processing. In the selective reminding format (wherein examinees are reminded only of stimuli "forgotten" or unrecalled), when items once recalled are unrecalled by the examinee on later trials, problems are revealed in the transference of stimuli from working memory and immediate memory to more long-term storage. Cueing is also provided at the end of Word Selective Reminding Delayed

TABLE 3. Description of TOMAL-2 Subtests

Core

Memory for Stories. A verbal subtest requiring recall of a short story read to the examinee. Provides a measure of meaningful and semantic recall and is also related to sequential recall in some instances.

Facial Memory. A nonverbal subtest requiring recognition and identification from a set of distractors: black-and-white photos of various ages, males and females, and various ethnic backgrounds. Assesses nonverbal meaningful memory in a practical fashion and has been extensively researched. Sequencing of responses is unimportant.

Word Selective Reminding. A verbal free-recall task in which the examinee learns a word list and repeats it only to be reminded of words left out in each trial: tests learning and immediate recall functions in verbal memory. Trials continue until mastery is achieved or until six trials have been attempted. Sequence of recall is unimportant.

Abstract Visual Memory. A nonverbal task assessing immediate recall for meaningless figures where order is unimportant. The examinee is presented with a standard stimulus and required to recognize the standard from any of six distractors.

Object Recall. The examiner presents a series of pictures, names them, has the examinee recall them, and repeats this process until mastery is achieved or until five trials have been attempted. Verbal and nonverbal stimuli are thus paired and recall is entirely verbal, creating a situation found to interfere with recall for many individuals with learning disabilities but to be neutral or facilitative for individuals without disabilities.

Visual Sequential Memory. A nonverbal task requiring recall of the sequence of a series of meaningless geometric designs. The ordered designs are shown followed by a presentation of a standard order of the stimuli and the examinee indicates the order in which they originally appeared.

Paired Recall. A verbal paired-associative task on which the examinee is required to recall a list of word pairs when the first word of each pair is provided by the examiner. Both easy and hard pairs are used.

Memory for Location. A nonverbal task that assesses spatial memory. The examinee is presented with a set of large dots distributed on a page and asked to recall the locations of the dots in any order.

Supplementary

Digits forward. A standard verbal number recall task. Measures low-level rote recall of a sequence of numbers.

Visual Selective Reminding. A nonverbal analogue to Word Selective Reminding where examinees point to specified dots on a card, following a demonstration by the examiner, and are reminded only of dots recalled incorrectly. Trials continue until mastery is achieved or until five trials have been attempted.

Letters Forward. A language-related analogue to common digit span tasks using letters as the stimuli in place of numbers.

Manual Imitation. A psychomotor, visually based assessment of sequential memory where the examine is required to reproduce a set of ordered hand movements in the same sequence as presented by the examiner.

Digits Backward. This is the same basic task as Digits Forward except the examinee recalls the numbers in reverse order.

Letters Backward. A language-related analogue to the Digits Backward task using letters as the stimuli instead of numbers.

to add to the examiner's ability to probe depth of processing.

Subtests are included that sample sequential recall (which tends strongly to be mediated by the left hemisphere, especially temporal regions; e.g., see Lezak et al., 2004) and free recall in both verbal and visual formats to allow localization; purely spatial memory tasks are included that are very difficult to confound via verbal mediation to assess more purely right hemisphere functions.

Well-established memory tasks (e.g., recalling stories) that also correlate well with school learning are included along with tasks more common to experimental neuropsychology that have high (e.g., Facial Memory) and low (e.g., Visual Selective Reminding) ecological salience; some subtests employ highly meaningful material (e.g., Memory for Stories) while some use highly abstract stimuli (e.g., Abstract Visual Memory).

Aside from allowing a comprehensive review of memory function, the purpose for including such a factorial array of tasks across multiple dimensions is to allow a thorough, detailed analysis of memory function and the source of any memory deficits that may be discovered. The task of the neuropsychologist demands subtests with great specificity and variability of presentation and response and that sample all relevant brain functions in order to solve the complex puzzle of dysfunctional brain–behavior relationships. Kaufman (1979) first presented a detailed model for analyzing test data in a comprehensive format (later elaborated, Kaufman, 1994) that likens the task of the clinician to that of a

detective. The thoroughness, breadth, and variability of the TOMAL-2 subtests, coupled with their excellent psychometric properties, make the TOMAL-2 ideal for use in an "intelligent testing" model and particularly in the analysis of brain–behavior relationships associated with memory function.

Standardization

The TOMAL-2 was standardized on a population-proportionate stratified (by age, gender, ethnicity, race, socioeconomic status, region of residence, educational attainment of parents, and exceptionality status) random sample of children, adolescents, and adults throughout the United States. Standardization and norming was conducted for ages 5–59. Details of the standardization and specific statistics on the sample are provided in Reynolds and Voress (2007b).

Reliability

The TOMAL-2 subtests and composite indexes show excellent evidence of internal consistency reliability. Reynolds and Voress (2007b) report coefficient alpha reliability estimates that routinely exceed 0.90 for individual subtests and 0.93 for composite scores. Stability coefficients for the composite scores are typically in the 0.80s.

Validity

The TOMAL-2 scores correlate around 0.50 with measures of intelligence and achievement, indicating the TOMAL-2 is related to but not the same as these measures. Measures of intelligence typically correlate with one another around 0.75–0.85 and with measures of achievement around 0.55–0.65 (Reynolds & Voress, 2007b). These validity studies that are specific to the TOMAL-2 are reported in detail in the manual.

The TOMAL-2 has been published for only about 60 days as of this writing. Therefore, no independent studies of the TOMAL-2 have been published. However, the first and second editions are extremely similar in content, with only a small number of items being changed, and the

core battery being shortened by one subtest on the verbal and on the nonverbal scales. The subtests moved from the core battery remain as supplementary subtests. Scores from the first and second editions appeared to be highly equivalent. The manual discusses in detail the evidence supporting the equivalence of scores from the first and second editions. Therefore, we are comfortable relying upon research on the first edition as providing insights and evidence regarding score interpretation for the new edition of the TOMAL, the TOMAL-2.

Several studies have provided evidence of convergent and divergent validity of the TOMAL subtests as measures of various aspects of memory by examining patterns of correlations among TOMAL subtests and the Rey Auditory Verbal Learning Test and the Wechsler Memory Scale-Revised. The verbal components of the TOMAL correlate well with these measures but the nonverbal sections are relatively independent (Barker et al., 1994; Mueller et al., 1994; Russo et al., 1994). The TOMAL-2 nonverbal subtests, unlike a number of other purportedly visual and nonverbal memory tests, are difficult to encode verbally, making the TOMAL-2 nonverbal subtests more specific and less contaminated by examinees' attempts at verbal mediation. On the nonverbal or visual memory portions of existing memory batteries, examiners should expect larger differences across tests than on verbal memory measures.

Validity is a complex concept related to the interpretation of scores on tests, and many approaches to the question of meaning of performance on tests such as the TOMAL-2 are appropriate. Case studies, group comparisons, and views of the internal structure of tests all add to this knowledge. We next turn to the internal structure of the TOMAL-2.

Factor Structure of the TOMAL-2

Given the equivalents of the first and second editions of the TOMAL, we have relied upon information regarding the internal structure of the original version as research on the second edition has not yet had time to appear. Reynolds and Bigler (1996) provided extended information on the factor structure of the TOMAL and the derivation of the empirically derived *factor indexes* noted in Table 2. Using

the method of principal factors with Varimax and Promax rotations, the correlation matrix for all 14 TOMAL subtests was examined. Factors were extracted for three age groups (5–8, 9–12, and 13–18) and were found to be consistent across age levels. The analyses reviewed below are based on the full sample of 1342 children from the first edition. It is worthy of note that those analyses are based on normal, non-referred children and that factor analyses do not always demonstrate the same results with exceptional samples, especially samples with CNS dysfunction (e.g., see review material by Kamphaus & Reynolds, 1987). The following is based substantively on the presentation by Reynolds and Bigler (1996).

The two-factor solutions of the TOMAL did not support the division of the subtests into a verbal and a nonverbal scale. Clearly the structure of the TOMAL is more complex than is represented by these two groupings. There is a general factor present, much as with the intellectual factor, g, but weaker, that nevertheless supports the use of a composite score such as the CMI with normal populations. Tables 4 and 5 show the two-factor Varimax and Promax results for the TOMAL when these factors are forced.

The unconstrained, exploratory factor analyses are also given in Tables 4–6. The use of the criteria for factor extraction recommended by Reynolds (1982) including an examination of scree plots across age, absolute value of the eigenvalues, and the psychological meaningfulness of each statistically viable solution indicated the possibility that three-, four-, and five-factor solutions had the potential to be the most appropriate alternative. A visual inspection of each of these solutions indicated that the four-factor solution best met the criteria given by Reynolds (1982) and essentially made the most psychological sense. The first and strongest factor appearing in the Promax solution appears to be a reflection of overall memory skills that perhaps represents more complex memory tasks and cuts across all modalities and memory processes. This first factor is designated primarily by the large loadings of Memory for Stories, Word Selective Reminding, Object Recall, Paired Recall, Facial Memory, and Visual Selective Reminding.

The second factor emphasizes sequential recall and attention and is composed principally of large loadings by Digits Forward, Letters Forward, Visual Sequential Memory, and Manual Imitation. The third factor consists of Digits

TABLE 4. Two- and Four-Factor Promax Solutions of TOMAL Subtests

Subtest	Subtest g_m[b]	Fac specificity[c]	Two-factor solution[a]		Four-factor solution[a]			
			Fac 1	Fac 2	Fac 1	Fac 2	Fac 3	Fac 4
Memory for Stories	0.53	0.56	0.17	*0.45*	*0.37*	0.05	0.19	0.19
Word Selective Reminding	0.59	0.46	0.01	*0.67*	*0.73*	0.08	0.03	0.19
Object Recall	0.55	0.51	0.05	*0.58*	*0.57*	0.08	0.01	0.01
Digits Forward	0.64	0.45	*0.71*	0.00	0.03	*0.74*	0.05	0.06
Paired Recall	0.55	0.48	0.03	*0.67*	*0.68*	0.05	0.07	0.04
Letters Forward[d]	0.68	0.40	*0.78*	0.03	0.01	*0.76*	0.10	0.03
Digits Backward[d]	0.63	0.59	*0.64*	0.06	0.06	0.10	*0.63*	0.01
Letters Backward[d]	0.64	0.46	0.72	0.00	0.02	0.13	*0.66*	0.07
Facial Memory	0.39	0.66	0.02	*0.47*	*0.37*	0.01	0.08	0.224
Visual Selective Reminding	0.45	0.69	0.02	*0.47*	0.37	0.01	0.08	0.24
Abstract Visual Memory	0.54	0.60	0.14	*0.49*	0.32	0.01	0.03	*0.38*
Visual Sequential Memory	0.55	0.61	0.28	*0.34*	0.26	*0.38*	0.13	0.18
Memory for Location	0.31	0.68	*0.24*	0.12	0.06	0.00	0.09	*0.44*
Manual Imitation[d]	0.61	0.57	*0.59*	0.09	0.02	*0.38*	0.15	0.29

[a]Largest loading is in italics.
[b]First unrotated factor loading, taken to represent a general memory factor.
[c]Subtest-specific variance, using median values across age.
[d]Supplementary subtest.

TABLE 5. Two- and Four-Factor Varimax Solutions of TOMAL Subtests

Subtest	Two-factor solution[a]		Four-factor solution[a]			
	Fac 1	Fac 2	Fac 1	Fac 2	Fac 3	Fac 4
Memory for Stories	0.29	*0.48*	*0.42*	0.12	0.25	0.29
Word Selective Reminding	0.21	*0.65*	*0.68*	0.20	0.14	0.02
Object Recall	0.21	*0.57*	*0.57*	0.19	0.11	0.13
Digits Forward	*0.68*	0.21	*0.21*	*0.69*	0.23	0.09
Paired Recall	0.16	*0.64*	*0.64*	0.11	0.15	0.08
Letters Forward[b]	*0.74*	0.20	0.19	*0.72*	0.28	0.13
Digits Backward[b]	*0.63*	0.25	0.22	0.32	*0.60*	0.18
Letters Backward[b]	*0.68*	0.21	0.16	0.35	*0.63*	0.23
Facial Memory	0.12	*0.45*	*0.39*	0.08	0.02	0.27
Visual Selective Reminding	0.19	*0.45*	*0.37*	0.12	0.07	0.32
Abstract Visual Memory	0.27	*0.54*	0.40	0.13	0.14	*0.43*
Visual Sequential Memory	0.37	*0.41*	0.36	*0.38*	0.05	0.26
Memory for Location	*0.26*	0.18	0.06	0.10	0.14	*0.43*
Manual Imitation[b]	0.59	0.27	0.17	*0.45*	0.28	0.38

[a]Largest loading is in italics.
[b]Supplementary subtest.

TABLE 6. Three-Factor Promax and Varimax Solutions

	Varimax[a]			Promax[a]		
	Fac 1	Fac 2	Fac 3	Fac 1	Fac 2	Fac 3
Memory for Stories	0.20	*0.43*	0.31	0.05	*0.38*	0.25
Word Selective Reminding	0.24	*0.67*	0.01	0.10	*0.79*	0.12
Object Recall	0.16	*0.58*	0.08	0.08	*0.58*	0.00
Digits Forward	*0.72*	0.23	0.05	*0.78*	0.66	0.00
Paired Recall	0.16	*0.64*	0.10	0.00	0.15	0.08
Letters Forward[b]	*0.76*	0.21	0.10	*0.82*	0.00	0.06
Digits Backward[b]	*0.54*	0.19	0.37	*0.51*	0.01	0.28
Letters Backward[b]	*0.58*	0.14	0.42	*0.55*	0.06	0.34
Facial Memory	0.06	*0.42*	0.21	0.08	*0.43*	0.16
Visual Selective Reminding	0.12	*0.40*	0.27	0.02	*0.39*	0.22
Abstract Visual Memory	0.15	*0.44*	0.39	0.02	*0.40*	0.35
Visual Sequential Memory	0.35	*0.40*	0.15	0.27	*0.33*	0.05
Memory for Location	0.12	0.10	*0.41*	0.02	0.02	*0.43*
Manual Imitation[b]	0.50	0.21	0.37	*0.45*	0.04	0.28

[a]Largest loading is in italics.
[b]Supplementary subtest.

Backward and Letters Backward, pointing clearly to the need for separate scaling of backward and forward memory span tasks. Backward digit recall is known to be a more highly *g*-loaded task than forward digit recall and is likely to be more demanding mentally (e.g., see Jensen & Figueroa, 1975). The fourth factor, as seen in Table 4, is composed of Abstract Visual

Memory and Memory for Location. This factor seems to tap spatial memory more strongly than other tasks. The four-factor Varimax solution provides the same results, essentially, but once again shows stronger secondary loadings of the various subtests than was true with the Promax solution. Both solutions demonstrate clearly that the TOMAL is factorially complex and indicate that it measures multiple components of memory. The content-driven division into verbal and nonverbal memory indexes and the various expert-derived supplementary indexes described originally in Reynolds and Bigler (1994b) for the TOMAL and by Reynolds and Voress (2007b) for the TOMAL-2 may be supplemented further for some examinees by the groupings discovered in these analyses.

Table 6 presents the three-factor Promax and Varimax solutions. The three-factor solutions suggest common factors across the Varimax and Promax rotations, but once again the Promax solution seems more distinctive in nature. When three factors are extracted, the first factor is quite similar to the second factor derived in the four-factor solution and consists primarily of tasks such as letter and digit recall that require intense concentration and sequential recall. Manual Imitation loads on this factor as well, but carries a large secondary loading on

the third factor where it is paired once again with Memory for Location. The second factor appears to be much the same in the three-factor solution as the first factor that appeared when two- and four-factor solutions are examined and is a factor made up of more complex memory tasks. Essentially, the three-factor solution presents a single as a third factor although Digits and Letters Backward tend to gravitate toward this factor which is defined by Memory for Location and may indicate that there is indeed a spatial component to backward memory span (via the use of visualization strategies) as has been suspected by many clinicians. The four-factor solution, as can be seen, however, provides significantly greater clarity than the three-factor solution. A five-factor solution was also examined and was not viable. Table 7 presents the two- and four-factor Promax solutions for the TOMAL-2. Corresponding factors show clear congruence across the TOMAL and the TOMAL-2, demonstrating the factorial equivalence of the two editions of the TOMAL.

Overall, these results suggest that memory as evaluated on the TOMAL and the TOMAL-2 is more process driven than content driven. Although the verbal–nonverbal memory distinction is useful clinically and may be more viable with clinical populations, especially those with

TABLE 7. Two-Factor and Four-Factor Promax Solutions of TOMAL-2 Subtests

Subtest	Two-factor solution[a]			Four-factor solution[a]			
	g_m	Factor 1	Factor 2	Factor 1	Factor 2	Factor 3	Factor 4
Memory for Stories	0.54	*0.56*	0.03	*0.38*	–0.03	0.08	0.22
Facial Memory	0.43	*0.56*	–0.09	*0.36*	0.02	–0.10	0.26
Word Selective Reminding	0.51	*0.50*	0.04	*0.70*	0.13	0.00	–0.18
Abstract Visual Memory	0.53	*0.46*	0.11	0.09	–0.01	0.01	*0.51*
Object Recall	0.52	*0.68*	–0.13	*0.71*	–0.01	–0.07	0.01
Visual Sequential Memory	0.60	*0.45*	0.21	0.06	0.03	0.08	*0.52*
Paired Recall	0.55	*0.64*	–0.04	*0.49*	–0.11	0.12	0.15
Memory for Location	0.57	*0.44*	0.17	–0.11	0.01	–0.07	*0.80*
Digits Forward[b]	0.58	–0.16	*0.82*	–0.01	*0.81*	0.02	–0.04
Visual Selective Reminding[b]	0.39	*0.42*	0.01	0.19	–0.02	–0.02	*0.31*
Letters Forward[b]	0.63	–0.06	*0.77*	0.02	0.75	–0.01	0.08
Manual Imitation[b]	0.59	0.31	*0.35*	0.03	0.14	0.12	*0.40*
Digits Backward[b]	0.62	0.08	*0.62*	–0.04	–0.02	*0.83*	–0.02
Letters Backward[b]	0.67	0.09	*0.67*	0.01	0.10	*0.71*	0.00

[a] Pattern matrix, largest loadings(s) is in italics.
[b] Supplementary subtests.

TBI or highly localized space-occupying lesions, when memory function is examined in normal individuals, process appears to be more salient than item content or modality of presentation. It will be extremely useful in the future to conduct large-sample factor analyses of a broad-based set of memory tasks such as is available on the TOMAL-2 using a clearly defined neurologically impaired sample. A large-sample analysis with a more heterogeneous group of learning-disabled children would also be quite informative in understanding the structure of memory and its role in learning problems among such populations.

Cross-Ethnic Stability of Factor Indexes

When using tests outside the majority group in a population, one is always concerned about making common interpretations of performance. Black–white differences on various aptitude measures are well documented, well known, and are present on many neuropsychological measures. This has led to claims of cultural bias in diagnostic psychological testing with blacks. Very little research has been done with neuropsychological measures and the cultural test bias hypothesis particularly relative to the plethora of bias research on intelligence tests (e.g., see Reynolds, 1995).

Reynolds and Bigler (1994b) report item-level bias studies of the TOMAL, indicating that individual test items on the TOMAL function in highly similar ways for blacks and for whites. Since no new items appear on the second edition, these analyses remain appropriate in considering issues of cultural bias in items for the TOMAL-2. The question of the stability of the TOMAL factor indexes across race for blacks and whites arises as well, and here again, since these subtests are common across the two editions of the TOMAL, generalization to the second edition appears appropriate. Research on intelligence tests reports comparability of factor structures across race for most major tests (Reynolds, 1995). There is but one such study of memory batteries, a study of the TOMAL by Mayfield and Reynolds (1997).

Mayfield and Reynolds (1997) analyzed the factor structure of the TOMAL separately for blacks and whites using the model of Reynolds and Bigler (1996) and recommendations of Reynolds (1982) for comparing factor-analytic results across groups. Tables 8 and 9 present the rotated four-factor solutions for the Promax and Varimax rotations, respectively, as derived separately for blacks and for whites by Mayfield and Reynolds (1997). These factors represent factors similar to those proposed by Reynolds and Bigler (1996) for the combined sample. The coefficients of congruence (r_c) indicate that, regardless of the method of rotation (oblique or orthogonal), the latent structure of children's memory, at least as assessed by the TOMAL, is constant for blacks and whites. The values of s (Cattell's salient variable similarity index) for each comparison are also statistically significant in each case bolstering the argument for comparability of the latent structure of the TOMAL for these two ethnic groups. The designation of each factor continues to be reasonable as suggested in prior research as well: Factor 1, Complex Memory; factor 2, Sequential Recall; factor 3, Backwards Recall; and factor 4, Spatial Memory.

The general memory factor, designated from the first unrotated factor, reveals a strong overall tendency of these memory tasks to trend in a constant direction although the "g" of memory is less powerful than the general factor associated with intelligence. This also supports the distinction of memory from intelligence although the two surely overlap (Reynolds & Bigler, 1994b). The large value of r_c (0.98) and maximal value of s (1.00) show that this general memory factor is constant across race as are the four rotated factors (see Tables 8 and 9).

The values of r_c all exceed 0.90 for the Promax solution with values of 0.94, 0.93, 0.84, and 0.83 (for factors 1–4, respectively) for the Varimax solution and s is significant for each pair of factors. Although the values of r_c for factors 3 and 4 of the Varimax solution are below 0.90, they are very close to this value and the Varimax solution is a poorer fit overall to the data than the Promax solution in the combined samples (Reynolds & Bigler, 1996); s is significant in each case. The strong fit across groups of the Promax solution and the reasonably good fit of an inferior solution support a consistent view of these factors across groups.

The consistency of the factor structure of the TOMAL across race for blacks and whites indicates the test materials are perceived and reacted to in a highly similar manner for these

TABLE 8. Four-Factor Promax Solution for Blacks and Whites[a]

Subtest	g_m[b]		Factor 1[c]		Factor 2[c]		Factor 3[c]		Factor 4[c]	
	Black	White	Black	White	Black	White	Black	White	Black	White
Memory for Stories	0.74	0.45	0.59	0.35	*0.80*	0.41	0.55	0.19	0.22	*0.45*
Word Selective Reminding	0.68	0.59	0.60	0.35	*0.66*	*0.70*	0.45	0.30	0.23	0.15
Object Recall	0.72	0.53	0.65	0.28	*0.69*	*0.61*	0.53	0.29	0.13	0.23
Digits Forward	0.78	0.58	0.74	0.49	0.47	0.33	*0.80*	*0.72*	0.16	0.27
Paired Recall	0.47	0.58	0.28	0.35	*0.64*	*0.66*	0.26	0.29	0.38	0.24
Letters Forward[d]	0.82	0.65	*0.82*	0.55	0.51	0.39	0.72	*0.78*	0.21	0.27
Digits Backward[d]	0.81	0.59	*0.90*	*0.70*	0.52	0.37	0.54	0.47	0.21	0.18
Letters Backward[d]	0.74	0.57	*0.87*	*0.72*	0.48	0.31	0.36	0.51	0.29	0.34
Facial Memory	0.54	0.42	0.37	0.21	*0.65*	*0.48*	0.36	0.18	0.32	0.30
Visual Selective Reminding	0.47	0.43	0.35	0.21	0.40	*0.47*	0.28	0.25	*0.63*	0.27
Abstract Visual Memory	0.70	0.52	0.57	0.31	0.54	0.50	*0.59*	0.28	0.46	*0.50*
Visual Sequential Memory	0.53	0.54	0.33	0.30	0.40	*0.53*	*0.46*	0.46	0.34	0.17
Memory for Location	0.40	0.26	0.24	0.21	0.29	0.14	0.41	0.17	*0.53*	*0.45*
Manual Imitation[d]	0.82	0.45	*0.73*	*0.44*	0.59	0.27	*0.73*	0.38	0.38	0.42
Coefficient of Congruence	0.98		0.98		0.96		0.94		0.91	
Salient Variable Similarity Index[e]	1.00		1.00		0.96		0.88		0.78	

[a] Modified from Mayfield and Reynolds (1997).
[b] First unrotated factor loading, taken to represent a general memory factor.
[c] Largest loading is in italics.
[d] Supplementary subtest.
[e] Where salience ≥ 0.20.

TABLE 9. Four-Factor Varimax Solution for Blacks and Whites[a]

Subtest	Factor 1[b]		Factor 2[b]		Factor 3[b]		Factor 4[b]	
	Black	White	Black	White	Black	White	Black	White
Memory for Stories	0.36	0.21	*0.68*	0.32	0.28	0.01	0.11	*0.38*
Word Selective Reminding	0.43	0.18	*0.53*	*0.68*	0.18	0.12	0.13	−0.01
Object Recall	0.48	0.09	*0.55*	*0.58*	0.27	0.14	0.03	0.10
Digits Forward	*0.60*	0.25	0.18	0.16	*0.60*	*0.65*	0.12	0.14
Paired Recall	0.07	0.17	*0.61*	*0.63*	0.04	0.10	0.28	0.09
Letters Forward[c]	*0.69*	0.29	0.22	0.21	0.46	*0.69*	0.16	0.13
Digits Backward[c]	*0.84*	*0.60*	0.25	0.21	0.20	0.27	0.11	0.17
Letters Backward[c]	*0.83*	*0.61*	0.23	0.13	−0.01	0.31	0.22	0.20
Facial Memory	0.16	0.05	*0.57*	*0.45*	0.15	0.04	0.23	0.21
Visual Selective Reminding	0.19	0.04	0.24	*0.43*	0.05	0.13	*0.59*	0.18
Abstract Visual Memory	0.38	0.10	0.32	*0.42*	0.35	0.11	*0.40*	0.41
Visual Sequential Memory	0.12	0.08	0.21	*0.47*	*0.58*	0.36	0.30	0.04
Memory for Location	0.07	0.08	0.21	0.04	0.28	0.09	*0.52*	*0.43*
Manual Imitation[c]	*0.55*	0.28	0.31	0.14	0.46	0.25	0.32	*0.34*
Coefficient of Congruence	0.94		0.93		0.84		0.83	
Salient Variable Similarity Index[d]	0.80		0.90		0.67		0.71	

[a] Modified from Mayfield and Reynolds (1997).
[b] Largest loading isin italics.
[c] Supplementary subtest.
[d] Where salience ≥ 0.20.

two groups. Consistent interpretation of performance across race on the TOMAL is thus supported and changes in interpretation as a function of race do not appear to be appropriate based on current results.

Forward Versus Backward Recall

One feature of the TOMAL-2, which has received a great deal of positive feedback from clinicians, is the allowance of contrasts, in scaled score form, of forward and backward recall. Often, forward and backward recall are combined into a single score such as on the Wechsler Digit Span tasks. This is inappropriate and will mask important neurologic and diagnostic information (Ramsay & Reynolds, 1995; Reynolds, 1997). Following a review of 27 relevant articles, Ramsay and Reynolds (1995) concluded that forward and backward memory span tasks should be treated separately. While forward memory span has strong attentional and sequential demands, backward memory span appears to have spatial and/or transformative element not apparent in forward memory span.

Reynolds (1997) examined this issue specifically with the TOMAL, which, as does the TOMAL-2, contains a variety of forward and backward recall tasks. The TOMAL-2 has six different sequential recall tasks, four forward ordered (Digits Forward, Letters Forward, Visual Sequential Memory, and Manual Imitation) and two backward ordered (Digits Backward and Letters Backward). An examination of these sequential recall tasks (described in Table 2 and in Reynolds & Bigler, 1994b and

Reynolds & Voress, 2007b, in greater detail) independent of other measures of memory is useful in determining whether backward and forward recall tasks on the TOMAL-2 should be combined into a single score. The analyses of Reynolds and Bigler (1996) are presented below examining these subtests and the two digit recall and two letter recall subtests to determine whether multiple factors are present and if so whether they conform to a forward–backward division. Reynolds (1997) analyzed all six sequential recall tasks and the four digit and letter recall tasks separately. For all six sequential tasks, he found that a two-factor solution was most appropriate. Table 10 presents the Varimax and Promax rotated solutions reported therein. In both cases, it is clear that the forward and backward recall tasks form two factors. Manual Imitation is the only task to load nearly equally on the two tasks arguing for the salience of imagery on this task, a finding echoed in the results of analyses of the K-ABC where a similar task (Hand Movements) shifts from high loadings on a sequential scale below age 5 to a simultaneous scale at older ages (see Kamphaus & Reynolds, 1987, for a review and discussion). The Promax solution is the most distinctive of the two solutions, but both argue strongly for a two-factor interpretation of these six tasks as forward recall and backward recall.

When the four most similar tasks, except for order of recall (forward versus backward), were examined, Reynolds (1997) again found that a two-factor solution was best. Table 11 presents the Varimax and Promax rotated solutions. There is no mistaking the clarity of the patterns evident in these loadings. The two forward memory span tasks clearly break apart from the

**TABLE 10. Six-Variable Varimax and Promax Two-Factor
Solutions of Sequential Memory Tasks**

Subtest	Varimax solution		Promax solution	
	Factor 1	Factor 2	Factor 3	Factor 4
Digits Forward	0.70	0.31	0.73	0.05
Letters Forward	0.71	0.38	0.71	0.13
Digits Backward	0.32	0.69	0.07	0.69
Letters Backward	0.32	0.69	0.07	0.69
Visual Sequential Memory	0.42	0.20	0.43	0.04
Manual Imitation	0.42	0.39	0.33	0.29

TABLE 11. Four-Variable Varimax and Promax Two-Factor Solutions of Sequential Memory Tasks

Subtest	Varimax solution		Promax solution	
	Factor 1	Factor 2	Factor 3	Factor 4
Digits Forward	0.70	0.31	0.73	0.04
Letters Forward	0.70	0.38	0.71	0.12
Digits Backward	0.32	0.66	0.09	0.68
Letters Backward	0.33	0.67	0.09	0.69

backward memory span tasks, with the Promax solution once again the most distinctive.

These patterns are clearly evident in the correlation matrix for the digit span and letter span tasks seen in Table 12. Digits Forward correlates at a statistically significantly higher level ($p < 0.001$) with Letters Forward ($r = 0.70$) than with Digits Backward ($r = 0.44$). Digits Forward correlates about equally well with Letters Backward ($r = 0.43$). Digits Backward correlates at a statistically significantly higher level ($p < 0.001$) with Letters Backward ($r = 0.65$) than with Letters Forward ($r = 0.47$).

Based on these correlations, it is known that 25–30% of normal children will show at least a one standard deviation (3 scaled score points) difference between their scores on Digits Forward versus Digits Backward and on Letters Forward versus Letters Backward. Nearly half of a normal sample will show a scaled score difference of two or more points. Thus, statistically significant differences in forward and backward memory span are relatively common in scaled score terms and should not be overinterpreted when scaled separately just as they should not be ignored by simply viewing a composite of forward and backward memory span as the difference in the two is potentially informative for many patients, especially those with TBI or CHI.

TABLE 12. Zero-Order Pearson Correlations for Digits and Letters Forward and Backward

Subtest	Letters Forward	Digits Backward	Letters Backward
Digits Forward	0.70	0.44	0.43
Letters Forward		0.47	0.50
Digits Backward			0.65

When the current results are considered in the context of various theoretical works such as that of Jensen (1980; Jensen & Figueroa, 1975), Kaufman and Kaufman (1983), and the review and reanalyses of Ramsay and Reynolds (1995), there seems to be little justification for continuing the practice of summing raw scores on forward and backward memory span tasks. Indeed, this practice is clearly not necessary to enhance reliability of the measurements as might be argued. Reynolds and Bigler (1994a) reported reliability coefficients (coefficients alpha) for the six tasks noted above of greater than 0.92. Collapsing these variables routinely without making separate scores available is likely to mask useful information as is clear from the clinical studies of patients reviewed but also now in multiple factor-analytic studies (e.g., Reynolds & Bigler, 1996) of large samples of normal individuals. This break between forward and backward memory span is enhanced in certain minority populations as well (e.g., Jensen & Figueroa, 1975; Mayfield & Reynolds, 1997).

While combining forward and backward memory span may be useful at times (e.g., Smyth & Scholey, 1994; Vanderploeg, Schinka, & Retzlaff, 1994), the evidence now seems overwhelming that separate scaled scores for forward nd for backward memory span tasks should be provided routinely on any standardized assessment. This practice will facilitate clinical practice and research applications concerning the differential meaning of performance on the two tasks. Current evidence seems to support forward span tasks as being simpler, perhaps verbally oriented, and strongly sequential while backward memory span invokes more complex processes that require transformations not necessary with forward memory span. Backward recall may also invoke, for many

individuals, visuospatial imaging processes even for ostensibly verbal material such as letters. Potential differences in the attentional demands or components of these two types of tasks deserve additional study as well. Forward memory span measures may have a stronger attentional component than backward recall measures, which are more highly correlated with general intelligence and require cognitive transformation, an element missing from rote, forward recall. Surprisingly, much remains to be done to understand the distinction between forward and backward memory span and what it means both clinically and to theories of brain–behavior relationships, but it is clear the tasks are sufficiently different to be assessed separately for clinical purposes, and are so presented on the TOMAL-2.

Delayed Recall

Delayed recall, asking an examinee to recall previously exposed material after some period of time of engagement in other tasks, is a routine component of the psychiatric mental status examination. It has been a part of the major memory batteries for over 50 years and there is a delayed recall (although briefer than on other tests) component to the Tactual Performance Test of the Halstead–Reitan Neuropsychological Test Battery.

Delayed recall on the TOMAL-2 requires the examinee to recall stimuli from two verbal subtests – Memory for Stories and Word Selective Reminding – 30 min after testing has been initiated. Delayed recall is frequently significantly affected by brain injury. Delayed recall is often more impaired than immediate and short-term memory in cases of TBI. The Verbal Delayed Recall Index (VDRI) acts as a measure of forgetting and may be of interest when contrasted with the Composite Memory Index (CMI). Most examinees will score within about 10 points of their CMI on the TOMAL-2. The manual also contains values for assessing the significance of the difference between VDRI and CMI; this is checked automatically by the TOMAL-2 computer scoring program (available from www.proedinc.com).

VDRI scores significantly below the CMI are often an indication of an organically based disturbance of memory. Memory scores can be suppressed by various psychiatric disturbances, especially depression; however, in these disorders, delayed recall is relatively preserved. In some research (e.g., Grossman, Kaufman, Mednitsky, Scharff, & Dennis, 1994), depressed patients actually score higher on delayed recall than immediate recall. This has been attributed to motivation. Whenever VDRI exceeds CMI to a significant degree, level of effort on immediate recall should be evaluated carefully. VDRI allows the clinician to explore a variety of hypotheses about depth of processing (especially in conjunction with selective reminding which may show more intermediate forgetting if examinees forget on later trials material recalled correctly on earlier trials), forgetting, and motivation.

Ethnic Differences in Mean Levels of Performance

As noted earlier, black–white differences in mean level of performance are well documented on IQ tests and average, over different tests and nearly 100 years of data collection, about one standard deviation (Jensen, 1980). Memory tests behave quite differently. Mayfield and Reynolds (1997) calculated mean levels of performance separately for blacks and whites on all 14 subtests of the TOMAL. Table 13 reports the essential results of their findings. A multivariate analysis of variance revealed a single significant difference with blacks scoring higher than whites on Letters Forward by 0.07 standard deviation – statistically significant, but of no real clinical significance. No changes of a substantive nature occurred in moving from the TOMAL to the TOMAL-2. Variations in profiles of blacks then cannot be related reasonably to artifacts of the test and most likely reflect real variations in memory for individual children.

Interpretive Strategies

The TOMAL-2 manual reviews a basic top-down interpretive strategy that mimics Kaufman's (1979, 1994) basic philosophy of intelligent testing and that requires integration of history and other test data. The additional information presented here and in other papers cited throughout this chapter supplements the strategies given by Reynolds and Voress (2007b) who also provide

TABLE 13. Mean and Standard Deviations of Subtest[a] Performance on the TOMAL for Black and White Children from the Standardization Sample

Subtest	Mean		Standard deviation		
	Black	White	Black	White	D^b
Memory for Stories	10.10	10.02	2.94	3.06	−0.03
Word Selective Reminding	9.90	10.00	3.00	3.03	0.03
Object Recall	10.13	9.96	3.30	2.97	−0.06
Digits Forward	10.09	9.99	3.18	3.00	−0.03
Paired Recall	9.96	10.00	3.00	3.00	0.01
Letters Forward[c]	10.17	9.97	3.51	2.88	−0.07*
Digits Backward[c]	9.97	9.98	3.30	2.97	−0.00
Letters Backward[c]	10.09	9.97	3.69	2.88	−0.04
Facial Memory	10.12	9.95	3.33	2.94	−0.05
Visual Selective Reminding	9.96	9.99	3.93	3.00	0.01
Abstract Visual Memory	9.97	9.99	3.03	3.00	−0.01
Visual Sequential Memory	10.14	9.99	3.30	2.91	−0.05
Memory for Location	9.90	10.00	2.73	3.03	0.03
Manual Imitation[c]	10.13	9.98	3.54	2.94	−0.06

[a] Mean $= 10$; SD $= 3$.
[b] Difference expressed as a function of the white sample standard deviation: (white mean – black mean)/ white standard deviation.
[c] Supplementary subtest.
*$p \leq 0.02$; all other differences, $p \geq 0.08$.

data on within-test scatter and the relationship of the TOMAL-2 to the major intelligence scales and to achievement tests as well.

Brief Case Examples

Thomas

At 14 years old, Thomas sustained severe carbon monoxide poisoning. The gas heater in the closed garage where he was working malfunctioned, releasing carbon monoxide into the area. His mother found him unconscious and seizing. An MRI showed basal ganglia lesion, a classic sign for carbon monoxide poisoning.

Prior to the accident, Thomas was in good health. He was an honor student with a GPA of 3.8. Thomas is now in the eleventh grade and is experiencing difficulties with his math classes and poor eye–hand coordination His current functioning is believed to reflect a decrease from premorbid performance.

Figure 1 summarizes the TOMAL-2 scores obtained by Thomas some 15 months postaccident and in a format obtained from the TOMAL-2 computer scoring program (Szasz, Reynolds, & Voress, 2007). The first section of the summary presents the scaled score, percentile rank, and a qualitative descriptor ranging from Very Deficient to Very Superior for each subtest. Details for the index scores are provided in the second section. This includes confidence intervals for the index scores and comparisons of various index scores. Thomas's VDRI (83) is below average and falls significantly below immediate recall performance as reflected on the VMI (107), clearly a significant deviation from his premorbid ability, and a common sign of organically based memory deficits as well as carbon monoxide poisoning. His Attention/Concentration Index is also depressed relative to other scores. Memory then shows an overall decline from expected preaccident levels.

His WISC-III scores were VIQ $= 109$, PIQ $= 82$, and FSIQ $= 95$. WRAT-3 scores showed reading of 110, spelling of 107, and math of 95. Word fluency was slightly below expectation for his age. His TOMAL-2 learning curves showed great inconsistency across trials reflecting considerable variability in attentional processes. The learning curves are displayed in the third section of Figure 1.

TOMAL-2

3/17/2004

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Examinee: Thomas   **Examiner:**

Core Subtests *Verbal Subtests*	Raw Score	Scaled Score	Percentile Rank	Description	Age Equivalent	Subtest Significance
Memory for Stories	27	10	50	Average	-	ns
Word Selective Reminding:	66	13	84	Above Average	-	ns
Object Recall:	61	11	63	Average	-	ns
Paired Recall:	26	10	50	Average	-	ns
Nonverbal Subtests						
Facial Memory:	36	14	91	Above Average	-	ns
Abstract Visual Memory:	28	10	50	Average	-	ns
Visual Sequential Memory:	37	13	84	Above Average	-	ns
Memory for Location:	15	10	50	Average	-	ns
Supplemental Subtests						
Verbal Subtests						
Digits Forward:	64	12	75	Average	-	
Letters Forward:	21	6	9	Below Average	-	
Digits Backward:	31	10	50	Average	-	
Letters Backward:	15	8	25	Average	-	
Nonverbal Subtests						
Manual Imitation:	44	12	75	Average	-	
Visual Selective Reminding:	29	8	25	Average	-	
Verbal Delayed Recall Subtests						
Memory for Stories Delayed:	12	7	16	Below Average	-	
Word Selective Reminding Dely:	7	8	25	Average	-	

FIGURE 1. Thomas's TOMAL-2 results as obtained from the TOMAL-2 computer scoring program.

TOMAL-2

3/17/2004

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Examinee: Thomas   **Examiner:**

Index Scores	SS Total	Index Score	85% CI	Percentile Rank	Description	Cumulative Intersubtest Scatter
Verbal Memory Index (VMI)	44	107	102-112	68	Average	65%
Nonverbal Memory Index (NMI)	47	111	105-117	77	Above Average	52.4%
Composite Memory Index (CMI)	91	110	105-115	75	Average	86.7%

Supplemental Index Scores

	SS Total	Index Score	85% CI	Percentile Rank	Description	
Verbal Delay Recall Index (VDRI)	15	83	77-89	13	Below Average	
Attention/Concentration Index (ACI)	48	97	94-100	42	Average	
Sequential Recall Index (SRI)	43	105	101-108	63	Average	
Free Recall Index (FRI)	34	108	101-115	70	Average	
Associative Recall Index (ARI)	20	100	94-106	50	Average	
Learning Index (LI)	42	104	98-110	61	Average	

Core Comparisons

	Difference	Significance Level	Discrepancy Frequency
VMI vs. NMI	4	ns	80.2%
VMI vs. VDRI	24	.01	5.9%
NMI vs. VDRI	28	.01	7%
CMI vs. VDRI	27	.01	4.6%

Supplementary Comparisons

	Difference	Significance Level	Discrepancy Frequency
CMI vs. ACI	13	.01	36.7%
CMI vs. SRI	5	ns	72.5%
CMI vs. FRI	2	ns	86.7%
CMI vs. ARI	10	ns	31.9%
CMI vs. LI	6	ns	52.9%

FIGURE 1. (*Continued*).

Examinee: Thomas   **Examiner:** |
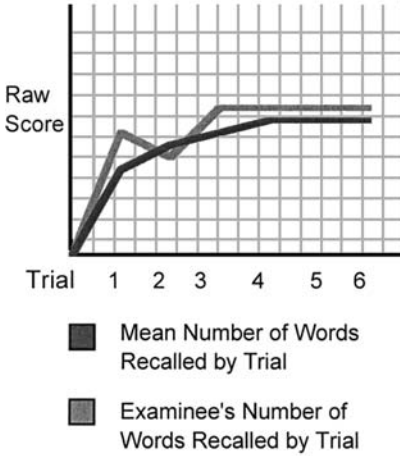
Subtest 3. Word Selective Reminding

Raw Score

Trial   1   2   3   4   5   6

■ Mean Number of Words Recalled by Trial

■ Examinee's Number of Words Recalled by Trial

Subtest 5. Object Recall

Raw Score

Trial   1   2   3   4   5

■ Mean Number of Objects Recalled by Trial

■ Examinee's Number of Objects Recalled by Trial

Subtest 7. Paired Recall

Raw Score

Trial   1   2   3   4

■ Mean Number of Dot Positions Recalled by Trial

■ Examinee's Number of Dot Positions Recalled by Trial

Subtest 10. Visual Selective Reminding

Raw Score

Trial   1   2   3   4   5

■ Mean Number of Dot Positions Recalled by Trial

■ Examinee's Number of Dot Positions Recalled by Trial
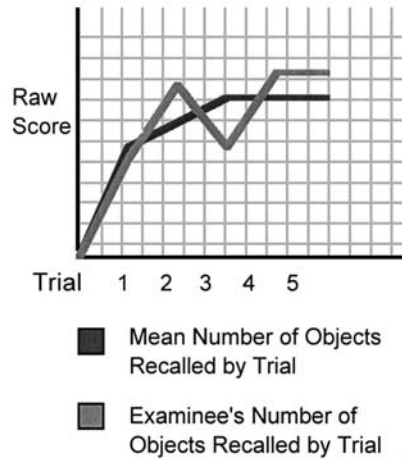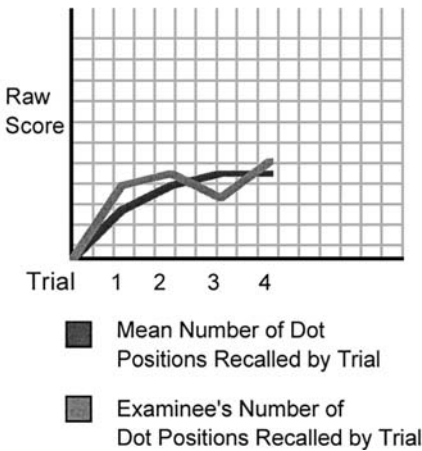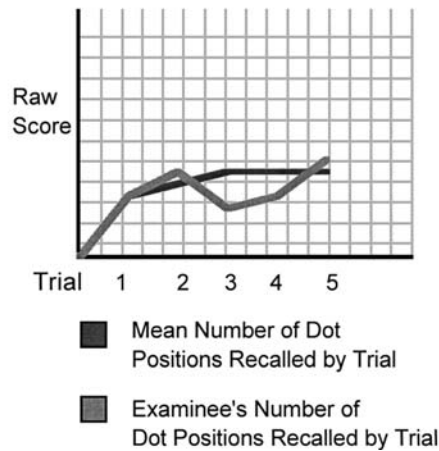
FIGURE 1. (*Continued*).

Maria

At age 5, Maria was in an automobile accident and sustained a closed head injury. She was rendered unconscious and hospitalized for several weeks. An EEG demonstrated physiological abnormalities in the right temporal lobe region. Before the accident, Maria was enrolled in kindergarten and there were no school-related academic or behavioral difficulties noted. Maria is now in 6 and in the first grade. Her teacher indicated Maria was having difficulty with visual processing and retention.

There were no pre-injury intellectual assessments, but given Maria's developmental history, it would be assumed the she was of at least average intelligence prior to her injury. Recent WISC-III scores were VIQ = 95, PIQ = 112, and FSIQ = 102. Figure 2 provides Maria's scores on the TOMAL-2. Maria's VMI of 88 is in the loser range of average in contrast to the

NMI of 71, which is clearly in the subaverage range of memory performance. The overall CMI of 77 is in the deficient range of memory performance. The global score comparisons indicate the VMI is significantly different from the NMI. It is apparent that Maria's nonverbal tests are generally reduced in comparison to the verbal tests. The Learning Index was lower than would be expected given Maria's academic history; the learning curves are presented in the third section of Figure 2. The low Learning Index is consistent with the teacher's

observation that Maria had difficulty learning new information.

Conclusion

Memory assessment has much to offer the clinician when viewing the neuropsychological processing of children and adolescents, especially those with CNS compromise. The TOMAL-2 is the most detailed and comprehensive of approaches and allows for a careful look at how

TOMAL-2

10/15/2006

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Examinee: Maria   **Examiner:**

Core Subtests	Raw	Scaled	Percentile		Age	Subtest
Verbal Subtests	Score	Score	Rank	Description	Equivalent	Significance
Memory for Stories	20	11	63	Average	7-3	.05/.01
Word Selective Reminding:	32	8	25	Average	below 5-0	ns
Object Recall:	25	6	9	Below Average	below 5-0	ns
Paired Recall:	11	8	25	Average	5-0	ns
Nonverbal Subtests						
Facial Memory:	10	4	2	Deficient	below 5-0	ns
Abstract Visual Memory:	2	7	16	Below Average	below 5-0	ns
Visual Sequential Memory:	8	7	16	Below Average	5-0	ns
Memory for Location:	3	6	9	Below Average	below 5-0	ns
Supplemental Subtests						
Verbal Subtests						
Digits Forward:	24	9	37	Average	5-3	
Letters Forward:	23	11	63	Average	7-0	
Digits Backward:	11	11	63	Average	7-9	
Letters Backward:	7	9	37	Average	5-6	
Nonverbal Subtests						
Manual Imitation:	17	10	50	Average	6-3	
Visual Selective Reminding:	4	2	below 1	Very Deficient	below 5-0	
Verbal Delayed Recall Subtests						
Memory for Stories Delayed:	14	10	50	Average	6-3	
Word Selective Reminding Dely:	2	8	25	Average	below 5-0	

FIGURE 2. Maria's TOMAL-2 results as obtained from the TOMAL-2 computer scoring program.

TOMAL-2   10/15/2006

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Examinee: Maria   Examiner:

Index Scores	SS Total	Index Score	85% CI	Percentile Rank	Description	Cumulative Intersubtest Scatter
Verbal Memory Index (VMI)	33	88	83-93	21	Below Average	30.3%
Nonverbal Memory Index (NMI)	24	71	65-77	3	Deficient	71.1%
Composite Memory Index (CMI)	57	77	72-82	6	Deficient	37.3%

Supplemental Index Scores

Verbal Delay Recall Index (VDRI)	18	92	86-98	30	Average	
Attention/Concentration Index (ACI)	50	99	96-102	47	Average	
Sequential Recall Index (SRI)	37	94	90-97	35	Average	
Free Recall Index (FRI)	17	70	63-77	2	Deficient	
Associative Recall Index (ARI)	19	97	91-103	42	Average	
Learning Index (LI)	24	72	66-78	3	Deficient	

Core Comparisons

	Difference	Significance Level	Discrepancy Frequency
VMI vs. NMI	17	.01	24.1%
VMI vs. VDRI	4	ns	75.3%
NMI vs. VDRI	21	.01	17.7%
CMI vs. VDRI	15	.01	20.1%

Supplementary Comparisons

	Difference	Significance Level	Discrepancy Frequency
CMI vs. ACI	22	.01	12.1%
CMI vs. SRI	17	.01	19.7%
CMI vs. FRI	7	ns	45.4%
CMI vs. ARI	20	.01	5.1%
CMI vs. LI	5	ns	60%

FIGURE 2. (*Continued*).

Examinee: Maria   **Examiner:**

Subtest 3. Word Selective Reminding
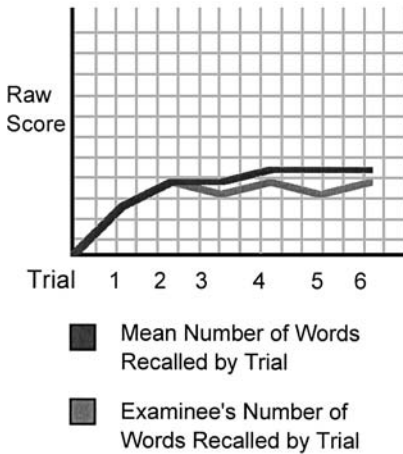
Raw Score

Trial   1   2   3   4   5   6

■ Mean Number of Words
  Recalled by Trial

▇ Examinee's Number of
  Words Recalled by Trial

Subtest 5. Object Recall

Raw Score

Trial   1   2   3   4   5

■ Mean Number of Objects
  Recalled by Trial

▇ Examinee's Number of
  Objects Recalled by Trial

Subtest 7. Paired Recall

Raw Score

Trial   1   2   3   4

■ Mean Number of Dot
  Positions Recalled by Trial

▇ Examinee's Number of
  Dot Positions Recalled by Trial

Subtest 10. Visual Selective Reminding

Raw Score

Trial   1   2   3   4   5

■ Mean Number of Dot
  Positions Recalled by Trial

▇ Examinee's Number of
  Dot Positions Recalled by Trial
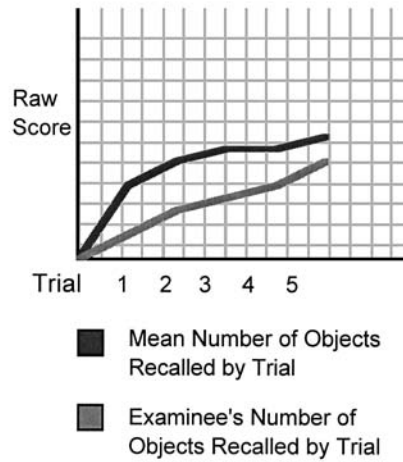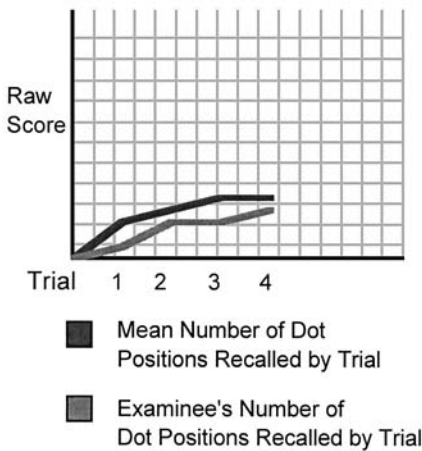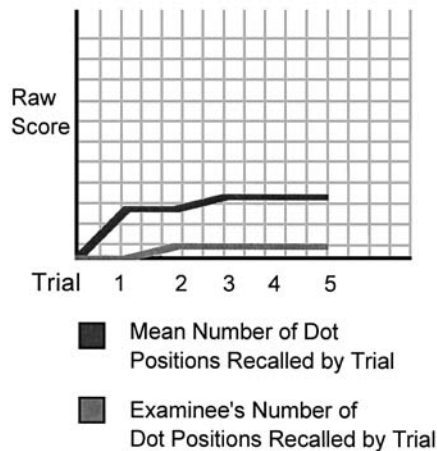
FIGURE 2. (*Continued*).

children are processing and learning information as well.

We have much to learn about memory in children and especially about the use of delayed recall indices that have proven so valuable with adults. Current work is focused on delineating diagnostic and remedial implications of test results and is promising. The ubiquitous nature of memory in daily life and memory complaints in CNS compromise makes clinical assessment of memory crucial to the tasks of the neuropsychologist.

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15

Utilizing a Neuropsychological Paradigm for Understanding Common Educational and Psychological Tests

ROBERT L. RHODES, RIK CARL D'AMATO,
AND BARBARA A. ROTHLISBERG

The field of psychology has long been marked by philosophical diversity and theoretical movements devoted to the investigation of individual differences (D'Amato & Rothlisberg, 1992/ 1997). Scores of single paradigm assessment approaches designed to provide appropriate diagnosis and treatment of individual difficulties have come to the forefront, only to be eclipsed later by rival viewpoints or different theoretical perspectives (e.g., psychoanalysis, behaviorism, neuropsychology). Throughout this procession of developing philosophies, theories, and interventions, countless educational and psychological tests have been administered and interpreted in an effort to understand the abilities and needs of the individuals under study (Lezak, Howieson, Loring, & Hannay, 2004). The purpose of this chapter is to help consolidate available information by offering

the reader the knowledge, skills, and dispositions that are needed to understand and interpret common formal and informal measures from a neuropsychological paradigm. This paradigm is offered as our *taproot*, the only paradigm that can organize all information into a scientifically defensible but at the same time practical approach that provides direction for both understanding current data and offering evidence-based rehabilitation for the future (Traughber & D'Amato, 2005; Work & Choi, 2005).

This chapter is designed to be of special assistance to practitioners who work with children and young adults and who, perhaps more than any other members of the field, have seen the greatest amount of emphasis placed on the assessment of individual differences (Dean, 1985a, b). Currently, more than six million children living in the United State have been referred, assessed, placed, and served in special education programs (Institute of Educational Sciences, 2006). This staggering number of children brings with them the myriad possibilities of potential hypothesis regarding the etiology and prognosis of their individual conditions (Crockett, 2003; D'Amato, Fletcher-Janzen, & Reynolds, 2005; Garbarino, 1995; Kalat & Wurm, 1999).

ROBERT L. RHODES • Special Education/Communication Disorders Department, New Mexico State University, Las Cruces, New Mexico 88003-8001.   RIK CARL D'AMATO • Department of Psychology, Faculty of Social Sciences and Humanities, Av. Padre Tomas Pereira, Taipa, Macau SAR, China.   BARBARA A. ROTHLISBERG • Department of Educational Psychology, Ball State University, Muncie, Indiana 47306.

As assessment, specialists, psychologists, clinical neuropsychologists, and school neuro-psychologists must quickly and accurately wade through the cumulative data available about the child in order to select the most viable alternative hypotheses to explain the findings (Selz & Wilson, 1989). The strategy the practi-tioner uses to accomplish this task must, of necessity, be based on well-grounded, empiri-cally validated theories of behavior (Hynd & Obrzut, 1981; Traughber & D'Amato, 2005). Only through the use of a suitable theoretical framework are specific predictions regarding per-formance under a given set of ecological circum-stances made possible (Christenson, 2003). Unfortunately, aside from neuropsychology, no single diagnostic paradigm or theory has proven sufficient to explain the vagaries of behavior (D'Amato & Rothlisberg, 1992/1997; Rapp-Paglicci, Dulmus, & Wodarski, 2004). Psychoana-lytic, behavioral, and humanistic views as well as other theoretical positions have been continually challenged, not only to describe behavior but also to provide effective interventions for the popula-tions whom they serve (D'Amato & Dean, 1988; Rothlisberg, D'Amato, & Palencia, 2003; Sheri-dan & Gutkin, 2000). For example, prepackaged programs dealing with psycholinguistic develop-ment, visual–motor training, and sensory integration have all failed to meet the demands of this challenge (D'Amato et al., 2005; Lee & Riccio, 2005). Gradually, the field has acknowl-edged that the effective use of assessment proce-dures is reliant on a theoretical foundation considering multiple data sources and environ-ments in such a manner as to increase the amount of effective and appropriate interventions generated.

Why Consider a Neuropsychological Perspective?

Neuropsychology represents a view thou-ght to be important for assessment, pedagogy, and the development of intervention-related hypotheses (Gaddes & Edgell, 1994; Hartlage & Telzrow, 1986; 1987; Hynd & Reynolds, 2005; Reynolds & French, 2005). Serving as a conscious and continuing attempt to look both *inward*, at the brain, and *outward*, at behavior, it is the goal of neuropsychology to integrate both the neurobiological and psychological aspects of functioning (Davis, Johnson, & D'Amato, 2005; D'Amato, Chittooran, & Whitten, 1992). Many argue that it bridges the nature-nurture primeval abyss (e.g., D'Amato et al., 2005). Numerous authors have advocated for a neuro-psychological interpretation of traditional assessment measures, with many advocating that school psychologists should receive applied training in neuropsychology (D'Amato et al. 1992; Root, D'Amato, & Reynolds, 2005).

A major impetus behind this approach is the number of children with learning problems, as well as behavior problems, who have been found to have some degree of cerebral impair-ment (Dean, 1985a, 1986a, b; Gaddes & Edgell, 1994; Hynd & Reynolds 2005; Selz & Wilson, 1989). This large number of learners who have considerable neurobiological difficulties often fail in the public schools and later have a similarly problematic connection with the juvenal justice system. A neuropsychological view of data allows for the consideration of a wider spectrum of functions and has been shown to improve the differential diagnosis of learning problems both between and within groups of learners (D'Amato, 1990; D'Amato & Dean, 1988; Das, Naglieri, & Kirby, 1994; Hynd & Obrzut, 1981). Table 1 presents several of the reasons why con-sideration of a neuropsychological paradigm is attractive. Of particular utility is the amount of information generated regarding the neuropsy-chological functions on which learning is predi-cated (e.g., sensory perceptions, motor functions; Chittooran, D'Amato, Lassiter, & Dean, 1993; D'Amato, Gray, & Dean, 1988). Overall, it appears that the information provided by a neu-ropsychological perspective facilitates a better understanding of etiology, which, in turn, may result in an increased ability to rehabilitate exist-ing problems, or prevent future difficulties (D'Amato et al., 2005; Dean, 1985a, b, 1986a; Sattler & D'Amato, 2002a, b). It is important to note that many of the measures routinely admi-nistered by psychologists (e.g., Wechsler Scales, Minnesota Multiphasic Personality Inventory-2) are included as part of the neuropsychological examination (D'Amato et al.). The neuropsycho-logical interpretation of these measures may dif-fer greatly, however, from thetraditional psychological interpretation of performance. More specifically, the neuropsychological inter-pretation of these measures is based on research

Table 1. Why Must We Follow a Neuropsychological Paradigm If We Are to Understand Human Behavior?

Because

- Brain development is sequential and predictable
- Neurodevelopment is the product of an interaction between intact neurological systems and cerebral dysfunction
- The developing brain is vulnerable to forces from both neurobiology (e.g., nature) and the environment (e.g., nurture)
- Perinatally, many children are exposed to drugs as well as to toxins in the environment
- In the United States and around the world many children suffer from malnutrition which has irreversible neurodevelopmental consequences
- An understanding of common neurodevelopmental benchmarks can offer appropriate differential diagnosis and chart the course of a disorder
- The demarcation separating the science of psychology from the medicinal sciences is tenuous at best
- Many disorders with long-term neurobiological sequelae require a neuropsychological approach if we are to understand the underpinnings of related disorders
- Abnormalities in brain functioning increase the risk of developing psychiatric disorders
- Prediction and treatment of reading disabilities can be best explained from a neuropsychological paradigm
- The study of applied neuropsychology offers the most comprehensive view of human behavior currently available

Adapted from Root et al. (2005)

that has examined the relation of the specific test utilized and the functional integrity of the brain, rather than on research that has focused exclusively on school-based achievement outcomes (Davis & Dean, 2005; Reynolds & French, 2005).

Approaches to Neuropsychological Assessment

The field of clinical neuropsychology began with a focus on adults with brain damage as well as examining the intriguing relationship between site of damage and behavioral outcomes (Davis & Dean, 2005; Dean, 1985b, 1986a; Reynolds & French, 2005). With this in mind, a considerable database developed relating specific tests or procedures to areas of cerebral damage in adults. The emphasis was often on localization, lateralization, and lesion detection (Lezak, 1995). Not surprisingly then, while neuropsychologists have become experts in studying the connection between damaged areas of the mature brain and overt behavior, the educational relevance of how to teach individuals with brain damage has not been well understood, particularly among children (D'Amato & Dean, 1987, 1988; Root et al., 2005; Telzrow, 1990; Telzrow, Beebe, & Wojcik, 2005). This relates to the fact that many tests and procedures are simply downward extensions of adult batteries, with little relevance offered for the educational enterprise, and with little

acknowledgment given to the developmental variations seen in the immature nervous system. Indeed, the developmental aspects of brain injury are only now becoming clear, increasing the complexity of the evaluation process and leading to a modified view of educational and psychological test data (Root et al.). Thus, the thrust of this chapter will be to address commonly used educational and psychological instruments from a neuropsychological perspective and focus on those tests or assessment areas that hold the greatest promise for intervention (D'Amato et al., 2005; Sattler & D'Amato, 2002a, b; Work & Choi, 2005).

Quantitative Standardized Approaches

Like psychology in general, assessment techniques and related methods have reflected different psychological paradigms (Dean 1985a, 1986a). In Britain and North America, the most popular approach to neuropsychological assessment has been a standardized battery-based quantitative approach that offers data-based psychometric scores used to make actuarial predictions (Davis & D'Amato, 2005; Lezak, 1995). This atheoretical approach stresses short-term client involvement, where deficits are measured accurately with structured assessment techniques (Reitan, 1989; Reitan & Wolfson, 1993). Thus, clinicians carefully consider a variety of scores that are viewed as products (like

summative scores), as opposed to a focus on the process. The assemblage of standardized tests is generally held constant for everyone, to evaluate a variety of functions for *all* individuals. If 10 brain functions are deemed important, then all patients would be tested with a core standardized battery that covers those 10 primary systemic areas.

Practitioners from this quantitative camp who have administered an invariant battery to all of their patients have developed an impressive database and have become experts in evaluating the meaning of those diagnostic measures (Dean, 1986b). A typical battery from this area with a strong educational focus may include a visual–motor screening test, the appropriate Wechsler Scale, the *Woodcock-Johnson Achievement Battery*, a finger tapping test, a grip strength test, a parent behavior rating scale, a teacher behavior rating scale, a self-report personality measure like found in the *Behavior Assessment System for Children*, a memory test, a review of school records, and a clinical interview with the parent and child, and often the teacher. Some comprehensive neuropsychological batteries like the *Halstead-Reitan Neuropsychological Test Battery* and the *Dean-Woodcock Neuropsychological Assessment System* also fall within this quantitative paradigm (Davis et al., 2005; Dean & Woodcock, 2003). This systematic method of data collection is consistent with most batteries of tests used by psychologists in the public schools. In fact, some public laws require that areas like intelligence, achievement, and processing skills be evaluated, parents be interviewed, and students be observed in school, if learners are to receive special services like those offered for children with learning disabilities or traumatic brain injuries (D'Amato et al., 2005).

Historically, this standardized content focus has been quite popular, although recent laws and classic applied practices have begun to focus less on assessment and more on intervention, implementing unique and promising approaches such as a *Response to Intervention* model (Tuesday Heathfield, Pompa, & Clark, 2005; Work & Choi, 2005). Such a model can help schools and those utilizing a school neuropsychological approach, in that this model offers classroom-based psychoeducational services for children with less serious issues and as a result can offer additional time for school psychologists to deal with those children suffering from significant neuropsychological impairments.

Unfortunately, one obvious difficulty with the quantitative approach relates to the cost-effectiveness of such a system. Although a certain number of functions need to be evaluated with everyone, rarely do practitioners have the time to evaluate areas that do not appear compromised. The quantitative approach also has been criticized for its emphasis on differential diagnosis, its easy link to localization of cerebral dysfunction, its product orientation, and its lack of utility in linking assessment data to suitable interventions. The strength most evident from this view relates to the impressive standardized and normative foundation that many of the tests used in this area enjoy (Reitan, 1989; Reitan & Wolfson, 1993). Indeed, individuals with high-profile cases or court-mandated assessments may want to use a data-based, standardized, quantitative approach to evaluation.

Qualitative Clinical Approaches

In an attempt to evaluate people in an individualized fashion, Luria and his colleagues (Luria, 1966, 1970, 1980; Luria & Majovski, 1977) offered a qualitative approach to neuropsychological assessment focusing on clinical interactions and "the process" to provide a comprehensive understanding of the individual. From this view, each client is uniquely evaluated with a comprehensive set of what the untrained eye has seen as informal, clinical, process-focused measures. Luria (1966, 1980) organized a dynamic, interactive assessment process that culminates in an understanding of the patient's functional systems (Hynd & Semrud-Clikeman, 1990). The qualitative approach has been popular in European and Asian countries (Dean, 1985a,b; Davis & Dean, 2005; Reynolds & French, 2005). This approach utilizes extensive long-term client involvement to offer what is essentially a case-study analysis. While the major areas traditionally covered in a qualitative evaluation seem comprehensive (e.g., investigations of motor functions, expressive speech, writing, reading), this view does not rely on standardized comparisons to a normative population base as its foundation (Hynd & Semrud-Clikeman, 1990; Korkman, 1999; Semrud-Clikeman, Wilkinson, & McMahon-Wellington, 2005). Instead, the selection of tests utilized follows

prominent clinical patient–practitioner interactions. For example, Luria (1970, 1980) described a detailed method of examining mathematical functions. He began by asking the subject to read numbers then measured whether the subject understood the relation between numbers, and the quantities associated with numbers. Next, Luria evaluated whether the subject could read and then write one-digit numbers accurately. Finally, automatic number skills were explored. Many additional steps could be utilized to capture the subject's understanding of mathematical processes (see Gaddes, 1985).

Luria's procedure demonstrates how neuropsychological data can be gleaned from work samples, informal tests, criterion-based measures, clinical interactions, observations, and review of classroom benchmarks. Here, the rich clinical relationship, where evaluation becomes the first step of the intervention process, offers important information that is used to develop and evaluate treatment outcomes. Instead of focusing simply on identified deficits, this approach considers what the child knows and can achieve, melding the assessment phase with the intervention process. For example, the practitioner may evaluate single-digit addition skills concomitantly teaching the single-digit addition facts that have not been mastered. While the focus of this chapter is not centered on qualitative assessment, such an approach offers much for practicing psychologists or neuropsychologists. It is our hope that all evaluations would utilize qualitative information from the learner under consideration, as well as information from peers, classroom teachers, other school personnel, and parents. One could argue that consideration of this readily available information flows from a real-life, common sense approach to assessment. Information considered should include cognitive and academic data, and social and emotional information, together with how the student interacts with others including his or her teacher (e.g., Leu & D'Amato, 1994; Sattler & D'Amato, 2002a, b; Work & Choi, 2005). Moreover, this approach would seem to have the most promise for future educational and psychological service models.

The qualitative perspective has been faulted because of its subjective foundation, its use of process-based interactions, use of case reports, and emphasis on clinical impressions and interactions. The ability to evaluate the reliability and validity of the qualitative approach has been problematic. Similar to the issues reported with "projective" testing in personality assessment, some individuals following this process approach view themselves as "believers," which makes empirical validation extremely thorny. However, its obvious strengths relate to how the practitioner understands the processes each client displays in areas of difficulty, and this has clear and obvious links to education and intervention.

An Integrative Flexible Battery Model

Basic Assumptions

To combat the respective weakness of the quantitative and qualitative approaches, an integrative model of assessment was proposed to aid practitioners in utilizing common tests to understand the neuropsychological functioning of children and youth. This model, designed to be comprehensive in scope, is based on a multitrait, multisource, multisetting assessment strategy (D'Amato et al., 2005; Kaufman, 1979, 1990). Stated simply, it encourages exploration of the totality of the individual's behavioral repertoire—including intellectual functioning, academic functioning, and social/emotional functioning through quantitative and qualitative interviews, observations, and tests. Such an approach should consider the views of parents, family members, friends, and teachers (D'Amato, Rothlisberg, & Leu Work, 1999; Hynd & Semrud-Clikeman, 1990; Savage & Wolcott, 1994). Formal tests provide the needed quantitative data, whereas interviews, observations, and collection of informal measures such as work samples offer the qualitative information necessary for an inclusive profile (Kaufman & Kaufman, 1983, 1993).

The Flexible Battery Approach

This integrative model is based on a contemporary understanding of the evaluation process (Dombrowski, Kamphaus, Reynolds, 2004; Sattler, 2002). Kaufman (1979, 1990) has argued that the focus of any assessment should be on the *person* being assessed, not on the *test* being used. The goal of any examination must be better than the tests that were used. Notably, information collected only represents illustrative samples of

behavior (and is not meant to be exhaustive); tests are meant to be administered and interpreted individually; and finally tests are to be used to generate hypotheses for helping the person being evaluated. With this as a backdrop, we offer the *flexible battery* approach. Although it is clear that all individuals need to be evaluated in the eight areas displayed in Table 2, the selection of tests utilized to evaluate these abilities will

Table 2. Brain-Based Areas That Should Be Formally and Informally Assessed in Neuropsychological Evaluations

1. Perceptual/Sensory
   - Visual
   - Auditory
   - Tactile-kinesthetic
   - Integrated
2. Motor Functions
   - Strength
   - Speed
   - Coordination
   - Lateral preference
3. Intelligence/Cognitive Abilities
   - Verbal functions
     Language skills
     Concepts/reasoning
     Numerical abilities
     Integrative functioning
   - Nonverbal functions
     Receptive perception
     Expressive perception
     Abstract reasoning
     Spatial Manipulation
     Construction
     Visual
     Integrative functions
4. Attention/Learning/Processing
   - Visual processing
   - Motoric processing
   - Auditory processing
   - Spatial Processing
   - Linguistic/verbal processing
   - Simultaneous processing
   - Sequential processing
   - Memory/learning
5. Communication/Language Skills
   - Receptive vocabulary
   - Expressive vocabulary
   - Speech/language
   - Written language

Table 2. (*Continued*)

6. Academic Achievement
   - Preacademic skills
   - Academic Skills
     Reading decoding
     Reading comprehension
     Arithmetic facts
     Arithmetic calculation
     Social studies
     Language arts
     Science
7. Personality/Behavior/Family
   - Adaptive behavior
     Daily living
     Development
     Play/leisure
   - Environmental/social
     Parental
     Siblings
     Family
     Peers
     Community
   - Student coping/tolerance
   - Family interpersonal style
8. Educational/Classroom Environmental
   - Learning environment fit
   - Peer reactions
   - Community reactions
   - Teacher/staff knowledge
   - Learner competencies
   - Teacher/staff reactions
   - Classroom dispositions

Adapted from D'Amato and Rothlisberg (1996) and D'Amato, Rothlisberg, and Work Leu (1999).

vary greatly because of the unique needs of the individual—considered in tandem with the reason for referral.

In the neuropsychological area, age expectations based on normal development can be misleading and must be cautiously scrutinized in light of the usual abilities of the child or adolescent. For example, an individual who has sustained a traumatic brain injury and is reportedly functioning at grade level may in actuality exhibit specific skill deficits that are at variance with what has been observed in the classroom, and these deficits may interfere with continued educational progress (Begali, 1994). Stated differently, the child may be compensating in ways that are not recognizable   by   teachers   (D'Amato   &

Rothlisberg, 1996; Work & Choi, 2005). For instance, some children will benefit from a multiple-choice format, which decreases memory requirements, while others will be overwhelmed with the number of choices available in such a situation. Telzrow 1986, 1987, 1990) and others have advocated for determining the essential and nonessential features of a measure before considering its use (D'Amato et al., 2005; Kaufman, 1990; Savage & Wolcott, 1994). From this view, tests can be utilized if modifications are made to nonessential features opposed to essential features. A case in point may be a child who is not able to point to a template, but could signal verbally without violating the intent of the measure. Indeed, consideration should be given to the type of response required, and alternate responses accepted if they do not violate the integrity of the measures being used. Such modifications may be necessary if valid and reliable instruments are not available in the areas to be evaluated.

Areas the Evaluation Should Encompass

The eight key areas that best reflect a comprehensive, developmentally appropriate examination are displayed in Table 2: (1) Perceptual/Sensory Functions, (2) Motor Functions, (3) Intelligence/Cognitive Abilities, (4) Attention/Learning/Processing Capacity, (5) Communication/Language Skills, (6) Academic Achievement, (7) Personality/Behavior Functioning, and (8) The Educational/Classroom Environment. All of these areas should be considered both formally and informally. Direct observations and interviews with the individual and family members are vital components in evaluating any individual's performance in these areas. Behavior rating scales and self-report measures, a review of records, and a collection of work samples should also be among the methods used to collect information (Lezak, 1995; Sattler, 2002a, b; Telzrow, 1986, 1987; Telzrow et al., 2005). As demonstrated in Table 3, a great variety of testing instruments are appropriate in all areas discussed. The practitioner must take responsibility for carefully matching the learner with potential assessment options—after considering the distinct features of the instruments and the unique needs of the student. Indeed, the uniqueness of the individual should drive the selection of instruments.

Table 3. Common Instruments and Procedures Used to Evaluate Neuropsychological Systems

1. Perceptual/Sensory
   - Child and classroom observations
   - *Dean-Woodcock Neuropsychological Battery* (e.g., Lateral Preference, Near Point Visual Acuity, Palm Writing, Finger Identification)
   - Developmental or clinical history
   - *Goldman-Fristoe Woodcock Test of Auditory Discrimination*
   - Mental status examination
   - *Motor-Free Visual Perception Test*
   - *Neuropsychological Questionnaire*
   - Vision and hearing screening
   - *Wepman's Auditory Discrimination Test*
2. Motor (Fine and Gross)
   - *Bender Visual–Motor Gestalt Test II*
   - *Dean-Woodcock Neuropsychology Battery Motor Tests* (subcortical and cortical; e.g., Gait and Station, Romberg, Construction Test, Finger Tapping)
   - *Detroit Tests of Learning Aptitude-4 (Motoric Composite)*
   - *Developmental Test of Visual–Motor Integration*
   - *Kaufman Assessment Battery for Children-2 Nonverbal Index* (e.g., Hand Movements subtest)
   - *Wechsler Scales* (e.g., Bock Design, Coding Subtests)
3. Intelligence/Cognitive Abilities
   - *Battelle Developmental Inventory 2*
   - *Bayley Scales of Infant Development, Third Edition*
   - *Das-Naglieri Cognitive Assessment System*
   - *Differential Ability Scales*
   - *Kaufman Adolescent and Adult Intelligence Test*
   - *Kaufman Assessment Battery for Children-II*
   - *Wechsler Scales*
   - *Woodcock Johnson III—Test of Cognitive Abilities*
4. Academic Achievement
   - *Basic Achievement Skills Invention* (e.g., Language, Reading, Math computation, Math application subtests)
   - *Differential Ability Scales*
   - *Kaufman Test of Educational Achievement II*
   - *Key Math Diagnostic Inventory-Revised, Normative Update*
   - *Peabody Individual Achievement Test-Revised, Normative Update*
   - *Wechsler Individual Achievement Test 2nd Edition*
   - *Woodcock Johnson III—Tests of Achievement*
   - *Woodcock Reading Mastery Test-Revised-Normative Update*
5. Communication/Language Skills
   - *Bracken Basic Concept Scale-Revised*
   - *Clinical Evaluation of Language Fundamentals*

(*Continued*)

Table 3. (*Continued*)

- *Comprehensive Test of Phonological Processing*
- Peabody Picture Vocabulary Test-Revised
- Revised Token (Oral Comprehension) Test
- Test of Adolescent and Adult Language, Third Edition
- Test of Early Language Development, Third Edition
- Test of Language Development, Primary, Third Edition
- Test of Written Language, Third Edition

6. Attention/Learning/Processing
   - Children's Auditory Verbal Learning Test
   - Detroit Tests of Learning Ability-4
   - Test of Memory and Learning
   - Test of Nonverbal Intelligence
   - Wechsler Memory Scale-Revised
   - Wide Range Assessment of Memory and Learning

7. Personality/Behavior
   - Behavior Assessment System for Children-2
     Parent Rating Scales
     Self-Report of Personality
     Teacher Rating Scales
   - Clinical Interview with Child or Adolescent
   - Family Environment Scale
   - Home Visit and Family/Parent Interview
   - Kinetic Family or School Drawings
   - Minnesota Multiphasic Personality Invention-2
   - Multidimensional Self-Concept Scale
   - Parent Stress Inventory
   - Personality Inventory for Children II
   - Revised Children's Manifest Anxiety Scale
   - Sentence Completion Test
   - Vineland Adaptive Behavior Scales
   - Wishes and Fears Inventory

8. Educational /Classroom Environment
   - *Attention/Distraction: Inhibition/Excitation Classroom Assessment*
   - *Behavioral and Emotional Rating Scale*
   - *Classroom Environment Scale*
   - Classroom Observations
   - *Early Childhood Environment Rating Scale*
   - *Instructional Environment Scale*
   - *Social Skills Rating Scale*
   - Sociograms
   - Teacher Interviews

The Evaluation-Intervention Link

The development of appropriate interventions from neuropsychological data has a long history replete with many difficulties. For decades many neurophysiologists have focused on the documentation of deficits (e.g., visual-spatial problems) with interventions geared to reduce the effects of or compensate for the deficit areas (e.g., visual–motor training). Another great body of research probes the relation of behavior change to specific areas of brain insult (D'Amato et al., 2005; Lezak, 1995). Although it may be of interest to realize that a child suffered frontal lobe damage in an automobile accident last summer, that an infant has general cerebral impairment caused by anoxia at birth, or that an adolescent has right parietal damage (and seizures) as a result of surgery, this causative information relating to individuals' difficulties offers little, if any, direction for the uninitiated regarding rehabilitation. All practitioners must select data-gathering approaches that offer information deemed directly relevant for understanding the educational and life needs of children and young adults.

The hypothesis-testing approach is offered as a heuristic guide for understanding individual learners. Practitioners evaluate the data generated from individuals examined and begin to problem solve concerning the abilities the student displays. Many have argued for strength-based approaches (D'Amato et al., 1999; Dean & D'Amato, 1989; Kaufman & Kaufman, 1983; Reynolds, 1981, 1986) as opposed to a focus on student weaknesses. Hypotheses based on the data can be utilized to develop learner profiles concerning environmental stimulation, endurance and stamina, instructional tactics, organizational abilities, and an evaluation of resulting student feelings given the profile exhibited. Most evaluations traditionally focus exclusively on the area where learners display deficiencies (e.g., in reading decoding or mathematical computations; D'Amato et al.); a flexible neuropsychological approach to assessment for intervention must consider both how and why learners best process information (D'Amato, 1990). For example, learners who vary on modality strength profiles may require different teaching strategies to accommodate student-learning styles (e.g., independent workbook tasks versus chalkboard work; Leu & D'Amato, 1994). In addition, each learner may exhibit a preferential hemispheric processing style (e.g., simultaneous or sequential processing; Davis & Dean, 2005). An evaluation must also consider if the individual would profit from compensatory teaching methods (used to circumvent a deficit) or remedial instruction

(geared to address and improve an academic weakness; D'Amato et al.; Gaddes & Edgell, 1994; Rothlisberg et al., 2003; Telzrow, 1986, 1990). The answers to these questions offer the foundation for the development of a broad-based rehabilitation program.

Interview and Generation of Assessment Plan

Developmental History

Any assessment of function would be incomplete without the compilation of a comprehensive developmental history. Information regarding prenatal, perinatal, and postnatal development should be gathered through a combination of structured interviews and the administration of more formalized measures like the Maternal Perinatal Scale (Gray, Dean, & Rattan, 1987). Significant deviations from normal developmental patterns may indicate potential areas of difficulty that warrant further investigation. Current medical issues and a gross observation of perceptual and motor functioning are also of interest during this contact. Knowledge of the individual's perception and motor skills, current health status, and physical limitations is essential for the formulation of an appropriate assessment battery. This same information should later be integrated in the interpretation of results.

Perceptual/Sensory and Motor Functions

Perceptual and motor functions form the basis of children's understanding of the world and their response to it. Therefore, differences in these primary areas may portend difficulties in other areas of functioning. For example, the reproduction of a visual stimulus in response to a request involves both perceptual discrimination of fine motor development, as well as the ability to integrate visual, tactile, and auditory skills. Therefore, inadequate performance in copying geometric designs developed to assess these skills may stem from: a misperception, or faulty interpretation of the input information; problems in executing the fine motor response, or output; and/or difficulties integrating the input and output, otherwise known as integrative or central processing difficulties. Other variables that contribute to poor performance include poor motivation, maturational delays, limited development, neurological impairment, sensory deprivation, and other disabilities or illnesses, including fatigue, stress, and injury (Sattler, 2002). The following sections will offer information on representative tests that are used to evaluate these processes.

Perceptual/Sensory Functions

Perception of stimuli is a complex process involving many different aspects of brain functioning (Lezak, Howieson, Loring, & Hannay, 2004). The assessment of these functions is useful in determining the extent to which visual, auditory, and tactile-kinesthetic information is received and integrated.

The Motor-Free Visual Perception Test, Third Edition (MVPT-3; 2002). Structure: A 65-item measure assessing five facets of visual perception—spatial relations, visual discrimination, figure-ground, visual closure, and visual memory. The MVPT-3 is intended for children and adults 4–95 years of age.

The MVPT-3 is designed to assess visual perception in the school age through adult population. The child is required to pick the correct response from four options arranged in a multiple-choice format (King, 2002). The MVPT-3 is used when the results from measures such as the Bender leave the clinician uncertain as to whether difficulties displayed are the result of visual and/or motor concerns. Clinical observations and other methods of data collection may also prove inconclusive regarding the etiology of performance difficulties. The MVPT-3 can offer information essential for the differential diagnosis of motor versus visual processing problems. However, when used in isolation from other measures or techniques, the MVPT-3 offers information regarding visual processing difficulties but is unable to rule out motor concerns.

Practical implications. Assesses perception without the confounding motor component present in popular visual–motor integration measures. Thus, the MVPT-3 can offer important diagnostic and rehabilitation information.

Motor Functions

Motor dysfunctions that are best explored using a neuropsychological paradigm are fine motor in nature (those that occur despite the appearance that the person moves normally through space) (Lezak, Howieson, Loring, & Hannay, 2004). Numerous paper-and-pencil tests have been developed to assess motor functions as they relate to visual–motor integration. Two of the most popular measures for this purpose are the Bender Visual–Motor Gestalt Test and the Developmental Test of Visual–Motor Integration.

Bender Visual–Motor Gestalt Test, Second Edition (Bender-Gestalt II, 2003). Structure: Individually administered test containing 16 geometric figures that the child or adult copies depending on their age. While historically this test was seen as a general measure of organicity, it is more appropriately used as a measure of visual–motor skills. Standard scores are provided for children and adults aged 5–85 and over.

Most commonly known as the Bender, this measure is perhaps the best known and most widely used visual–motor assessment procedure available today (Bender, 1938; Reynolds & Kamphaus, 2003). As a component of a comprehensive assessment battery, performance on the Bender has long been thought to reveal visual–motor difficulties that may be associated with cerebral impairment (Sattler, 2002). Traditionally used to assess an individual's constructional praxic skills, the Bender provides an evaluation of motor integration employed in the execution of complex learned movements (Hartlage & Golden, 1990). The information generated through this process may then be compared with levels of performance across other measures of functioning. Contrary to once-common practice, the Bender is inappropriate as a test of brain damage. In fact, the very idea of single screening instrument having the potential for evaluating the complex nature of the brain has proven to be naïve at best (D'Amato, 1990).

Alternate uses of the Bender include its administration as a memory test and then as copying test. This dual administration process can be employed to assess different mental functions (short-term visual memory and visual perception) that utilize the same modalities in perception and task execution (Sattler, 2002).

An additional technique available when interpreting Bender performance is to have the child compare the figure that he or she produced with the corresponding stimulus design. If the child is unable to recognize obvious differences between the two designs, a perceptual deficit may be involved. Likewise, if the child is able to detect differences between the two figures, but is unable to make them alike, motor involvement may be influencing performance (Hartlage & Golden, 1990). In the personality area, performance on the Bender may also be used to develop hypotheses regarding impaired performance caused by poor planning, impulsivity, or compulsivity. Extremely large or small figures, heavily reinforced lines, and second attempts, are examples of the item reproduction difficulties that are thought to indicate emotional concerns on the part of the individual.

Practical implications: The Bender provides information relevant to visual–motor skills and visual–motor integration. Results from this measure can be useful in evaluating pre-reading, reading, and penmanship concerns, and other areas requiring the input and output of information. However, because of the Bender's marginal differentiation between visual and motor components of performance, it is not practical for use if isolated from other measures.

The Beery-Buktenica Developmental Test of Visual–Motor Integration, Fifth Edition (VMI, 2004). Structure: Involves copying a sequence of 24, increasingly complex, geometric figures. The VMI may be administered in either an individual or a group setting and requires a relatively short administration time. It is designed primarily for ages 2–18.

The VMI was first published in 1967 and is now in its fifth edition. Because the VMI does not require a verbal response, it has often been used to assess visual–motor processes among non-English-speaking children. The VMI has also been previously employed when investigating the reliability and validity of other tests of visual–motor integration, such as the Bender self-drawing tasks, progressive matrices, and neuropsychological tests (Goldstein, Smith, & Waldrep, 1986; Palisano & Dichter, 1989). The most common use of the VMI, however, seems to be in assisting with the diagnosis of children who are suspected of having visual–motor difficulties related to learning problems.

The VMI offers several advantages as a tool for assessment and is widely used in psychological evaluation and research. From a neuropsychological perspective, the VMI differs from the Bender on two variables: age range and level of planning required. First, the age range of the VMI is more extensive than that of the Bender. Whereas the Bender has limited application to children under 5 years, the VMI is able to be used in the assessment of children as young as 2 years. Second, unlike the Bender in which the child is allowed to copy the stimulus design on any section of the paper, the VMI requires the design to be placed within a predesignated area. This restriction omits analysis of planning, but does allow for the evaluation of visual–motor integration in a structured format. The VMI can provide a measure of how the child completes a perceptual-motor task within specific limitations and then can be contrasted with the Bender, which is more ambiguous and requires more planning, in order to evaluate how he or she learns and approaches a task (Semrud-Clikeman et al. 2005).

Practical implications: The VMI allows for relatively fine differentiation of individual performance on tasks requiring visual–motor integration. The age range and structured format of the measure render the VMI applicable to a wide range of children.

Cognitive/Intellectual Functioning

Aptly described as a cornerstone of the testing movement, intelligence tests predate efforts to efficiently measure neuropsychological constructs (Kamphaus, 2005). Ability tests probably are considered among the most acceptable types of measurement currently available because of their public aura of infallibility born from society's expectations of the tests' capability to gauge the true intellectual level of individuals. Unfortunately, the tests cannot live up to their public persona; they are simply tools that measure the individual's status as the person compares to others who have engaged in the same task. However, available measures do still provide the most valid test of skill when they are used to help predict the future performance of the individual in educational contexts and can provide insight into preferred processing style.

Intelligence testing is a useful adjunct to standard neuropsychological testing. Neuropsychological instruments try to evaluate one or more of the areas of sensory or motor skills, language processing, visual-spatial skills, memory and learning, attention, and abstract reasoning. Cognitive/intellectual instruments arguably assess these same constructs/areas and thus may offer valuable corroborative data in the overall profile of the individual's performance. In fact, some researchers have found information from intelligence tests to add a unique element to that discerned from standard neuropsychological tests (D'Amato, Gray, & Dean, 1988; Dean & Gray, 1990; Donders & Nesbit-Greene, 2004). However, interpretation of an individual's performance on intelligence tests is complicated by the fact that no two ability tests conceive of intelligence in exactly the same way or include items that measure only one capacity at a time. Instead, tests that purport to measure the broad construct of intellect can differ substantially from one another and be made up of items that tap multiple skills (Kamphaus, 2005). In general, children who have experienced some form of neuropsychological dysfunction or damage display general cognitive impairment; specific profile subtypes on intelligence tests have not been found (Kamphaus, 2005).

Although tests of cognitive skill cannot provide a ready means of interpreting performance and selecting intervention options, careful analysis of all aspects of the tests (i.e., formal and informal observations) can provide a starting point for integration with other data sources using a neuropsychological framework. Practitioners should be encouraged to go beyond the superficial aspects of the tests (e.g., the global scores when building hypotheses and interpreting assessment findings). Review of the test features—in terms of theoretical orientation, subtest construction, and item characteristics, modality of presentation and response—can be helpful clues to understanding children's performance. For the instruments discussed, such features will be addressed.

Battelle Developmental Inventory, *Second Edition* (BDI-2; 2004). Structure: Five domains incorporating 24 subdomains are assessed in making up the Total Battery score. The domains (and associated subdomains) are as follows— Personal-Social (Adult Interaction, Self-Concept and Social Growth, and Peer Interaction); Adaptive (Personal Responsibility and Self-Care); Motor (Fine Motor, Perceptual Motor, and Gross Motor); Communication (Receptive

Communication and Expressive Communication); and Cognitive (Perceptual Discrimination/ Conceptual Development, Reasoning and Academic Skills, Attention and Memory). The BDI-2 was normed for individuals from birth to 8 years.

The BDI was initially designed as a means of evaluating the government's Handicapped Children's Early Education Program (Kamphaus, 1993; Salvia & Ysseldyke, 1991). As such, it was functionally oriented to provide a profile of developmental strengths and weaknesses suitable for generating individualized programs for children at risk (Snyder, Lawson, Thompson, Stricklin, & Sexton, 1993). Items were chosen based on existing infant and preschool measures to provide a comprehensive view of early functioning.

The BDI and other measures of early cognitive performance have had the difficult task of trying to explain the factors potentially relevant for later success. The rudimentary nature of infant behavior and the lack of agreement as to the structure of intelligence (i.e., its continuity versus its discontinuity) lessen the influence that information about infant behavior can provide (Lewis, Jaskir, & Enright, 1986). However, for diagnostic purposes and for gauging the needs of these youngest learners, the press for assessment of behaviors has continued.

The BDI-2 is unique in that it addresses the idea that infant and preschool behavior can be conceived of as multifaceted. It depends on parent interview, observation, and structured assessment in the collection of data; however, its length and formal administrative procedure may make it difficult for examiners to accurately survey the child's functioning. For instance, Bailey, Vandiviere, Dellinger, and Munn (1987) found that teachers trained to administer the original BDI needed multiple sessions to complete the assessment and made many computational errors in scoring the test. Adaptations (or procedures) for children with disabilities were only partially successful and the restricted range of scores lessened the BDI's value for children with severe delays.

The BDI-2 is also available in Spanish. The BDI-2 Spanish is an adaptation/translation of the BDI-2 English materials and according to the publisher is designed for the screening, diagnoses, and evaluation of early childhood development of non-English-proficient children and their caregivers. It allows both the child and parent to document the child's mastery of critical skills or behaviors of typically developing children. The BDI-2 is designed for use by a bilingual examiner, by an English-speaking examiner and a Spanish-speaking colleague, or by a team of professionals.

Practical implication: Although neither the BDI-2 nor its predecessor has resolved all of the questions concerning appropriate assessment of early development, its attempt at multidimensional evaluation and its functional approach to intervention strategies make it an appropriate addition to traditional assessment methodology. By acknowledging that infant behavior can be viewed in a diversified fashion and grouped in what some see as neuropsychological domains, the BDI has helped to advance the conceptualization of early intelligence.

Bayley Scales of Infant Development, Third Edition (Bayley, 2006). Structure: The Bayley-III assesses development across five domains: cognitive, language, motor, socio-emotional, and adaptive behavior. This recently revised version of the Bayley was normed for individuals 1–42 months of age. Administration time takes between 30 and 90 min depending on the age of the child (Salvia & Ysseldyke, 2007).

The Bayley has long been considered one of the finest norm referenced instrument available to assess the cognitive and motor status of infants and toddlers (Kamphaus, 2005; Whatley, 1987). It attempts to look at the infant's sensorimotor functioning, rudimentary communication, and problem-solving abilities as well as the child's early fine and gross motor capacities. The measure is based on Bayley's research with infants and her belief that a picture of current functioning relative to other infants is our best way of understanding the progress of very young children. Moreover, infants may display idiosyncratic rates of skill attainment based on their characteristics and the environments to which they are exposed (Bendell-Estroff, Greenfield, Hogan, & Claussen, 1989). Consequently, the Bayley-III provides the infant with the opportunity to experience a range of tasks in a rather fluid format to determine how each child's pattern of performance compares with that commonly found.

The Bayley-III includes the addition of a social-emotional subtest and an adaptive behavior subtest. Information for these two subtests is provided by the parent or caregiver through a

questionnaire format. The Bayley-III also provides an abbreviated screening test to help determine if more extensive testing is needed. Reliability and validity information for the Bayley-III is limited because of the recent date of publication, but is reported by the publisher to be consistent with previous versions of the measure.

Practical implications: The Bayley-III provides to the examiner the psychometric sophistication and control that ensures the most reliable estimate of infant behavior currently available. It is supported by decades of research. Although it does not allow for extensive explanation of different domains of cognitive function, it does provide the child an opportunity to display progressive growth in its series of skills.

Differential Ability Scales (DAS, 1990). Structure: Two levels with cluster scores for all ages except lower preschool. A General Conceptual Ability (GCA) score is computed based on level subtests. Preschool includes lower (ages 2 years 6 months to 3 years 5 months) and upper (3 years 6 months to 5 years 11 months) levels. GCA is made up of Block Building, Verbal Comprehension, Picture Similarities, and Naming Vocabulary for the Lower Preschool Level while cluster scores, Verbal (Verbal Comprehension, Naming Vocabulary) and Nonverbal (Picture Similarities, Pattern Construction, Copying) as well as an Early Number Concepts subtest appear for the Upper Preschool Level. At the school-age level, GCA is defined by three clusters: Verbal (Word Definitions, Similarities), Nonverbal Reasoning (Matrices, Sequential and Quantitative Reasoning), and Spatial (Recall of Designs, Pattern Construction). The DAS was normed for children from 2½ to 17 years. It also includes diagnostic subtests (Recall of Digits, Recall of Objects—Immediate and Delayed, Speed of Information Processing (school age only), Matching Letter-Like Forms (preschool only), Recognition of Pictures (preschool only) for both levels and Achievement tests (Basic Number Skills, Spelling, Word Reading) for the school-age level.

The DAS is based on the British Ability Scales and is unique in that it can promote itself as a "full-service" test. The DAS has two distinct levels, preschool (2 years 6 months to 5 years 11 months) and school age (6 years to 17 years, 11 months) made up of core subtests related strongly to "*g*," i.e., general ability. In addition, several diagnostic tests and a brief achievement screener are available if the examiner wishes to examine different aspects of performance. Packaging different components of performance within one scale with common norms across ability and achievement may make analysis of examinee responses clearer and more clinically relevant (Elliott, 1990).

One aspect of interest in the structure of the core battery is the acknowledgment of the developmental changes occurring in intellectual skills during the early years of life. The lower preschool level provides only a general conceptual ability scale, reflecting the lack of differentiation of ability present among the very young. The upper preschool version offers verbal and nonverbal components, whereas the school-age version includes verbal, nonverbal, and spatial clusters. Unfortunately, the DAS is not based on a particular model of intelligence, so the tendency may be to shift interpretive schemes with each case. Also, since clusters are made up of only two subtests, one may be limited in the breadth of options or measures of behavior; performance is either equivalent across subtests in a cluster or one subtest proves to be significantly higher in score than its partner.

The authors have found the DAS to be an appealing test to individuals of all ages—suggesting that motivation to perform is less a problem than with some other instruments. In fact, the preschool level of the DAS is one of the more physically attractive measures for this population. Colorful objects, pictures, and an item format based on item sets rather than common basal and ceiling rules engage examinees in the items covered. Teaching items that allow the examiner to offer feedback and the alternate untimed method of administration for the Pattern Construction provide options in the examiner technique unlike those of other tests. Language demands may be less than those for the Standford-Binet V and the WISC-IV in that simple phrases or one-word responses may suffice to answer vocabulary or similarity items. In terms of neuropsychological principles, the DAS may be viewed as fitting under a verbal/nonverbal dichotomy, with nonverbal skills including both nonverbal reasoning and spatial clusters at the school-age level. However, depending on the examinee, even the nonverbal tasks may involve verbal mediation. For instance, even Recall of Designs, where the individual must remember

and reproduce a line drawing, is aided when the child can attach a verbal label to the design. This is also factor in Matrices and Sequential and Quantitative Reasoning where concept formation can be facilitated through verbal rehearsal of cues.

Diagnostic subtests available for the DAS can be useful adjuncts to the core battery. Both Recall of Digits and Recall of Objects involve the use of verbal labels to determine success; however, Recall of Objects includes a delayed component which may indicate the degree of incidental learning under way when the individual is rehearsing the items seen on the card. Similarly, at the preschool level, Matching Letter-Like Forms and Recognition of Pictures may anticipate the child's need to be aware of the spatial orientation of letters and shapes and attend to meaningful detail.

Practical implications: The DAS, now an outdated instrument, is scheduled to be replaced with a revised version in the very near future. Similar to the original DAS, the newly revised DAS-II (2007) is designed to offer the examiner a broad array of assessment options. Including both a preschool and a school-age level, the addition of diagnostic and achievement tests affords the examiner ways of exploring hypotheses about learning difficulties. The core subtests basically describe verbal versus visual-spatial-numerical reasoning, while the diagnostic subtests explore auditory and visual short-term recall as well as processing speed. The engaging items available may make the measures very attractive to preschoolers in particular.

Kaufman Adolescent and Adult Intelligence Test (KAIT, 1993). Structure: Two scales—Crystallized (Definitions, Auditory Comprehension, Double Meanings) and Fluid (Rebus Learning, Logical Steps, Mystery Codes)—make up the Core Battery. Although a Composite score is available, it is only suggested for interpretation if there is no significant difference between Crystallized and Fluid scales.

The Expanded Battery adds the subtests Famous Faces (alternate, Crystallized Scale), Memory for Block Designs (alternate, Fluid Scale), and Rebus Delayed Recall and Auditory Delayed Recall (Measures of Delayed Recall). A Mental Status Examination is also provided. The KAIT was normed for individuals 11–85 years of age.

The KAIT was originally designed to compete with the WAIS-R for assessment of the adult population. However, unlike the WAIS-R, the KAIT has attached to it a strong theoretical direction that unites classical views of crystallized and fluid abilities with the abstract reasoning abilities associated with Piaget's concept of formal operations (Kaufman & Kaufman, 1993). Whereas one would expect the KAIT to be congruent in design to the Kaufman Assessment Battery for Children (K-ABC), the two Kaufman tests are not extensions of one another. In fact, Kaufman (1993) illustrated this point in a factor-analytic study that compared the KAIT with the K-ABC. The fluid components of the K-ABC are defined by measures of simultaneous and sequential processing; however, planning and formal operational features are believed to address fluid abilities on the adult scale. Kaufman defended the shift in his theoretical orientation by ascribing the differences in the tests to the different reasons behind testing in childhood and adulthood. Although the K-ABC presumes to assess crystallized ability through a separate achievement scale and reserves fluid tests as those that best represent cognitive potential, the KAIT sees the mature individual as a functional composite of both problem-solving abilities and the rich store of experiences to which the person has been exposed.

In a way, the structure of the KAIT is somewhat deceiving. A cursory preview of the materials may suggest a simple measure that takes little time to administer. Actual practice and administration of the KAIT will disavow that notion. Adolescent and adults will be challenged by the apparently modest stimuli to uncover the relations between concepts. To generate the most complete picture of the adolescent or adult, both the core and expanded battery sections must be administered. The expanded battery may provide the best picture of learning among its examinees because the instrument includes what it considers to be measures of immediate, long-term and remote memory. Rebus Delayed Recall and Auditory Delayed Recall will test out the examinee's ability to retrieve information learned recently and Famous Faces involves retrieval of past experiences. Certainly, informal observations of examinee strategies to handle the various situations will add clinical insight about the individual's approach to problems.

In terms of a neuropsychological orientation to the task, the KAIT defies easy analysis. The breakdown of subtests into measures of classic fluid and crystallized ability suggests that the subtests given over to crystallized skills are analogous to those found in the WAIS III that tap predominately verbal knowledge and those designated as fluid hold the strongest connection to WAIS III performance items. Indeed, the subtle novelty of the subtests of the KAIT may require openness to new problem-solving situations even when the response involves retrieving verbal information from memory. Likewise, the fluid subtests may tap logical or purportedly left-hemisphere functions (Logical Steps), simultaneous or purportedly right-hemisphere functions (Memory for Block Designs), and integrative functions (Mystery Codes). It seems that, in nearly every task, a verbal organizational strategy could aid in problem solution. Given the innovative item types, however, individuals who are operating at more concrete levels of reasoning or who have experienced significant trauma may be unable to understand the questions with enough clarity to respond.

Practical implications: The KAIT, overdue for an update and revision, is unique in that it seeks to examine the complexity of mature cognition through the combined use of crystallized/fluid distinctions and presence of formal operational thought. Formal operational skills may help to describe frontal lobe function, but the neuropsychological relations in the test are not clearly delineated.

Kaufman Assessment Battery for Children, Second Edition (KABC-II, 2004). Structure: Four scales plus one optional scale—Simultaneous (Triangles, Face Recognition, Pattern Reasoning, Block Counting, Story Completion, Conceptual Thinking, Rover, Gestalt Closure), Sequential (Hand Movements, Number Recall, Word Order), Planning (Pattern Reasoning and Story Completion), Learning (Atlantis, Atlantis Delayed, Rebus, Rebus Delayed) and Knowledge (included in the Cattell–Horn–Carroll model only; Riddles, Expressive Vocabulary, Verbal Knowledge) make the Mental Processing Index, Fluid-Crystallized Index, and Nonverbal Index. The KABC-II was normed for children 3–18 years old.

The KABC-II was developed along two theoretical perspectives, a Lurian model and a Cattell–Horn–Carroll model, so that practitioners can interpret their results based on the referral question and the child's background. The test offers an expanded age range and, like the original, a nonverbal battery option and answers in Spanish for those items that require an oral response (Hess & Rhodes, 2005).

The separate simultaneous and sequential scales of the Mental Processing Index of the KABC-II propose that the learner must exhibit that particular processing style when completing the subtests within each scale. Use of simultaneous or sequential processing is believed to be independent of modality of presentation. Unfortunately, like its predecessor, the KABC-II has had difficulty providing proof that its view of processing style can be relevant for intervention (Braden & Ouzts, 2005). Soon after publication of the original K-ABC, a great deal of activity tried to establish the linkage of the simultaneous/sequential processing to academic behavior (e.g., see Rothlisberg, 1989), but when straightforward connections between processing and academic skill development did not materialize, interest in the test waned (Chattin & Bracken, 1989). It may be that the novel theoretical orientation of the test and its limited verbal requirements made the K-ABC too discrepant from practitioner notions of intelligence as to make it appear a less viable option than other scales. Nevertheless, comparisons with other measures of ability offered evidence that the K-ABC measures similar constructs to those assessed by the Wechsler and Stanford-Binet scales of intelligence.

Practical implications: The K-ABC was one of the first major assessment tools to define its structure in terms of a specific theoretical orientation. Conceiving of intelligence as involving the simultaneous and sequential fluid processing strategies, the K-ABC sought to offer a closer match between diagnosis and intervention. Sequential skills were tied to left-hemisphere, step-by-step analysis, whereas simultaneous abilities were purported to tap right-hemisphere strengths. The KABC-II allows for interpretation of performance from a Lurian model and/or Cattell–Horn–Carroll model perspective. The ability to link performance on the KABC-II to intervention has been questioned.

Stanford-Binet Intelligence Scale, Fifth Edition (SBV, 2003). Structure: Five domain scores—Fluid Reasoning (Nonverbal subtest; Object Series/Matrices and Verbal subtests;

Early Reasoning, Verbal Absurdities, Verbal Analogies), Knowledge (Nonverbal subtests; Procedural Knowledge, Picture Absurdities and Verbal subtest; Vocabulary), Quantitative Reasoning (Nonverbal subtest; Quantitative Reasoning and Verbal Subtest; Quantitative Reasoning), Visual-Spatial Processing (Nonverbal subtests; Form Board, Form Patterns and Verbal subtest; Position and Direction), and Working Memory (Nonverbal subtests; Delayed Response, Block Span and Verbal subtests; Memory for Sentences, Last Word)—make up the Composite standard age score. The SBV was normed for individuals 2 to over 85 years of age.

The SBV is the latest revision in the test's venerable history. Prior to the Stanford-Binet Fourth Edition, earlier versions of the instrument were organized according to an age scale format and provided a single or composite score to characterize cognitive skill. In addition, the Stanford-Binet had a unique adaptive format that allowed examiners to route the examinee through items and skills considered to be indicative of intellectual performance at various age levels. Functional in nature, the early versions of the Stanford-Binet gave examiners the luxury of a wide age range for testing and item groupings that often piqued younger children's interest while challenging children of higher capabilities.

Salvia and Ysseldyke (2007) note that the SBV maintains continuity with the past while also making use of advances in the field of psychometrics. The SBV continues to be based on a hierarchical model of intelligence, recognizing a global *g* factor and several broad factors that comprise *g*. Item response theory was used in creating the routing, subtest, and functional levels. In its latest form, the SBV differs from the SBIV in the addition of a fifth factor, the requirement of fewer verbal responses from the examinee, the inclusion of items that measure very low and very high levels of functioning, and a significantly expanded age range (Salvia & Ysseldyke, 2007).

In an effort to address noted limitations of the SBIV, the SBV revised the artwork and manipulatives, added toy and game-like materials, and streamlined administrative options (Becker, 2004). The SBV covers the widest age range of any Stanford-Binet and included revisions designed to address previous criticism of verbal content, norms, and the standard deviation. The standard deviation is now 15 for the SBV IQ scales rather than the 16 point standard deviation of previous versions.

Practical implications: Designed to support a hierarchical model of intelligence, the structural integrity of the modern Stanford-Binet scales has not lived up to their hypothesized ideal. Difficulties in administration, scoring, and interpretation have cast doubts on the overall utility of the Stanford-Binet for analysis from any neuropsychological perspective. If used, the most salient aspects, verbal versus nonverbal/visualization areas, may be thought of as analogous to verbal versus performance breakdowns. The latest version of this long-standing measure, the Stanford-Binet V, has attempted to address previous concerns and appears to be a worth revison.

Wechsler Adult Intelligence Scale, Third Edition (WAIS-III, 1997). Structure: Two scales—Verbal IQ Index and Performance IQ Index—make up the Full Scale IQ Score. The measure contains a four-factor structure that includes Verbal Comprehension, Perceptual Organization, Working Memory, and Processing Speed. The WAIS-III was normed for individuals 16–89 years of age.

The WAIS-III and the WAIS-R and the WAIS before it have been used as an integral part of neuropsychological testing (e.g., see Tulsky et al., 2003; Goldstein, Katz, Slomka, & Kelly, 1993; Moore et al., 1990, 1992; Russell, 1987). As such, each subtest has been analyzed and reviewed as to the unique contributions it makes to the neuropsychological battery. In some cases, an individual's WAIS-III profile is interpreted relative to the three-factor structure of the measure, Bannatyne's categorization, fluid versus crystallized skill, or a host of other configurations (Kaufman & Lichtenberger, 2005). In any case, interpretive strategies must take into account the match between performance on the WAIS-III and other documented evidence.

Perhaps one of the greatest contributions that Wechsler made to the study of intelligence was his recognition of the importance of nonverbal abilities in the evaluation of cognitive skill. Today, the basis of much of interpretation is grounded in the appearance of verbal/performance splits in an individual's protocol. Verbal skills such as vocabulary, understanding of similarity of concept, and comprehension of social situations may be resilient in the face of cerebral insult. At the same time, the spatial or fluid skills

associated with construction tasks such as Block Design or with fine motor control tasks such as Digit Symbol may not be spared. In any event, clinicians' familiarity with the WAIS-III makes it a trusted addition to any assessment situation.

Practical implications: The WAIS-III is the adult measure to which all others are compared. Offering an extensive age range as well as an impressive research base relative to neuropsychological testing, the WAIS-III differentiation between verbal and performance abilities along with related neuropsychological interpretive strategies is among the most widely known in the world.

Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV, 2003). Structure: Four index scores—Verbal Comprehension (VCI), Perceptual Reasoning (PRI), Working Memory (WMI), and Processing Speed (PSI)—make up the full scale IQ score (FSIQ) of the WISC-IV. The measure includes 10 core subtests and 5 supplemental tests. The FSIQ score derives from the 10 core subtests included in the four indices. Unlike previous versions of the WISC, the FSIQ of the WISC-IV is influenced by working memory and information processing speed. The WISC-IV was normed for individuals 6–16 years old.

The publisher reports that neurocognitive models of information processing provided the basis for the new structure of the WISC-IV, which replaces the traditional Verbal IQ (VIQ)/ Performance IQ (PIQ) dichotomy. The index scores that were supplemental in the WISC-III have been given primary importance and each has been enhanced based on contemporary research (Williams, Weiss, & Rolfhus, 2003). Three subtests from the WISC-III were eliminated and five new subtests were developed for the WISC-IV. Picture Concepts, Letter-Number Sequencing, Matrix Reasoning, and Word Reasoning were adapted from other Wechsler intelligence scales and were modified specifically for use with school-age children. Cancellation was developed as a new subtest as a measure of visual selection and processing speed (Williams, Weiss, & Rolfhus, 2003).

The WISC-IV is the latest version of the highly successful Wechsler series. Created as a clinical tool and as a downward extension of Wechsler's adult measure, the WISC has been embraced as the instrument of choice for the assessment of children's ability by school practitioners and neuropsychologists alike.

Practical implications: As with the WAIS-III, this latest revision of the WISC has the strength of many years of acceptance on its side as the premiere measure of intellectual functioning in childhood. The WISC-IV continues to offer a clinically relevant overview of intelligence, but the expected associations between test scores and academic performance may need to be modified in accord with the changing psychometric nature of the test. Children who have experienced some sort of trauma will typically exhibit a depression of scores with the performance scale more adversely affected than the verbal scores.

Academic Achievement

Although some would hold that there is little difference in the measure of ability and the measure of achievement (Anastasi & Urbina, 1997), it would seem that the operationalization of the two areas allows for a comparison of more generic problem-solving and verbal tasks to those directly involved in scholastic performance. Thus, the measure of ability may be conceived of as attempting to address the concept of underlying skills or capacities, whereas the measure of achievement is tied to the notion of the individual's facility in applying those faculties in a functional way to master real-world skills. For the purposes of this discussion, several norm-referenced instruments will be used to represent the area. Although it could be argued that alternate methods to norm-referenced assessment are preferable (i.e., curriculum based), the availability of a standard normative context allows for comparison of skills across a wide variety of curricular contexts.

The broad-based tests listed all have a similar organizational structure. For example, measures of a particular area, such as reading, are typically divided into basic skill (reading recognition) and some form of applied skill (reading comprehension) so that variation in the aspects of that academic task can be noted. The difference between instruments often lies in the method by which they obtain their information (i.e., whether visual–motor or oral responses are required).

Peabody Individual Achievement Test-Revised-Normative Update (PIAT-R/NU, 1997). Structure: Five subtest scores (General Information, Reading Recognition, Reading Comprehension, Mathematics, Spelling) are provided

in addition to the Total Reading and Total Test scores. A Written Expression and optional Written Language score are also available. The PIAT-R/NU was normed for individuals aged 5–22 years old in kindergarten through 12th grade.

The PIAT-R/NU is a normative update of the 1989 version of the measure. It is made up of five subtests and does what few other achievement tests do, namely it provides a composite achievement score. The utility of such a score is puzzling, however, as it averages the child's performance over disparate academic categories and essentially hides performance discrepancies. Of greater benefit to the practitioner will be subtest scores based on specific content.

The PIAT-R/NU is different from other tests in that it includes a larger pictorial component in its item types, letting children avoid the need for verbal reply, and instead of expecting them to point at the correct answer (out of four) for reading, spelling, and mathematics items. Because the task demands for recognition of information do not appear to be the same as for recall, this response format may aid children with retrieval difficulties or those who have developed some background knowledge of the area in question. It should be noted, however, that this response-type advantage may not give a good indication of the expectations for student performance in the classroom where recall and more integrated answers are the norm.

One aspect of the PIAT-R/NU that is of great benefit to the evaluator is the inclusion of the Written Expression subtest. Previously, when spelling skill was used to assess the written language area, children who could manage to spell words in isolation may have been perceived as being able to translate those spelling skills into fully developed written discourse. Unfortunately, this estimation of writing skill may have complicated the student's ability to have written language deficits recognized. On the PIAT-R/NU, students above the second grade are asked to create a story for one of two pictures. This writing experience allows the examiner to begin to evaluate ability in terms of organization, grammar, and development of ideas. This testing situation more closely approximates classroom activities in writing than do the other subtests.

Practical implications: The PIAT-R/NU is a well-constructed instrument that requires less oral language and makes greater use of

recognition as a response type than other achievement tests. The inclusion of a written expression subtest helps to address the notion of a continuum of skills in written discourse beyond spelling.

Wechsler Individual Achievement Test, Second Edition (WIAT-II, 2001). Structure: Four composites—Language (Oral Expression, Listening Comprehension), Writing (Written Expression, Spelling), Reading (Basic Reading Skill, Reading Comprehension), and Math (Mathematics Calculation, Mathematics Reasoning)—make up the battery. Basic Reading, Mathematics Reasoning, and Spelling can also be used as a screener. The WIAT-II was normed for individuals 4–85 years of age.

The WIAT-II is unique in that its subtests were designed to reflect major aspects of the definition of learning disabilities; hence, oral expression, listening comprehension, and written expression will sound familiar to those well versed in classification criteria. Unfortunately, it should be noted that little agreement as to the key elements of the definition exists so that specific aspects of the WIAT-II may relate to artifacts of our difficulties in understanding the nature of learning disorders. Be that as it may, the WIAT-II matches others of its genre in its basic structure and intent. It samples basic academic skill areas through the use of two tests per area and provides composite scores for reading, writing, language, and mathematics.

Although it appears to match the PIAT-R/NU in its inclusion of a Written Expression subtest, the most distinctive parts of the WIAT-II are the Listening Comprehension and Oral Expression components of this instrument. Listening Comprehension requires that the child listen to a paragraph and then respond orally to questions. The ability to understand orally presented material in an educational setting cannot be underestimated. Yet, although care has been taken to minimize the effect of the knowledge base on the child's ability to answer, it is possible in several instances to take educated guesses and receive credit for the items in this subtest. In contrast, Oral Expression appears to be different than any other subtest from competing achievement tests. Given a task, this subtest looks at the child's capacity to describe in an organized fashion the steps needed to complete an activity, recognize relations between objects, and take another person's perspective. This type

of activity would seem to be extremely difficult if a nonverbal disability existed that interfered with the interpretation of social perspective taking or if the pragmatic aspects of speech were underdeveloped.

Practical implications: The WIAT-II attempts to measure aspects of academic skill largely unaccounted for by other instruments. The addition of a language component may afford practitioners a greater capacity to compare components of language function. The purported relation of test construction and scoring to the educational category of learning disability may also prove attractive in a clinical setting.

Woodcock-Johnson Tests of Achievement, Third Edition (WJTA-III, 2001). Structure: Two batteries are included. The Standard Battery is divided into four cluster areas: Reading (Letter-Word Identification, Reading Fluency, Passage Comprehension), Oral Language (Story Recall, Understanding Directions), Mathematics (Calculation, Math Fluency, Applied Problems), and Written Language (Spelling, Writing Fluency, Writing Samples) and allows for scores for each subtest and area. An Extended Battery is also available to expand the Standard Battery Coverage. It includes Word Attack, Picture Vocabulary, Oral Comprehension, Editing, Reading Vocabulary, Quantitative Concepts, Academic Knowledge, Spelling of Sounds, Sound Awareness, and Punctuation and Capitalization subtests. Employing one or more of the supplemental subtests gives the examiner the option of computing additional areas of achievement such as Academic Knowledge, Phoneme/Grapheme Knowledge, and Academic Skills. The WJTA-III is normed for individuals 2 to over 90 years old.

The WJTA-III cluster areas parallel the areas of evaluation mandated by IDEA 2004. This broad range of assessment coverage and options is unique among available measures of academic achievement. With the inclusion of the supplemental or extended battery, academic areas such as reading or mathematics can be approached from more than a single direction. For example, five subtests looking at different aspects of reading can be included if the examiner so chooses. Similarly, the Academic Applications cluster allows the examiner to evaluate the child's ability to apply specific or discrete academic skills to common academic tasks.

The WJTA-III can be used in combination with the Woodcock-Johnson Tests of Cognitive Ability, Third Edition, as part of the Woodcock-Johnson Psychoeducational Battery, Third Edition, or with other recognized measures of cognitive ability. The overall Woodcock-Johnson Psychoeducational Battery is based on the Cattell–Horn–Carroll theory of cognitive abilities and identifies-broad CHC factors for each Standard and Extended Battery subtest of the WJTA-III.

Practical implications: The WJTA-III may be the most versatile of the norm-referenced individual achievement tests. This measure includes a standard and extended battery, providing practitioners with flexibility in the sampling of achievement-related behavior. In addition to covering more areas, the WJTA-III also features an extended age range.

Communication/Language Skills

When attempting to assess the potential for cerebral dysfunction, communication and language skills are prime candidates for analysis. A comprehensive assessment should include an analysis of receptive vocabulary and the ability to analyze and integrate information presented in a verbal format, since a common difficulty among children experiencing traumatic brain injury is a decreased capacity to coordinate the social aspects of language. Instruments useful for this purpose (in addition to the diagnostic information gained through the clinical evaluation of language-based measures of general intelligence and achievement) include the Bracken Basic Concept Scale-Revised, the Test of Written Language-III, and the Test of Language Development-III. Importantly, speech-language pathologists frequently contribute significantly to this area through the multidisciplinary process. In many cases, they serve as critical team leaders, when individuals have lost or nearly lost the ability to communicate clearly. Despite this, clinicians considering this key skill may choose to utilize measures such as the following instrument to gain a clearer picture of receptive language.

Peabody Picture Vocabulary Test, Third Edition (PPVT-III, 1997). Two parallel forms, each of which includes 204 picture plates designed to measure receptive vocabulary. The

PPVT-III was normed for individuals from 2½ to over 90 years of age.

The PPVT-III is one of the most frequently used measures of receptive language because it addresses the development of vocabulary in a relatively brief and flexible way (Kamphaus, 2005). The PPVT-III is untimed and requires the examinee to select from each plate of four pictures the one that best represents the target word. The test requires no reading ability, nor is the ability to point or provide an oral response essential. Starting and stopping points for the PPVT-III are determined by both the individual's chronological age and basal and ceiling requirements.

Although limited to the assessment of receptive language, the PPVT-III is particularly useful in establishing the level of verbal understanding children have when expressive language is not required. Comparing such receptive skills with those expressive skills needed for other tests may help in developing hypotheses about the qualitative nature of verbal performance and in framing potential intervention efforts.

Practical implications: The PPVT-III remains a frequent instrument of choice for the assessment of receptive vocabulary. The PPVT-III's wide range of applicable age groups and the absence of reading and motor requirements are especially beneficial for work with children with limited intellectual and physical abilities. This measure addresses an important area that is critical for intervention development. A newly revised version of this measure is scheduled for release in the near future.

Attention/Learning/Processing

Generally, three approaches have been utilized when evaluating how students preferentially process information. The first approach, seen as the traditional test approach, utilizes established measures (such as the WISC-IV), with the practitioner seeking to understand information processing through an analysis of common test results such as reviewing global score, subtests, and clusters of subtests (Kaufman & Lichtenberger, 2005). The second view of information processing, regarded as the informal approach, considers classroom data, observations, checklists, and learning style inventories to understand how students learn. From this view, students who seem to profit most from visual clues may be seen as visual learners and might be taught utilizing multimedia presentations, overheads, visual diagrams, and worksheets. The final approach to understanding processing stems from the administration and analysis of the many unique measures that have been offered as learning style, memory, or processing tests. This approach is seen as the nontraditional test approach.

These specialized measures of performance in learning, memory, or processing do not fall neatly within the traditional domains of intelligence, achievement, or neuropsychological processing. These tests, including the Detroit Tests of Learning Aptitude-4, the Children's Auditory Verbal Learning Test-2, the Wechsler Memory Scale-III, the Wide Range Assessment of Memory and Learning-2, the Test of Memory and Learning (TOMAL), and others can offer valuable information concerning how children deal with information. Although practitioners have used these instruments to document student strengths and weaknesses, diagnose learning problems, and chart the course of disorders, these instruments offer more practical information concerning rehabilitation or program planning than for diagnostic activities. Whereas all of these tests have been helpful in different circumstances, space does not permit review of these instruments. One measure that has a long history in the evaluation of processing styles is the Detroit. This measure has historically been one of the most popular processing instruments used in special education. The Detroit has been especially helpful when evaluating children who have suffered traumatic brain injuries. The TOMAL will be discussed as a measure representative of the contributions that tests in this domain offer for delineating student skills.

Test of Memory and Learning (TOMAL, 1994). Structure: Four Core Indexes, including Verbal Memory, Nonverbal Memory, Composite Memory, and Delayed Recall, are provided. Supplementary Indexes include Learning, Attention and Concentration, Sequential Memory, Free Recall, and Associative Recall. Subtests include Memory for Stories, Facial Memory, Word Selective Reminding, Visual Selective Reminding, Object Recall, Abstract Visual Memory, Digits Forward, Visual Sequential Memory, Paired Recall, Memory for Location, Manual Imitation, Letters Forward, Digits Backwards, and Letter

Backwards. The TOMAL was standardized for children aged 5–19 years.

The TOMAL is one of the most reliable measures available to evaluate children and adolescent memory. The evaluation of memory has long been a staple in the neuropsychological testing arena. Indeed, an understanding of memory and related learning processes is critical in all areas of neuropsychology including working with students who display learning disabilities, traumatic brain injuries, or psychiatric disabilities. The TOMAL boasts many unique features, including a great variety of memory indexes (Reynolds & Bigler, 1994). Although some of the subtests appear similar to other memory measures, some unique features of the test include a learning index where teaching is permissible (similar to some K-ABC subtests), a sequential memory index, and an attention and concentration index. Delayed recall subtests are also available and are offered as an evaluation of forgetting or memory decay. It is possible to compare the examinee's own personal learning curve with a standardized learning curve.

The test is easy to administer and generally user friendly. For example, directions are clear and many memory comparisons are readily utilized by virtue of the side-by-side layout of the measure. Unfortunately, the black-and-white templates are dated and do not seem engaging for young children. The TOMAL has many positive features for evaluating neuropsychologically impaired children and youth.

Practical implications: The TOMAL is psychometrically sound and has several features that are clinically relevant. Although it is not the only option when choosing a measure of memory, it remains an instrument of choice for many practitioners.

Personality Variables

Piers-Harris Children's Self-Concept Scale, Second Edition (Piers-Harris 2, 2002). The Piers-Harris 2 is a self-report questionnaire designed to assess how children and adolescents feel about themselves. Six cluster scales provide information concerning physical appearance and attributes, freedom from anxiety, intellectual and school status, behavioral adjustment, happiness and satisfaction, and popularity. An overall assessment of self-concept is provided. The Piers-Harris 2 was developed for individuals 7–18 years of age.

The Piers-Harris 2, in contrast to projective measures, evaluates the conscious self-perceptions/self-concept of the individual. This measure defines self-concept as a relatively stable set of attitudes reflecting both a description and an evaluation of one's own behavior and attributes. Through the use of the Piers-Harris 2 the practitioner is able to directly access the child's view of himself or herself in various situations and settings, rather than relying on interpretive inference.

The individual's responses to the questions of the Piers-Harris 2 allow for the evaluation of both general and specific dimensions of self-concept. The six separate cluster scales provide for a detailed interpretation of the individual's self-perception. The normative information gathered from this measure serves to round out the clinical hypotheses developed through the use of other measures.

Practical implications: The Piers-Harris 2 is a wide-band measure that offers insight into the individual's perception of his or her strengths and difficulties. The breadth of information gathered through this measure provides an overview of all major areas of a child's life. However, because of the use of one respondent, results are not adequate for differential diagnosis.

The Personality Inventory for Children, Second Edition (PIC-2; 2001). Structure: The PIC-2 is a multidimensional, objective measure typically completed by a parent of the child. Three measures of informant response style, 9 adjustment scales, and 21 adjustment subscales are included. The PIC-2 was designed to assess the functioning of individuals from 5 through 19 years of age.

The PIC-2 is one of several well-developed actuarial measures that are currently available for the evaluation of a school-age population (Urbina, 2005). An adult who is knowledgeable about the child (typically a parent) completes the inventory items. Results from this measure are then used to identify domains that may relate to specific behavioral problems. The individual's PIC profile may also be compared with the profiles of children exhibiting similar traits in order to predict behaviors and patterns of behavior.

The measures of informant response style included (e.g., Inconsistency, Dissimulation, and Defensiveness Scales) are designed to assist in

determining the validity of results. The nine adjustment scales of the PIC-2 are Cognitive Impairments, Impulsivity and Distractibility, Delinquency, Family Dysfunction, Reality Distortion, Somatic Concern, Psychological Discomfort, Social Withdrawal, and Social Skill Deficits. Each of the adjustment scales has two or three subscales made up of relatively homogenous subsets of items from their respective scales (Urbina, 2005).

The PIC-2 offers actuarially based information regarding the behavioral functioning of the child when included as part of a comprehensive battery. The information gathered from a parent or guardian is unique in comparison with that provided by a teacher or self-report. This information may then be used to evaluate situation-specific behaviors and parental perception of difficulties. The PIC scales have also been used as an instrument for characterizing the behavioral sequelae of a head injury, for following the course of a disorder, and for examining personality correlates in light of development of a rehabilitation program (Knoff, 2003; Hynd & Willis, 1988).

Practical implications: The PIC-2 assesses the parent's or guardian's view of individual functioning across various settings and demands. Results provide empirical analysis of a child's behavior, affect, ability, and family functions. The great variety of scales included in the PIC-2 allows for a more detailed description of behavior than is typically provided by parent report measures. The clinical specificity of this measure offers the neuropsychological evaluation an actuarial component important in the diagnosis and treatment of individual difficulties.

The Behavior Assessment System for Children, Second Edition (BASC-2; 2004). Structure: The BASC-2 provides an actuarially based approach to the evaluation of behavior. This measure includes a structured developmental history, a self-report inventory, a parent rating scale, a teacher rating scale, and a student observation form. The BASC-2 scales are designed for use with children and adolescents 2–21 years old.

The BASC-2 is a multimethod, multidimensional approach to evaluating the behavior and self-perceptions of children and adolescents. The multimethod feature of the BASC-2 is found in the five separate components available for use: a structured developmental history, a self-report scale completed by the child, rating scales for both parents and teachers, and a form for recording and classifying observed classroom behavior. The multidimensional feature of the BASC-2 is found in the numerous aspects of behavior and personality measured, including adaptive and clinical dimensions.

Perhaps the most clinically useful aspect of the BASC-2, in comparison with other instruments such as the PIC-2, is the provision of information from three separate sources: child, parent, and teacher. The Self-Report of Personality, the Parent Rating Scales (PRS), and the Teacher Rating Scales provide information from multiple points of reference and across multiple settings. The Self-Report of Personality assesses the respondent's level of clinical maladjustment, school maladjustment, depression, sense of inadequacy, and personal adjustments. The PRS evaluates the individual's actions toward others, actions toward self, attention problems, withdrawal, and adaptive skills. The Teacher Rating Scales include the areas evaluated by the PRS as well as specific school-related concerns such as study skills and learning problems. Overall, the inclusion of information from multiple points of reference provides for a more complete and balanced picture of the current functioning and concerns of the child in question.

Practical implications: A clear strength of the BASC-2 is the inclusion of information from the perspective of the individual, the parent, and the teacher. The analysis of behavioral information from multiple sources and settings should be of great utility to practitioners of neuropsychology. Overall, the BASC-2 integrates a variety of perspectives that are often lacking in traditional neuropsychological evaluations.

Vineland Adaptive Behavior Scales, Second Edition (VABS II, 2005). Structure: Each of the four versions of the VABS II (Survey Interview Edition, Parent/Caregiver Rating Form, Expanded Interview Form, and Teacher Rating Form) measures adaptive behavior across four separate domains: Communication, Daily Living Skills, Socialization, and Motor Skills. A Maladaptive Behavior Index is also provided as an optional area of evaluation. An Adaptive Behavior Composite, a combination of the four adaptive behavior domains, provides an overall analysis of personal and social sufficiency. The

VABS measures adaptive skill across the age range from birth to adulthood.

The VABS II is designed to assess the living skills of individuals through the report of a parent, caregiver, or teacher. The current form of the VABS is the latest revision of the Vineland Social Maturity Scale (Doll, 1935). Each of the four adaptive behavior domains is composed of subdomains that provide specific information regarding the individual's ability to function within his or her environment. The Communication domain contains Receptive, Expressive, and Written subdomains, examining what the individual understands, says, reads, and writes. The Daily Living Skills domain evaluates the individual's ability to independently eat, dress, perform household tasks, and use time, money, and job skills through the Personal, Domestic, and Community subdomains. The Socialization domain includes the three subdomains of Interpersonal Relationships, Play and Leisure Time, and Coping Skills, examining how the individual acts with others, plays, uses leisure time, and demonstrates responsibility and sensitivity to others. Finally, the Motor Skills domain evaluates how the individual uses large and small muscle movements to accomplish daily tasks through the Gross Motor and Fine Motor subdomains.

The VABS scales provide standardized evaluation of behavioral status in those situations in which the individual is unable to consistently respond to evaluation questions or tasks. This measure is most typically used in school psychology evaluations considering the real-life performance of children suspected of or diagnosed as having limited intellectual capacity. In neuropsychology, the VABS may be used following traumatic brain injuries, degenerative disorders, or other cerebral impairments to document the loss or return of adaptive behaviors (Lezak, Howieson, Loring, & Hannay, 2004). In fact, the VABS II is often a key component in the development of rehabilitation plans for individuals experiencing injury or impairment.

Practical implications: The VABS II considers life skills to a greater degree than any measure previously discussed. The information provided by the VABS is important in discerning what tasks the individual is capable of performing independently. In addition to the evaluation of living skills related to limited intellectual capacity, the VABS II is also of use in determining the skills of children following neuropsychological impairment.

The Thematic Apperception Test (TAT, 1943). Structure: The TAT is a projective test consisting of 31 cards, with 30 cards depicting various scenes and people, and 1 card being blank. Specific male/female, children, adolescent, and adult issues are presented. Typically, 10 cards that relate to the issues thought be faced by the individual are selected for use.

The TAT was the first widely used thematic technique. Developed by Murray (1938, 1943), the TAT was designed to facilitate the psychoanalytic exploration of an individual's dominant drives, emotions, traits, and conflicts. By identifying significant needs, presses, and themes, the inhibited and unconscious personality characteristics of the individual were thought to be brought to the surface. Through the use of projective interpretation, the TAT offers insight into the etiology of behavior and allows for a better understanding of the issues presented by the individual in question (Bellak & Abrams, 1997). Few personality tests provide the depth of insight relative to the child's view of the world. This wide-band, open-ended technique offers data regarding how the individual responds to authority, popularity, male/females roles, dominant personality traits, and familial relationships.

The validity and reliability of the TAT have been difficult to establish because of the open-ended, free-response nature of the measure, and limited avenues through which to validate inferences (Knoff, 2003). In an effort to address this difficulty, a number of quantitative scoring methods have been established. Although these methods have aided practitioners in developing a more normative approach to interpretation, the clinical use of the TAT often remains rather informal and idiosyncratic (Lanyon & Goodstein, 1997). A distinct advantage of including the TAT as part of a comprehensive assessment battery is the opportunity it provides for examining the individual's ability to organize and maintain ideas (Lezak, Howieson, Loring, & Hannay, 2004). Practitioners operating from a neuropsychological paradigm are able to evaluate the individual's verbal behavior. Those individuals with cerebral impairment are more likely to use fewer words and ideas in telling the stories, tend to take longer to respond

to the stimuli, are more likely to describe the picture than make up a story, and may present inflexible, concrete responses to the various cards (Lezak, Howieson, Loring, & Hannay, 2004). An alternate administration technique is to have the individual write his or her response to each pictorial card. The written product may then be used to compare verbal and written response styles.

Practical implications: The TAT enables individuals to relate their thoughts and feelings through a free-response, open-ended technique. In comparison to other personality measures, this measure does not limit the individual to a set choice of responses. The projective nature of the measures is useful in alleviating response sets resulting from social constraints. The TAT allows for a thorough analysis of verbal behavior, as well as a glimpse into the individual's view of their world.

Conclusions

Because neuropsychological assessment is geared to treat all manifestations of behavior as related to the functional integrity of the central nervous system, it follows that the tests commonly ascribed to psychological and educational functioning can provide a wealth of information to that enterprise. The strength of the flexible battery view of assessment as proposed here lies in its adaptability to clinical need. By integrating knowledge of brain function with the overt aspects of behavior detailed by formal and informal techniques, the clinician can gain a balanced picture of individuals in their interactions with various environmental systems. The domains of a behavior discussed here have offered insight into the breadth of evaluation available to probe the diverse nature of cognition, affect, and action. Once the practitioner identifies the assessment needs of the individual child, and a decision is made as to the components most relevant for exploring the dimensions of behavior, the process can begin. It is only through the quality of the data obtained that the effectiveness of potential intervention strategies can be gauged. To this end, this chapter intended to give the practitioner a range of assessment options from which to make wise choices.

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16

Assessment of Behavior and Personality in the Neuropsychological Diagnosis of Children

PHYLLIS ANNE TEETER, LAURA ECKERT, AMY NELSON, PETER PLATTEN, MARGARET SEMRUD-CLIKEMAN, AND RANDY W. KAMPHAUS

For many clinicians, behavior and personality have been traditionally evaluated by assessing behavior patterns and interpolating these behaviors as reflecting underlying personality variables (Martin, 1988). Behavior has been defined as the *what* a child does with personality defined as the *why* the child does what he or she does. Behaviors can be quantified and graphed fairly easily, whereas personality variables are more difficult to measure and are generally described qualitatively. Such differentiation is artificial and the boundaries between these concepts become blurred when observing a child. For the purposes of this chapter, behavior will be conceptualized as the outward expression of inner experience and personality will be viewed as the overarching principle encompassing behavior. Personality, therefore, is the constant

principle across situations whereas behaviors may vary depending on situational characteristics (Martin, 1988). A discussion of distinctions between the concepts of behavior and personality is beyond the scope of this chapter. The interested reader is referred to further discussions by Martin (1988) and Lewis and Miller (1990).

Historically, behavioral and personality disorders have been the purview of psychology and psychiatry; however, recent conceptualizations of childhood disorders have emerged from neuropsychiatry.

> Although there is considerable disagreement about just what neuropsychiatry comprises, fundamental to any definition is the indelible inseparability of brain and thought, of mind and body, and of mental and physical. Neuropsychiatry spans these interrelationships to enlarge understanding of cognitive, emotional, and behavioral function and dysfunction.
>
> (Yudovsky & Hales, 1989, p. 363)

On the other hand, neuropsychology focuses on broad brain–behavior relationships, which generally include investigation into how brain function/dysfunction affects the cognitive–intellectual, memory, psychomotor, perceptual, and attentional functions of children. Although neuropsychologists frequently study

PHYLLIS ANNE TEETER ELLISON, LAURA ECKERT, PETER PLATTEN AND AMY NELSON • Department of Educational Psychology, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53201. **MARGARET SEMRUD-CLIKEMAN** • Department of Psychology, Michigan State University, East Lansing, MI 48824. **RANDY W. KAMPHAUS** • Department of Educational Psychology, University of Georgia, Athens, Georgia 30602.

neurodevelopmental (e.g., learning disorders), traumatic brain injury, and central nervous system disease processes, the overlap between neuropsychiatric and neuropsychological disorders is quite extensive. Recently, neuropsychologists have advocated for a transactional framework for investigating childhood disorders, where personality and resulting behaviors are viewed as an integration of learned and biologically predisposed variables (Teeter Ellison & Semrud-Clikeman, 1996, 2007). In such a transactional, neuropsychological approach, the interplay of biogenetic and environmental factors with the maturation and development of the central nervous system is considered (Teeter Ellison & Semrud-Clikeman, 2007). Similarly, Achenbach (1991) suggests that childhood psychopathology should be conceptualized as a combination of "microparadigms" including neuropsychological, cognitive– behavioral, psychodynamic theory, and family systems which are then formed into a "macroparadigm." The assessment of the child's support system, prior developmental history and behavior, social and emotional development, as well as neuropsychological deficits provides a comprehensive and useful picture for the understanding of the whole child and for the subsequent development of appropriate interventions.

The purpose of this chapter is to discuss common behavioral and psychiatric disorders of childhood from a neuropsychological–neuropsychiatric viewpoint. The first part of this chapter will review various disorders from a neuropsychological–neuropsychiatric viewpoint. The neurobiological contributions, the associated behaviors frequently noted with common disorders of children referred for neuropsychological assessment, and the impact of neurobehavioral deficits on development are discussed. The second section of this chapter discusses psychosocial and behavioral measures for evaluation of neuropsychiatric and psychological disorders of childhood. Finally, guidelines for incorporating behavior and personality assessment in neuropsychological evaluations are presented.

Neuropsychology of Emotions

Although the brain has a defined neuroanatomy at birth, the myelination of axons, the formation of synaptic connections, and the arrangement of these into synapses begin in infancy and continue into adolescence with the environment effecting changes in neuroanatomy (Teeter Ellison & Semrud-Clikeman, 2007). Such neurodevelopment generally corresponds to the emergence of complex human behaviors. Childhood disorders (i.e., obsessive–compulsive disorder, attention deficit hyperactivity disorder, and Tourette's syndrome) may involve neurodevelopmental abnormalities for regulation when the brain is overproducing and then pruning the axonal– synaptic processes (Cook & Leventhal, 1992). Moreover, disorders in childhood rarely affect an isolated function (e.g., language, motor, or cognitive processes) because interference in the developmental process of one brain region will affect the development of other areas as well (Reitan & Wolfson, 1985; Tranel, 1992).

An example of the interplay between systems and resulting behavior following faulty development or traumatic injury is discussed by Bear (1983). Bear details the relationship between temporofrontal (ventral system) and parietofrontal functions (dorsal system), and psychological behavior in adults. The ventral temporofrontal systems (inferotemporal visual cortex to limbic structures to orbital frontal structures) are thought to assist in the storage of associations made between visual and emotional processes, the evaluation of basic drives, and the development of response strategies to environmental stimulation. Bear (1983) hypothesizes that damage to temporal or orbital prefrontal regions interferes with the ability to access previously learned emotional responses including the ability to utilize social restraint. When this system is dysfunctional, an individual may engage in aggressive (or sexual) responses to the environment with little or no regard for learned consequences. Damage in any part of this functional network results in discrete emotional and behavioral deficits. The inferior parietal lobe to limbic system to dorsolateral frontal cortex is involved in the activation of emotions, and lesions to this region result in apathy of neglect.

Through an integration of the findings from numerous studies (Dimond, Farrington, & Johnson, 1976; Geschwind, 1965; Heilman, Schwartz, & Watson, 1978), Bear hypothesizes that the cognitive processing functions of the left hemisphere are related to reflective and rigid or stereotypic responding. Conversely, the right

hemisphere is thought to be particularly suited for incidental learning as well as the addition of affective qualities to cognitions in order to provoke emotional responses, recognize threats, and initiate goal-directed responses. The temporofrontal portions of the right hemisphere have been implicated in memory functioning, discrimination of vocal intonations, identification of facial expressions, and the ability to decode and assign emotional meaning to perceptions (Semrud-Clikeman & Hynd, 1990).

Although several studies have addressed the neuropsychological basis of emotions in adults, the research base for understanding the neuropsychology of emotions in children is sparse. Measuring childhood emotions and their development is confounded by maturational variations, environmental influences, and the onset of injury on the developing brain.

Fletcher and Taylor (1984) conceptualize developmental neuropsychology as the study of how moderator variables (i.e., including environmental and social factors) can influence the basic competencies/deficits present in a child. In this model, the central nervous system is viewed as just one of several influences on the developing child. Therefore, developmental neuropsychology focuses on the sequence in which skills are developed and how these skills change with each developmental stage. Fletcher and Taylor (1984) further suggest a need to focus on how a deficit interferes with or disrupts normal development instead of focusing on localization of deficient brain areas. Thus, if we are interested in assessing how brain function affects behavior and personality, it is important to (1) determine the effects of damage or dysfunction on behavioral and psychosocial functioning and (2) determine how moderator variables (e.g., intelligence, therapeutic interventions, social support) affect the overall adjustment of the child.

Childhood Psychopathology from a Neuropsychological–Neuropsychiatric View

Studies investigating children with psychopathology have looked for cognitive and/or neuropsychological patterns across different types of psychiatric disturbance. Results from recent research suggest that many psychiatric disorders may well have an underlying organic etiology (Dean, 1986). There is mounting evidence that diagnoses previously considered to be functional in origin may, in fact, be organically based. Furthermore, it is believed that organic and environmental components interact with development and that each variable, in turn, affects the other variable.

Difficulty in differentiating between functional and organic etiology for diagnosis is found in child and adolescent samples (Dean, 1985, 1986). A study by Hertzig (1982) found that roughly a third of an adolescent sample with a history of psychiatric disorders also possessed neurological impairments. Another study found 60% of child and adolescent psychiatric patients to have neuropsychological deficits (Tramontana, Sherrets, & Golden, 1980). The duration of the psychiatric disorder predicted the severity of neuropsychological dysfunction. For example, when the duration of the psychiatric disorder exceeded 2 years, there was a higher probability of neuropsychological disorder. In addition, complex cognitive and perceptual abilities were the most severely affected.

In summary, the frequent distinction that is made between psychiatric and organic syndromes may be erroneous. Historically, such a distinction was based on the assumption that psychiatric disorders were the result of psychosocial influences. In contrast, organic disorders have been ascribed to biological influences. Mounting evidence from new technology allowing for the visualization of the brain suggests that biochemical and structural neurological abnormalities are present in many psychiatric disorders (Andreasen, Olsen, Dennert, & Smith, 1982; Semrud-Clikeman, Hynd, Novey, & Eliopulos, 1991; Zametkin et al., 1990). Neurochemical differences have also been found in patients with affective disorders (Jarvik, 1977), as well as some forms of schizophrenia (Andreasen et al., 1982). As a result of this new body of evidence, Dean (1986) suggests that the "organic–functional distinction for mental disorders" is better understood as a continuous and not as an all-or-none phenomenon (p. 95). Thus, a combined view of child psychological disorders utilizing a neuropsychological–neuropsychiatric interface would be most informative and lead to a more comprehensive understanding for these diagnoses. The following section reviews influences of various neuroanatomical structures on behavioral functions.

The Role and Development of Frontal Lobes in Children

One of the regions implicated in several childhood disorders is the frontal lobe. In order to more fully understand its role in childhood dysfunction, it is important to first discuss normal frontal lobe development. Studies have recently focused on the neurodevelopment of cognitive abilities in an effort to determine when specific brain areas become functionally operational in children. These studies have focused on the frontal lobes in children because attentional and behavioral control, planning, flexibility, and self-monitoring (executive functions) have been attributed to this area. The frontal lobes are also thought to play a prominent role in the control of human emotions in adults (Bear, 1983; Grafman, Vance, Weingartner, Salazar, & Amin, 1986).

The frontal lobes are a large and heterogeneous anatomical structure that make up one-third of the cerebral cortex (Stuss, 1992). The frontal lobes are richly connected to almost all of the other parts of the central nervous system (Stuss & Benson, 1984). The myelination of the frontal lobes takes place throughout development (Dennis, 1991). Some suggest that the frontal lobes of children begin to develop between the ages of 4 and 7 years (Luria, 1973); others suggest that development begins in adolescence and continues up to about age 24 (Golden, 1981). Current research suggests that children and even infants exhibit behaviors thought to be mediated by the frontal lobes much earlier than previous estimates (Bell & Fox, 1992; Dawson, 1994). In an EEG study, Thatcher (1992) found that there are continuous and discontinuous growth processes with growth spurts in the early postnatal period and again after puberty. Such growth spurts are characterized by increases in the amount of neural connections between the frontal lobes and other portions of the brain. Thatcher suggests that the growth spurt in the right frontal pole, which occurs at about age 4½ years, corresponds with the ability to take another person's perspective. Such a correlation between brain maturation and psychological processes suggests that there is a direct relationship between anatomy and function.

Brain mapping research with structural magnetic imaging resonance imaging (MRI) shows remarkable changes in brain maturation in children with healthy brain. Studies show that the brain undergoes successive synaptic overproduction, where brain regions reach maximum synaptic density followed by selective pruning or cell death. While fetal life marks the most rapid proliferation, migration and maturation, this process continues into adulthood depending on the region. The infant brain is about one-fourth to one-third the size of the adult brain and undergoes rapid changes based on genetic programming which is influenced by both experience and stimulation. Thus, environmental factors impact the genetic program thereby affecting myelination, dendritic growth for rapid and elegant connectivity between neurons—dendritic pruning and synaptic elimination allowing for more efficient brain functions (Toga, Thompson, & Sowell, 2006). For example, synaptic overproduction of the visual cortex reaches peak during the fourth postnatal month, followed by pruning which reaches adult stages by preschool age. Medial prefrontal regions involved with executive controls reach peak maturation between 3 and 4 years of age but continues well into adolescence where substantial decreases are prominent. "Indeed, much of the potential and many of the vulnerabilities of the brain might, in part, depend on the first two decades" (Toga et al., 2006, p. 148).

Scientists investigating brain maturation have found that gray-matter volume reaches peak levels in early childhood (after 6–7 years of age) and continues to decline into early adolescence, while white-matter volume shows a linear increase into early adulthood (age 20; Giedd et al., 1999). White-matter volume appears to increase until about 12.4% between the ages of 4 and 22, with some variations found in male and female brain maturation. Maximum gray-matter volume peaks at age 12.1 for males and earlier for girls (11 years). Giedd et al. (1999) suggest that there may be a second wave of overproduction of synapses in frontal regions accounting for the gray-matter increases. Furthermore, "it may hearld a critical stage when the environment or activities of the teenager may guide selective synaptic elimination during adolescence"(Giedd et al., 1999, p. 863).

Frontal lobe development is thought to involve a hierarchical, dynamic, and multistage process (Case, 1992; Thatcher, 1992). A study by Becker, Isaac, and Hynd (1987) supports this hypothesis. Becker et al. (1987) found that

10- and 12-year-olds had mastered the capability of inhibiting motor responses, of remembering the temporal ordering of visual designs, of using strategies for memory tasks, and of attending to relevant details and ignoring distracting stimuli. All of these skills are thought to be mediated by the frontal lobes. In contrast, 6-year-olds had more difficulty inhibiting motor responses and had trouble remembering the order of designs. Therefore, a developmental shift for 8-year-olds occurs that allows for inhibition of motor response. Moreover, while children at all age levels were able to verbalize directions, they were not always able to inhibit perseverative responding until about age 8. In contrast, older children (10- and 12-year-olds) displayed verbal and nonverbal strategies that aided their performance.

Similarly, Passler, Isaac, and Hynd (1985) found a developmental progression through stages requiring mastery of some frontal-mediated tasks at 6 and 8 years of age, whereas other tasks were not mastered by the age of 12. These findings suggest that the greatest period of development for frontal lobe functioning occurs between the ages of 6 and 8, with continued growth beyond age 12 for more complex skills. Although basic research is useful for building a neurodevelopmental model for children, research with psychiatric populations can provide further information concerning the relationship between personality, behavior, and neuropsychological functioning.

Evidence from Childhood Psychopathology

Frontal lobe dysfunction has been found in children with various behavioral and psychological difficulties; however, frontal lobe dysfunction does not appear to be specific to one particular disorder. For example, a study that compared children with diagnoses of externalizing (i.e., ADD, conduct disorder), internalizing (i.e., anxiety, depression), and comorbid psychopathology found frontal lobe dysfunction in all of these disorders (Kusche, Cook, & Greenberg, 1993). Children with these diverse disorders performed more poorly on neuropsychological measures thought to be implicated in frontal lobe functioning.

From initial reports, it appears that the frontal lobe is charged with the modulation of behavior and is heavily implicated in "functional" and psychiatric disorders of childhood. Evidence from children with traumatic brain injury (TBI) also sheds light on our understanding of the neuropsychological basis of behavior and personality.

Evidence from TBI

Although brain injury in adults frequently produces highly focal damage, childhood behavioral disorders are hypothesized to be a result of neurodevelopmental disorders in an otherwise healthy brain rather than caused by lesions or degenerative disorders (Cook & Leventhal, 1992). The question of whether early damage to the developing brain has a better prognosis than later damage is currently under debate.

Marlowe (1992) discussed a case study of a boy who experienced a focal prefrontal injury at age 3. Neuropsychological evaluations at 5 and 6 years indicated that the injury at 3 years disrupted the acquisition of executive and emotional control. Behavioral changes after the accident included emotional lability, difficulty falling asleep, and increase in impulsivity, agitation, and aggression. Although no decrease in intelligence scores was found, the boy experienced difficulty in school on tasks thought to be prefrontally based (i.e., self-regulation, planning and carrying out a strategy). Another study by Mateer and Williams (1991) investigated four children with nonfocal frontal lobe injuries in childhood. Maladaptive social behaviors were present in all four. Three main areas were found to be impacted: self-regulation, attention, and the ability to carry out plans. These difficulties were present despite normal intellectual, linguistic, and perceptual functioning. Welsh, Pennington, and Groisser (1991) also found that intelligence tests are not related to frontal lobe damage.

Thus, these investigations lead one to believe that frontal lobe dysfunction may be responsible for social adjustment difficulties in children. Particular problems are found in self-regulation and planning. These behaviors are frequently implicated in childhood disorders. Frontal lobe damage seems to result in difficulty in executive planning and strategic behaviors, as well as interference with or loss of previously learned skills. It is not clear whether frontal lobe damage inhibits, alters, or halts the process of continuing development. What is known is that age of injury has an

important role in the severity of the injury on later development.

Age of injury. Age plays a role not only in brain development but also in outcome following trauma. Injuries prior to age 8 have been found to produce more severe cognitive deficiencies than injuries after age 10 (Brink, Garrett, Hale, Woo-Sam, & Nickel, 1970; Woo-Sam, Zimmerman, Brink, Uyehara, & Miller, 1970). Woods (1980) found that children injured in the first year of life tend to have severe verbal and nonverbal deficits, and children injured after age 1 show more lateralized effects from the injury. Left-hemisphere damage between the ages of 5 and 12 often produces transitory aphasia, and adultlike aphasia is seen with left-hemisphere damage after age 16 (Boll & Barth, 1981).

Reading difficulties following TBI. Reading deficits are sequelae of some forms of TBI (Klonoff, Low, & Clark, 1977; Schaffner, Bijur, Chadwick, & Rutter, 1980). Neurodevelopmental processes, particularly in the left planum temporale, have been implicated in reading difficulty in dyslexic children (Galaburda, 1991). Over time, reading deficits can depress overall verbal intelligence, vocabulary attainment, and verbal comprehension abilities of children (Stanovich, 1993). Thus, brain trauma at an early age, as well as neurodevelopmental disorders resulting in reading deficits, may reduce the overall ability of children to acquire basic knowledge across the life span.

Swanson (1982, 1993) asserts that previously acquired information influences a child's ability to encode, process, and utilize new information. Reitan and Davison (1974) have argued that early damage to the immature, developing brain can have serious long-term effects. It may be that the longer the brain is "normal," the greater is its capacity to increase the richness and complexity of the knowledge base which is ultimately related to new learning.

Since brain damage appears to have its greatest effect on new learning (Hebb, 1942), young children, who by definition have less accumulated knowledge and experience, would experience difficulty with new learning. Severe deficiencies may not show up until later years when cognitive flexibility and independent thinking are required for learning and social–psychological functioning. These findings coupled with knowledge gained about the effect of frontal lobe damage on social functioning indicate that children with head injuries may well evidence behavioral difficulties that significantly affect their adjustment. Even mild head injury has been implicated in behavioral difficulties that may appear to be functionally based (Boll, 1983). Functional differences between the two hemispheres are important factors affecting emotional, behavioral, and psychosocial adjustment in children.

Psychosocial and behavioral functioning. Children with TBI frequently experience behavioral and psychosocial difficulties following injury, and these problems cause the most difficulty in the home and school settings (Di Scala, Osberg, Gans, Chin, & Grant, 1991; Levin, 1987). During the initial stage of recovery behaviors such as agitation, difficulty following directions, and regression are frequently seen and generally resolve after a short period of time (Jaffe, Brink, Hays, & Chorazy, 1990). For some children, the self-awareness of these difficulties is accompanied by feelings of depression and anxiety (Semrud-Clikeman, 1992). Following this initial recovery time, the emotional difficulties that do not resolve are generally thought to become more permanent with premorbid functioning very predictive of postmorbid recovering. A child who has experienced significant behavioral and emotional difficulties prior to the TBI and whose TBI is severe has the poorest prognosis (Semrud-Clikeman, 1992). Those children who have fewer social supports and who come from chaotic or disruptive family backgrounds show the poorest recovery (Jaffe et al., 1990).

Of particular concern to parents are difficulties with attention, hyperactivity, and irritability as well as a low frustration tolerance and poor motivation (McAllister, 1992; Michaud, Duhaime, & Batshaw, 1993). In addition problems with anger modulation, aggression, mood disorders, and social isolation are particularly worrisome for children with TBI and require close monitoring during the recovery period (Kehle, Clark, & Jenson, 1996). Early expression of irritability has been found to be related to later development of aggressive behavior, and these difficulties do not resolve as quickly as more "hard-wired" skills (McKinlay, Brooks, Bond, Martinage, & Marshall, 1981; Silver & Yudofsky, 1987). When psychosocial and emotional difficulties are present with an underlying cognitive component (inability to

learn from behaviors, memory deficits, and/or attentional difficulties), the emotional problems are more difficult to remediate and take significantly more time to resolve (Di Scala et al., 1991).

The suggestion that children with TBI will show social difficulties is consistent with the above findings for the persistence of depressive and anxiety symptoms as well as the likelihood that younger children will experience difficulty in developing social competence. Some researchers have suggested that children with TBI may show a deterioration in social skills over time due to an awareness of previously obtained but now lost skills (Begali, 1992; Fordyce, Roueche, & Prigatano, 1983). This hypothesis has not been carefully studied and should be viewed as clinical observation rather than as an expectation.

The Role of the Right and Left Hemispheres

Differences between the two hemispheres appear early in life, and these functional asymmetries may underlie variations in behavior (Teeter Ellison & Semrud-Clikeman, 2007). Goldberg and Costa (1981) describe the basic anatomical differences between the hemispheres related to the ratio of gray matter to white matter: the left hemisphere has greater gray matter than white and the right hemisphere has more white than gray matter. These structural differences may relate to the capacity of each hemisphere to deal with complex and novel information in social–psychological situations.

Anatomical asymmetries are present at birth, and functional differences in the processing of emotional stimuli appear early in life. For example, the right hemisphere appears central to the discrimination of facial expressivity and emotional tone; and the left hemisphere is more reactive to emotional stimuli, especially in younger children (9-year-olds). It has been hypothesized that as the right hemisphere matures, it has a modulating effect on the more reactive left hemisphere (Heller, 1990).

Adult research suggests that damage to the left hemisphere results in depression and catastrophic reactions, whereas damage to the right produces abnormal emotional reactions (e.g., euphoria or indifference) (Kolb & Whishaw,

1990). The extent to which these patterns hold true for children needs further investigation.

In a report of clinical case studies, Teeter (1989) found that children with signs of significant depression demonstrate various profiles depending on the hemisphere involved. For example, a child (CA, chronological age = 10 years, 5 months) with a right frontal pattern showed left-handed tactual deficits, left-handed motor weaknesses, poor nonverbal reasoning abilities, visual–perceptual deficits, and abnormal EEG findings (bilateral anterior regions). Behavioral and psychological problems were noted as dysthymia, impulsivity, disinhibition, social imperception, and suicidal ideation. Conversely, a child (CA = 9 years-8 months) with a left frontal lobe pattern displayed right-handed motor weaknesses, tactile imperception, auditory sequential memory problems, verbal reasoning weaknesses, lower verbal IQ, and abnormal EEG ratings of a diffuse nature. In this instance, the child demonstrated anxiety, denial of emotions, isolation from peers, dysphoria, and inappropriate affect. Further examination revealed abnormal dexamethasone suppression results. The extent to which right frontal regions are involved with attention to social cues, execution of social interaction skills, and control over the left frontal regions for the appropriate expression of emotions in children with depression needs further study.

In summary, the apparent ratio of activation between the right and left hemispheres appears important—such that the right hemisphere might inhibit or modulate the left. Maturation of later-developing interhemispheric regions (i.e., corpus callosum) may also play a role in the control and modulation of emotional processes. Kolb and Whishaw (1990) suggest that differences between the front/back (anterior/posterior) quadrants are as essential as right–left differences in the control of human emotions. Furthermore, it must be noted that controversy over whether the two hemispheres operate in autonomous, interactive, or domain-specific ways when it comes to complex behaviors still remains (Teeter Ellison & Semrud-Clikeman, 2007).

The following section discusses different types of psychopathology from a functional organizational approach utilizing a combined neuropsychological–neuropsychiatric and personality paradigm.

Externalizing Disorders of Childhood

Externalizing disorders are defined as those behaviors involving aggression, inattention, overactivity, and antisocial behavior. These problems are often classified as disruptive behavior disorders in infancy, childhood, and adolescence (APA, 2000). Behavior problems affect academic achievement in an age-dependent way. A strong correlation exists between delinquent behavior and underachievement for children and adolescents (Fergusson & Horwood, 1995; Hinshaw, 1992). Furthermore, early learning problems have also been found to be highly related to later psychopathology (Pianta & Caldwell, 1990). Two externalizing disorders—ADHD and conduct disorders—are briefly reviewed from a neuropsychological–neuropsychiatric point of view.

ADHD

According to the National Survey of Children's Health, ADHD is one of the most commonly diagnosed disorders in children (Blanchard, Gurka, & Blackman, 2006). General population estimates of children aged 6–17 years suggest that it has a prevalence rate of 8.8% (Blanchard et al., 2006), although estimates have ranged from 3 to 11% (Daley, 2005). This diagnosis falls second in prevalence only to learning disabilities, which may be found in as many as 11.5% of the school-age population (Blanchard et al., 2006). In addition, epidemiological studies of preschool children suggest that as many as 1.0–5.7% have ADHD (Blanchard et al., 2006; Egger & Angold, 2006).

The clinical presentation of ADHD in children appears to be similar to that in adolescents; research examining the diagnostic continuity of ADHD from childhood to adolescence suggests that the prevalence of symptoms does not vary by age, nor do children with ADHD compared to adolescents with ADHD differ in psychiatric comorbidity, cognitive functioning, school functioning, or overall functioning (Faraone, Biederman, & Monuteaux, 2002). The *Diagnostic and Statistical Manual, Fourth Edition-Text Revision* (DSM-VI-TR) currently has three classification subtypes of ADHD: (1) ADHD, Combined Type (ADHD-C), (2) ADHD, Primarily Inattentive Type (ADHD-PI), and 3)

ADHD, Primarily Hyperactive-Impulsive Type (ADHD-HI; APA, 2000).

Attempts to refine and clarify the diagnostic subtypes of ADHD have utilized methods such as latent class analysis (LCA), a statistical technique that partitions individuals into phenotypically homogenous groups based on profiles of symptoms (Volk, Henderson, Neuman, & Todd, 2006). Recent studies using this technique have suggested that there may be as many as seven population-based profiles of ADHD symptoms (Few Symptoms, Mild Inattentive, Severe Inattentive, Talkative-Impulsive, Mild-Combined, Severe-Combined, and Hyperactive; Volk, Henderson, Neuman, & Todd, 2006; Volk, Neuman, & Todd, 2005). The profiles that were found to be the most prevalent included the Few Symptoms (53.4%), Mild Inattentive (12.3%), and Severe Inattentive (12.1%) groups (Volk et al., 2005).

Even though several profiles of ADHD were identified, three subtypes of ADHD may be particularly clinically relevant based on endorsed levels of impairment and competency. The three groups identified were the Severe Inattentive, Mild-Combined, and Severe-Combined subtypes (Volk et al., 2006). Children classified into one of these three groups were found to have significantly greater social impairment than the other four latent classes identified (Few Symptoms, Talkative-Impulsive, Mild Inattention, and Hyperactive). Similarly, school functioning was significantly lower for the Severe-Combined, Mild-Combined, and Severe Inattentive groups compared to the other latent classes. Finally, while the Severe-Combined class had the most impairment in total competency scores, mild competency impairment was found for the Severe Inattentive, Mild Inattentive, and Mild-Combined classes (Volk et al., 2006). Identification of the impairment associated with the Mild-Combined subtype is important considering this group is often left undiagnosed. Furthermore, twin heritability studies have recently suggested that Mild- and Severe-Combined ADHD have different genetic influences (Volk et al., 2006).

Besides subtype classification, Frick and Lahey (1991) suggest that it is important to differentiate primary symptoms from associated problems in children with ADHD. These authors state that the main variables involved in ADHD are those of inattention/disorganization

and motor hyperactivity/impulsivity. Associated behaviors are poor academic achievement, problematic peer relationships, and low self-esteem. Other common areas of poor functioning include language impairments, impaired motor coordination and perception, lower cognitive functioning, greater unintentional injuries, and increased presence of sleep disturbances (Bruce, 2006; Cortese, Konofal, Yateman, Mouren, & Lecendreaux, 2006; Daley, 2005; Faraone, Biederman, & Monuteaux, 2002; Miller, Miller, Bllom, Hynd, & Craggs, 2006). Comparisons of children and adolescents with ADHD to controls indicate significantly lower full scale IQ and math achievement, and significantly higher rates of a learning disability, with reading achievement differences approaching significance (Faraone et al., 2002). Furthermore, while approximately 5–13% of children and adolescents without ADHD repeat a grade, as many as 18–31% of children and adolescents with ADHD repeat a grade (Faraone et al., 2002). Common sleep disturbances of children with ADHD include more movements during sleep, greater daytime drowsiness, and higher indexes of apnea-hypopnea (Cortese et al., 2006).

The issue of comorbidity is pertinent, given that as many as 87% of children with ADHD have at least one other comorbid disorder, and as many as 67% had at least two additional diagnoses (Kadesjö & Gillberg, 2001). Prevalence rates of other *DSM-IV* disorders suggest that some of the most common comorbid diagnoses associated with ADHD include oppositional defiant disorder (ODD; 60%), developmental coordination disorder (47%), reading/writing disorder (40%), and tic disorders (33%), although internalizing problems such as anxiety and depression were not examined (Kadesjö & Gillberg, 2001). Biederman et al. (1992) and Biederman, Newcorn, and Sprich (1991) have found that children with ADHD have a tendency to develop affective disorders in about 30% of cases. Moreover, children with ADHD tend to have parents and/or siblings who evidence ADHD or affectively based psychopathology. In addition, ADHD continues into adulthood for approximately 50% of subjects perhaps as a result of their difficulty in developing compensatory techniques. For the adolescent or adult with ADHD, continuing difficulty with the law, substance abuse problems, difficulty holding a job, and problems with interpersonal relationships also occur (Biederman & Steingard, 1989). When prevalence rates of conduct disorder and depression are examined concurrently in a clinical sample, as many as 25% of children and 30% of adolescents have comorbid major depression, whereas approximately 15% of children and 23% of adolescents have been found to have a comorbid conduct disorder (CD; Faraone, Biederman, & Monuteaux, 2002).

If comorbidity is examined by ADHD subtype, again ODD is the most prevalent, with 48.3% of children with ADHD-C, 33.3% of children with ADHD-HI, and 23.3% of children with ADHD-PI meeting criteria for comorbid ODD (Volk et al., 2005). Comorbid depression is slightly less prevalent, with approximately 10.3% of children with ADHD-C, 8.7% of children with ADHD-HI, and 8.6% of children with ADHD-PI found to have a co-occurring depressive disorder (Volk et al., 2005).

Such comorbid or associated behaviors often cloud the diagnostic picture and have led clinicians to believe that they are part of the disorder. Further studies have attempted to separate out correlated symptoms from the main area of difficulty (Frick & Lahey, 1991; Pennington, 1991). Pertinent to this issue of comorbidity was a study drawn from the NIMH Collaborative Multisite Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (MTA) suggesting there may in fact be three distinct clinical profiles of ADHD comorbidity (Jensen et al., 2001). Separate profiles of ADHD with co-occurring internalizing disorders (primarily anxiety; ADHD + ANX), ADHD with co-occurring oppositional defiant disorder/conduct disorder (ADHD + ODD/CD), and ADHD with both comorbid problems (ADHD + ANX + ODD/CD) were found based on consistent differences in clinical baseline characteristics, outcomes, and response to treatment, suggesting a need for discriminating between these comorbid subtypes of ADHD (Jensen et al., 2001). For example, presence of anxiety with ADHD was prognostically beneficial. These children, regardless of ODD/CD status, tended to be more responsive to treatment than children with either ADHD + ODD/CD or ADHD-only. In addition, children with ADHD + ANX responded positively to any of three treatments (behavioral, medication management, or combined treatment), whereas the ADHD + ANX + ODD/CD had the greatest benefits from the combined treatment. Finally, the

ADHD + OCC/CD or ADHD-only groups generally only responded to the treatments with medication (Jensen et al., 2001).

The long-term outcome for children with ADHD and conduct disorder has been found to be the poorest compared with any other childhood disorder (Barkley, Fischer, Smallish, & Fletcher, 2006; Mannuzza & Klein, 2000; Moffitt & Henry, 1989). Poor long-term functioning occurs across multiple domains, including educational, occupational, financial, criminal, emotional, and social realms and persists into adolescence and adulthood (Barkley et al., 2006; Mannuzza & Klein, 2000).

Further complicating matters of separating associated behaviors from the core behaviors include potential genetic overlap for common comorbid problems often associated with ADHD. A recent large genetic comorbidity twin study found that shared genetic heritability estimates were strong for comorbid reading disabilities and ADHD-PI (31%), conduct disorder and ADHD-HI (37%), and oppositional defiant disorder with ADHD-HI (42%; Martin, Levy, Pieka, & Hay, 2006). Future research needs to tease out whether the genetic connections are due to similar shared biological pathways or due to the environmental impact one set of behaviors have in the development of other destructive behaviors.

Another area of impairment that is often related to ADHD involves the social domain, such as poor social skills or social competence (Semrud-Clikeman & Schafer, 2000). There appears to be significant differences in social competence between children who are overactive with inattention and those with inattention without overactivity. Children with ADHD plus aggressive behavior have been found to be less popular, more disliked, and more likely to be rejected by their peers (Atkins & Pelham, 1991). Although these children do not evidence skill deficits, they do experience difficulty in carrying out their intentions in a social situation. In contrast, children with ADD and withdrawn behaviors are often isolated and seem to lack needed social skills (Hynd et al., 1991). These children also appear to be at higher risk for mood disorders including anxiety and depression (Hynd et al., 1991; Milich & Landau, 1989). Social impairments also appear to increase when depression is present as well. For example, a recent community sample study

comparing ADHD with and without comorbid depression suggested that children with a diagnosis of ADHD have greater impairment in social competence, academic achievement, and conduct problems than control children. However, children who present with comorbid ADHD + depression have even greater impairments in social functioning than those children with ADHD-only (Blackman, Ostrander, & Herman, 2005). Because inattention symptoms explained nearly all of the depression variance, this suggests that the link between ADHD and depression goes beyond simple association. Contrary to previous research, which tended to use clinical samples and single method formats allowing for potential rater bias, no differences were found in academic achievement, ADHD severity, or conduct problems between children with ADHD + depression and those with ADHD-only, although these results need to be further studied (Blackman et al., 2005).

Thus, children with ADHD with comorbid externalizing or internalizing disorders appear to be at risk for poor academic achievement and for the development of concurrent psychopathology. It is currently unclear whether these developmental disorders with co-occurring psychopathology are mutually independent or whether they are interrelated; that is, it is possible that having one disorder (i.e., ADHD) makes one vulnerable for the development of another disorder (e.g., conduct disorder or oppositional defiant disorder). However, ADHD children are at risk for the development of psychopathology.

In terms of the educational domain, a sample of children with hyperactivity followed over a minimum of 13 years were found to have significantly higher rates of grade retention, greater number of suspensions, higher rates of special education, lower grade point averages, lower college enrollment status, fewer years of education completed, and lower graduation rates, with as many as 32% failing to complete high school (Barkley et al., 2006). Occupational and financial outcomes include higher rates of being fired from a job (more than twice as often), owing money to others (twice as much as controls), more trouble paying bills, and lower prevalence of credit card ownership and having a savings account (Barkley et al., 2006). Higher rates of arrests, multiple arrests, and incarcerations have also been found in comparison to controls (Mannuzza & Klein, 2000). Finally, in the social

domain, individuals with hyperactivity have been found to have significantly fewer close friends, greater number of social problems, shorter duration of dating relationships, younger age when first sexually intimate (15.5 compared to 16.3), and higher numbers of sexual partners within the last year compared to controls (Barkley et al., 2006).

Predictors of specific functional outcomes were also examined by these authors, including high school graduation, employment stability, work performance, age of sexual initiation, parenthood involvement, number of close friends, and social problems (Barkley et al., 2006). The best predictors of high school graduation status included severity of childhood hyperactivity, number of lifetime CD symptoms, and grade retainment. Employment stability was best predicted by total ADHD symptoms and severity of ODD symptoms, whereas current job performance was predicted by employer-rated ADHD symptoms and the intensity of childhood hyperactivity. Age of sexual activity initiation predictors included number of lifetime CD symptoms, severity of childhood CD, and IQ. Involvement during a pregnancy was predicted by lifetime CD symptoms and child hyperactivity severity. Finally, the number of close friendships and social problems were best predicted by severity of childhood hyperactivity and severity of current ADHD and hyperactivity, respectively (Barkley et al., 2006). Early aggressive tendencies plus neuropsychological delays in early childhood have been found to be highly predictive of delinquent behavior in adolescence and criminal behavior in adulthood (Fergusson & Horwood, 1995; Mannuzza, Klein, Abikoff, & Moulton, 2004; Moffitt & Silva, 1988; Toupin, Déry, Pauzé, Mercier, & Fortin, 2000).

Neuropsychology of ADHD

The neurophysiology and neuropsychology of ADHD continue to be extensively studied using multiple techniques, including magnetic resonance imaging (MRI; Eliez & Reiss, 2000; Miller et al., 2006; Schrimsher, Billingsley, Jackson, & Moore, 2002), functional magnetic resonance imaging (fMRI; Booth et al., 2005; Konrad, Neufang, Hanisch, Fink, & Herpertz-Dahlmann, 2006; Mitterschiffthaler, Ettinger, Mehta, Mataix-Cols, & Williams, 2006; Vaidya et al., 2005; Zang et al., 2005), magnetoencephalography (MEG; Mulas et al., 2006), cerebral blood flow (Kim, Lee, Shin, Cho, & Lee, 2002), and tests of executive functioning (Drechler, Brandeis, Földényi, Imhof, Steinhausen, 2005; Fischer, Barkley, Smallish, & Fletcher, 2005; Oosterlaan, Scheres, & Sergeant, 2005).

Some of the cognitive deficits associated with ADHD that are often revealed in neuropsychological testing fall within the executive function realm. Executive functions (EF) have been defined as "a collection of interrelated higher level cognitive processes involved in the selection, initiation, execution, and monitoring of complex cognitive and motor responses. Stated more broadly, executive functions are concerned with the self-regulation of behavior" (Roth & Saykin, 2004, p. 84). Specific abilities often included under the umbrella of EF's include cognitive flexibility, initiation, interference control, planning/organization, response inhibition, self-monitoring, and working memory (Roth & Saykin, 2004).

Deficits in EF have often been found in individuals with ADHD and are the hallmark of major theories of ADHD (Fischer et al., 2005; Swanson, Castellanos, Murias, LaHoste, & Kennedy, 1998). For example, young adults who had a diagnosis of ADHD during childhood have been found to have significantly greater impairment in attention and inhibition compared to controls (Fischer et al., 2005). Reaction time to alertness tasks has also been found to be highly variable in children with ADHD compared to controls, often conceived as the result of inattention (Dreschler et al., 2005). Children with ADHD have been found to make more false alarms and produce fewer correct responses on spatial interference/inhibitory control tasks which are often indicative of hyperactivity/impulsivity (Dreschler et al., 2005). Finally, processing speed has also been found to be an area of weakness (Calhoun & Mayes, 2005).

Executive function deficits have been found in children with ADHD particularly when overactivity and comorbid aggressive behaviors are present. While presence of lifetime CD does not appear to affect severity of inattention, inhibition, reaction time, or increased ADHD behavior during tasks, CD has been shown to be specifically related to increased response perseveration (Fischer et al., 2005). These deficits were found on measures thought to evaluate

planning, inhibition, and divided attention (Gorenstein, Mammato, & Sandy, 1989). Other EF deficits may be more specific to ADHD. A recent study suggests that when ODD/CD symptoms or ODD/CD diagnosis status were controlled, planning and working memory were still significantly predicted by the presence of ADHD (measured continuously or categorically), while verbal fluency was no longer associated with ADHD (Oosterlaan, Scheres, & Sergeant, 2005). Furthermore, ODD/CD often appeared to enhance performance. For example, increased ODD/CD symptom endorsement was associated with making fewer errors in a planning task, children with ODD/CD performed significantly better on the planning task than controls, and comorbid ODD/CD problems in children with ADHD appeared to be associated with reduced impulsive planning behavior. Thus, this suggests that ADHD may be specifically related to executive dysfunctions such as deficits in planning and working memory (Oosterlaan, Scheres, & Sergeant, 2005).

In support of these behavioral findings, brain scanning techniques have found lowered metabolism in the prefrontal brain regions on sustained attention tasks in both children and adults with ADD (Lou, Henriksen, & Bruhn, 1984; Zametkin et al., 1990). Structural and functional neuroimaging of children and adults with ADHD often indicate abnormalities in frontal cortex areas (often the right hemisphere), subcortical structures such as the basal ganglia (caudate nucleus) and corpus callosum, and the cerebellum (Eliez & Reiss, 2000; Miller et al., 2006; Roth & Saykin, 2004; Vaidya et al., 2005). Reviews of recent MRI neuroimaging studies indicate findings of smaller total brain volume, smaller global and posterior parietal–occipital white-matter volumes, and smaller cerebral volume in children with ADHD. The degree of asymmetry of the caudate nucleus, a subcortical basal ganglia structure, has been found to significantly predict ADHD inattentive behaviors as opposed to hyperactive/impulsive symptomatology (Schrimsher et al., 2002), but research has been inconsistent as to whether the abnormalities pertain to the right or left hemisphere (Eliez & Reiss, 2000; Roth & Saykin, 2004; Schrimsher et al., 2002). Reports of abnormalities of the corpus callosum have included suggestions of smaller anterior and posterior sections of the corpus callosum in

individuals with ADHD, including the rostral areas, genu, and splenium areas (Eliez & Reiss, 2000). Finally, several studies have suggested decreased cerebellar volume, particularly posterior vermis and inferior posterior vermis areas (Eliez & Reiss, 2000; Roth & Saykin, 2004).

Atypical cerebral blood flow patterns of children with ADHD compared to controls during a resting state have also been found in prefrontal cortex areas using single photon emission computerized tomography (SPECT; Kim et al., 2002). For example, areas of decreased cerebral blood flow have been found in the right lateral prefrontal cortex, both orbital prefrontal cortex, and the cerebellum (both cerebellar cortices; Kim et al., 2002). Areas of increased blood flow may include mainly posterior cortex regions such as the upper parietal cortex (left and right postcentral gyrus, left and right angular gyrus) and the left parieto-occipital cortex (inferior and superior occipital gyrus; Kim et al., 2002).

These structural and functional abnormalities of the frontal cortex, basal ganglia, and cerebellum have been corroborated using fMRI techniques (Vaidya et al., 2005; Zang et al., 2005). In one study, children with ADHD on and off methylphenidate (MPH) were compared to controls on a task developed to elicit a Stroop effect (where an interference condition requires greater response time and greater activation volumes of brain regions than a neutral condition; Zang et al., 2005). Children with ADHD off MPH were found to have smaller activation volumes of the prefrontal cortex in both the neutral and interference condition than controls. Activation volumes of the basal ganglia, insula, and cerebellum were also smaller in the interference condition for children with ADHD off MPH than controls. Finally, when MPH was administered, the Stroop effect appeared (increased activation volume and increased behavioral reaction time), suggesting that ADHD is a disorder of hypofrontality and may also involve subcortical structures such as the basal ganglia and cerebellum (Zang et al., 2005).

These findings serve to demonstrate a possible relationship between brain function and the resulting behavior. Moreover, given the negative impact of deficient executive functions on day-to-day functioning, brain differences coupled with problematic behavior and difficulty in learning from experience may often result in feelings of lowered self-esteem and self-efficacy.

It is reasonable to speculate that there is an interaction between genetics and environment which affects how ADHD is manifested (Teeter Ellison & Semrud-Clikeman, 2007). Close inspection of 20 recent twin heritability studies of ADHD suggest that heritability rates average around 76%, ranging from around 60 to over 95% heritability (Faraone et al., 2005). Variation in heritability rates is speculated to be due to differences in how ADHD is defined, rater effects, differences in environment, and comorbidity (Levy, Hay, & Bennet, 2006). While heritability estimates derived from twin studies using DSM-IV criteria for ADHD have frequently been very high (between 90 and 95%), twin studies using quantitative methods such as the Child Behavior Checklist scales or the Conner's Rating scales to define the presence of ADHD have found smaller rates of genetic influence (60–70%; Hudziak, Derks, Althoff, Rettew, & Boomsma, 2005). When examined further, genetic dominance factors may comprise 48% of a model of ADHD, additive genetic factors 30%, and unique environmental factors contributing another 22% of an ADHD model (Hudziak et al., 2005). It is suggested that use of dimensional models of attention problems that allow for phenotypic variation and rely on normative data for comparison may not only reduce the large estimates of rater bias of ADHD symptom criteria in twin heritability studies, but also allow for investigating genetic dominance (Hudziak et al., 2005).

It may well be that a biological predisposition interacts with environmental variables (e.g., parental psychopathology, parenting styles) to foster the development of a more severe type of ADHD. A study of ADHD sibling pairs suggests that these parents rate their families as having significantly more problems in cohesiveness, expressiveness, achievement orientation, organization, and conflict compared to control families, and significantly higher than control "distressed families" without ADHD for conflict, organization, and achievement orientation (Pressman et al., 2006). When family environment variables were included in a model of sibling ADHD impairment, the sibling correlation of impairment dropped from 67 to 38%, indicating that approximately 40% of ADHD impairment is accounted for by family conflict. Furthermore, parental psychopathology such as parental mood disorders or substance abuse accounted for between 3 and 9% of the variability in ADHD impairment, and tended to be linked to sibling impairment through family conflict as a mediator. In most instances, the eldest sibling was the most vulnerable to a negative family environment (Pressman et al., 2006). Thus, children with ADHD who have parents with ADHD, parents with additional comorbid psychopathology, or who live in a chaotic environment may be at highest risk for the disorder to appear and for comorbid disorders to also be present (Pfiffner, McBurnett, Rathouz, & Judice, 2005).

Conduct Disorder

Children with conduct disorder appear to have significantly lower intelligence than non-conduct-disordered children (Nieves, 1991; Semrud-Clikeman, Hynd, Lorys, & Lahey, 1993). Conversely, higher intelligence may mitigate against the development of delinquent behavior in high-risk children, as well as in adults (Kandel et al., 1988; White, Moffitt, & Silva, 1989). Scholastic failure has also been suggested to be a potential cause of delinquency, although a 15-year longitudinal study examining several causal pathways suggested that both scholastic achievement and later delinquent problems were influenced by the common effects of early behavior and IQ (Fergusson & Horwood, 1995). Thus, this finding supports a view that scholastic problems and later delinquent behavior may be due to problems that are already established by 8 years of age, such as lower cognitive ability and early behavior problems (Fergusson & Horwood, 1995). A study using linear structural equations found that poor school achievement in middle elementary school and adolescence is predicted by disruptive behaviors in first grade (Tremblay, Masse, Perron, & Leblanc, 1992). In this study, academic difficulties were found in both first and fourth grades. However, when first-grade disruptive behaviors were used as a covariate, the relationship between first- and fourth-grade achievement and delinquency at age 14 diminished. These findings suggest that the primary foci of intervention strategies need to be placed on early behavioral control, as well as on academic acquisition.

Most studies have found language-related deficits in aggressive children and adolescents with conduct disorders, which may suggest

involvement of the left hemisphere (Coy, Speltz, DeKlyen, & Jones, 2001; Moffitt, 1992; Vance, Bowen, Fernandez, & Thompson, 2002). Adult males diagnosed as conduct disordered have also been found to have poorer verbal processing skills, with less language lateralization than adults without conduct disorder (Hare & Connoly, 1987). However, executive functioning deficits may also be relevant in addition to language deficits in CD, particularly at a younger age of development. For example, a study examining verbal ability and executive function in children aged 7–12 years with conduct disorder found no significant differences in any of the verbal measures compared to the non-CD group (Toupin et al., 2000). However, children with CD (even when controlling for ADHD and socioeconomic status) performed significantly worse than the non-CD group on nearly every EF measure of inhibition impulsivity, cognitive flexibility, and planning/organization. In particular, the Rey-Osterrieth Complex Figure Test (ROCF) was the most discriminant measure between CD and non-CD groups, a task that taps visual–motor–spatial organization and construction, planning strategy, and sustained attention. Predictors of the development of CD in children, in order of importance, included: greater ADHD symptomology, poorer performance on ROCF copy accuracy, greater reports of parental punishment, and lower socioeconomic status. Predictors of the persistence of CD were the number of ADHD and CD symptoms present a year earlier (Toupin et al., 2000).

In contrast to left-hemisphere involvement found in conduct disorder, some researchers have suggested that chronic delinquents may show impairment in right frontal regions (Yeudall, Fromm-Auch, & Davies, 1982). Furthermore, Teeter and Smith (1993) found that severely emotionally disturbed children with conduct-related disorders (e.g., severe physical aggression and sexual-acting out) had lower verbal intelligence, and significantly weaker nonverbal reasoning abilities.

Support for atypical processing of environmental stimuli and potential genetic influences is provided through recent psychophysiological research. A meta-analysis of antisocial behavior in children suggests that youth with ASB have a significantly lower resting heart rate and lower heart rate during a stressor, regardless of gender, culture, or country of origin (Ortiz & Raine,

2004). Effect sizes were moderate, reaching $d = 0.44$ for resting heart rate and an even higher effect size for heart rate during a stressor ($d = -0.76$). Furthermore, age did not impact the effect size, which, coupled with the strong predictive ability of low resting heart rate in predicting ASB and prospective studies of criminal parents and their offspring having low resting heart rates, gives support for a potential genetic transmission or predisposition for ASB (Ortiz & Raine, 2004).

Lowered physiological response to stress and resting heart rate appears to be a relatively specific marker of ASB. Children with either CD alone or who have comorbid ADHD have significantly lower physiological reactions to aversive stimuli than children with ADHD, psychiatric controls, or healthy comparisons, measured using self-reports, skin conductance, and heart rate (Herpertz et al., 2005; Ortiz & Raine, 2004). Theories of why low heart rate is a marker of ASB include stimulation-seeking theories, fearlessness theories, and biosocial theories, although neurophysiologic research suggests that other processes may be involved (Ortiz & Raine, 2004). More specifically, low heart rate may be an artifact of right-hemisphere dysfunction, which controls autonomic functioning and has been shown to be lower in antisocial populations, or reduced noradrenergic functioning (Ortiz & Raine, 2004). In summary, determining the extent to which clear-cut lateralizing signs are present may not be as important as determining the types of associated neuropsychological deficits (i.e., language and reasoning problems), and assessing their effect on later psychophysiological, psychosocial, and emotional development.

Studies with delinquents have yielded equivocal findings about the nature and extent of neuropsychological deficits that are present (Appellof, 1986; Berman & Siegal, 1976). It may be that these equivocal findings are a result of different levels of violent and nonviolent behaviors reported in children across various studies (Linz, Hooper, Hynd, Isaac, & Gibson, 1988). Delinquents with aggressive behavioral difficulties have been found to perform poorly on measures of receptive language skills (Linz et al., 1988). These children may experience difficulty understanding the consequences of their actions and thus are unable to mediate their behaviors appropriately.

Thus, it would appear that a child with a predisposition to develop a conduct disorder with co-occurring poorly developed language skills and/or overall lower cognitive ability has a higher risk factor for developing significant antisocial behavior as an adolescent and as an adult. Environmental factors should also not be ignored, such as poor early attachment relationships, family conflict and aggression, and maternal depression. For example, disorganized attachment styles, which are associated with factors such as family adversity, hostile parenting, and parental depression, have been shown to predict school-age aggressive behavior (Lyons-Ruth, 1996). In addition, a twin study of child antisocial behavior (ASB) and maternal depression found support for both nature and nurture effects (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005). In this study, only maternal depression that occurred *after* the birth of twins (as opposed to before the births) was found to be associated with later child ASB. However, parental history of an antisocial personality disorder (ASPD) also contributed to approximately one-third of the variance of child ASB, and a combination of both maternal depression and history of a parental ASPD posed the greatest risk for later ASB (Kim-Cohen et al., 2005).

The importance of understanding the biological, cognitive, and environmental precursors to a conduct disorder is demonstrated by the grim outcomes of children with CD. Severe childhood conduct problems between the ages of 7 and 9 years have been associated with significantly increased risk of crime activities such as property offending, violent offending, arrests and convictions, repeated traffic offences, and imprisonment (Fergusson, Horwood, & Ridder, 2005). Increased risk of substance use (nicotine, illicit drug dependence) and mental health problems (MDD, anxiety disorder, antisocial personality disorder, suicide attempts) have also been found, with as many as 42.1% of children with severe conduct problems having a comorbid MDD or anxiety by age 25, and as many as 14.6% of adults with a diagnosis of CD in childhood being addicted to an illegal drug (Fergusson et al., 2005). Finally, sexual/partner problems and education/employment problems are also increased, including higher risks of: having multiple partners, becoming pregnant or getting one pregnant, parenthood, being involved in inter-partner violence, no educational or employment

qualifications, failing to obtain a university degree, unemployment for 12 months or more, or welfare dependency. These findings occurred even when controlling for demographics such as gender, ethnicity, SES, parental adjustment problems, child abuse, child attention problems, and child IQ (Fergusson et al., 2005).

It should be noted that the developmental trajectory of physical aggression in children through adolescence is highly variable. Most children with antisocial behavior do not have extreme behavior problems as adults, indicating that aggression has relatively low stability (Brame, Nagin, & Tremblay, 2001). However, youth with high aggression levels in childhood are far more likely to have high levels of aggression in adolescence compared to children with low levels of aggression during childhood (Brame, et al., 2001).

Although as many as 8.7% of children with CD develop antisocial personality disorder (APD) later in life, it is unknown exactly how cognitive, language, and environmental variables contribute to the development of APD. (Fergusson et al., 2005). Reasoning problems may also play a role in the development and progression of conduct-related disorders. Moreover, which variables are correlated and which are causative is currently under investigation. Nonetheless, it appears that intervention strategies need to address the cognitive, reasoning, and language deficits that have been linked to delinquent behavior and conduct disorder as well.

Internalizing Disorders of Childhood

Although some believe that internalizing disorders in children are more closely related to brain dysfunction than are externalizing disorders (Tramontana & Hooper, 1989), there is a paucity of published research to support this hypothesis. Moreover, this picture is complicated by the finding that internalizing disorders such as depression and anxiety have been found to co-occur with disruptive behaviors (Jensen et al., 2001; Semrud-Clikeman & Hynd, 1991). As mentioned previously, approximately 20–40% of ADD children also experience depression and/or anxiety disorders (Biederman et al., 1991; Faraone et al., 2002). Moreover, ADD children have a significantly higher tendency to

have parents with diagnoses of anxiety disorder and/or depression than do normal children or children with other psychiatric diagnoses. Thus, it is often difficult to obtain a sample of children with only internalizing symptomatology and research that has done so is rare (Kusche et al., 1993).

Childhood Depression

Based on extensive investigation of depression, Weinberg suggests that the following criteria be applied when diagnosing children and adolescents: "depressed mood; self-deprecatory ideation; aggressive behavior; sleep disturbance; change in school performance; diminished socialization; change in attitude toward school; somatic complaints; loss of usual energy; and change in appetite/weight" (Emslie, Kennard, & Kowatch, 1995, p. 43). Further distinctions should be made concerning the type of depression, including differentiating major depressive disorder, minor depressive disorder, dysthymic disorder, and bipolar disorder.

Correlational research suggests that depressive symptoms are negatively related to cognitive ability, although the relationship may be stronger for boys (Priess & Franova, 2006). Performance and verbal intelligence quotients are not generally depressed as a whole, but over time depression does have a negative effect on the child's performance on these measures (Emslie et al., 1995). Furthermore, depressed children often show poor academic achievement (Kovacs & Goldston, 1991; Priess & Franova, 2006) and possess cognitive distortions on initial admittance into psychiatric hospitals (Tems, Stewart, Skinner, & Hughes, 1993).

Environmental factors also play a role in childhood depression, and may well shape the development of physiological and genetic processes (Dawson, Hessl, & Frey, in press; Leech, Larkby, Day, & Day, 2006; Kaufman et al., 2006). Childhood trauma, maternal depression, and maltreatment are environmental stressors that have been implicated in neurobiological consequences such as dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; De Bellis et al., 1994; Ronsaville et al., 2006). The HPA axis is vital to maintaining homeostasis in response to stress, a process termed "allostasis" (McEwen, 1998; McEwen &

Seeman, 1999). The neuroendocrinology of the HPA acute stress response consists of three cascading events. First, the central nucleus of the amygdala activates the ventromedial nucleus of the hypothalamus, causing the synthesis and release of corticotrophin releasing hormone (CRH) and arginine vasopressin (AVP). Second, immediately after CRH and AVP are detected, the anterior pituitary releases adrenocorticotropic hormone (ACTH) into the bloodstream, activating the adrenal cortex. Finally, the adrenal cortex releases corticosteroids (i.e., cortisol), which travel into the bloodstream and exert effects on many systems throughout the body. The circulating glucocorticoids provide the negative feedback to shut off the initial cascading processes (Checkley, 1996; Heim & Nemeroff, 2001). Thus, in a healthy acute allostasis response, the initial stressor activates biological pathways that deactivate once the stressor is past through negative feedback systems.

Chronic stress, however, can lead to excessive cycling of allostasis, resulting in wear and tear on the body and inefficiency in the systems (McEwen, 1998; McEwen & Seeman, 1999). The effect of chronic stress on the body is termed "allostatic load" and has been shown to affect cardiovascular systems, metabolic systems, specific brain regions, and the immune system (McEwen, 1998). A high allostatic load over time may affect the turnover of the feedback inhibition systems for the production of cortisol in the HPA axis, as well as cause adrenal hypertrophy. Because cortisol can be easily sampled through salivary, urinary, and plasma cortisol levels, it is often utilized as an observable mediator of stress and psychological or physiological functioning (Checkley, 1996; McEwen, 1998). Long-term stress can lead to atrophy of the hippocampal neurons, an area that is involved in verbal memory and emotional memories (McEwen, 1998). For reviews of the role of HPA in depression and anxiety disorders, the reader is referred to Heim and Nemeroff (2001) and Shea, Walsh, MacMillan, and Steiner (2004).

Neuroimaging studies have also implicated hippocampal, amygdala, and frontal lobe abnormalities in childhood depression. Children with depression have been shown to have significantly smaller left and right amygdala volumes compared to healthy children (Rosso et al., 2005). White-matter hyperintensities, which are

areas of possible increased water density, have been found in the frontal regions of children with unipolar depression or bipolar disorders (Lyoo, Lee, Jung, Noam, Renshaw, 2002). Cognitive and sensorimotor dysfunction associated with right-hemisphere processes has been found to frequently occur in children with depression (Brumback, 1988). Right-hemisphere dysfunction has also been implicated using studies of receptive affective prosodic ability (Emerson, Harrison, & Everhart, 1999), facial emotional recognition studies (Lenti, Giacobbe, & Pegna, 2000), and EEG studies indicating less right-hemisphere activity in children with low positive emotionality (Shankman et al., 2005). Moreover, a much lower incidence of left-hemisphere dysfunction was found with approximately 10% showing this type of lateralization compared with 50–66% with right-hemisphere dysfunction, and 30% of depressed children showing bilateral dysfunction.

Neuropsychological test battery support for the hypothesis of right-hemisphere involvement in depression came from studies that reported poor performance on the Wechsler Intelligence Scale for Children-Revised (WISC-R) subtests of Block Design, Coding, and Digit Span (Kaslow, Rehm, & Siegel, 1984; Wechsler, 1974). These WISC-R subtests are thought to be sensitive to right-hemisphere function (Teeter, 1986). Conversely, these children performed at an average level on measures thought to be sensitive to left-hemisphere function, such as the Vocabulary subtest of the WISC-R, or Trails A and B of the Reitan batteries (Reitan & Wolfson, 1995). For further information on the neuroscience and neurodevelopment of depression in children and adolescents, interested readers can refer to Pine (2002) and Steingard (2000), respectively.

The percentage of persons with major depression who have been found to have family members with depression is six times greater than those without depression (Downey & Coyne, 1990). Twin studies have found a 65% concordance rate for affective disorders for monozygotic twins versus 14% for dizygotic twins. Genome-wide linkage studies investigating affective disorder susceptibility have found association in chromosomal regions such as 1q31-32, 4p16, 6pter-p24, 9q31-q33, 10p14, 10q21-26, 12q23-24, 13q31-32, 18p11, 18q21-23, 21q11-13, and Xq24-28 (Venken, Claes, Sluijs, Paterson, van Duijn,

Adolfsson, et al., 2005). While these findings suggest a genetic risk factor for depression, environment and biology may interact in this disorder. Mothers who are depressed may interact differently with their children and an insecure attachment may occur (Quay et al., 1985). Such insecure attachment has been found to be a significant risk factor in the development of childhood depression (Cummings & Cicchetti, 1990).

Dawson, Grofer-Klinger, Panagiotides, Hill, and Spieker (1992) found that infants of mothers with depression had more activation in the right versus left frontal lobe even when placed in neutral conditions. This is considered to be an atypical pattern of activation and is also found in subjects who are in remission for depressive symptoms (Henriques & Davidson, 1990). What is not clear is whether the patterns of brain activity are the consequence of the environmental impact of a depressed episode or episodes or whether a biologically mediated depressive tendency is present. Thus, depression, as with many other disorders, appears to have multiple facets that likely interact to produce the syndrome.

Childhood Anxiety

Anxiety disorders have not been as extensively studied from a neuropsychological perspective as other disorders of childhood. Performance difficulties have been found in anxious children on the WISC-R, including Digit Span, Arithmetic, and Coding (Kaufman, 1979; Strauss, 1991). Dependent behavior coupled with signs of motor clumsiness, associated movements, and/or fine motor delays appears to be high risk factors for the development of long-term problems in children with anxiety and withdrawal (Shaffer et al., 1985).

Anxiety disorders have been found to be highly comorbid with ADHD (Biederman et al., 1991) and depression (Brumback, 1988). The neuropsychological differences between children with comorbid internalizing and externalizing disorders (i.e., conduct disorders and anxiety or depression) and those with co-occurring internalizing disorders (i.e., anxiety and depression) have not been investigated. Children with various comorbid psychiatric disorders may well present differences behaviorally as well as neuropsychologically. Further research is needed in this area to more fully determine

characteristics that are unique to each combination of diagnosis.

Conclusions

Children with internalizing and externalizing psychiatric disorders appear to present with both functional–behavioral and neuropsychological–organic markers. These domains are intertwined and are difficult to separate out. It seems safe to conclude that children who have more than one disorder are more likely to be referred for assessment and are more likely to demonstrate severe types of psychopathology and neuropsychological dysfunction. For example, Kusche et al. (1993) evaluated neuropsychological differences among children with internalizing-only, externalizing-only, and mixed symptoms. They found that while all groups performed more poorly than a control group, the mixed symptom group showed the most severe and widespread deficits. The internalizing-only group was the closest to the control group and showed the least amount of neuropsychological impairment; the externalizing-only group showed moderate amounts of impairment. Unfortunately, parental psychopathology was not evaluated in this study so that contributing familial–environmental factors could not be ascertained.

Many of the personality assessment measures evaluating a child's behavior utilize parent report, and therefore it is reasonable to speculate that parental psychpathology may be related not only to the child's behavior but also to parental report. Given the relationship between neuropsychological measures and environmental correlates reported in most of the studies of childhood disorders, it is important to be cognizant of these influences when assessing a child. The following section discusses methods for assessment of children's behavioral and psychosocial difficulties.

Specific Assessment Methods

The technology for assessing behavioral/emotional problems in neurologically impaired children and adolescents has lagged behind the methods available for assessing other domains of functioning, including intelligence and academic achievement (Martin, 1988). Fortunately,

this lag in innovation is beginning to abate somewhat as evidenced by the pace of publication of new instruments with improved psychometric properties (Kamphaus & Frick, 1996).

In this section, a brief overview of available personality/behavioral assessment methodology is provided. Although not an exhaustive list, the focus will be on increasingly popular methods of parent and teacher ratings of child behavior. The reader is referred to other resources for detailed information regarding peer assessment methods, self-ratings, history-taking schemes, structured diagnostic schedules, projective techniques, observations, and other methods (e.g., see Kamphaus & Frick, 1996).

The assessment of behavioral/personality constructs is emphasized as opposed to specific isolated behaviors, which is consistent with the expressed purpose of most of the instrumentation that will be reviewed. Thus, an overview of specific behavioral assessment (i.e., molecularly defined behaviors) for intervention planning is not offered. The utility of assessing constructs or dimensions of behavior that have broader implications for case conceptualization, diagnosis, and treatment planning for neurologically impaired children will be explored.

Although a broad introduction to each measure will be presented, a detailed analysis of reliability and validity evidence is beyond the scope of this review. An analysis of important strengths and weaknesses of each measure is provided in an effort to assist clinicians in selecting and using specific instruments. The content of each scale is also reflected in tabular format.

Parent Rating Scales

Children who are referred for psychological or neuropsychological evaluations do not always demonstrate sufficient reading or oral expression skills for self-report purposes, which has led to the increasing popularity of parent rating scales (Lachar, 1990). Parent ratings of child behavior possess additional advantages, including ease and brevity of assessment and cost efficiency in the evaluation process. The minimal time involved in obtaining parent ratings makes it easy to collect parental information about child behavior problems or assets. Parent rating scales also provide a method for obtaining broad-based assessment of the child's problems as well as her or his assets. Although

unstructured interviews may allow the clinician to carefully evaluate a specific area of the child's functioning, other important behavior problems may be missed (Witt, Heffer, & Pfeiffer, 1990). Furthermore, the parental perspective, regardless of its validity, is often of value when conceptualizing a case. Given the importance of parental influences on child behavior, parent perceptions of behavior problems, in particular, should routinely be collected for neurologically involved children and adolescents.

Although parent rating scales are helpful, they are not interchangeable. With the seemingly exponential growth of such measures, psychologists have to make many decisions about the utility of various measures. This chapter attempts to aid the clinical neuropsychologist in the process of test selection by providing an overview of a variety of recently developed scales. Particular attention is devoted to defining the strengths and weaknesses of each measure.

Furthermore, discussion will be limited to a coverage of multidomain/multisyndrome/omnibus measures as opposed to the universe of single domain/syndrome measures that are designed to measure specialized traits (e.g., ADHD symptoms only). An omnibus measure is preferred for most assessment purposes in order to ensure that comorbidity of other disorders is not overlooked (Kamphaus & Frick, 1996). A review of the strengths and weaknesses of five popular parent rating scales follows.

Behavior Assessment System for Children-Second Edition Parent Rating Scales (BASC-2-PRS) (Reynolds & Kamphaus, 2004)

The Behavior Assessment System for Children (BASC, Reynolds & Kamphaus, 1992) was revised in 2004 (Reynolds & Kamphaus, 2004). The BASC-2-PRS is part of the larger BASC-2 system that was published concurrently with a teacher and self-reports rating method (Reynolds & Kamphaus, 2004). It also includes a structured developmental history survey and a student observation system. The BASC system was first published in 1992 and has a current revision published in 2004. Revisions from the original version include the following: improved reliability standardization, the addition of more scales such as Functional Communication and Activities of Daily Living, standardization sample was

re-normed and matches current U.S. Census data, parent and teacher rating scales are more similar in regard to content to make comparisons easily, teacher rating scale is shortened, age range expansion of use of the scale up through age 21, and it was specifically designed to facilitate differential diagnosis in order to design more effective treatment plans for children with emotional and behavioral disorders. The re-normed standardization sample also includes those diagnosed with LD and ADHD and separate norming tables for such disorders. Unfortunately, there is little independent empirical research to date in regard to the revised edition's validity.

The BASC-2-PRS has three separate forms that are composed of similar items and scales spanning the early childhood (2–5 years), child (6–11 years), and adolescent to adult (12–21 years) age ranges. The PRS allows the clinician to take a broad sampling of the child's behavior in home and community settings (see Table 1). In the revision of the BASC, no key features were eliminated (Reynolds & Kamphaus, 2004). Initial reports of the original version find that the BASC (1) possessed strong psychometric properties (Adams & Drabman, 1994; Jones & Witt, 1994); (2) had a large number of scales that may be useful for differential diagnosis (e.g., attention problems versus hyperactivity, and anxiety versus depression) (Adams & Drabman, 1994); (3) provided useful

validity indexes (Adams & Drabman, 1994); and (4) possessed adaptive scales, such as social skills and leadership (Adams & Drabman, 1994). With regard to the inclusion of adaptive scales, Jones and Witt (1994) observed that "by delineating positive as well as negative behaviors, the BASC may be more useful than other similar scales in identifying target alternative behaviors for intervention."

The BASC-2 also includes Spanish versions of the parent rating scales, self-report, and structured developmental history. These scales were translated from the original versions and reviewed by bilingual psychologists.

Conners' Parent Rating Scale-Revised (CPRS-R) (Conners, 1997)

The Conners' Rating Scales-Revised CRS-R is a widely used behavior rating scale that was

TABLE 1. Overview of Parent and Teacher Rating Scales and Scale Content

Parent rating scales

BASC-2 Parent Rating Scales (BASC-2-PRS; Reynolds & Kamphaus, 2004)	Activities of Daily Living, Adaptability, Aggression, Anxiety, Attention Problems, Attitude to Teachers, Atypicality, Conduct Problems, Depression, Functional Communication, Hyperactivity, Leadership, Social Skills, Somatization, and Withdrawal
Child Behavior Checklist (CBCL; Achenbach, 1990)	Aggressive Behavior, Delinquent Behavior, Anxious/Depressed, Somatic Complaints, Social Problems, Attention Problems, Thought Problems, Withdrawn
Conners' Parent Rating Scales (CPRS-R; Conners, 1997)	The Conners' short form (CPRS-R: S; 27 items) provides Conduct Problem, Learning Problem, Psychosomatic, Impulsive–Hyperactive, and Anxiety scales.
Devereux Scales of Mental Disorders (DSMD; Naglieri, LeBuffe, & Pfeiffer, 1994)	Internalizing Composite: Anxiety Scale (Anx), Depression Scale (Dep), Critical Pathology Composite: Autism Scale (Aut), Acute Problems Scale (AP), Externalizing Composite: Conduct Scale (Con) (ages 13–18 only), Delinquency Scale (Del) (ages 13–18 only), Attention Scale (Att) (ages 5–12 only)
Personality Inventory for Children-Revised (PIC-R, Wirt, Lachar, Klinedinst, & Seat, 1990)	Lie Scale (L), Frequency Scale (F), Defensiveness Scale (DEF), Adjustment Scale, Achievement Scale (ACH), Intellectual Screening Scale (IS), Development Scale (DVL), Depression Scale (D), Family Relations Scale (FAM), Delinquency Scale (DLQ), Withdrawal Scale (WDL), Anxiety Scale (ANX), Psychosis Scale (PSY), Hyperactivity Scale (HPR), Social Skills Scale (SSK)

Teacher rating scales

Behavior Assessment System for Children— Second Edition Teacher Rating Scales (BASC-2-TRS; Reynolds & Kamphaus, 2004)	Adaptability, Aggression, Anxiety, Attention Problems, Attitude to Teacher, Atypicality, Conduct Problems, Depression, Functional Communication, Hyperactivity, Leadership, Learning Problems, Social Skills, Somatization, Study Skills, and Withdrawal
Child Behavior Checklist-91—Teacher's Report Form (TRF, Achenbach, 1990)	Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, Aggressive Behavior
Comprehensive Behavior Rating Scale for Children (CBRSC; Neeper, Lahey, & Frick, 1990)	Three scales focus on learning problems and cognitive and cognitive processing (Reading Problems, Cognitive Deficits, Sluggish Tempo), three scales are related to attention deficits and motor hyperactivity (Inattention–Disorganization, Motor Hyperactivity, Daydreaming), and one scale each assesses conduct problems (Oppositional–Conduct Disorders), anxiety (Anxiety), and peer relations (Social Competence)
Conners''Teacher Rating (CTRS-R; Conners, 1997)	The Conners' Revised long form (CTRS-R: L; 59 items) includes Oppositional, Cognitive Problems/ Inattention, Hyperacitivity, Anxious-Shy, Perfectionism, and Social Problems scales. The Conners' Revised short form (CTRS-R: S; 28 items) includes Oppositional, Cognitive Problems/ Inattention, and Hyperactivity scales
Devereux Behavior Rating Scale—School Form (DBRS-SF; Naglieri, LeBuffe, & Pfeiffer, 1993)	Interpersonal Problems, Inappropriate Behaviors/Feelings, Depression, andPhysical Symptoms/Fears—40 items

primarily used for research purposes until it was commercially published in 1989. It was revised in 1997 with new norms and an addition of a self-report scale. The original scale was designed to be "used to characterize the behaviors of a child and compare them to levels of appropriate normative groups" (Conners, 1989, p. 3). Parent forms are designed for ages 3–17; and two parent forms are available, a long form with 80 items and a short form with 27 items.

Kamphaus and Frick (2005) note that some of the strengths of the revised Conners' scale are

that (1) multiple forms are available such as parent, teacher, and self-report forms, (2) forms are easy for parents to complete and can also be easily scored by clinicians, (3) the scales appropriately cover the symptomatology of ADHD according to the DSM-IV-TR, and (4) it is rather brief. They also agree that the 10-item Conners Global Index is effective for measuring treatment effects and can be used as a progress monitoring technique especially for students who are undergoing medication for treatment. However, they argue that the response forms do not offer much space for distinguishing between normed age groups. There are also separate T-score tables for males and females which makes scores problematic in generalizing. Another weakness is that the wording used in the scales tends to be rather negative and may encourage negative responses. Furthermore, the measure does not provide depression or competency scales.

Sattler and Hoge (2006) agree that the revised version of the Conners' Rating Scales is a significant improvement from its original version. The scales show appropriate reliability and validity with the exception of the Social Problems scale. However, they do argue that the standardization samples are small and do not match the U.S. Census data. The sample was normed with 2,482 samples in the United States and Canada and 83% of the sample was European American (Kamphaus & Frick, 2005).

Aman (1994) further expresses reservations about the use of the CPRS with children who have diagnoses of cognitive or mental retardation. He concludes as follows:

> The first is that hyperactivity may not manifest itself identically in children with and without mental retardation. For example, two groups found that both classic attention deficit item types and noncompliance items tend to cluster onto one factor in those with mental retardation ..., whereas this is not the case in normal IQ children. The second reservation is that teachers have complained that aspects of the Conners Scales are not relevant to the handicapped children they teach. Items like "appears to lack leadership" may be examples. The success of the Conners scales cannot be denied, and there is merit in using a standard instrument to bridge the work with children who are and are not mentally retarded. With time, however, this field must find its own identity, and it is hoped that the Conners scales will either be validated for this

population or that investigators will begin to use tools that are. (p. 7)

So, while the CPRS may have a role to play in medication monitoring, it may be less useful to the clinician in the initial assessment and diagnosis of children with particular behavioral/personality problems.

Teacher Ratings

It has not always been customary for clinicians to use teacher ratings as centerpieces of the assessment of child and adolescent social/emotional functioning (Kamphaus & Frick, 1996). There are several reasons, however, why teacher ratings should be part of the evaluation of all school-age children. Among the most important reasons is that schooling constitutes much of the child's daily activity. In some ways the school is a metaphor for the workplace. Schooling is as important for child evaluation as occupational issues are for adult assessment. Second, it is important to note how a child responds to the demands to sit still, participate in group activities, complete assignments, and engage in other activities required in academic and social settings in the school. Finally, it can be valuable to understand how a child responds to schooling at different stages of development. The demands of schooling change considerably from grade to grade which produces many opportunities for a mismatch between the child's strengths and weaknesses and the demands of the environment.

Clinicians are increasingly recognizing the importance of obtaining teacher ratings for screening, intervention design, treatment evaluation, and diagnostic purposes. As children with brain injuries are increasingly integrated into the regular schooling process, teacher ratings will be essential, particularly for monitoring the progress of these children.

The following section is a presentation and discussion of some of the newly available and widely used teacher rating scales.

Behavior Assessment System for Children-Second Edition Teacher Rating Scales (BASC-2-TRS) (Reynolds & Kamphaus, 2004)

The BASC-2-TRS was designed to gather information regarding a child's observable

behaviors and then place this information in the context of other data obtained in the overall BASC system (e.g., self-report scale, parent rating scales, class-room observation system) (Kamphaus & Frick, 1996). Many aspects of the BASC-2-TRS are comparable to its companion parent form (PRS) including (1) comparable age ranges; (2) separate levels for preschool (2–5), child (6–11), and adolescent (12–21); (3) four-point scales to describe the frequency of occurrence of the behavior, ranging from "Never" to "Almost Always"; (4) different numbers of items for the three forms: 100 items for the preschool form and 139 items for the child and adolescent forms; (5) inclusion of items that were chosen to measure multiple aspects of a child's personality and behavior, including both positive (adaptive) and pathological (clinical) dimensions.

The BASC-2-TRS continues to include components of a multimethod, multi-informant system compared to the original version, item content covering important domains of classroom behavioral and emotional functioning, and excellent sampling from a large national normative group on which norm-referenced scores are based. These apparent strengths allow the clinician to make norm-referenced interpretations of scores with confidence.

Conners' Teacher Rating Scales-Revised (CTRS-R) (Conners, 1997)

The CTRS-R is a well-known research instrument that was published commercially in 1989 by Multi-Health Systems, Inc. The CTRS-R: L (59 items) describes behaviors that are scored on a four-point frequency scale ranging from "Not at all" (0) to "Very Much" (3). It has been normed for use with children between the ages of 3 and 17 years similar to the parent version and has separate T-score tables for males and females. The CTRS-R: S is a 28-item version of the CTRS-R that includes three scales (see Table 1). For both versions of the CTRS-R there is a 10-item scale, labeled the Conners Global Index, composed of the "ten items most sensitive to drug effects" (Conners, 1989, p. 2) in the treatment of childhood hyperactivity. This index is argued to be the most valid measure for its purpose (Kamphaus & Frick, 2005).

A major strength of the revised scale is that rather than building on the original version, it was revised to reflect current conceptualizations of childhood psychopathology while maintaining content validity (Kamphaus & Frick, 2005). Also, there is correspondence between the teacher and parent forms which make comparisons possible for a more holistic multi-informant assessment. However, this scale also has its weaknesses. Mainly, this scale only includes oppositional types of misconduct and not more serious problems such as stealing or lying. Additionally, the norming samples include children beginning at age 3, but there is little research regarding its validity with preschool children.

Teacher's Report Form (TRF; Achenbach & Rescorla, 2001) and Caregiver-Teacher Report Form (C-TRF; Achenbach & Rescorla, 2000)

The TRF is part of a multi-informant system that has a long and prominent history of assessing children's emotional and behavioral functioning (Kamphaus & Frick, 1996). The CBCL is a widely used rating scale system, and the dimensions of functioning covered by these scales are often considered the "standard" by which the content of other rating scales is judged. Similar to the most recent revision of the CBCL, the TRF has individual forms for children aged 1½–5 and 6–18 years. For the most part, these revisions follow the format of the 1991 version of the TRF. However, the wording of several items has been changed and three rarely endorsed items were excluded to increase the TRF's sensitivity for assessing conduct and depression problems. The content of the TRF was designed to be analogous to the original parent-completed CBCL, which explicitly attempted to be atheoretical in the development of the item pool.

Use of the TRF is supported by a large research literature showing correlations between CBCL scales and important clinical criteria, especially for the externalizing scales. Obtained scores on the TRF are also based on a national normative sample that is geographically and ethnically representative of the population. However, the standardization sample of the TRF combines two norm groups, one group representative of 1999 U.S. Census data and another

representative of information from the 1989 U.S. Census. Likewise, the TRF-C combines norm information representative of norm groups from the 1999 and 1997 U.S. Census. Additionally, the TRF and C-TRF exhibit variable test–retest and interrater reliabilities. Thus, clinicians should practice caution when interpreting these scales.

Student Behavior Survey (SBS) (Lachar, Wingenfeld, Kline, & Gruber, 2000)

The SBS is a 102-item teacher rating scale designed as a screening measure to assess the classroom behaviors of children aged 5–18 years. Despite belonging to the same family of assessment measures as the PIC-2, the SBS consists of rating statements that were derived independent of the PIC-2 (Lachar & Boyd, 2005). Moreover, 58 of the 102 items on the SBS specifically refer to in-class or in-school behaviors that can only be observed members (Wingenfeld, Lachar, Gruber, & Kline, 1998).

The SBS consists of three sections related to academic achievement, academic resources, and adjustment problems, and contains a total of 14 subscales. A four-point Likert scale is used for 13 of the scales, with responses as follows: 1 (never), 2 (seldom), 3 (sometimes), and 4 (usually). Responses in the academic performance section are based on a five-point Likert scale: 1 (deficient), 2 (below average), 3 (average), 4, (above average), and 5 (superior). There are separate norms for males and females, and for two age groups (children aged 5–11 and 12–18 years).

Although the SBS possesses satisfactory psychometric properties, questions exist regarding the clinically and educationally referred norm groups (Sattler & Hoge, 2006). Despite these limitations, the SBS can be used as an effective screening measure of student behavior.

Devereux Behavior Rating Scale-School Form (DBRS-SF) (Naglieri et al., 1993)

The DBRS-SF is a revision of the Devereux rating scales published in the 1960s by the Devereux Foundation (Spivack & Spotts, 1966; Spivack, Spotts, & Haimes, 1967). The DBRS-SF is a brief measure containing two 40-item forms, one for children (ages 5–12 years) and a second for adolescents (ages 13–18 years). Based on their occurrence in the previous 4 weeks, items are rated on a five-point frequency scale ranging from "Never" to "Very Frequently." The DBRS-SF was designed to be completed by either a parent or a teacher.

The DBRS-SF possesses acceptable reliability indexes and its scores are based on an extensive normative base. Evidence is presented in the manual that the scales can discriminate between emotionally disturbed children and nonhandicapped children. The main weakness of the DBRS-SF is its item content. The DBRS-SF measures a very limited range of behavioral domains with a noteworthy absence of externalizing behaviors. This situation is unfortunate given that teachers are most adept at providing information regarding externalizing problems. Also, there is a significant lack of items relating to symptoms of inattention and motor hyperactivity.

Conclusions Regarding Parent and Teacher Rating Scales

There has been a substantial improvement in the technology available to the child neuropsychologist who assesses behavioral and emotional functioning. This situation is welcome news given that we are well aware of the need to assess these behavioral domains (Prigatano, 1992).

Clinical neuropsychologists may use the large armamentarium of parent and teacher rating scales in concert with other measures to assess the numerous sequelae associated with TBI. Prigatano (1992), for example, provides a useful review of some of the postmorbid difficulties associated with various childhood disorders that require assessment (see Table 2). Some of these problems, and others, are conveniently assessed with the newer parent and teacher methods described above.

The manner in which the behaviors associated with TBI are measured depends in part on the characteristics present. However, a combination of parent and teaching rating scales, self-report measures, observational formats, and clinical interviews will afford methods for broad-based evaluation.

TABLE 2. Behavioral/Emotional Disturbances Associated with TBI

Irritability
Agitation
Belligerence
Anger
Violence
Impulsiveness
Restlessness
Inappropriate social responses
Emotional lability
Hypersensitivity to noise or distress
Anxiety
Suspiciousness
Delusions
Paranoia
Mania
Aspontaneity
Sluggish
Loss of interest or drive
Fatigue
Depression
Immature behavior
Helplessness
Poor insight

Adapted from Prigatano (1992).

Integrating Psychological–Behavioral Assessment Findings into Neuropsychological Evaluation Results

Clinical child neuropsychologists historically have focused on investigation of the brain–behavior relationship in children, with special attention to cognitive, memory, language, visual–spatial, sensory–perceptual, reasoning, alertness, and motor functions. Recent integrated, transactional conceptualizations of child neuropsychology call for the inclusion of methods to identify associated psychosocial and behavior problems that may accompany brain-related disorders or disease processes (Teeter Ellison & Semrud-Clikeman, 2007). In order to fully appreciate the manner in which neuropsychological dysfunction affects the psychosocial and behavioral functioning of children, several guidelines are recommended. As the assessment process should ultimately assist in the determination of appropriate interventions, clinicians may want to consider the following when assessing childhood disorders, and when subsequently designing and implementing intervention plans.

Identify Neuropsychological Assets and Deficits

It is critical to fully assess the child's neuropsychological assets and deficits and to determine their impact on the psychosocial and behavioral functioning in the home and school settings. In an effort to appreciate the effects of neuropsychological dysfunction on behavior, the following deficit patterns need to be assessed.

First, does the child have intact or dysfunctional frontal lobe systems? The extent to which disinhibition (motor and attentional), poor planning and execution of plans, inflexibility and rigidity, inadequate language and verbal skills, and impaired reasoning strategies are affecting the child's overall adjustment should be ascertained. These behaviors affect the child's social interaction patterns and acceptance by the age peers.

Second, does the child have intact temporal lobe association regions? Temporal lobe impairment often results in significant memory deficits, an inability to analyze affective qualities of stimuli, and trouble recognizing nonverbal social cues. Memory deficits may significantly impair the child's ability to learn and profit from experience. The extent to which the child is plagued by temporal association region deficits may affect the manner in which social and emotional problems are manifested. Differences in right- and left-hemisphere systems should also be assessed, and deficits may affect the manner in which verbal and nonverbal information is perceived and remembered.

Third, does the child have neurodevelopmental disorders affecting sensory–perceptual systems? For example, children with tactile defensiveness often recoil from touch and are not easily soothed as infants. Children with these deficits may have displayed temperamental difficulties as infants, and may not have established firm emotional bonds. These neurological sensitivities may result in bonding and attachment problems with the primary caretaker (i.e., the mother), which may persist into early childhood and adolescence. In other instances, children with significant psychomotor delays or weaknesses may avoid physical-play activities, such as bicycle riding, swimming, baseball, soccer, basketball, and tennis. The extent to which

avoidance isolates the child from her or his peers is of concern. These physical activities are a significant part of the early socialization of childhood. When children withdraw from play activities and become isolated from peers, depression is a likely outcome.

Fourth, does the child have a particular pattern of neuropsychological deficits and assets? A number of syndromes have been described that appear to have a fairly reliable set of neuropsychological asset/deficit patterns, associated psychosocial, academic, and behavioral features, and relatively consistent developmental course (e.g., nonverbal learning disabilities). It is critical to ascertain the child's capacity to develop compensatory skills, and the child neuropsychologist is advised to identify potential strengths and assets that can be used in the intervention phase of treatment.

Finally, to what extent do basic neuropsychological assets/deficits affect the psychosocial and behavioral functioning of the child? While causal relationships are difficult to determine, a number of childhood disorders do have rather predictable clusters of neuropsychological problems that interfere with normal adjustment. (See the discussion of specific disorders at the beginning of the chapter.) While assessing the functional neuropsychological status of children is critical, it is also important to identify comorbid psychiatric and learning problems in children.

Identify Comorbid Disorders

It is imperative to obtain a total picture of the child's functional and dysfunctional systems—neuropsychological, psychosocial, behavioral, and academic. Thus, the clinician must determine the presence of comorbid disorders when assessing the child and when developing intervention programs. For example, are psychological disorders also present with neuropsychological symptoms? Are externalizing, internalizing, or combined disorders obvious? Do learning disabilities interfere with the child's overall functional capacity? Do parental psychopathology and family stress or dysfunction exacerbate the child's problems? The extent to which associated features, full-blown syndromes or disorders, and/or environmental stress are identified may significantly increase intervention outcomes. When these important features are

ignored, children with neuropsychological-based disorders are often unable to adequately profit from treatment programs.

Furthermore, it is important to note that neuropsychological deficits are more likely to be present in children with chronic and severe forms of psychopathology. In summary, the presence of comorbid disorders may affect the child's ability to profit from interventions, to remember past experiences, and to anticipate consequences of their behavior—all of which are related to positive intervention and developmental outcomes.

Identify the Developmental Course of the Disorder

The process of neuropsychological assessment and determination of associated psychosocial and behavioral features should consider developmental issues. The clinician should be well versed in the developmental course of various childhood brain-related and neuropsychiatric disorders of childhood. It is also important to determine/ascertain the following: (1) which behaviors are expected to improve with little or no interventions? (2) which behaviors are likely to increase without interventions? (3) which behaviors may improve when other behaviors are targeted for intervention? (4) which behaviors, if left untreated, are likely to produce other more serious disorders?

Answers to these questions are critical for setting treatment priorities. Although the developmental course of some disorders of childhood (e.g., ADHD) has been described (Barkley, 1998; Teeter, 1998), other disorders are not well delineated (e.g., depression and anxiety). Furthermore, very little research has been conducted on how specific deficits affect other behaviors over time. There are a few exceptions. For example, a causal link has been established between early aggression and later achievement deficits. However, the extent to which early intervention targeting aggression may reduce subsequent academic problems needs to be investigated. It may also be helpful to determine whether interventions in verbal language and reasoning deficits also assist in improving the long-term prognosis of children with conduct-related problems. This is certainly a rich area for future research.

Identify Child Competencies

Identification of the child's unique assets, interests, and competencies should be explored. By describing the child's strengths and incorporating these into intervention plans, the clinician may help to avoid the cycle of low self-esteem that often accompanies long-term school failure, social isolation, and/or rejection that many children with problems experience. Levine (1993, 1994) advocates for "demystification" processes in treatment programs that specifically address the children's knowledge and perceptions about their own disorders. Thus, measures that assist in the identification of assets as well as deficits should be utilized by the clinician. The newly developed BASC system for parents, teachers, and the child seems perfectly well suited to this end. Interview and observational techniques also provide information about what the child excels at, or "feels at home" doing. These can be powerful factors to increase self-esteem and motivation in children with various disorders.

Identify Ecological Factors

Child neuropsychologists are advised to incorporate ecologically valid assessment and intervention methods when treating children with various disorders. With this in mind, three factors seem pertinent. First, understanding the child's social, cultural, and family context is important. Resources available to the family, psychological as well as economic, should be assessed. Intervention plans should be developed with these assets/limitations in mind. Second, selection of ecologically valid, empirically based intervention strategies is recommended. Numerous behavioral, psychosocial, and cognitively based interventions have proven effective for children with behavior and personality disorders (Semrud-Clikeman, 1995). Pharmocotherapy may also be warranted for some disorders of childhood (Teeter Ellison & Semrud-Clikeman, 1995). Third, intervention plans should include strategies for parents and teachers. Although we may not always be able to change the neuropsychological profile of a child, we may effect significant change in the child's adjustment by modifying parenting strategies, coping skills, learning environments, and classroom management techniques. Thus, careful evaluation and planning for the school and home environment is essential.

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17

Psychophysiological Evaluation of Neuropsychological Disorders in Children

THALÍA HARMONY

Introduction

In recent years the differential diagnosis of neuropsychological disorders in children has been of considerable interest, both from the clinical and neurophysiological points of view. Contradictory results based on quantitative electroencephalography (qEEG) may be related to small sample sizes or differences in sample selection, age ranges, or subtyping a particular deficit. The use of different labels to characterize specific samples has complicated the controversy; for example "poor readers" or less skilled readers have been defined as children who are reading between 1 and 2 years below their expected level and have been differentiated from children with dyslexia or severe reading impairments in childhood that tend to persist into adolescence and adulthood (Rayner & Pollatsek, 1989). The controversy is whether dyslexics and poor readers are qualitatively different groups or whether they suffer from the same deficiency at different degrees (Bernal et al., 2004).

At present, many authors use the classification by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV, APA, 1994),

which facilitates comparison of results between different reports. One of the most controversial issues in child psychiatry is whether there is a clear distinction between subjects with AD/HD and children with LD. There is considerable comorbidity between these two classes of disorders. Further, both are associated with an increased incidence of other psychiatric problems, such as anxiety, oppositional defiant, obsessive–compulsive, or mood disorders (Michele, Prichep, John, & Chabot, 2005). Current diagnostic assessment relies primarily on observations of the child's behavior, as reported by parents and teachers which can be highly subjective. Magee, Clarke, Barry, McCarthy, & Selikowitz (2005) and Michele et al. (2005) have emphasized the need for objective and independent tests. These authors propose that quantitative methods in electrophysiology may help the clinician in the diagnosis.

In this chapter we shall review some of the psychophysiological findings reported in studies of the major neuropsychological syndromes in childhood. We have two goals: (1) to describe the results that may be applied in the clinic and (2) to analyze the neuropsychological processes that are affected in these children.

In the evaluation of neuropsychological disorders in children there are two important factors that should be taken into account: the sociocultural environment (Spear-Swerling &

THALÍA HARMONY • Instituto de Neurobiología, Universidad Nacional Autónoma de México, Campus Juriquilla, 76230, Querétaro, Qro, Mexico.

Sternberg, 1994) and the presence of antecedents of risk factors of brain damage. We have demonstrated that children with clear sociocultural disadvantages, coming from marginal urban areas or poor rural environments, have an EEG developmental pattern different from that of other populations (Harmony et al., 1988; Harmony, Marosi, Díaz de León, Becker, & Fernández, 1990a). Otero, Pliego-Rivero, Fernandez, and Ricardo (2003) compared the quantitative EEGs of children at high and low risk of developing learning problems caused by residing in economically, socially, and culturally disadvantaged environments. These children were tested at 18–40 months, 4 years, and 5–6 years of age. High-risk children were found to have increased delta and theta in frontal regions and decreased alpha in posterior regions. Although these EEG differences decreased with age, frontal theta excess and posterior alpha deficits persisted.

Children with neuropsychological disorders also frequently have antecedents of risk factors of brain damage, such as perinatal asphyxia and prematurity (Díaz de León, Harmony, Marosi, Becker, & Alvarez, 1988; Selassie, Jennische, Kyllerman, Viggedal, & Hartelius, 2005). In some cases these antecedents may be related to the presence of lesions observable in computed tomography or magnetic resonance images that were not detected by the neurological examination (Fernández-Bouzas et al., 1991).

Developmental Learning Disorders

Learning disorders (LD) are diagnosed when the individual's achievement on individually administered, standardized tests in reading, mathematics, or written expression is substantially below that expected for age, schooling, and level of intelligence. The learning problems significantly interfere with academic achievement or activities of daily living that require reading, mathematical, or writing skills. There are children with specific disorders in these areas. LDs not otherwise specified are disorders in learning that do not meet the criteria for any specific LD. This category might include problems in all three areas that together significantly interfere with academic achievement (DSM-IV, 1994).

"Poor readers" or less skilled readers are defined as children who are reading between 1 and 2 years below their expected level. Such children make up about 10% of the school population. When IQ differences are controlled, it appears that good and poor readers differ primarily in terms of short-tem memory for linguistic information and in the ability to code information phonetically in short-term memory (for a review see Rayner & Pollatsek, 1989). Silva, Harmony, Bernal, Fernández, and Rodríguez (1995), using a computerized reading skill test composed of different types of tasks (naming, reading comprehension, picture naming, syntactic tasks, phonological categorization tasks, and visual perception tasks), observed that syntactic tasks, consisting of the ordering of words to complete a sentence, differentiated less skilled readers from normal readers better than other tasks. They concluded that, because the participation of working memory is needed to perform the syntactic tasks, the deficit observed may be related to a decreased capacity for short-term memory, according to the capacity theory of language comprehension advanced by Just and Carpenter (1992).

Based on behavioral studies accessing vocabulary, phonological awareness, general name retrieval ability, decoding skill, word recognition speed, and the ability to use context to speed word recognition, Stanovich (1988) showed that the profiles of skilled third-grade readers and less skilled fifth-grade readers were quite similar. Based on the findings of Stanovich and some other authors, it has been proposed that less skilled readers may suffer from some type of developmental lag.

Using EEG frequency analysis, many authors have shown that absolute and relative power in the delta and theta bands (the slow EEG bands) decrease with age, while alpha relative power increases (Fonseca et al., 2003; Gasser, Verleger, Bacher, & Stroka, 1988; Harmony, Hinojosa et al., 1990; John et al., 1980; Matousek & Petersén, 1973). Therefore, an increase in delta and theta powers, with a concomitant decrease in alpha power, seems to be characteristic of an immature EEG pattern. Analysis of EEG spectra obtained during resting conditions has yielded conflicting results with respect to the presence of differences between children with reading disorders. Such contradictory results may reflect differences in sample selection, age range, or the subtyping of reading disorders. Whereas children with dyslexia have no differences in their EEG during resting

conditions when compared with children without dyslexia (Fein et al., 1986; Yingling, Fein, Galin, Peltzman, & Davenport, 1986), it appears that less skilled readers do show such differences. Ahn et al. (1980), John et al. (1983), Harmony, Hinojosa et al. (1990), Chabot, di Michele, Prichep, & John (2001), and more recently Gasser et al. (2003) described an abundance of delta and theta powers during rest in LD.

In order to analyze the differences between LD and normal children with a more powerful analysis, we calculated the sources of the EEG currents at different frequencies in a group of LD not otherwise specified and a group of normal controls. Source analysis frequency-domain variable resolution electromagnetic tomography (Fd-VARETA) was used to calculate the distributed sources, each 0.39 Hz of frequency. This is a method that provides volumetric solutions on the gray matter of an averaged brain (Evans et al., 1994, average of MRI images) for each frequency. Previous papers describe this method in detail (Bosch-Bayard et al., 2001; Fernández et al., 2002). Current sources of different EEG frequencies were studied in 25 normal children and 46 LD (not otherwise specified) children between 8 and 10 years of age (Fernández et al., 2002). Significant differences between groups were observed. LD children had more

theta activity (3.5–7.02 Hz) in frontal lobes and control children had more alpha (9.75–12.87 Hz) in occipital areas. These results support the maturational lag hypothesis, as the neurobiological cause of learning deficiencies not otherwise specified. Figure 1 shows the probability maps (projected in the averaged brain) that result from the comparisons of the current sources between LD and control children for the different frequencies. It is possible to observe significant differences in blue color, LD children with more theta than control children in frontal lobes, and control children with more alpha in posterior regions.

Harmony, Hinojosa et al. (1990) analyzed EEG in three groups of children, according to their performance on a reading–writing test. Children from group 1 had adequate performance for their age and grade; children from group 2 had below-level performance with minor difficulties; and children from group 3 had below-level performance with severe difficulties. Children from groups 2 and 3 had more diffuse theta absolute power and relative power and less alpha relative power than group 1. Children from group 3 also had a higher amount of delta in frontotemporal leads than the other two groups. These results led the authors to conclude that the diffuse increase of theta and decrease of
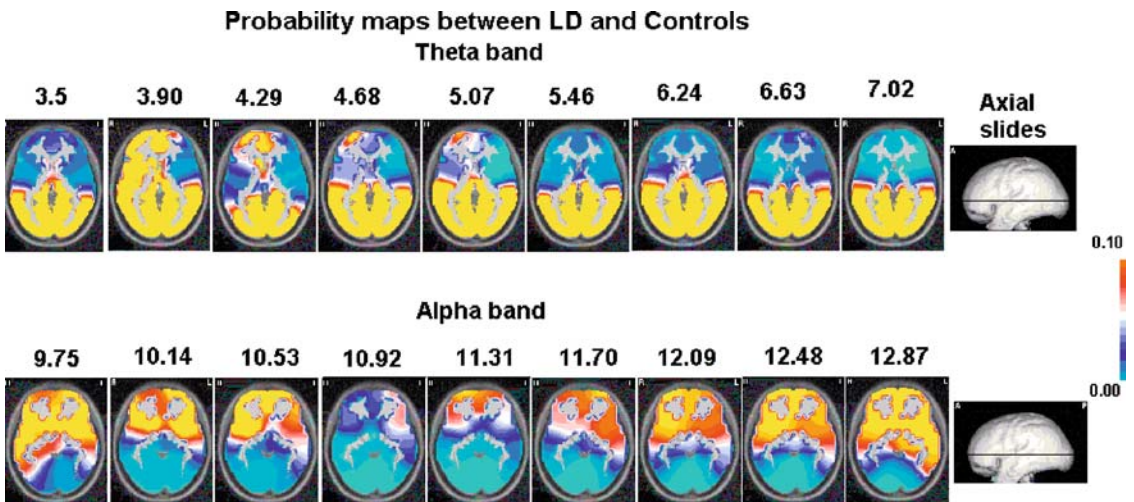
FIGURE 1. Comparison between LD and control children: probability maps (*blue* highly significant). Frequencies correspond to the *columns*. *Upper*: frequencies within the theta band. *Bottom*: frequencies within the alpha band. LD children had more theta in frontal regions than control children. Control children had more alpha in posterior regions. The level of the slices is shown at the *right*.

alpha may be related to a maturational lag, but that in group 3 children, frontotemporal delta power reflected an underlying dysfunction in these areas.

However, subsequently, in a longitudinal quantitative EEG study of the same groups of children, we observed that children with mild and severe difficulties on the test had a maturational spurt of their EEG between the ages of 10 and 13. The age of the children during the first session was 9.0 ±1.6 years; the second recording was carried out 3 years later. A greater decrease of theta absolute power between sessions was observed in children from groups 2 and 3 than in children from group 1. Our quantitative EEG (qEEG) results agree with the hypothesis of a maturational lag in children with mild and severe problems in reading up to the age of 10. Later, a maturational spurt caused less skilled readers to almost reach grade level by the age of 13 (Harmony et al., 1995).

On the other hand, we have reported a significant positive correlation between higher delta and theta powers in the EEG at rest and the number of incorrect responses, the reaction times in a selective visual attention task and in a memory task in normal children. Significant correlations were observed between reaction times in the memory task and relative power in delta and alpha bands in the various leads. Lower alpha and higher delta values correlated with longer reaction times (Harmony et al., 1992). Therefore we postulated that a slow EEG might be the underlying cause for cognitive deficiencies. To investigate this hypothesis, in our laboratory Fernández et al. (1998) have performed a series of experiments with skilled and less skilled readers, recording EEG during a Continuous Performance Task and a memory task using Sternberg's paradigm. The results showed that the EEG prior to the presentation of the stimulus was slower when incorrect responses were given than when correct responses were obtained. These results supported the maturational lag hypothesis as an explanation for the deficits observed in a group of LD.

In the reports of Klimesch, Doppelmayr, Wimmer, Gruber, et al. (2001), Klimesch, Doppelmayr, Wimmer, Schwaiger, et al. (2001), the EEG of dyslexic children was recorded while subjects were reading numbers, words, and pseudowords. Although the sample in these papers was very small (eight control children and eight dyslexic), the results were of interest: large differences with a control group were found in the lower theta band in occipital sites where dyslexics showed a complete lack of pseudoword processing. Differences were also found at upper and lower alpha and beta bands. The authors concluded that dyslexics lack the ability to encode pseudowords in visual working memory, and they lack attentional control during the encoding of words at left occipital sites.

Using topographic mapping of EEG and sensory-evoked responses during rest and during various tasks (reading and recall, listening to speech, memorization and recall of geometric figures, listening to music, forming associations between geometric forms and nonsense words), Duffy and McAnulty (1985) found the following significant differences between normal control subjects and subjects with dyslexia ranging in age from 10 to 12 years: (1) group differences were better demonstrated during EEG-activated tasks than during resting states; (2) EEG differences between groups were largely anterior; (3) although the classical left temporal and parietal speech regions were prominent as a locus of dyslexic versus normal differences, a between-group difference was also found in frontal regions, with more alpha activity in frontal regions in the dyslexics during active states.

Duffy and McAnulty interpreted the abundance of alpha activity as a tendency toward inactivity or functional "idleness" (Gevins et al., 1979) or as a lack of electrophysiological responsiveness to different experimental situations. Lower alpha and beta-2 responsiveness was also reported by Ortíz et al. (1992) in a group of children with dysphonemic dyslexia during an auditory phonemic discrimination task. Galin et al. (1992) observed a significantly smaller change in theta power between oral and silent reading in subjects with dyslexia. What all of these studies have in common is a decreased responsiveness of EEG during different active states, which may reflect cognitive differences between children with versus without reading disabilities (RD).

Other quantitative EEG measures, such as coherence, have also provided results suggesting that a different pattern of EEG maturation exists in learning-disabled children. Coherence is a measure of covariation of the spectra of two EEG signals. High coherence between EEG signals has been interpreted as evidence of a structural and functional connection between

cortical areas underlying the recording electrodes. Marosi et al. (1992) observed that the maturation of EEG coherences in skilled readers was characterized by an increase with age in coherence values between vertex and the posterior regions and by a decrease with age in the coherence of frontal interconnections. Decreased frontal coherence with age may be related to an increase in cortical differentiation (Thatcher, Krause, & Hrybyk, 1986). Children with learning disabilities showed a different pattern of EEG coherence maturation, demonstrating that age affects the coherence of skilled and less skilled readers in a differential way.

The comparison of coherence values between three groups of children with different performances on a reading and writing test showed that between the ages of 7 and 9, children with below-average performance had higher coherence in the delta, theta, and beta bands and lower coherence in the alpha band. However, in older children (9–11 years old), while the same tendency was observed, differences between groups were significant only in the delta band. In this age range, the significant group differences were almost entirely in interhemispheric coherence; in the youngest group the significant differences were observed in both intrahemispheric and interhemispheric coherence. These results also suggest that less skilled readers have a developmental spurt of EEG coherence at age 9 (Marosi et al. 1995).

Based on the analysis of coherence another explanation has been proposed for dyslexia: that it is a functional hemispheric disconnection syndrome. Leisman (2002) found that normal subjects have significantly greater sharing between hemispheres at symmetrical locations than dyslexic children, and dyslexics demonstrate significantly greater sharing within hemispheres than do normals. The comparison of EEG intrahemispheric coherence in a group of nonverbal LD and a group of verbal LD children showed that the nonverbal LD present long-distance gamma band hypoconnectivity in the right hemisphere and lower gamma interhemispheric coherence than verbal LD over F7/F8 and T3/T4 (Njiokiiktjien, de Rijke, & Jonkman, 2001).

Another important aspect in the evaluation of LD children's EEG is the presence of paroxysmal activity in the EEG, which is defined as a group of waves that appear and disappear abruptly; it is clearly distinguished from background activity by different frequency, morphology, and amplitudes. Spikes, multispike complexes, sharp waves, spike and slow-wave complexes, and paroxysmal slow waves are recognized as the fundamental patterns. In normal children, such activity is rarely observed (Petersén, Sellden, & Eeg-Olofsson, 1975), whereas in various groups of children with cognitive impairments, a significantly higher proportion of paroxysmal activity has been described (Hughes, 1971; Lezny, Provasnik, Jirasek, & Komarek, 1977; Murdoch, 1974). Becker, Velasco, Harmony, Marosi, and Landazuri (1987) reported more paroxysmal (25%) and atypical (39%) EEG activity in children with learning disabilities than in normal controls.

The presence of paroxysmal EEG discharges, even in persons not considered to have epilepsy, may in fact produce subclinical phenomena. In 1939, using a simple reaction time task during EEG recording, Schwab showed that apparently subclinical discharges may be accompanied by subtle decreases in cognitive function. Many subsequent investigators have confirmed the occurrence, in patients with subclinical discharges, of a momentary cognitive deficit, to which Aarts, Binnie, Smith, and Wilkins (1984) gave the name transitory cognitive impairment (TCI). Binnie, Channon, and Marston (1990) pointed out that paroxysmal activity may produce learning disabilities through disruption of longer-term processes of elaboration, storage, and retrieval and by a prolonged or permanent reduction in the brain's capacity to react adaptively to incoming information.

The presence of TCI was also demonstrated by Binnie (1993) in children with benign epilepsy characterized by Rolandic spikes. He demonstrated TCI using a test of short-term memory for spatial material. In this group of children, behavioral or cognitive problems such as dyslexia, speech delay, underachievement, and inattentiveness were reported. Binnie (1993) concluded that it might be expected that all children with TCI would have behavioral or cognitive difficulties. The practical implication of this finding was that subclinical EEG discharges that produce TCI could be ameliorated by the use of medication to suppress epileptiform EEG activity. Binnie was the first to present such evidence observed under controlled conditions.

Alvarez, Pérez-Avalo, and Morenza (1992) assessed the effect of paroxysmal activity in the performance of a psychological task in two groups of children: nine epileptic children who attended a special education school and nine learning-disabled children without clinical diagnosis of epilepsy. In each group, TCI could be demonstrated in three children. In a recent report, the same group of authors administered, in a counterbalanced design, three variants of a Continuous Performance Test in which visual stimuli had to be classified according to color, semantic, or phonological criteria. TCI was found in a significant proportion of nonepileptic learning-disabled children. The tasks in which TCI was present differed from one child to another. Thus, the paroxysmal activity apparently interfered with diverse mental processes in different children (Alvarez, Morgades, Pérez-Avalo, Rojas, & Díaz-Comas, 1994).

In conclusion, EEG recordings and qEEG may be very useful in the evaluation of less skilled readers and dyslexia. The presence of paroxysmal activity suggests the possibility of TCI affecting the cognitive functions of the child. Controlled experiments have not yet been carried out using anticonvulsive medication in nonepileptic children with TCI, but such applications remain a possibility. Etchepareborda (2003) studied four groups of patients with a paroxysmal EEG without seizures: language and speech disorders, specific LD, AD/HD, and a group with mixed neuropsychological symptoms. This author concluded that the pharmacological treatment was found to be favorable in 80% of the cases for the four groups under study. In our laboratory, Porras-Katzz et al. (2005) evaluated 10 LD children with paroxysmal EEG but without seizures in different psychophysiological tasks. The children received anticonvulsive therapy over the course of 6 months and were re-evaluated after treatment. Significant improvement was observed in many items of the tasks (WISC, standardized battery for the evaluation of different processes that are involved in reading).

Tallal (1987) has proposed a different concept of the underlying mechanisms involved in dyslexia, considering developmental dysphasia and dyslexia as the same syndrome. Recent formulations of the underlying deficits in this syndrome have focused on three major areas: (1) deficits in the ability to rapidly integrate presented nonlanguage auditory stimuli (Tallal, Galaburda, Llinás, & von Euler, 1993); (2) deficits in the functioning of the transient visual system (Galaburda & Livingstone, 1993; Lovegrove, 1993); and (3) deficits in verbal short-term memory (Baddeley, 1979; Vellutino, 1983).

According to Tallal, Miller, and Fitch (1993), the dysfunction of higher-level speech processing, which is necessary for normal language and reading development, may result from difficulties in the processing of basic sensory information rapidly entering the nervous system (within milliseconds). They provided data showing that this deficit affects processing in multiple sensory modalities, as well as motor output within the millisecond time frame. They linked these basic temporal integration deficits to specific patterns of speech perception and speech production deficits in children with language impairment (LI). They also suggested that these basic temporal deficits cause a cascade of effects, starting with disruption of the normal development of the phonological system and leading to a subsequent failure to learn to speak and read normally. That is, for Tallal et al., both language and reading problems derived from a deficiently established phonological processing and decoding.

Neville, Coffey, Holcomb, and Tallal (1993) recorded auditory-evoked responses (AERs) to a standard tone of 1,000 Hz and to a target tone of 2,000 Hz, with different interstimulus intervals in a group of normal children and a group of children with LI. They observed significant differences between groups only when the children with LI were split into two subgroups based on their behavioral performance on the rapid sequencing subtest of the Tallal Repetition Test. Only those children scoring between 0 and 16 who were classified as "low rep" showed AERs of lower amplitude in the N140 component following the shortest interval and in the N260 and N440 components for all intervals. The authors concluded that in some children with LI/RD (language impairment/reading disorders), reduced and slowed activity within primary and associated auditory areas contributed to their language impairment. The fact that the subsequent responses, N260 and N440, were also reduced to all interstimulus intervals suggested that auditory sensory processing might be abnormal even at moderate rates of stimulus presentation in a subset of children with LI/RD.

Other very interesting results that show abnormal auditory processing in children with LI/RD are those of Lang et al. (1993). They analyzed the mismatch negativity (MMN) in a group of dysphasic children. The MMN component appeared when a deviant tone was presented embedded in a series of tones (Näätänen, Gaillard, & Mantysalo, 1978). The deviant tones were characterized by a different pitch or a different duration relative to the standard tones. The MMN seems to reflect a neural mismatch process triggered by a sensory input from a deviant stimulus at the presence of a neural trace of the frequent (standard) stimuli. That process serves as an automatic, preconscious, change-detection mechanism that initiates a sequence of brain events that lead to an attention switch to a stimulus change when some threshold is exceeded (Näätänen, Paavilainen, Tiitinen, Jiang , & Alho, 1993). In children with dysphasia, MMN is significantly attenuated especially to pitch difference and it has a somewhat different scalp distribution than in normal children. These results indicate that dysphasia might, at least partially, be the result of a functional disturbance in the preattentive auditory discrimination stage and the echoic memory (Lang et al., 1983).

With regard to deficits in visual processing in subjects with dyslexia, although it was a common clinical assumption that reading disability was not attributable to visual deficits, since the early 1970s recordings of visual-evoked responses (VERs) have shown that children with dyslexia display amplitude attenuation of these responses (Cohen, 1980; Conners, 1971; Preston, Guthrie, & Childs, 1974) and greater variability of VERs in parietal areas (Harmony, 1989; Harmony & Díaz de León, 1982). Lovegrove (1993) has proposed a theory to explain dyslexia on the basis of deficits in the transient visual system. Information is transmitted from the eye to the brain via a number of separate parallel pathways or channels. The different channels transmit their information at different rates and respond differently to different rates of temporal change. Some channels are sensitive to very rapidly changing stimuli and others to stationary or slow-moving stimuli, and two subsystems have been proposed within the visual system: the transient and sustained systems. The transient system is highly sensitive to contrast, most sensitive to low spatial and high temporal frequencies; fast cellular and parvocellular systems of the visual pathways are often equated with the transient and sustained systems, respectively.

Lovegrove (1993) used measures of low-level visual processing as visible persistence, which is measured by the temporal separation required for distinguishing between two presentations. Flicker fusion rate, which is the fastest rate at which a contrast reversal of a stimulus can be seen, led to the observation that approximately 75% of children with dyslexia showed reduced transient system sensitivity, but they did not differ from controls in the functioning of the sustained vision system. Galaburda and Livingstone (1993) analyzed the brains of five dyslexic subjects and five nondyslexics, observing that the magnocellular layers of the lateral geniculate nuclei were more disorganized in the dyslexic brains, thereby supporting the hypothesis of a deficit in the transient visual system. Dyslexics also have specific visual deficits in processing moving stimuli, which also supports the hypothesis of an impairment of a specific magnocellular function (Schulte-Korne, Bartling, Deimel, & Remschmidt, 2004).

Visual-evoked responses (VERs) to pattern reversal stimuli are of smaller amplitude in children with reading disorders (RD) (May, Lovegrove, Martin, & Nelson, 1991; Mecacci, Sechi, & Levi, 1983; Solan, Sutija, Ficarra, & Wurst, 1990). Neville et al. (1993), in the same sample of children with LI/RD mentioned above, reported that children with LI had smaller amplitudes of N230. These findings are further evidence for the proposed deficits in visual processing in dyslexia.

The third set of underlying deficits that have been postulated to explain LI/RD in children are those related to short-term memory. It is assumed that short-term memory plays a role in reading. Strong theoretical evidence for a link between linguistic coding and reading disability has been provided by Torgesen (1988) and Vellutino (1983). These authors pointed out, in general, the importance of language processes for reading and, in particular, the vulnerability of decoding processes to deficiencies in encoding abilities.

Event-related potentials (ERPs) can be used for chronometrical analysis of cognitive processes (McCarthy & Donchin, 1981) yielding information not available from behavioral measures and therefore offering the possibility of investigating the cognitive processing required

for reading. Among the most frequent components of the ERPs studied is P300. This is an endogenous positive wave with a latency of 300 ms or greater that is typically elicited by rare target stimuli in a detection task. In selective attention tasks, when the signal is correctly detected the ERP shows a large P300 component that does not appear when targets are missed. P300 seems to be related to stimulus evaluation processes and to be independent of response selection and execution processes. It is the activation of a unique processor, a subroutine, with a specific function, that is indicated by the appearance of P300. Any stimulus, once identified and categorized, is thought to initiate two processes, one concerned with response selection and the other with what might be called "context updating," which depends in turn on stimulus evaluation. If the unexpected happens, the model of the operating context must be revised. Donchin, Ritter, and McCallum (1978) hypothesized that this context revision is manifested by P300. Because context updating involves the activation of working memory, P300 has also been related to processing of stimuli in memory. Posner (1978) proposed that the higher-level process responsible for the generation of P300 is conscious attention. A large P300 would indicate that the subject was focusing a substantial amount of available attention resources on the stimulus event, while a small or nonexistent P300 would indicate that these resources were unavailable or diverted elsewhere.

Smaller P300 responses are commonly found in children when using a language-related task (Barner, Lamm, Epstein, & Pratt, 1994; Erez & Pratt, 1992; Lovrich & Stamm, 1983; Ollo & Squires, 1982; Silva et al., 2003; Taylor & Keenan, 1990). Holcomb, Ackerman, and Dykman (1985) reported a dissociation of findings between children with RD and those with AD/HD using words and symbols as stimuli: children with AD/HD had lower amplitudes of P300 in both conditions. However, the amplitude of P300 better differentiated LD and control groups when word stimuli were contrasted with nonlinguistic symbols. Because symbols elicited larger P300 than words in children with LD, whereas the two kinds of stimuli elicited equivalent amplitudes in controls, the results were interpreted as displaying a selective deficit in the group with LD when processing word stimuli. Using a spatial task, Harter, Anllo-Vento, and Wood (1989) found a greater

enhancement of N100 and reduced P300 in children with LD. However, the effects of LD on ERP did not vary as a function of AD/HD, indicating that these two disorders are distinct. These authors conclude that children with LD, while deficient in their ability to select a target stimulus – as indexed by smaller P300 component – nevertheless had enhanced spatial attention abilities. Also longer P300 latencies have been observed in LD children suggesting that the time needed to identify a target stimulus is longer in these children (Silva-Pereyra et al., 2001). However, Stelmack, Saxe, Noldy-Cullum, Campbell, and Armitage (1989), using word recognition memory tasks in normal and LD groups, found differences in P200 but not in P300.

Another very interesting component of the ERPs is N400, which typically has a peak latency of 400 ms and a broad scalp distribution, although it is usually largest at more posterior sites. Semantic manipulations, such as presenting a target word following an appropriate context versus an inappropriate context, modulate the amplitude of N400. N400 are larger for words after an inappropriate context (Kutas & Hillyard, 1980). As N400 amplitude shows a strong negative correlation with word frequency, semantic context, and controlled processing, it is reasonable to assume that it indexes processes invoked by the integration of a word into context (Brown & Hagoort, 1993; Holcomb & Neville, 1990; Kutas & Hillyard, 1984; Rugg & Doyle, 1992). Holcomb, Coffey, and Neville (1992) recorded subjects aged 5–26 as they listened to and read sentences that ended either with an appropriate and highly expected or with a semantically inappropriate word. ERPs to sentence final words displayed effects of contextual priming in both modalities, in all age groups. An important finding was that there were significant reductions in semantic priming effects with age. The results suggest that as children acquire better language skills, they rely less on semantic context for language comprehension.

Neville et al. (1993), in the same paper studying children with LI/RD quoted above, found that N400 enhancement to semantic anomalies tended to be longer, although not significant ($p < 0.08$), than in control children. The authors interpreted this result to indicate that the auditory and visual sensory processing deficits observed in this group of children led to compensatory increases in the effect required to

integrate words into context and a greater reliance on context for word recognition than in control subjects. In another study it was reported that the LD group's N400 responses were significantly delayed at the Pz electrode site. The authors concluded that the significant delays of N400 suggest inefficiency in the semantic processing in these individuals, in both automatic and attention-based aspects of lexical access (Rubin & Johnson, 2002). However, in another study in an auditory lexical decision test, using words and nonwords as primes, dyslexics showed anomalous N1 and N2 responses, related to the phonetic/phonological level, but later N400 priming effects were comparable to those of normal readers (Bonte & Blomert, 2004).

The final conclusion of the Neville et al. (1993) study of the auditory and visual recovery cycles and the N400 (in the same group of children with LI/RD) was that multiple factors contribute to the emergence of language-processing deficits, and that these deficits are heterogeneous across populations of children with LI/RD.

Attention-Deficit/Hyperactivity Disorder (AD/HD)

The essential feature of AD/HD is a persistent pattern of inattention and/or hyperactivity–impulsivity that is more frequent and severe than is typically observed in individuals at a comparable level of development. Some hyperactive–impulsive or inattentive symptoms that cause impairment must have been present before an age of 7 years. Three subtypes are recognized: combined type, predominantly inattentive type, and predominantly hyperactive–impulsive type (DSM-IV, 1994). AD/HD occurs in 3–5% of children and accounts for approximately 50% of the child psychiatric clinic population. If left untreated it can significantly impair cognitive and behavioral functioning, increasing the risk of social problems and psychopathology in later life Excellent reviews relating qEEG and AD/HD syndrome have appeared in the last year: Chabot et al. (2005), Michele et al. (2005), Magee et al. (2005), Loo and Barkley (2005).

Chabot et al. (2005) reported that most children with AD/HD in the normal and low IQ groups showed qEEG abnormalities when compared with a normal database. The qEEG frequency abnormality occurred in more than 80% of the 407 children in this population, with theta and alpha excess the most prevalent abnormal finding. Frontal and central regions were the most likely to be involved, and when the abnormality was generalized, its magnitude was usually greatest in these regions. Increased theta power is the most consistent finding in AD/HD literature, indicating that cortical hypoarousal is a common neuropathological mechanism in AD/HD (Loo & Barkley, 2005). Chabot et al. also reported differences between normal and AD/HD children in inter- and intrahemispheric values of EEG coherence. When the population with AD/HD was compared with the population of children with LDs not secondary to an attention problem, qEEG differences were observed. Children with AD/HD could be distinguished from children with LDs with a sensitivity of 97% and a specificity of 84%.

As AD/HD is a heterogeneous group, Magee et al. (2005) calculated a cluster analysis, identifying three distinct groups. Cluster 1 ("maturational group") consisted of 47.8% of the sample. Compared to controls, this cluster had decreased frontal delta and alpha, increased frontal and central theta. Cluster 2 ("cortical hypoarousal group") consisted of 36% of the sample and, compared to controls, it had increased frontal, central, and posterior total power and theta and decreased frontal, central, and posterior alpha and beta. Cluster 3 ("beta group") comprised 16.2% of the AD/HD sample and, compared to controls, it had increased frontal and central total power, decreased frontal delta, decreased frontal and central theta, decreased frontal delta, decreased frontal alpha, and increased frontal, central, and posterior beta.

The preliminary results of Chabot et al. (2001) using Fd-VARETA for source analysis showed specific regional abnormalities, with the most significant abnormalities at 11 Hz (alpha band) and at 5.4 Hz (theta band). VARETA images were localized within basal ganglia and right anterior cortical regions at 11 Hz and in the hippocampal, para-hippocampal, and temporal cortical regions at 5.4 Hz. Evidence exists that two different but interconnected neural systems are involved in the generation of EEG within the theta and alpha frequency bands. Theta seems to be generated within the septal–hippocampal pathway, whereas the alpha

frequency involves thalamocortical and cortico-cortical circuitry. A theta or alpha excess might result from low dopamine levels, and qEEG findings are in agreement with the dopaminergic theory of AD/HD, which conceptualizes AD/HD as a disorder of the polysynaptic dopaminergic circuits between prefrontal and striatal centers of activity (Levy, 1991; Chabot et al., 2005).

Another possible explanation for the heterogeneity of AD/HD is the range of age studied. Ricardo-Garcell et al. (2004) compared children and adolescents with AD/HD. Fd-VARETA was calculated for each group, and for statistical analyses permutational tests were used. The comparisons were made using Z values in order to eliminate the age effect in each group. More current was observed in children than adolescents at frequencies from 3.51 to 5.07 Hz in the medial parietal cortex, right hemisphere, parietal, and cingulate cortex. The adolescents showed higher currents in frequencies between 10.14 and 15.82 Hz in the prefrontal cortex, right frontotemporal, right parietal, and cingulate cortex.

Using ERPs, it has been shown that LD and AD/HD are distinct disorders (Harter et al., 1989; Holcomb et al., 1985). It is generally accepted that P300 amplitude between targets and nontargets is smaller in AD/HD using auditory or visual stimuli (Holcomb et al., 1985; Loiselle, Stamm, Maitinsky, & Whipple, 1980; Satterfield, Schell, Nicholas, & Backs, 1988). Satterfield, Schell, and Nicholas (1994) analyzed the ERPs from 36 hyperkinetic AD/HD and 35 normal 6-year-olds to auditory and visual stimuli in a two-choice discrimination task. When normal subjects paid attention to stimuli in a given modality, enhanced N200 and P300 responses (as compared with responses to non-attended stimuli) were found for auditory and visual target stimuli. In contrast, when subjects with AD/HD attended, little or no enhanced negative responses were found in either modality, and P300 responses were found only to visual target stimuli. Auditory N100, N200, and P300 and visual N200 to attended target stimuli were significantly reduced in subjects with AD/HD versus controls. No between-group differences were found for responses to nontarget stimuli. The authors concluded that the lack of enhancement of brain response to attended stimuli reflects deficits in cognitive processes essential to the discrimination of novel and important stimuli (as reflected by small N200 responses) and deficits in cognitive processes – thought to be crucial to memory and learning (as reflected by small P300 responses) – in young males with hyperkinetic AD/HD.

Another element of the practical importance of ERPs in the study of AD/HD is their use in the evaluation of medication. In two different sessions, one before treatment and the second after a drug dose, it is possible to reach conclusions as to whether a particular child will respond to pharmacological treatment. In "responders," amphetamines and methylphenidate produced improvement of the ERP measures toward normalization (Halliday, Callaway, & Naylor, 1983; Klorman, Salzman, Coons, Borgestedt, & Halpen, 1983; Prichep, Sutton, & Hakerem, 1976; Saletu, Saletu, Simeon, Vitamontes, & Itil, 1975).

Childhood Autism

From a neurophysiological point of view, studies on infantile autism have tried to identify defects in information processing and defects in mechanisms of orienting to novel stimulation. Because of serious problems in obtaining the cooperation of these children, technical difficulties are frequent and for this reason some studies have been carried out during unmedicated sleep. Moreover, it is often difficult to distinguish the roles played, respectively, by autism and mental deficit.

The largest study of quantitative EEG analysis (qEEG) examined autistic children, normal controls, mental age-matched toddlers, and age-matched mentally handicapped individuals (Cantor, Thatcher, & Hrybyk, 1986). The autistic children showed increased frontal-temporal and left temporal total power and decreased power asymmetry when compared with normal or mentally handicapped controls. The autistic children and mental age-matched toddlers showed greater intra and inter cerebral hemispheric EEG coherence than the other two groups. The autistic children's EEG findings indicated decreased cerebral hemispheric and topographic differentiation, which suggested a severe maturational lag.

Studies of brain stem auditory responses (BAERs) in children with autism have yielded contradictory results. Sohmer and Student

(1978) observed an increase in latency of all waves and a prolonged transmission time, and similar findings were reported by Skoff, Mirsky, and Turner (1980) and Rosemblum et al. (1980). Although these results per se do not clarify the question as to whether this functional deviation was caused by a specific lesion of the auditory pathways or was a sign of diffuse brain damage, Sohmer and Student concluded that diffuse lesion was the most probable explanation. However, Rumsey, Grimes, Pikus, Duara, and Ismond (1984) found no differences in BAER characteristics in their study of 25 children and adults with pervasive developmental disorders, including autism, versus sex- and age-matched controls.

Exaggerated reactions to even small changes in the environment and abnormal behaviors in response to auditory stimuli are frequently observed in children with autism (Khalfa et al., 2004). Brain mechanisms involved in the automatic detection of auditory frequency change were studied by recordings of mismatch negativity (MMN). At the middle frontal electrode (Fz) site children with autism showed significantly shorter latency of MMN than the control group. Scalp current density mapping demonstrates a temporal component in both groups; the shortest latency occurred in the group of children with autism and was preceded by an abnormal, early left frontal component, suggesting a left frontal cortex dysfunction (Gomot, Giard, Adrieu, Barthelemy, & Bruneau, 2002; Ferri et al., 2003).

Martineau, Garreau, Barthelemy, and Lelord (1984) measured amplitude and latencies of peak N100, P200, and P300 of the ERPs to sound alone and to paired sound and light stimuli in 18 normal and 15 autistic children. Latencies of auditory-evoked responses (AERs) to sound alone were smaller in children with autism than in normal controls. P300 amplitude to sound alone was also larger in the autistic group. Pairing sound with light caused little changes in latencies but the amplitude of all peaks increased in controls and diminished in children with autism. P300 showed greater variability in children with autism. This finding agrees with that of Novick, Vaughan, Kurtzberg, and Simon (1980), who examined the standard deviation of the mean ERP in children with autism and found considerable variability. Late auditory-evoked potentials recorded at the temporal site were of smaller amplitude in the group of autistic children than in a normal

group, and increasing-intensity related amplitude was observed in both sides in the normal group and only on the right side in children with autism. In this report it was also shown that the greater the amplitude of the right temporal N1c wave of the AERs, the better the verbal and nonverbal communication abilities (Bruneau, Bonnet-Brihault, Gomot, Adrien, & Barthelemy, 2003).

Another approach to the study of infantile autism has been followed by Courchesne, Lincoln, Kilman, and Galambos (1985) and is based on the clinical observation that individuals with autism do not orient toward information in a normal fashion. Visual-evoked responses (VERs) and AERs to stimuli requiring simple classification decisions and ERPs to unexpected, novel information, presented without forewarning the subjects, were analyzed in a group of 10 nonretarded subjects with autism aged between 13 and 25 years. Two conditions were studied in each session of AERs and VERs: no task condition, where children simply looked at or listened to these stimuli, and a task or performance condition where they pressed a button at the occurrence of target stimuli intermixed with unexpected, novel stimuli and also with expected, familiar stimuli. In the task condition, auditory stimuli evoked AERs of smaller amplitude in autistic subjects to novel sounds in the vertex, to target (N100, P300) and nontarget sounds (N100, P300) in frontal regions. In the visual modality the autistic group had smaller VER amplitudes at the frontal sites to novels and targets. The results suggested (1) nonretarded subjects with autism may have a limited capacity to process novel information – they are neither hypersensitive to novel information nor do they misperceive it as non-novel and insignificant; (2) classification of simple visual information may be less impaired than auditory; and (3) with the exception of only one latency difference, visual and auditory ERP abnormalities do not seem to reflect maturational delay.

This study was performed in high-functioning subjects with autism to permit the analysis of the relationship between neurophysiological variables and information processing not confounded by mental retardation, poor attention, poor cooperation, and low performance capacity. The results supported the findings of Martineau et al. (1984) and Novick et al. (1980) in relation to a decreased P300 to auditory stimuli

in subjects with autism and reflects the fact that some particular aspects of information processing are abnormal in autism. Such reproducibility between laboratories, designs, and quantification approaches strengthens the hypothesis that long-latency ERP components associated with cognitive processing could prove valuable in determining the neurobiological dysfunction of autism (Courchesne et al. 1985). On the other hand, Courchesne et al. did not find the striking changes, in the AERs and VERs, during nontask conditions, that have been reported by others. Such differences may relate to the fact that children with autism may display a pattern of ERP abnormalities different from that of adolescents and young adults with autism.

It has also been suggested that autism involves face recognition impairment. ERPs recorded to photos of the child's mother versus an unfamiliar female face and to photos of a favorite versus an unfamiliar toy showed that in normal children there were differences between faces and between objects, whereas in children aged 3–4 years with autism failed to show ERP differences between a familiar versus an unfamiliar face (Dawson et al., 2002; Dawson, Webb, & McPartland, 2005).

Autism is frequently associated with epilepsy. In a report by Hughes and Melyn (2005), abnormal EEGs were found in 75% of the autistic children and 46% of them had clinical seizures. Nearly all children with seizures had epilepsy, but almost 20% of those with spike discharges did not have clinical attacks. Canitano, Luchetti, and Zapella (2005) have reported similar findings.

Conclusion

AD/HD and LD constitute the most frequent syndromes in child psychiatry. Children with AD/HD and LD are heterogeneous groups with no clear limits between them. However, we recommend the clinical utilization of qEEG not only in the initial screening and treatment evaluation stages of LD and AD/HD, but also for the detection of organicity as the cause of brain dysfunction in these children. Some other electrophysiological procedures, such as the recording of ERPs, give us valuable information on deficits of specific processes in these children.

Although they are not routine evaluations important advances have been made in their experimental evaluation, and we expect their clinical application will also be recommended in the near future.

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18

The Assessment of the Hispanic Child

MARGO A. CANDELARIA AND ANTOLIN M. LLORENTE

The Assessment of the Hispanic Child

Childhood is a complex construct that is difficult to define. Childhood is not clearly demarcated by physiological variables. Nor is it clearly delineated by psychological, social, or legal variables. From a physiological standpoint, some may argue that the end of childhood could be pinpointed by specific endocrinological changes, such as the arrival of menarche. However, such a posture would represent a poor definition of childhood as there is tremendous variability in the onset of menarche even in normal states. Whereas some aboriginal girls in Central America may reach menarche onset by age 9, girls who are active in competitive, high-level, athletics anywhere in the world may not have the onset of menarche until their early 20 s or beyond. Therefore, there is substantial variance in the onset of menarche, and this variable poorly defines the end of childhood.

With regard to psychological factors, adopting a Piagetian framework (c.f., Piaget, 1952), it is not clear when an individual leaves behind "Concrete Operations" and enters the "Abstract Operations" stage. In fact, some individuals, including those from healthy populations, may never fully arrive at a level consistent with "Abstract Operations." Similar conclusions can be reached adopting other developmental psychological models, particularly models of moral development including conceptual definitions such as postconventional morality (Kolberg, 1981). Hence, in this sense, psychological variables also fail to clearly demarcate childhood. From a social standpoint, societies around the world have defined adulthood at different ages and definitions have changed throughout history. For example, during World War II, different nations changed their laws that demarcated childhood, to assist in the war effort (Tuttle, 1995). Similarly, variables associated with social behaviors and legal factors such as age of legal drinking may substantially differ by country. In this regard, some nations around the globe do not stipulate a legal drinking age (Azerbaijan) whereas other use the ages of 16 (Spain), 18 (Chile), or 21 (United States, U.S.; c.f., U.S. Government, 1984). Finally, from a legal standpoint, if we take the U.S. as an example, different states have different laws that define legal adulthood, and indirectly childhood. For example, states throughout the Union use different ages to define an emancipated minor. Whereby some states may use the age of 17 years, others adopt an earlier age, in some instances it is dependent on the child's ability to sustain herself/himself. States also have regulations or laws associated with a child's ability to be left alone or to care for himself/herself or to care for his/her siblings in his/her home. Maryland has laws that stipulate that children younger than 8 years of age should not be left alone or be able to care for other children, where other states do not have such regulations or any stipulated age (e.g., Minnesota). Such differences in legal definitions

MARGO A. CANDELARIA • Department of Pediatrics, University of Maryland School of Medicine, Baltimore, Maryland 21201. **ANTOLIN M. LLORENTE** • Department of Pediatrics, University of Maryland School of Medicine, Baltimore, Maryland 21209.

among the states partially emerge because legislatures in each state devise their own laws, and indirectly play a major role in the very definitions of childhood. For example, states where English Common Law based on legal precedent is the rule (i.e., Maryland), an age may legally define childhood, but it may be different from Louisiana where French Law prevails. Louisiana is the only American state with a legal system based on civil law established on French and Spanish codes that had their origination in Roman Law. Therefore, it should be clear that definitions of childhood vary significantly, not simply on a disciplinary-based referential framework (e.g., psychology, law), but even within the same discipline, for example, among legal definitions, and within the same country.

Thus, an inquisitive reader may ask: if these variables do not define childhood, what or who does? When is an individual considered no longer a child and is substantively and subsequently considered an adult? The answer to these logical and proper questions lays in another complex construct, namely, the child's culture (Kessen, 1979; Luria, 1976; Vygotsky, 1978; Vygotsky & Luria, 1930/1993; Wartofsky, 1983). Contrary to popular or misguided professional beliefs, a culture, not a natural or social science discipline, defines childhood, and childhood emerges in the crucible of a society and is forged in the cultural context in which the child develops (c.f., Wartofsky, 1983). However, these are not our or recent novel ideas, but rather, complex and extremely elaborated conceptualizations of childhood developed during the last century (c.f., Luria, 1976). In fact, distinguished students of childhood, including Kessen (1979), properly and explicitly have noted that childhood is a construct defined by culture to the extent that childhood is a "cultural invention" (c.f., Kessel & Sigel, 1983).

Because childhood is indeed defined by culture, and culture significantly impacts the central nervous system (CNS) and brain development (c.f., Ardila, 2003; Blonder, 1991; Kennepohl, 1999; Mandal, Ida, Harizuka, & Upadhaya, 1999; Moss, Davidson, & Saron, 1985), it is proper and meritorious to examine the neuropsychological assessment of the Hispanic child, a cultural minority within American society, in a dedicated chapter in a comprehensive volume of this nature. The chapter initially presents population statistics regarding Hispanics in order to demonstrate the prevalence of this group within the U.S. population. Before addressing specific, pragmatic assessment issues, the chapter first provides an introduction to important topics to consider when assessing youths from this ethnic minority group including demographic characteristics, ethical issues, immigration patterns and their impact upon neuropsychological assessment and inference, and other critical topics addressing cultural factors and neuropsychological assessment. Finally, although a detailed simple path could have been adopted addressing narrow assessment issues, such as what test to administer, a posture was taken to address more general but important issues associated with the assessment of Hispanic youth, and the reader is referred to more comprehensive volumes (Llorente, 2008) or dedicated chapters (c.f., Gonzalez, 2001; Marlowe, 2000) for such topics.

A Brief Look at Current and Future Statistics on Hispanics

Over the past two decades, there have been significant changes in the ethnic composition of the U.S. population. Between 1980 and 2000, minority populations (non-Caucasian) have grown 11 times faster than the Caucasian population (U.S. Census Bureau, 2001). Immigration and population growth has dramatically increased the racial and ethnic diversity with a 142% increase in the Hispanic population (U.S. Bureau of the Census, 2004). The projected population in 50 years predicts striking changes in the composition of the U.S. population. The U.S. Census Bureau predicts in the year 2050 the percent of population by race will be: 72.1% Caucasian, 14.6% African-American, 8.0% Asian-American, and 5.3% all other races. The percent of Hispanic origin jumps to 24.4% of the overall population, comprising one of the largest populations of Hispanics living on the globe. These predictions note marked increases in all minority groups, most notably, the Hispanic populations grow at significantly faster rates, nearly doubling their percentage in their share of the total population. This trend is predicted to continue and by the end of the century the number of inhabitants of Hispanic origin is predicted to nearly equal the number of inhabitants of Caucasian origin living in the U.S. (see Figure 1) (U.S. Bureau of the Census, 2004).
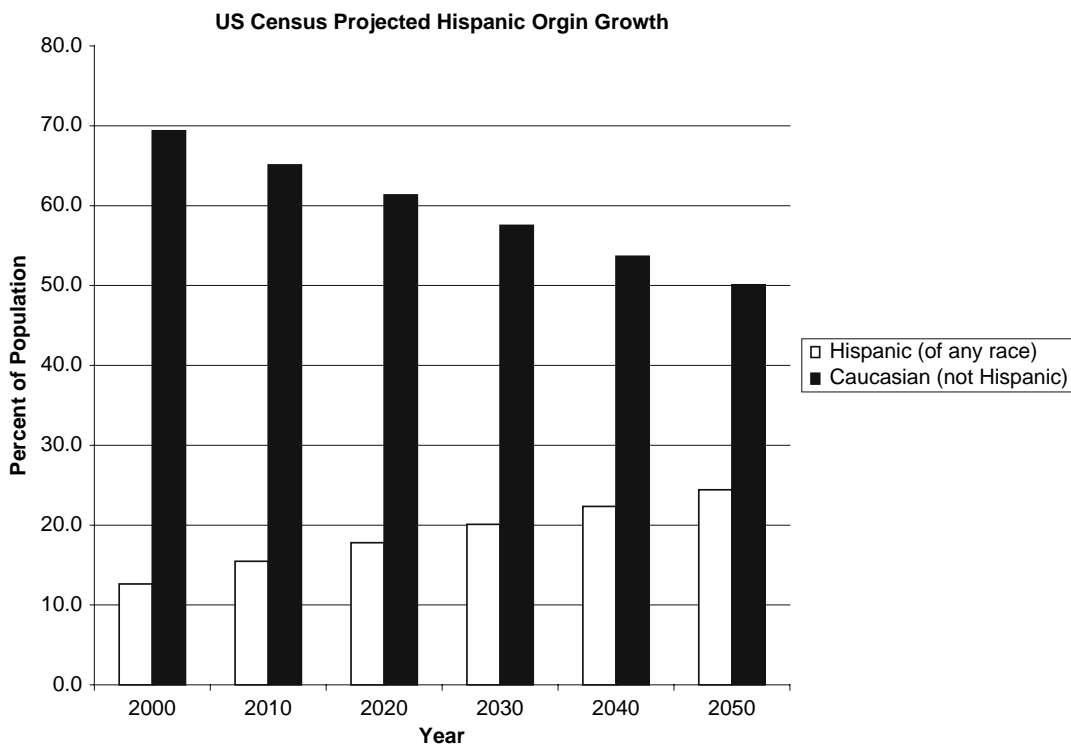
FIGURE 1. Hispanic Population in the U.S.: Expected Percent of Hispanic Relative to the Non-Hispanic White Population Across Decades (Adapted from U.S. Census, 2004).

More critical, as it relates to pediatric neuropsychological assessment of Hispanics, patterns of American immigration, moderating demographic variables of large numbers of individuals, are not the result of mechanisms driven by chance processes. The non-random nature of these mechanisms is the outcome of specific and selective influences affecting host and sending countries, be it humanitarian concerns, occupational needs, or geopolitical turmoil (Hamilton & Chinchilla, 1991). In addition, the proportion of immigrants from specific regions living in the U.S. or from foreign countries may vary substantially over large periods of time or for specific groups of individuals. Such immigration patterns can have significant impact on demographic variables and indirectly on neuropsychological assessment (Llorente, Pontón, Taussig, & Satz, 1999; Llorente, Taussig, Perez, & Satz, 2000). This inter-variability and intra-variability in immigration patterns is particularly important for demographic variables such as level of education, geographical allegiance within the U.S., and

occupational allegiance because gravitation exists toward specific areas of the U.S. and occupations and educational levels for specific groups of immigrants (Llorente, Pontón, Taussig, & Satz, 1999; Llorente, Taussig, Perez, & Satz, 2000). Most critical, it is important to note that ultimately, these factors moderate the utility of data obtained during the course of neuropsychological assessment (Harris & Llorente, 2005; Llorente, Pontón, Taussig, & Satz, 1999; Llorente, Taussig, Perez, & Satz, 2000; Rey, Feldman, Rivas-Vazquez, Levin, & Benton, 1999; Ries, Potter & Llorente, 2007).

In summary, the predicted changes in the racial and ethnic diversity in the U.S. population underscore the ever-increasing importance of understanding the dynamics between culture and pediatric neuropsychological assessment. It is also important to recognize that there is significant heterogeneity in racial groups, far too much to be accounted for by simple pan-ethnic labels such as those established by the U.S. Census. For example, the U.S. Census subdivides the Asian-American

category into seven separate racial categories which in and of themselves are extremely heterogeneous. In the federal statistical system race and ethnicity (or culture) are confounded concepts, a posture not to be adopted during the course of neuropsychological assessment (Llorente, 2008). Finally, it is important to recognize that culture may interact with other variables to create specific CNS epidemiology (c.f., Hanks et al., 2003; Kraus, Fife, Ramstein, Conroy, & Cox, 1986; LaRue, Romano, Ortiz, Liang, & Lindeman, 1999; Yeates, Taylor, Woodrome, Wade, Stancin & Drotar, 2002).

Race, Ethnicity, Culture, and the Assessment of the Hispanic Child

The terms race, ethnicity, and culture are often used interchangeably without properly understanding the repercussions of adopting such a definitional posture, and there has been significant confusion regarding distinctions between the three concepts. However, they are distinct concepts and should be understood and used independently. Race is typically viewed as the biological and genetic origins of an individual. The U.S. Census allows respondents to select from five specified race categories (white, black or African-American, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander) and also includes an "other" category (U.S. Census Bureau, 2004). Although there has been controversy about the accuracies of these racial labels, most dictionary definitions refer to race as "one of the different varieties of mankind" (Webster's Dictionary). Ethnicity and race are more complex as each is a compilation of many experiences and factors.

In the field of anthropology ethnicity refers to characteristics that defines an individual based on his or her ancestry, language, geography, history, religion, rituals, and values (Applebaum, 1987). To a certain extent, ethnicity is an individual characteristic that develops over time and may evolve in an individual as a result of many factors, including assimilation. Although race and ethnicity are each considered demographic variables, race is primarily viewed as one based on biological traits, whereas ethnicity is more often based on factors such as country of origin, traditions and beliefs. Jalali (1988) defined ethnicity as "the culture of [a] people

[that] is thus critical for values, attitudes, perceptions, needs, and modes of expression, behavior, and identity" (p. 10). Although race may be easier to discern in an individual, his or her ethnicity is not, and in some instances, it is even difficult for some persons to readily identify themselves with a specific ethnicity.

Culture can be thought of as a set of unifying beliefs, behaviors, ideas, and values that connect symbols to form a cultural integration in a group of individuals. A culture is composed of smaller subcomponents that transmit symbols such as family, groups, and institutions. Cultural characteristics and cultural patterns of behavior including beliefs, language, institutions, technology, and values are transmitted across generations as culturally learned traits leading to the very cultural definitions of its components (e.g., childhood; Wartofsky, 1983). Although culture and ethnicity can be considered to be similar because they are learned and flexible (Smedley, 1993), culture can be perceived as elements that define a group of individuals or society from which individuals may adopt specific characteristics which over time lead to their own ethnic identity (Smedley, 1993; Nagel, 1994, Shorris, 1992). In contrast, ethnicity is in the individual, and there can be many ethnicities represented within a culture.

It is also critical to note that ethnicity, culture, and race are not related to nationality. Individuals with the same nationality or country or region of origin may have different races, ethnicity, and cultural characteristics, and this is particularly true for Hispanics (Shorris, 1992). For example, Hispanic youths living in the U.S. may not only identify themselves to be racially black, white, or both, while simultaneously ethnically identifying themselves specifically (e.g., Puerto Rican, Cuban, Honduran) or globally (e.g., Hispanic or Latino), but also consider themselves to be part of the American culture. Thus, race, nationality, ethnicity, and culture are distinctive but interactive, and are often determined by the experiences and perceptions of the individual.

The term "Hispanic" is used throughout this chapter to refer to all individuals perceiving themselves as Latino, Spanish, and Spanish-speaking individuals. In this chapter, the term is intended to represent children from Latin or Central America and the Caribbean (i.e., Latino), as well as Mexico and individuals from other Spanish-speaking (e.g., Spain) origins and

the U.S., and youths who identify themselves as such because they perceive themselves as "Hispanic." As might be expected, and as noted by Harris and Llorente (2005), "Hispanic individuals living in the U.S." and other parts of the world "share many of their institutional and societal structures, including values, political, economic, and general educational systems." However, there is a great deal of heterogeneity within the group. Hispanics have various countries of origin, educational attainment, religions, use of language(s) and dialects, traditions and beliefs (Harris and Llorente, 2005), level of assimilation in their host country, and numerous other factors that distinguish individual members of the group, including children and adolescents.

The term "Hispanic" is in fact a pan-ethnic term used to identify a number of cultural or ethnic groupings, and Hispanic children and adolescents can claim one or more races as well as any Spanish-speaking country of origin, nationality, or ethnicity. Even within an intra-ethnic definition, youths emigrating from Mexico may identify themselves with any of many ethnic groups that reside in that country (Vásquez, 1994). In addition to traditional Spanish, many of these children and adolescents may use languages which exceed over 200 different indigenous *living* languages, including Mayan, Náhuatl, and Tamaulipeco (Harris & Llorente, 2005). Therefore, youths in the U.S. can be of any race or ethnicity and can be a combination of races (e.g., biracial) and ethnicities (e.g., parents with Puerto Rican and Colombian nationalities). In addition, they can be speak English, Spanish, multiple Spanish dialects, or any combination of these (e.g., English and Spanish or Spanish and Mayan), and English proficiency can range from minimal to fluent. Hispanic can refer to recent immigrants who do not speak English at one continuum to fourth generation children who may not speak Spanish at the other end. In sum, although the term Hispanic here is being used arbitrarily to encompass individuals of a Spanish or Latino background, who identify themselves as "Hispanic," our intention is to convey that Hispanics are not a homogenous group, as heterogeneity is the rule within this population (c.f., Harris & Llorente, 2005; Puente & Ardila, 2000; Shorris, 1992).

Ethical Issues and the Assessment of the Hispanic Child

When conducting neuropsychological assessments with Hispanic youths there are important ethical considerations to bear in mind. It is vital to process all cultural information available and seriously ponder how it informs and influences test selection, performance, and interpretation. The *Ethical Principles of Psychologists* (*Principles*; APA, 2002) and the *Standards for Educational and Psychological Testing* (1999) clearly note the importance of considering cultural factors and ethnicity. The preamble of the *Principles* (APA, 2002) notes

> Psychologists are committed to increasing scientific and professional knowledge of behavior and people's understanding of themselves and others and to the use of such knowledge to improve the condition of individuals, organizations, and society. Psychologists respect and protect civil and human rights and the central importance of freedom of inquiry and expression in research, teaching, and publication. They strive to help the public in developing informed judgments and choices concerning human behavior. In doing so, they perform many roles, such as researcher, educator, diagnostician, therapist, supervisor, consultant, administrator, social interventionist, and expert witness. This Ethics Code provides a common set of principles and standards upon which psychologists build their professional and scientific work.

Clearly, the Preamble indicates that the regulations intend to have psychologists take culture into consideration. This is further emphasized in Principle E, "Respect for People's Rights and Dignity," which states

> Psychologists are aware of and respect cultural, individual, and role differences, including those based on age, gender, gender identity, *race*, *ethnicity*, *culture*, *national origin*, religion, sexual orientation, disability, *language*, and socioeconomic status and consider these factors when working with members of such groups. Psychologists try to eliminate the effect on their work of biases based on those factors, and they do not knowingly participate in or condone activities of others based upon such prejudices [italics added].

Most relevant to neuropsychological assessment the *Principles* specifically refers to the interpretation of test results with the following

statement: "When interpreting assessment results, including automated interpretations, psychologists take into account the purpose of the assessment as well as the various test factors, test-taking abilities, and other characteristics of the person being assessed, such as situational, personal, *linguistic*, and *cultural differences*, that might affect psychologists' judgments or reduce the accuracy of their interpretations." (9.06 Interpreting Assessment Results) [italics added].

In brief, certain portions of the *Ethical Principles of Psychologists* (2002) refers to cultural sensitivity in general and applies to conducting work with Hispanic children and adolescents. Although similar to the *Ethical Principles*, the *Standards of Educational and Psychological Testing* (*Standards;* 1999) provides more specific and detailed guidelines that are applicable to work with Hispanic populations. For example, the *Standards* (1999) state the application and construction of tests should be suitable for the "background" (e.g., cultural, etc.) of the test taker. The construction of tests should also include information on validity and reliability of the inferences derived for such populations. Regarding test interpretation, the *Standards* indicate that contextual information should be provided in the interpretation of test scores, and when unavailable, cautions should be raised against the misinterpretation of test scores.

Thus, the *Ethical Principles of Psychologists* (2002) and the *Standards of Educational and Psychological Testing* (1999) both provide guidance related to the proper evaluative posture when conducting neuropsychological assessment with Hispanic youths. However, the guidelines do not guarantee that individual psychologists are sensitive to cultural differences and thoroughly address factors that influence assessment and intervention results when working with Hispanic children. Any professional conducting neuropsychological evaluations of Hispanic children, or any minority, should take the time and energy required to obtain as much information as possible (e.g., education status, level of acculturation, English proficiency, health status) in order to best inform the testing process. The next several sections of this chapter will explicate various factors that should be considered when working with Hispanic children.

Neuropsychological Assessment of the Hispanic Child: Special Topics

The effects of sociodemographic variables such as education on test performance are well established in the neuropsychological literature (Adams, Boake & Crain, 1982; Ardila, 1993, 2003; Ardila, Rosselli, & Rosas, 1989; Heaton, Grant, & Matthews 1986; Laosa, 1984). Therefore, it is important to understand the influence of these potential confounds in Hispanic populations, including children, during the course of neuropsychological evaluations (c.f., Acevedo, Loewenstein, Agron, & Duara, 2007 for elder adults). The intent in this section is to elucidate which demographic characteristics and other variables are most relevant and to discuss how each has an impact on neuropsychological assessments (c.f., Holmbeck, 1997). An exhaustive review of the literature is beyond the scope of this chapter, but a brief overview of education, economic status, occupation, perceptions of the Hispanic patient, and health status as they relate to neuropsychology is presented below.

Education

Education is perhaps one of the most relevant as well as one of the most researched demographics regarding neuropsychological performance (c.f., Heaton et al., 1986; Ostrosky-Solis, Ramirez, Lozano, & Velez , 2004; Acevedo et al., 2007). For illustrative purposes, this chapter now reviews a small sampling of investigations that have demonstrated that what is frequently assumed to be a result of cultural or ethnic differences is often explained by educational inequities. Pontón, Satz, Herrera, Ortiz, Urrutia, Young, D'Elia,& Namerow, (1996) exemplified the influence of education by demonstrating that in a sample of similar age individuals, performance was greater on neuropsychological assessments for those with higher levels of education across all age groups. Even within Hispanic samples, education can explain neuropsychological performance differences. Rey et al. (1999) uncovered performance differences between Cuban and Mexican normative samples in Dade County, Florida while conducting research to develop psychological instruments for Hispanics. Although one could attribute the discrepancy to differing

brain functions in the two ethnic groups, examination of sample characteristics revealed *selection biases* associated with lower levels of education in the Mexican cohort available to researchers relative to the Cuban cohort. The demographic differences of these two groups were most likely the result of distinct immigrations patterns, particularly geographical allegiance (Rey et al., 1999). Most recently, Acevedo et al. (2007) demonstrated that education attainment had broad and great influence on neuropsychological performance in a Spanish-speaking sample chiefly comprised of Cuban-born, healthy elderly.

It is crucial to examine education as a special factor because significant numbers of Hispanics living in the U.S., including children and adolescents, have reached low educational attainment. Harris and Llorente (2005) report that whereas 88.7% of the white non-Hispanic children graduate from high school, only 26.6% of children, adolescents, and adult 25 years or older from Mexico have graduated from high school and 48.6% have not received a high school diploma. Similarly 29.4% of whites achieve a minimum of a Bachelor's degree, compared to only 5.2% of Mexicans who achieved a minimum of a Bachelor's degree. This indicates that parents of pediatric Hispanic patients would often have low levels of education. Low educational attainment relates to other factors such as employment challenges, neighborhood and housing conditions, healthcare access, and nutritional status. As we discuss below, these factors interact to collectively influence neuropsychological status of children. Thus, it is vital to seriously consider education level when interpreting neuropsychological test performance and working with Hispanic youths.

Although Heaton et al. (1986) argued for increased consideration of education in neuropsychological test performance, research addressing culture and education, particularly for Hispanic children, is limited. Many tests and procedures, including those considered by many practitioners as gold standards in instrumentation have significant deficiencies regarding level of education, both for Hispanic youths as well as youths from other racial or ethnic groups. For example, many do not have normative data for specific Hispanic groups with limited or very advanced educational backgrounds (Ardila, 1998; Llorente, 1997; Llorente,

Pontón, Taussig, & Satz, 1999; Llorente, Taussig, Perez, & Satz, 2000.; Puente & Ardila, 2000). Moreover, such data may not even be available for individuals from the mainstream culture, yet clinicians continue to use such norms without questioning the validity or reliability of the inferences derived from them. For example, the reader is encouraged to determine how many 7- year-old Hispanic children from the Midwest of any parental educational backgrounds are found in the WPPSI-III standardization sample, or how many 16 to 17-year-old, "Hispanic," adolescents whose parents had >16 years of education are found in the WAIS-III standardization sample, or to make it ridiculously clear, how many 10-year-old "white" children who came from backgrounds whose average parental educational is < 8 years are found in the WISC-IV's standardization sample. Furthermore, as noted by Harris and Llorente (2005), education (or parent's education in the case of children) is often utilized as a proxy measure of SES status for stratification purposes within ethnic groups during standardization procedures because education and SES are strongly correlated (Prifitera, et al., 1998, Prifitera, Saklofske, & Weiss, 2005). Thus, when comparing scores across ethnic groups, the preponderance of the reference group will have not only a higher SES, but also higher education levels (Prifitera, et al., 1998). The lower performances of individuals from ethnic minority groups reflect both the correlation between SES and IQ (Prifitera et al., 2005), as well as the composition of the normative sample. This illustrates that education level warrants further consideration both within Hispanic children, as well as other minority groups.

Quality of education is also pertinent to neuropsychology (Byrd, Sanchez & Manly, 2005) because not all educational systems are equitable, both within the U.S. and abroad. Education quality can vary from school to school, by neighborhood or school district (e.g., suburban versus urban), by state, and by type of school (e.g., public, private, parochial). In the U.S., geographic location is particularly significant, as large numbers of Hispanic youths attend poor inner city schools. Another concern is that Hispanic children have higher school dropout rates compared to other ethnic minority and the majority populations (c.f., Harris and Llorente, 2005). Even for those youth with high school

diplomas or who appear to be steadily progressing toward a diploma, quality of education should be considered, as it has become common practice for many schools to promote students based on choronological age rather than academic merit. Quality of education is also an issue for those Hispanic children and adolescents who immigrated from rural and/or impoverished backgrounds from underdeveloped countries. They likely have received academic training in a poor educational system, and although they may have the same number of years of education as their U.S. counterparts, it may be a significantly lower quality of education.

Although at first glance issues related to quality of education may not be seen as important to neuropsychologists, it is vital because most neuropsychological tests and procedures used in daily practice with Hispanic children employ normative data that have been stratified according to years of education. However, quality of education is not taken into consideration. Equality is assumed in academic instruction and achievement, and most important, by test developers and indirectly test norms. Considering this, it may behoove the practitioner to attempt, at the very least, to informally ascertain the quality of the patient's education rather than make assumptions based on level of education (e.g., possession of a middle school diploma).

Poverty/SES

Socioeconomic status (SES) is especially relevant when working with Hispanic populations as they are overrepresented in low income and poverty samples both in the U.S. (U.S. Census Bureau, 2004) and abroad (World Health Organization, 1998). Hispanic children represent approximately 18% of all children living in the U.S., yet they constitute 30% of all children living below the poverty level in 2002 (U.S. Census Bureau, 2004). Internationally, Hispanics, including children, are often living in or immigrating from impoverished conditions, and global estimates indicate that Hispanic youths are one of the largest populations living in poverty worldwide (World Health Organization, 1998). Poverty has repeatedly been associated with neuropsychological and academic performance, particularly for young children (The National Research Council Institute of Medicine, 2000).

Literacy

A number of neuropsychologists (c.f., Ardila & Moreno, 2001; Nell, 2000) have argued that literacy plays a major role in the differences sometimes observed between Hispanics and members of other ethnic minority, and non-minority groups. However, literacy is in itself an extremely complex area of inquiry and a discreet understanding of the construct and its influence on neuropsychological performance is elusive. Currently there is controversy around what defines literary fluency and competency, such as specific cognitive processes, inability to read text, social literacy, and technological literacy (Kress, 2003; Tannen, 1980). Literacy also falls along a continuum (Tannen, 1980). Some individuals who have a rudimentary mastery of reading may have quite limited fluency. Furthermore, many youths who report certain degrees of literacy, or that reported by their parents, may not possess a sufficient degree of this characteristic to undergo evaluation in that language. This can be the case with their secondary (English), as well as their primary (Spanish) language.

The research literature has demonstrated the consequences of illiteracy on neuropsychological performance. For example, (Ardila et al., 1989; Ardila, Rosselli, & Puente, 1994) compared visuospatial and memory abilities in Hispanic illiterates and highly educated individuals. The results revealed significant differences in both areas. The investigators concluded that the cognitive skills typically examined during neuropsychological testing require abilities that are "highly trained," such as those provided by a formal educational system.

It is also worth noting that technological literacy is becoming increasingly relevant to neuropsychology because many tests and procedures administered to patients are technology dependent (e.g., computerized neuropsychological tests). Many Hispanic patients come from backgrounds where technological illiteracy is commonplace as they may have limited exposure to and experience with computers (c.f., Llorente, 2008).

Occupational Status

As with educational status, parents of Hispanic children and adolescents are often limited in the level of occupational status they can

obtain, and the prevalence of Hispanics is not distributed evenly across all occupational categories (c.f., Llorente, Taussig, Perez & Satz, 2000). In fact, large numbers of Hispanic families are over-represented in the farming/forestry industries or other low-level occupational categories at rates that sometimes exceed twice the rate of expectation based on U.S. population demographics (c.f., Llorente, Pontón, Taussig, & Satz (1999); Llorente, Taussig, Perez, & Satz (2000); Portes & Rumbaut, 1990). Low-level parental occupation often limits the child's life experiences and opportunities. In addition, if the parents are unable to sufficiently support the family there may be pressure for old children to work, often at the expense of attending school.

In addition, numerous Hispanic children and adolescents are at increased risks for exposure to occupational hazards including, but not limited to, neurotoxic substances that impact neuropsychological assessment (see Llorente, 2000). For example, Hispanic children and adolescents whose parents are employed in the farming industries may have chronic, low-level pesticide exposure if they live on the farm or assist in the workload, and may be referred for assessment due to the associated impact on neurological substrates and neuropsychological functioning (c.f., Llorente, 2008, 2000).

Housing

Although Hispanics in the U.S. have made recent gains in real estate ownership, significant disparities still remain between them and majority groups (Tomás Rivera Policy Institute, 2003). Quality of housing is relevant to neuropsychological assessment due to the potentially harmful environmental contaminants (e.g., lead, mercury, organophosphates, sulfur dioxide) with significant impact on brain functions, that occur with greater frequency in low-income neighborhoods with large Hispanic populations, including children, throughout the U.S. (Llorente, 2008). In addition, other housing factors, such as environmental deprivation, overcrowding, and the stress of sub-standard housing, hold significance for neuropsychological functioning.

Health

For specific health problems, illnesses, and diseases, Hispanic children living in the U.S. and abroad bear a disproportionate burden of disease, injury, morbidity, and mortality when compared with non-Hispanic whites (World Health Organization, 1998). In addition, the leading causes of death among Hispanics vary from those for non-Hispanic whites in the U.S. (U.S. Department of Health and Human Services [USDHHS], 2004). For example, compared to non-Hispanic whites, Hispanics of all ethnic backgrounds have greater mortality associated with stroke (18% more), chronic liver disease, and cirrhosis (62%), diabetes (41%), and human immunodeficiency virus disease (168%). Each of these health conditions has significant implications for neuropsychological assessment.

Nutrition in Hispanic children living in the U.S. and abroad, aside from humanitarian concerns, represents an important topic for neuropsychology. As noted previously, Hispanic children are overrepresented in poverty populations, and nutrition is heavily influenced by family income level. Not only does nutrition have an immediate influence on neuropsychological performance (e.g., hunger during testing), but long-term malnutrition has deleterious effects on cognition (Frongillo, de Onis, & Hanson, 1997). There is clear empirical evidence that appropriate nutrition is vital to healthy brain development (DeLong, 1993), and indirectly influences chemical brain functions underlying neuropsychological skills. Analysis of the brain's composition and metabolism reveals that a large proportion of the brain is made up of essential fatty acids and other nutrients (Sastry, 1985) that are obtained from a healthy diet. Lack of appropriate nutrition, including metals and other nutrients, has been associated with brain dysfunction in humans and animals (c.f., Winick & Noble, 1966; Winick and Rosso, 1969).

Children whose height is below the fifth percentile may be classified as stunted defined as height-for-age that is more than two standard deviations below the NCHS or World Health Organization (WHO) International Growth Reference. Stunting is a general indicator of a child's poor nutritional status over long periods of time. Growth stunting is a gradual process that occurs in response to chronic biological insults, including malnutrition and infectious diseases, during periods of linear bone growth. It often begins in utero and extends through the first two years of life. Childhood stunting is

closely associated with poverty and is often used as a population-based indicator to compare nutritional adequacy across countries. Without environmental changes, such as adoption, stunting can lead to a permanent reduction in growth. Thus, children who experience stunting early in life are often shorter during childhood and adulthood than peers who had adequate early growth. Studies have found that severe malnutrition, as evidenced by stunting, occurs at higher than expected rates in economically depressed Latin American areas (ACC/SCN, 2004), particularly in middle and late childhood, and is consistently linked with compromised cognitive performance (Berkman, Lescano, Gilman, Lopez & Black, 2002; Martorell, Rivera, Kaplowitz, & Pollitt, 1992). Thus, a history of severe malnutrition may be relevant for many Hispanic children seen for neuropsychological examinations.

Another relevant health factor for Hispanic children that influences neuropsychological performance is access to health care. For many immigrant Hispanic youths and their families, accessing and navigating the U.S. healthcare system can be overwhelming, burdensome, and aversive. The process can be complicated even further when attempting to obtain specialty services such as mental health and pediatric neuropsychological assessment. For those who are U.S. citizens or born in the U.S., lack of health insurance is common among the poor, particularly the working poor who may not qualify for any type of medical assistance (U.S. Census Bureau, 2001; USDHHS, 2004). Hispanic children in the U.S. have been found to have less access to and seek less dental, medical, and mental health services (c.f., Weinick, Zuvekas & Cohen, 2000). As noted above, Hispanic youth also have disproportionately higher rates of mortality (USDHSS, 2004) which is likely linked to lack of preventative health care.

Perceptions and Bias

Any neuropsychological assessment with Hispanic children is influenced by perceptions or preconceived notions of Hispanics in general. As Llorente, Taussig, Perez, & Salz (2000) noted, the empirical psychological literature is besieged with data documenting examiner and patient characteristics that bias evaluations. The expectations of the examiners (e.g., halo effects) may

limit the validity of the inferences derived from neuropsychological assessments of Hispanics, particularly if they are not acknowledged and controlled (Donahue & Sattler, 1971; Grossman, 1978; Sattler & Winget, 1970). The patient's history also can significantly impact how the examiner conducts, scores, and interprets the results of a psychological evaluation (c.f., Auffrey & Robertson, 1972). These issues may have even greater significance with immigrants since any characteristics considered to be stereotypical may be more pronounced, particularly those that are obvious, such as limited English proficiency.

There are numerous negative stereotypes about immigrants and ethnic minorities, including Hispanics, that have permeated American society and culture. As noted by Llorente, Taussig, Perez, & Salz (2000), "these stereotypes are capable of having deleterious impact upon" a neuropsychological evaluation, "despite their unsubstantiated nature and the fact that they have insufficient weight to withstand the rigor of scientific scrutiny." This issue is best exemplified within American society through the perceptions of the immigrant.

Negative perceptions of immigrants have been persistent throughout history, even within the mental health professions (Ødegaard, 1932; Sanua, 1970). During large-scale migrations to the U.S. at the beginning of the 20th century, methodologically flawed epidemiological studies suggested the process of immigration was correlated with higher rates of psychopathology. For example, although erroneous, studies indicated a higher incidence of mental illness among immigrants on the basis of hospital admissions (Jarvis, 1866; Rothman, 1971; Sanua, 1970), greater suicide rates among U.S. immigrants, and differential suicide rates in Europeans and U.S. immigrants of the same nationality (c.f., Farris & Dunham, 1939). These investigations were flawed in numerous ways, including biased samples, and sound research later demonstrated the majority of the observed differences could be attributed to the effects of objective variables such as age, poverty, and area of residence (Kohn, 1973; Hollingshead & Redlich, 1958; Kessler & Cleary, 1980; Srole, Langner, & Mitchell, 1962). Regrettably, the early inaccurate studies fed the mainstream perception of immigrants, and influenced how lay people and mental health professionals alike regard the

mental abilities of immigrants (Llorente, Taussig, Perez, & Satz 2000). These stereotypes are capable of biasing the outcome of a neuropsychological examination. Llorente, Taussig, Perez, & Satz (2000) noted that despite our current understanding of how contextual factors are relevant to the psychological status of immigrants (e.g., SES, education, reason for immigration), current neuropsychologists must be cognizant of these biases, and acknowledge how they encroach upon their assessments, before behaviors can successfully be changed. Although immigration can be one of the greatest stressors that any individual may experience in life, immigration per se, is not necessarily responsible for mental illness or the etiology behind abnormal brain–behavior relationships (c.f., Llorente, 2004).

In summary, the sections above have demonstrated that what are often assumed to be cultural or ethnic differences are truly demographic differences and that confounding factors need to be considered for each child assessed. In addition, it is clear that individual factors do not operate in isolation, but rather exert a collective influence on neuropsychological performance. For example, Harris and Llorente (2005) note that children of immigrants not born in the U.S. are eligible to go to U.S. schools, but are prevented from attending college in most states. This limitation constrains their employment opportunities, which in turn influences housing, healthcare access, and other factors for themselves and their children. They further remark that "These realities conspire to depress the SES" for Hispanic youths as a whole.

Confounds associated with certain demographic characteristics must continue to be scrutinized during the norms acquisition process when assessments are developed and revised. Careful consideration of these factors is also warranted to avoid attributing differences in neuropsychological performance between the majority group and Hispanics to non-existent abnormal brain–behavior relationships rather than differences in demographic and other characteristics (see Georgas, 2003).

Acculturation

Another highly relevant factor when evaluating Hispanic children is acculturation. Acculturation occurs when alien cultural traits and values are adopted by a society on a large scale or when a minority group or an individual adopts, assimilates, or conforms to and integrates the characteristics, norms, and values of another culture (c.f., Berry, 1997; Portes & Rumbaut, 1990). Assimilation is the process by which an individual partially or entirely gives up her cultural or ethnic identity in favor of the traditions, beliefs, and values of the majority culture. Acculturation is bidirectional, and the culture of a society is altered as a result of the acculturation of immigrating populations, such as the changes in American society associated with large-scale migrations of ethnic minority groups (e.g., Hispanics, Italians). Within this context, the terms acculturation and assimilation are being used to described the adoption of values and alien cultural traits by Hispanic children and youths as a result of immigration or residence within the U.S., and in the case of school-age children, upon enrolment and attendance to school in the U.S. regardless of birthplace.

Acculturation can occur in varying degrees along a continuum. For example, some Hispanic children are able to live in communities where little adoption of the U.S. culture is necessary as they are able to use Spanish for all social and community activities (e.g., play) and attend schools where English is only used in the classroom. For others, extensive acculturation may occur where they become proficient in English, participate in activities within the majority culture, and may come to adopt values and beliefs of the majority culture. It is critical to note that many variables influence degree of acculturation including age of the individual, residential area, and school environment, and for older children, employment (Portes & Rumbaut, 1990). Particularly for children who attend U.S. schools, a minimum amount of acculturation is necessary to succeed. Similarly, residence in areas with small Hispanic communities forces children to learn English and conduct a majority of interactions within the majority culture, whereas in areas with large Hispanic communities such as Miami, Florida or Los Angeles, California individuals can choose to acculturate to the extent they perceive it as desirable or necessary. Thus, for some level of acculturation is a choice, but for many the process of acculturation is necessary.

Acculturation is highly relevant to neuropsychology and must be considered when working with Hispanic children. Knowledge of the

patient's level of acculturation is critical because it assists the clinician with important pragmatic decisions regarding the assessment process including language use during the assessment, selection of assessment procedures, and test performance interpretation (Pontón, 2001). Acculturation is particularly relevant for test performance interpretation, and Llorente, Pontón, Taussig, & Satz (1999); Llorente, Taussig, Perez, & Satz (2000). and Llorente (2008) have argued that norms acquired in the U.S. for certain minority groups may not be representative of individuals from their respective country of origin or specific ethnic group if the standardization group differs from the recent immigrant in levels of acculturation. For those Hispanics with greater levels of language proficiency, comparisons with existing neuropsychological norms from mainstream populations are likely to be more valid.

There are several significant aspects of acculturation, beyond age, geography, and general experience with the majority culture, that influence neuropsychological performance. Below, bilingualism and language proficiency are reviewed as they relate to acculturation and neuropsychological performance. This is followed by a brief discussion of education and literacy as they relate to acculturation.

Language

Language proficiency and bilingualism are capable of impacting neuropsychological test performance (Llorente, 2008) and should be ascertained before conducting an assessment. The level of language proficiency and bilingualism in a Hispanic child has significant and direct bearing on the performance discrepancies observed between ethnic minority groups (e.g., Hispanics) and non-minority groups (Harris & Llorente, 2005). Although early studies suggested that bilingualism might represent a cognitive liability, later investigations revealed that such differences were the result of artifact associated with flawed research methodologies including failure to control for demographic characteristic (Adrenal, 2002; Paradis, 1978). It is important to understand that depressed test performance as it relates to language proficiency and bilingualism does not indicate innate brain-based differences, but rather the questionable validity of the inferences derived from neuropsychological tests and norms when used with children who are not proficient in English.

Research has suggested that second language acquisition, particularly English proficiency, takes long periods to reach a deep structural level, and that such mastery should not be confused with the simple ability to use English in social situations (Cummins, 1979). Cummins (1979) differentiated between "surface fluency" (basic interpersonal communication skills) and the more cognitively demanding and complex levels of processing of language proficiency. Cummins (1979, 1984) further argued that in social situations, comprehension is supported by contextual cues (e.g., facial expression), whereas test situations are context reduced. The lack of context and the cognitively demanding circumstances of a testing situation require significant language proficiency in excess of that utilized in basic social communication. Evidence has suggested that those arriving after the age of 6 years required an average of 5–7 years to approach grade norm levels of English proficiency (Cummins 1981). Thus, it is imperative to not assume sufficient fluency of English for test performance-based observed social communication skills.

As suggested above, lack of formal education and the interaction between education, literacy, and culture also are important to consider when understanding level of acculturation. Education cannot be equated with literacy as they are different constructs, and most likely play distinct roles in neuropsychology (Llorente, 2008). For example, literacy does not necessarily imply formal education beyond a few years of schooling. Therefore, education can have independent effects on acculturation and neuropsychological performance that are not associated with illiteracy. The relation between education and neuropsychological performance was discussed above and does not need repeating. However, it is worth noting that beyond the direct influence of education on neuropsychological performance, education is also linked to acculturation.

The extent to which a Hispanic individual is acculturated is largely determined by the amount of education he has received in the U.S. The more U.S. education received the more exposure a minority individual has to language, practices, values, beliefs, and general culture of the majority group, whereas being fully educated in one's

country of origin obviously does not require acculturation. In addition, the type of school influences acculturation to the extent that the student is required to participate in the majority culture. For many urban schools, the large numbers of Hispanics present may allow the individual to minimize the amount of acculturation necessarily, particularly for social interactions. Other educational factors discussed above (e.g., quality of the school, geographic location) also influence acculturation as they determine the content of the education and the local culture of the school. Thus education is a primary factor in level of acculturation.

Whenever possible, acculturation should be assessed formally during the course of neuropsychological examination. Acculturation scales that tap into preferred language use across various domains (e.g., at home, during leisure time, with friends) have been found to predict generational cohort and degree of acculturation (Marin et al., 1987). Several investigators have also developed acculturation measures that take into consideration variables such as timing of immigration, generational differences in migration, ethnic identification, and length of U.S. residence (Franco, 1983; Marin, Sabogal, Marin & Otero-Sabogal, 1984; Suinn, Richard-Figueroa, Lew, & Vigil, 1987).

If formal acculturation assessments are not available, acculturation also can be informally measured by obtaining information about indicators of acculturations. For example, one could inquire about language use in various contexts. In addition, literacy should be assessed with formal reading, reading comprehension, and phonemic processing tests (Llorente, 2008). Education should also be investigated, including information about the level and type of education (e.g., private versus public). In addition, if possible the practitioner should attempt to determine the quality of education (e.g., a poorly ranked inner city school, a highly regarded suburban school, completing high school is a small rural town in their country of origin).

In sum, neuropsychologists serving Hispanic populations should be cognizant of the effects of acculturation on neuropsychological evaluations. They should be aware of the methods available to them to determine the level of acculturation and the language proficiency, literacy, and education of a specific patient prior to the commencement of such an examination. It is also critical to recognize that individual variables such as level of education are capable of infringing on the assessment process, but that the interaction of multiple variables also should be given due weight.

Genetics: A Bridge Eliminating the Chasm Between Culture and Brain

Although the theoretical foundations presented above integrated culture and definitions of childhood, impacting Hispanic children and their assessment, the relationship between the brain and culture or a mediating mechanism capable of tying together these two concepts was not discussed. Hence, another logical question emerges related to the relationship between brain development and culture. In essence, how does the brain assimilate culture? Outside of environmental mechanisms (e.g., vicarious learning), how does culture enters the brain? From our vantage point at the onset of the 21st century, when great advances have emerged in genetics, particularly during the last part of the last century as a result of the Human Genome Project and other investigations, recent studies suggest that genes, and indirectly brains, and culture are closely intertwined. Studies conducted by prominent neuroscientists (c.f., Kohler, Keysers, Alessandra Umiltà, Fogassi, Gallese, & Rizzolatti, 2002) researching brain functions using functional MRI scans of the brain have demonstrated that "mirror neurons," which have been speculated to be responding to an "action," also respond to the "vision of an action," most likely a mechanism of brain function involved in imitation. In another study, they showed that these types of neurons may not respond to the observation and enactment of a behavior or action, but respond in a similar fashion to a noise associated with the action (Kohler, Keysers, Alessandra Umiltà, Fogassi, Gallese, & Rizzolatti, 2002). These findings are relevant as a critical aspect for the transmission of cultural variables including rituals and other cultural components, but most important, the presence of mirror neurons suggest that children may possess brain mechanisms that mediate interactions between biology and the environment, providing an interactive mechanism capable of permitting Hispanic children to assimilate complex cultural variables.

Another recent finding involves language, a domain closely involved with culture and brain functions. In this study, reported by Lai, Fisher, Hurst, Vargha-Khadem, & Monaca (2001), investigators discovered a mutation responsible for a severe type of speech and language disorder. This gene, known as forkhead box P_2, is responsible for modulating other genes and, when abnormal, leads to language and speech disorders, because the gene is necessary for the normal development of speech and grammar, language closely associated with the transmission of culture through narrative, songs, and other factors closely associated with CNS and language development.

In sum, it would appear from these examples that brains, through genetic mechanisms, and culture, through a myriad of mechanisms, including imitation and language, are closely intertwined. Behavior is partially shaped by the environment, particularly in humans, and humans are impacted by their culture. Culture affects brain development through genes and environment, and culture should be given due consideration when assessing Hispanic children.

The Assessment of Hispanic Children: Pragmatic Assessment Issues

Additional considerations when evaluating Hispanics are whether to test in Spanish or English, test translation, and the use of interpreters. The next session focuses on issues of translation, including the quality of test development in Spanish and the use of interpreters. In addition, we discuss the rising need for skilled assessors who are fluent in Spanish.

There are two unethical translation practices that will be discussed here – "live" translations and use of untrained professionals simply because they are bilingual. Occasionally, a test will be translated "live," where a trained bilingual professional translates the test from English to Spanish during the evaluation session. There are numerous problems with this scenario, including questionable validity and reliability, variable quality of translation, and the use of the existing norms for the English version. A less common questionable practice is when an untrained professional is asked to conduct an evaluation because they are bilingual. Both of these scenarios are certainly unethical (c.f., Artioli i Fortuny

et al., 2005, Artioli i Fortuny & Mullaney, 1998; Llorente, 2008) for obvious reasons, and the validity of any results yielded from either of these practices is highly questionable. There is no system to ensure the tests were administered correctly, and moreover the accuracy of test result interpretation is highly compromised. Any type of test translation and adaptation should take place during the test development phase by trained professionals (Artioli i Fortuny et al., 2005), as discussed below.

More recent tests developed for use with Hispanics involved comprehensive adaptations into Spanish, including examination of word usage and frequency of word appearance in the culture for which the test was being adapted (Carroll, Davies, & Richman, 1971), and use of similar populations for standardizations. Modern tests with Spanish versions (e.g., BASC-2, SENAS; WISC-IV in Spanish, WJ-III) have used more advanced statistical procedures to reduce bias (e.g., item analysis) and sampling methods (e.g., over sampling).

Creation and use of assessment instruments for research purposes also warrants mention. Often tests used for research purposes with Hispanic children are translated or created specifically for a study. In these cases the reliability and validity of a test may be unpublished or difficult to ascertain. Furthermore, these studies typically lack the large sample size required to create appropriate testing norms (Artioli i Fortuny et al., 2005). Findings from these studies enter the research literature and can influence future studies and how individual clinicians and researchers view the neuropsychological functioning of Hispanic children and adolescents. Artioli i Fortuny et al. (2005) call upon test developers and funding agencies to take responsibility for ensuring appropriate test construction strategies during the research planning phase. While they also encourage journal editors and reviewers to critically examine any investigations that utilize translated tests, they promote prevention of errors during the funding phase as the most appropriate form of intervention (Artioli i Fortuny et al., 2005).

Tests that are translated or created for Hispanics should adhere to a rigorous process of ensuring they are appropriate for the intended population. This includes translation, back translation, and vetting by several professionals who are fluent in Spanish. Moreover, there

should be thorough examination of local dialects, word usage, and frequency to be sure the content is appropriate. Many times a direct translation would not make sense and creation of a comparable Spanish testing language would be more appropriate. There are many examples in the literature of test material reading illogically in Spanish (Artioli i Fortuny et al., 2005, Artioli i Fortuny & Mullaney, 1998). The same strict scientific standards that are applied to English language tests should be applied to Spanish versions.

Although highly discouraged, the use of interpreters sometimes occurs and a discussion of its suitability is warranted. In addition to ethical considerations (APA, 2002), there are several factors worth addressing related to the use of interpreters during the course of neuropsychological evaluations. Every effort should be made to avoid the use of interpreters as it can be difficult to effectively and correctly translate and interpret the intricate language and verbal abstraction involved in neuropsychological assessment. The literature suggests that even an accurate translation of test protocols and other components of an evaluation may result in the loss of subtleties and connotational nuances of speech (Artioli i Fortuny et al., 2005; Artioli i Fortuny & Mullaney, 1998; Cervantes & Acosta, 1992), leading to diminished validity and reliability. In fact, some researchers and clinicians argue that simply changing the manner in which a test is administered without re-standardizing the tool to meet the ethnic, cultural, and linguistic requirements of the patient challenges the validity and reliability of test results (Melendez, 2001).

The use of interpreters during forensic neuropsychological evaluations should especially be avoided (DeJongh, 1991; LaCalle, 1987; Llorente, 2008). In these cases, important legal dispositions may have significant impact on the client, his family, his community, and in some instances, the establishments of critical legal precedents. Thus, the validity of the testing situation must be optimized rather than jeopardized with the use of interpreters. From a legal standpoint, the forensic psychology and cross-cultural literatures indicate that evaluations conducted through an interpreter may be invalid and must be avoided, not to mention unethical and easily challenged in a court of law (LaCalle, 1987). Additionally, there are specific ethical

principles associated with the appropriate conduct of neuropsychologists when acting in the forensic arena (APA, 2002), as well as legal issues to consider concerning admissibility of test results on the basis of their validity and reliability in such proceedings (c.f., Daubert *v.* Merrell Dow Pharmaceuticals [92–102], 509 US 579 [1993]).

While the use of interpreters is strongly discouraged, the use of family members as interpreters is highly inappropriate and strongly advised against (Llorente, 2008). It goes without saying that family members are untrained and are not aware of the ethical guidelines of translation or interpretation (Byrd, Sanchez & Manly, 2005). Beyond that, the use of family members as interpreters may lead to bias throughout the course of the assessment (Dodd, 1983). It might be argued that those close to the patient add the benefit of familiarity, they have a genuine interest in the patient, are easily accessible, and serve the client as a buffer related to anxiety-provoking and other assessment-related effects. However, any benefits from using a family member are far outweighed by the potential risks and problems that may arise (Blau, 1998; Kayser, 1993). One risk is misinterpretation, both intentional and unintentional. For example, if a Hispanic child is brought in for an assessment after a head injury that occurred during an abusive episode, the parent who inflicted the injury may not be objective in his report. Similarly, if a Hispanic adult relative with borderline intellect brings her niece for a feedback session, she may have difficulty objectively and comprehensively providing information that she perceives may be painful to her niece (Llorente, 2008).

In the event that the use of an interpreter is unavoidable, standards should be in place to maximize the quality of the evaluation. High-quality interpretative services with trained professional interpreters should be secured. Those with experience and training in the mental health profession are preferred as they are more likely to understand the context of the testing situation (Llorente, 2008). Family members should not be included in or relied upon for the interpretive process (Dodd, 1983).

In sum, neuropsychological assessments of Hispanics whose primary or preferred language is Spanish should be conducted in Spanish by a Spanish-speaking expert cognizant of the client's ethnic and cultural background with enough

language fluency to be able to conduct a competent examination. The complexity of such evaluations requires that they be conducted in the language in which the client can best comprehend the testing questions and most fluently communicate their responses. Assessment is typically conducted for educational, legal, medical, or other reasons where the outcomes influence some kind of determination (e.g., level of placement in school) with significant personal and social consequences for the client (Llorente, 2008). Thus, every effort should be made to ensure the validity of the assessment and to maximize the child's performance. The clinician must determine the appropriate language for the examinee, taking into consideration their dominant language, literacy in each language, and educational experiences in each language. If it is determined that assessment in Spanish is most appropriate, it is the responsibility of the clinician, if they are not competent to conduct the evaluation in Spanish, to conduct an exhaustive search for a fluent neuropsychologist (c.f., Brickman, Cabo & Manly, 2006).

Cultural Competency

Fortunately, there has been an increase in the number of individuals who are able to conduct neuropsychological assessments in Spanish, and the use of interpreters can often be avoided. Efforts have been made to increase cultural competency among educators, researchers, and practitioners, including awareness, language skills, standardized training and assessment procedures, and methods and instrumentation to address the growing need for neuropsychological services in Spanish. For example, as noted above the *Standards for Educational and Psychological Testing* (1999) established by the American Psychological Association (APA), the American Educational Research Association (AERA), and the National Council on Measurement in Education (NCME) has put greater emphasis on ensuring the fairness in assessments of individuals with diverse ethnic and racial backgrounds. The American Psychological Association (APA, 1991, 1985, 2003) has established the *Guidelines for Providers of Psychological Services to Ethnic, Linguistic, and Culturally Diverse Populations*, urging consultations, supervision, and continuing education to increase cultural competency in clinical practice.

Wong, Strickland, Fletcher-Janzen, Ardila, & Reynolds (2000) and others (Pontón & León-Carrión, 2001; van Gorp, Myers, & Drake, 2000) have recommended educators and practitioners be more sensitive in identifying and understanding cultural, linguistic, and ethnic differences through careful interviews, education, and the clinician's own awareness of individuals' biases. Furthermore, position papers and guidelines from major organizations and conferences within the discipline have also emerged addressing the importance of such factors. For example, educational and training guidelines require that neuropsychology "attempt to actively involve (enroll, recruit) individuals from diverse backgrounds at all levels of education and training" (Hannay et al., 1998).

Artioli i Fortuny and Mullaney (1997) propose that the assessment of monolingual Hispanics should be conducted by someone with an advanced degree in Spanish, a practice that does not occur in the U.S. or abroad during the course of most neuropsychological evaluations. They further point out that securing a fluent Spanish-speaking evaluator should be a logical step in the assessment process and decision-making process of competency, but this fails to occur at a rate much greater than one might suspect, including judicial proceedings (Artioli i Fortuny & Mullaney, 1997, 1998). Because an ethical course of action has not been followed by large number of practitioners, particularly in the U.S., Pedersen and Marsella (1982) have equated the current status of the field as a crisis (c.f., Hall, 1997).

This begs the question, should graduate and training programs include foreign language proficiency as a requirement or consider adding language proficiency as an optional subspecialty? Adding such components to graduate and training programs, with formal supervised training, has several benefits. First, it ensures a level of competency that the current informal system does not. Specific education around the issues of testing in Spanish (e.g., understanding language nuances, cultural sensitivity), beyond simple language training, would maximize the likelihood that validity and reliability are maintained during evaluations with Hispanics. Secondly, it would increase the number of competent fluent evaluators. Those who are

already in the field and speak Spanish would likely participate in such a program, but beyond that those who normally would not make the effort to become fluent may do so if such a program were readily available and encouraged. Knowing the Hispanic population is large and ever increasing, those with minimal Spanish skills may be attracted to programs that enable them to work proficiently with Hispanic patients.

The current informal system often results in assessments being performed by individuals who are assumed to be more fluent than they are. Often Hispanics or individuals with Hispanic Surnames are hired to conduct testing in Spanish with the assumption that they are competent to do so (Artioli i Fortuny et al., 2005). Being of Hispanic descent does not guarantee fluency in Spanish. Even for those who are socially fluent, the assumption that they can adequately translate neuropsychological material is often erroneous as this is much more complex process than social interactions. Individuals often overestimate their own abilities assuming they can accurately translate on a level far greater than they actually can (Artioli i Fortuny & Mullaney, 1998). A formal system would allow for a process to ensure a minimum level of language competency, whereas the current system relies on self-report and often erroneous assumptions. Furthermore, a formal system will secure adequate supervision by establishing standards for training. There has been speculation that the level of supervision given for those performing tests in Spanish is often variable or of poor quality (Artioli i Fortuny & Mullaney, 1998, Brickman et al., 2006)

Of course, creating such a program does not guarantee the production of qualified evaluators. As noted above, it takes more than being proficient in a language to truly understand a language beyond a surface or conversational level. In addition, language fluency is not static. It requires constant usage and practice to be maintained (Artioli i Fortuny & Mullaney, 1998). Nonetheless, creating such programs would benefit the field by increasing the number of Spanish-speaking testers available and securing the validity and reliability of more evaluations with Hispanics. Regardless of formal or informal training, all neuropsychologists should have training in issues related to race, culture, and ethnicity and how they relate to neuropsychological performance (Artioli i Fortuny & Mullaney, 1998; Wong, 2006)

Multicultural Diagnostic Considerations During Neuropsychological Assessment

The culture of a Hispanic child is also relevant to understanding neuropsychiatric disorders, as cultural context is inextricably intertwined with their expression and diagnoses (c.f., Bird, 1996; Mezzich & Lewis-Fernandez, 1997; Rhodes, Kayser, & Hess, 2000). In this regard, and despite its cursory approach, the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM IV, Appendix I) acknowledges the impact of culture on abnormal brain-driven affect, behavior, and cognition (APA, 1994, 2000).

This issue is important because the expression of neuropsychopathology in two different Hispanic children, or in the same youth at distinct points in time, may vary depending on whether the patient(s) attribute their problems to "*nervios*," a common cultural description of psychological problems, versus attribution to a known medical condition found in his or her family (Guarnaccia, Lewis-Fernandez, and Marano, 2003). Regardless of the fact that neuropsychopathology in two children may have the same neurobiological etiology (e.g., clinical depression consequent to diminished 5-HT availability in brain), their individual expressions and diagnoses may be different depending on the cultural context. This includes interpretation and assump- tions related to the symptoms (c.f., Simpson, Mohr, & Redman, 2000).

Again, as previously mentioned, many factors such as language and education are relevant to neuropsychological diagnoses. It is paramount to recognize that the phenomenology of a construct, such as depression in childhood, may be altered in its assessment or interpretation by the examiner due to a lack of language proficiency (Perez-Foster, 2001). As noted before, ethical considerations should prevail in the decision to assess or not to assess a Hispanic client, seek consultation, or supervision (APA, 2002). It is left to the clinician to determine whether their degree of professional competency is appropriate to evaluate and diagnose a specific Hispanic child in a specific language (c.f., Llorente, 2008). The intent of this section is to emphasize that

factors associated with neuropsychological evaluations also are highly relevant when diagnosing Hispanic children (c.f., Holm, Dodd, Stow, & Pert, 1999).

Conclusions

Neuropsychology faces the specific challenge of being able to develop comprehensive theoretical models and applied methods that are capable of incorporating culture into integrated explanations of complex brain–behavior relationships. Intricacies associated with the neuropsychological assessment of Hispanic pediatric populations is an area that also demands greater attention, as individuals of Hispanic descent are the fastest growing minority members in the U.S. (U.S. Census Bureau, 2001). The cultural, ethnic, and linguistic heterogeneity of Hispanic children also poses unique challenges and opportunities for neuropsychology and its applications as it strives to develop such comprehensive explanatory frameworks and assessment procedures capable of accounting for such heterogeneity. It is also important to recognize that the inclusion of culture in childhood within neuropsychology, and psychology in general, and more general, in cognitive mechanisms within developmental frameworks, is not the result of recent discoveries or scholarly thought, but rather, that they had their earlier and nascent formulations in the work of the environmentalists (e.g., Luria, Vygotsky, Wartofski). Given our recent advances in genetics, it would appear as if brain and culture are interwoven by biological developmental mechanisms, and children may actually possess "culture" genes that mediate such an interaction between biology and the environment, providing an interactive mechanism capable of permitting Hispanic children to assimilate complex cultural variables into their biological makeup, particularly the central nervous system, aside from nurturing mechanisms.

As indicated in this chapter, it is not easy to simply label "Hispanics" using pan-ethnic definitions and comprehend the variability and heterogeneity observed within such pediatric populations. Obviously, their beliefs, cultural values, practices, rituals, and other factors at the core of their self-identity fundamentally vary substantially. Furthermore, the distribution of the Hispanic pediatric population in the U.S. is not uniform, and there are regional idiosyncrasies as well as significant geographical affinity for specific groups of Hispanic youths. Large variability also can be found in the acculturation levels of U.S.-born versus foreign-born Hispanic children, and within these subgroups, including their linguistic skills. For these reasons, it is not sufficient, for example, simply to conduct an assessment in Spanish, to use norms based on a "Hispanic" sample, or to assume certain cultural similarities, in order to work competently with heterogenic Hispanic populations. In addition, race, culture, and ethnicity are often confused. Race reflects common descent and physical characteristics, while culture reflects a set of social beliefs and behaviors (Ardila, Rosselli, & Puente, 1994). Although culture and ethnicity can be considered to be similar because they may be learned and flexible (Smedley, 1993), culture, as noted above, can be perceived as a complex manifestation or expression or symbolic elements that define a group of individuals or society from which an individual may adopt specific characteristics which over time are learned and lead to their own, unique ethnic identity (c.f., Smedley, 1993). Whereas an individual adopts several characteristics capable of leading to his unique ethnic identity, there can be many ethnicities in a culture.

In addition, it is hoped that this chapter has conveyed that a large numbers of factors including acculturation, educational attainment and quality of education, literacy, SES, and others impact neuropsychological performance in Hispanic children. According to relatively recent U.S. Census Bureau Survey, Hispanic children tend to drop out of school at a rate greater, almost three times more, than Anglo- or European Americans and African-Americans. Hispanic children also are starting school later than average relative to other groups (Shorris, 1992). As noted by Harris and Llorente (2005), "As many neuropsychological test scores are correlated with education level," it is important to be cognizant of differences in educational opportunities, quality of education, educational experiences, and attitude toward education among Hispanics. Moreover, in the process of establishing normative data for neuropsychological instruments, people with 10–12 years of education and below are usually combined into a homogeneous educational group. However, reliable differences due to years of educational

attainment have been found in the neuropsychological performance among people who attained less than 10 years of education, while little differences have been found in the upper end (Ardila, Rosselli, & Puente, 1994). These factors lead to increased chance of errors in the inferences derived from neuropsychological assessment with Hispanic children and adolescents with low educational levels. Neuropsychological profiles of Hispanic children with limited education, for example, could mimic educated, brain-damaged persons (Ardila et al., 1989).

Individual differences in linguistic skills acquisition, fluency, and mastery as well as the differences in the nature of English and Spanish as languages also create significant challenges. Although a value judgment is not being made, many Hispanics in the U.S. use both Spanish and English in varied degrees of proficiency and frequency, and oftentimes combine these two languages to create what many have termed Spanglish (c.f., Cruz & Teck, 1998), in some instances with positive and/or negative consequences due their inability to truly master either language. Significant differences also exist in the structure of these two languages further complicating the assessment process. Oral and written proficiencies, language preferences, and the patterns of use depend on multiple factors, such as the age, language learning sequence, reasons behind learning these two or more languages, method of acquisition, early versus late exposure to the languages, degree of cultural identification, and individual differences in verbal abilities (c.f., Ardila, 1998). These and other factors influence children's performance not only on tasks measuring language development and abilities, but also on tasks that are intended to measure other abilities (e.g., attention, memory, processing speed, etc.) but often requiring verbal mediation and processing.

It is clear that language may present a barrier for neuropsychological test administration. How could neuropsychologists accurately assess the brain–behavior relationship of bilingual patients? As discussed above, there are considerable limitations to conducting neuropsychological evaluations with non-English speakers. For example, there is a misunderstanding that only a translation of the text is needed (Echemendía, Harris, Congett, Diaz, & Puente, 1997). Translating individual test items during evaluation procedures is not adequate, as it deviates from standardized procedure, and the accuracy and appropriateness of the translations would likely vary significantly among examiners. Translations must be conducted in a standardized fashion, and appropriate norms must be established. Brislin (1983) emphasized the use of back translation to ensure the comparability of the translated instrument. The changes in the nature and cognitive equivalency of the translated tests must be considered because of the differences in language and culture. For example, an object that is easy to name in one language may require significantly more sophisticated proficiency in another language, or a word may contain a greater number of syllables in one language than the other. The International Test Commission has also provided guidelines for the adaptation of tests (Muñiz & Hambleton, 1996). The guidelines not only address issues associated with translations, but also discuss the selection of appropriate tests, consideration of potential biases, appropriate scoring methods, appropriate communication of findings, revision of tests, etc. Even when using validated translated instruments, the test results should be interpreted with caution, and within an appropriate cultural context. Individuals assessing these patients should be competent to conduct such evaluations. It is also important to be aware of the unique needs of Spanish–English bilinguals living in the U.S. For many, using either Spanish or English testing materials and norms can underestimate their cognitive abilities (Puente & Ardila, 2000). To reduce bilingualism effects in testing, it would be ideal to have special norms for Spanish–English bilinguals and a bilingual examiner, who can provide instructions and understand answers in either language or any mixture of both languages. If this is not feasible, their results could perhaps be interpreted using both norms (English and Spanish versions) and both presented in the report.

Modern neuropsychological procedures have used more complex methods of tests development using operating-receiver curves or item analytic procedures creating standards for test development far more advanced and sophisticated than a simple adaptation, or worst, a translation of a test. If a patient's primary language is unfamiliar, it is best to refer the patient to a neuropsychologist who can competently perform an evaluation in that language. Only as a last resort and if necessary, an interpreter

should be used for clinical interviews and consultations. In such cases, clinicians must select interpreters carefully, and rapport should be established between a neuropsychologist and an interpreter prior to meetings with patients. It is important that interpreters are familiar with neuropsychological principles and terms as well as different Hispanic cultures and regional languages. Still, it is crucial that clinicians are aware of the increased possibility of miscommunications and misunderstandings. Having an interpreter in a room may change the comfort level and dynamics during meetings, and the subtleties in communications, such as non- verbal cues and complex language responses, can be lost easily through interpretations. It is also pivotal to note the use of interpreters during the course of neuropsychological assessment was not advocated or recommended in this volume, and such a practice should be avoided at all costs, particularly in forensic proceedings, and the use of family members as interpreters completely discarded.

In conclusion, significant attention toward ethical considerations should be given to scientific models and applied methods in neuropsychology addressing cross-cultural issues related to Hispanic children.

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III

Techniques of Intervention

19

Neurocognitive Interventions for Childhood and Adolescent Disorders: A Transactional Model

PHYLLIS ANNE TEETER

Interest in the neuropsychological basis of childhood and adolescent disorders continues to grow (Gaddes & Edgell, 1994; Obrzut & Hynd, 1991; Rourke, 1991), and neurocognitive models for designing effective interventions for treating various disorders show promise (Teeter Ellison & Semrud-Clikeman, 2007). Technological innovations in computed tomography (CT), magnetic resonance imaging (MRI), single-photon emission computer tomography (SPECT), positron emission tomography (PET), regional cerebral blood flow (rCBF) (Yudofsky & Hales, 1992), and functional magnetic resonance imaging (FMRI) (Binder, personal communication) have transformed our understanding of numerous neuropsychiatric disorders (e.g., attention-deficit hyperactivity disorder) and learning disabilities (e.g., dyslexia).

Recent technological advances have had a profound impact on our understanding of childhood disorders. Lewis Judd, M.D., director of the National Institute of Mental Health, stated that "95% of what we know about the brain as it relates to behavior has been discovered in the past 5 years" (Yudofsky & Hales, 1992, p. xxii). The fact that this statement was made in 1988 serves to highlight the dramatic scientific advances that have been made in our understanding of brain-related disorders. Further, study of recombinant DNA and complex genetic models of "at-risk" populations has also been important in this effort, stimulating a focus on the biochemistry of neuropsychological functioning (Rourke, 1991). Neurochemical models of human behavior may even begin to overshadow structural, neuroanatomical paradigms in the future (Rourke, 1991). The extent to which these findings advance the science of childhood psychopathology and learning disorders and improve intervention planning is under investigation.

Some argue that advances in neuropsychology have not furthered our knowledge about remedial and treatment programs for brain-related disorders, whereas others indicate that this information can be used as a basis for developing paradigms or models for intervention for childhood disorders (Gaddes & Edgell, 1994; Rourke, 1991, 1994; Teeter Ellison & Semrud-Clikeman, 2007). Several paradigms have been designed incorporating information about the neuropsychological functioning of children into intervention programs. This chapter

explores a number of intervention models and develops a rationale for using a transactional model for understanding and treating learning and neuropsychiatric disorders of childhood. Information about the child's neuropsychological, cognitive, academic, and psychosocial status forms the basis for designing integrated intervention and treatment plans for children and adolescents with brain-related and neurodevelopmental disorders (Teeter Ellison & Semrud- Clikeman, 2007).

The purpose of this chapter is to review current neuropsychological, neurocognitive, and neurobehavioral paradigms for designing interventions for children with various disorders, including phonological reading disabilities (PRD), nonverbal learning disabilities (NLD), and attention-deficit hyperactivity disorders (ADHD). Four models for intervention are discussed in this chapter: (1) the Multistage Neuropsychological Assessment–Intervention Model (Teeter Ellison & Semrud-Clikeman 2007); (2) the developmental neuropsychological remediation/habilitation framework designed by Rourke (1994); (3) rehabilitation procedures designed by Reitan and Wolfson (1992); and (4) the phenomenological model articulated by Levine (1993, 1994).

Techniques for addressing the cognitive, academic psychosocial, and attentional problems associated with selected disorders of childhood and adolescence are presented. Medications for treating neuropsychiatric disorders of childhood, medication monitoring, consultation with educational staff, and integrated intervention protocols are briefly discussed. Finally, guidelines for collaboration are addressed, including ideas for developing home–school–physician partnerships for treating childhood and adolescent neuropsychiatric, neurodevelopmental, and brain-related disorders.

Theoretical Orientations for the Study of Childhood Disorders

In the past, dichotomies such as "medical" versus "behavioral," "within-child" versus "environmental," and "neuropsychological" versus "psychoeducational" have served as stimuli for controversy and great debate over which orientation or theoretical approach is most relevant (Teeter Ellison & Semrud-Clikeman, 1995).

Further, some have adopted one approach exclusively in an attempt to diagnose and treat childhood disorders (Teeter Ellison & Semrud-Clikeman, 2007). Research adopting only one paradigm often oversimplifies the complex interaction of genetic, neurocognitive, psychosocial, and environmental factors that can affect various childhood disorders (Gaddes & Edgell, 1994), including traumatic brain injury (TBI) (Goldstein & Levin, 1990), ADHD (Barkley, 1990; Weiss & Hechtman, 1993), NLD (Rourke, 1994), and PRD (Teeter Ellison & Semrud-Clikeman, 2007). With this shortcoming in mind, Teeter Ellison and Semrud-Clikeman (1995, 2007) developed a transactional paradigm in an effort to assist in the diagnosis and design of intervention programs for children and adolescents with various learning and neuropsychiatric disorders.

Teeter Ellison and Semrud-Clikeman (1995) argue that multiple perspectives advance the science of childhood psychopathology and aid in our understanding of cognitive–intellectual development. Neuropsychological functioning should be considered with other cognitive, behavioral, and psychosocial factors for the assessment and intervention of children and adolescents. Diagnostic accuracy and intervention efficacy can also be explored within a developmental framework in a transactional neuropsychological paradigm. Definitions and a brief discussion of the features of a transactional paradigm follow.

Neuropsychological Component

Neuropsychology involves the study of the brain–behavior relationships, with the assumption that there is a causal relationship between brain functioning and behavior (Obrzut & Hynd, 1991). Teeter Ellison and Semrud-Clikeman (2007) outline the advantages of incorporating neuropsychology in the study of childhood and adolescent disorders:

> (1) it is a well established science with knowledge relevant to childhood disorders (Gaddes & Edgell, 1994); (2) there is a growing body of evidence suggesting that "behavior and neurology are inseparable" (Hynd & Willis, 1988, p. 5); (3) it provides a means for studying the long-term sequelae of head injury in children (Goldstein & Levin, 1990); (4) it provides a means for investigating abnormalities in brain function that increase the risk for psychiatric disorders in children

(Tramontana & Hooper, 1989); and, (5) it provides a means for early prediction and treatment of reading disabilities (Felton & Brown, 1991). (p. 7)

While it is virtually indisputable that all behavior is by mediated the brain (Gaddes & Edgell, 1994), the nature of this relationship is complex and our present knowledge is incomplete, especially in children. However, Gaddes and Edgell (1994) argue that child neuropsychology should not be abandoned because what we do know about the developing brain can be effectively utilized by knowledgeable clinicians. A number of behavioral psychologists have stated that child neuropsychology diverts attention from behavioral techniques with documented treatment validity (Gresham & Gansle, 1992; Reschly & Gresham, 1989), whereas clinical child neuropsychologists consider a broader framework for childhood disorders that includes the interaction of psychosocial, environmental, neurocognitive, biomedical, and neurochemical aspects of behaviors (Teeter Ellison & Semrud-Clikeman, 2007). The relationships between physiological and psychological systems are of interest; and, within a transactional neuropsychological model, environmental and behavioral factors must also be explored.

Although there have been advances in our understanding of the brain–behavior relations for many childhood disorders, child neuropsychology should not be exclusively employed when assessing and treating children (Gaddes & Edgell, 1994). Further, Levine (1994) argues that even though learning problems may result from neurodevelopmental dysfunctions, including gaps, maturational delays, or differences in how the child's brain is developing, he prefers a model that describes, accurately recognizes, and understands observable phenomena related to learning problems. Behavioral, psychosocial, and cognitive factors are thus important variables affecting both the diagnosis and treatment of children with brain-related disorders.

Behavioral Component

Behavioral approaches typically focus on describing and modifying the antecedents and consequences of behavior. Behavioral assessment and intervention techniques have been found to be valid and effective methods for many disorders of childhood (Kratochwill & Bergan, 1990; Mash & Terdal, 1988; Shapiro, 1989; Shinn, 1989). Behavioral models often incorporate an ecological as well as behavioral analysis, to describe how environmental factors contribute to and maintain learning difficulties in children (Shapiro, 1989). Others incorporate techniques of functional analysis for assessing, treating, and determining treatment efficacy for behavioral, psychosocial, and learning disorders (Kratochwill & Plunge, 1992). However, behavioral approaches can be effectively integrated into neurocognitive models, and child clinical assessment and intervention can be enhanced by this integration.

In other integrated paradigms, Horton and Puente (1986) employed behavioral assessment and intervention techniques with neuropsychological procedures for treating children and adolescents with brain-related disorders. On the surface it may appear that behavioral and neuropsychological paradigms are at odds with one another; however, Teeter Ellison and Semrud-Clikeman (2007) argue that important information can be gleaned about a child when these two approaches are integrated. Child neuropsychologists typically consider the influence of environmental factors when investigating numerous problems including malnutrition and brain development in young children (Cravioto & Arrieta, 1983); changes in brain morphology after intensive behavioral interventions (Hynd, 1992); environmental factors (e.g., school, home, and peer/family interactions) and their effect on recovery of function following brain impairment (Rourke, Bakker, Fisk, & Strang, 1983); the effects of nonneurological factors (e.g., preaccident behavioral, temperamental, and psychosocial problems and family reactions) when treating psychiatric disorders resulting from TBI (Rutter, Chadwick, & Shaffer, 1983); and applied behavioral intervention strategies for brain-injured children (Gray & Dean, 1989). Rourke (1989) also incorporates an integrated model for investigating the neuropsychological, social–emotional, cognitive, adaptational, behavioral, and academic factors for diagnosing and treating children and adolescents with NLD.

Horton and Puente (1986) advocated for the development of behavioral neuropsychology as a subspeciality within clinical neuropsychology. Behavioral neuropsychology refers to "the application of behavior therapy techniques to

problems of organically impaired individuals while using a neuropsychological assessment and intervention perspective" (Horton, 1979, p. 20). Although more research beyond single-subject designs is needed, Horton and Puente (1986) indicate that behavioral interventions have been helpful for disorders resulting from brain injury and learning disabilities.

Psychosocial and cognitive factors are also included in the transactional neuropsychological paradigm developed by Teeter Ellison and Semrud-Clikeman (2007) for the assessment and treatment model for childhood and adolescent disorders. The extent to which children with brain-related disorders evidence cognitive, psychological, and social problems will be briefly explored.

Psychosocial and Cognitive Components

Many neuropsychiatric and learning disorders of childhood and adolescence (e.g., ADHD and learning disabilities) have associated psychosocial and cognitive deficits (Teeter Ellison & Semrud-Clikeman, 2007). Teeter Ellison and Semrud-Clikeman (2007) suggest that these factors have a bidirectional relationship, such that cognitive and psychosocial characteristics interact with and can exacerbate disorders with a neuropsychological basis. Further, information about the brain–behavior relationship derived from neuropsychological models can be helpful for understanding the associated features (i.e., behavioral, cognitive, and psychosocial deficits) of ADHD and dyslexia (Semrud-Clikeman & Hynd, 1993; Teeter Ellison & Semrud-Clikeman, 1995). Conversely, cognitive abilities (i.e., premorbid intelligence) and psychosocial adjustment affect recovery of functions in children and adolescents sustaining TBI (Bigler, 1990). Thus, the influence of brain function on psychosocial and cognitive functions is transactional in nature and is intricately linked—each influencing and affecting the outcome of treatment programs and intervention plans.

Neurobiological and psychosocial functionings are intricately linked in children with ADHD. Barkley (1990) argues that ADHD is a disorder of dysregulation, which affects inhibition and self-regulation, most likely resulting from impairment in executive functions mediated by the frontal cortex. An inability to inhibit or to regulate one's own behavior can have significant negative consequences in social situations. A number of children with ADHD are described as noncompliant and rebellious (Johnston & Pelham, 1986), and rigid, domineering, irritating, and annoying in social situations (Milich & Landau, 1989). ADHD children with these characteristics are frequently rejected by their peers (Hynd et al., 1991), particularly when they are also aggressive (Milich & Landau, 1989). A transactional model thus provides a framework for investigating whether psychosocial outcomes are related to the primary features of impulsivity, distractibility, and disinhibition, which have been found to have a neurobiological basis (Teeter Ellison & Semrud-Clikeman, 1995), or whether these problems are related to secondary personality (i.e., aggression) or environmental factors (i.e., modeling and/or reinforcement history).

Associated cognitive and academic difficulties have also been found in children and adolescents with ADHD, including: school failure (Barkley, 1990) and academic underachievement and learning disabilities (Epstein, Shaywitz, Shaywitz, & Woolston, 1992; Lambert & Sandoval, 1980; Semrud-Clikeman et al., 1992). Further, only a small number of adolescents with ADHD ever finish college (Barkley, 1990). Declines in academic achievement, verbal IQ, and overall psychosocial adjustment may result from difficulties in self-regulation and response inhibition (Barkley, 1990). Thus, the manner in which neurochemical and/or neuropsychological functioning interact with social, psychological, and behavioral functioning in children with ADHD can be more fully investigated within a transactional model (Teeter Ellison & Semrud-Clikeman, 1995).

Children with learning disabilities (LD) also demonstrate psychosocial and cognitive deficits that may be associated with underlying dysfunctional neural mechanisms (Teeter Ellison & Semrud-Clikeman, 2007). For example, LD children with low verbal skills and relatively good visual–spatial abilities demonstrate high rates of depression (Nussbaum, Bigler, & Koch, 1986). Personality function appears related to the neuropsychological assets/deficits observed in this subgroup of LD children (Nussbaum et al., 1986). Further, children with NLD also tend to have high suicide rates (Rourke, Young, & Leenaars, 1989). The neuropsychological assets and deficits (i.e., right hemisphere dysfunction with

intact left hemisphere functions) may result in deficient social interaction skills, inappropriate verbal interactions, and poor social adjustment observed in children with NLD (Rourke, 1989).

By gathering data from different paradigms, the clinician can utilize an integrated model for the diagnosis and treatment of children and adolescents (Teeter Ellison & Semrud-Clikeman, 2007). Thus, when using a transactional neuropsychological paradigm, the clinician would conduct a thorough assessment addressing the pattern of neurocognitive strengths and weaknesses as the first step and then plan an integrated intervention program for addressing specific problems. By developing interventions within this model, the interaction of environmental–behavioral, psychosocial, and cognitive factors with neuropsychological functioning would result in a more complete clinical study of the child. These various factors are considered when approaching the task of child clinical assessment and intervention planning.

A Transactional Neuropsychological Paradigm for the Assessment and Treatment of Childhood Disorders

Neuropsychological assessment and intervention approaches are strengthened by a careful study of the relationship between brain function and the cognitive, psychosocial, and behavioral characteristics displayed by children with various disorders (Teeter Ellison & Semrud-Clikeman, 1995, 2007). (See Figure 1.) A transactional model provides a framework for investigating how intact versus impaired neuropsychological systems interact with and limit cognitive–intellectual and psychosocial adjustment in children and adolescents (Teeter Ellison & Semrud-Clikeman, 2007).
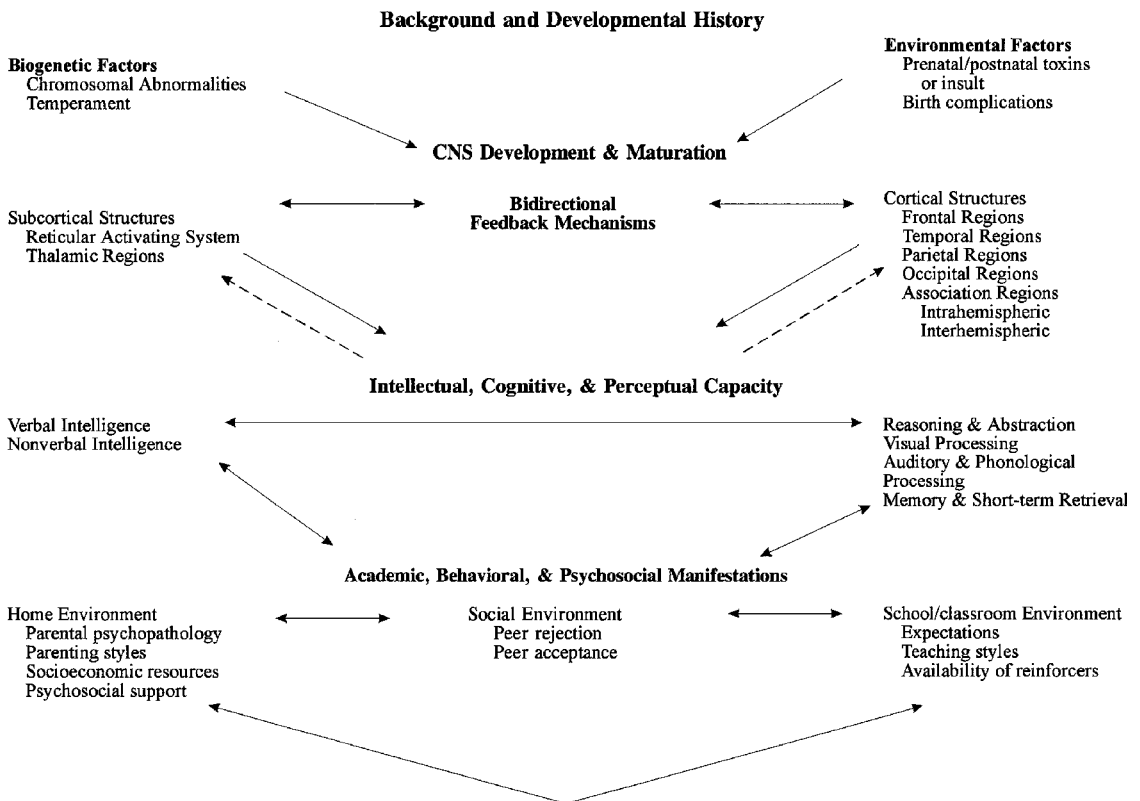
FIGURE 1. Transactional paradigm for understanding neurodevelopmental and neuropsychiatric disorders of childhood. (Adapted with permission from Teeter Ellison and Semrud-Clikeman, 2007).

Development and maturation of the brain is influenced by biogenetic as well as environmental factors (e.g., prenatal and postnatal toxins or insults). Subcortical and cortical regions have a bidirectional influence on neural functional systems impacting on the intellectual, reasoning, memory, attentional, and perceptual capacity of the child (Teeter Ellison & Semrud-Clikeman, 2007). Various functional systems in the brain interact with and influence the expression of the behavioral, psychosocial, and cognitive manifestations of a number of childhood disorders (Teeter Ellison & Semrud-Clikeman, 2007). Social, family, and school environments also interact and can either facilitate or inhibit the development of compensatory and/or coping skills in children with disorders.

A dynamic interaction among the biogenetic, neuropsychological, environmental, cognitive, and psychosocial systems is an essential feature of this transactional model (Teeter Ellison & Semrud-Clikeman, 2007). Although abnormal neural development can be detrimental, the course and nature of neuropsychiatric and learning disorders are not necessarily inevitable. Effective psychosocial and educational interventions, with modifications in the environment (i.e., home, school, and social environment), can reduce the negative effects of many neuropsychological or biogenetically based disorders (Teeter Ellison & Semrud-Clikeman, 2007). Further, pharmacotherapy may also be part of treatment programs for some disorders of childhood (e.g., ADHD, depression). Thus, dynamic relationships exist among these variables and should be considered in the clinical assessment and treatment of childhood disorders.

Models Linking Assessment to Interventions

A thorough understanding of the underlying features of a disorder precedes effective intervention; thus, a link between assessment and intervention is critical. Four models are described in the following sections, including (1) the multistage neuropsychological model developed by Teeter Ellison and Semrud-Clikeman (2007); (2) the developmental remediation model developed by Rourke (1994); (3) the REHABIT model designed by Reitan and Wolfson (1992); and (4) the Observable Phenomenon Model developed by Levine (1993, 1994). Table 1

summarizes stages of assessment and intervention planning and provides a description of the major features of each model.

Each model assumes that comprehensive clinical evaluation precedes intervention plans. A phenomenological model designed by Levine (1993, 1994) is also described. Although Levine's model does not specifically identify the neurodevelopmental mechanisms underlying learning difficulties, it is helpful for determining various observable phenomena (e.g., weak attention controls, reduced remembering, chronic misunderstanding) that affect a child's learning capacity. Levine (1993, 1994) also provides detailed intervention strategies to address various learning problems. These four neuropsychological/neurobehavioral models are discussed in more detail below.

Multistage Neuropsychological Model

Teeter (1992) first presented a multistage neuropsychological model (MNM) for linking neuropsychological assessment to intervention plans. Teeter Ellison and Semrud-Clikeman (2007) later expanded the model described below. The MNM uses structured behavioral–observational assessment techniques in the first stage; and if the child's problems do not improve after systematic behavioral interventions, then more extensive cognitive and psychosocial, neuropsychological, and/or neuroradiological evaluation and interventions are considered (Teeter Ellison & Semrud-Clikeman, 2007). Intervention strategies are developed and implemented after careful assessment and diagnosis at each level of the model. Intervention strategies described in later sections of this chapter can be selected to address the child's specific problems.

Effective interventions may reduce the need for further, more intensive evaluation (e.g., neuropsychological) of the child, particularly when disorders are not severe or chronic in nature (e.g., reading delays versus dyslexia). This requires ongoing and systematic evaluation to determine whether the initial diagnosis and description of the disorder is accurate and whether the specific intervention plan is effective. Thus, a working diagnostic hypothesis seems reasonable in early assessment–intervention stages. However, for more serious childhood disorders including TBI, CNS diseases, and seizure activity, the clinician may proceed

TABLE 1. Models for Neuropsychological Remediation and Rehabilitation: Linking Assessment to Interventions[a]

Models	Stages	Description
MNM (Teeter & Semrud-Clikeman, 1995)[b]	Stage 1: problem identification	Behavioral assessment
	Stage 2: behavioral-based intervention	Self-management Contingency management Learning strategies Peer tutoring
	Stage 3: cognitive child study	Comprehensive cognitive, academic, psychosocial assessment
	Stage 4: cognitive-based intervention	Pattern analysis Phonological awareness Activating schemata Organizational strategies
	Stage 5: neuropsychological assessment	Comprehensive neurocognitive assessment
	Stage 6: integrated neuropsychological intervention	Compensatory skills psychopharmacology
	Stage 7: neurological and neuroradiological assessment	Neurological, CT, MRI
	Stage 8: medical–neurological rehabilitation	Rehabilitation and medical management
DNRR (Rourke, 1994)[c]	Step 1: neuropsychological assets/deficits, academic and psychosocial assessment	Neuropsychological profile Ecologically based evaluation
	Step 2: demands of environment	Behavioral, academic, and psychosocial challenges within contextual framework
	Step 3: short and long term	Formulate short- and long-range predictions Which deficits will decrease? Specific treatment strategies
	Step 4: "ideal" remedial plans	"Ideal" plans Monitoring and modification
	Step 5: availability of resources	Therapeutic goals Prognosis Reduce redundant services
	Step 6: realistic remedial plan	Compare differences between Steps 4 and 5
	Step 7: ongoing assessment and intervention	
REHABIT (Reitan & Wolfson, 1992)[d]	Tract A: verbal–language	Materials to increase expressive–receptive skills
	Tract B: abstraction and reasoning	Materials to increase analysis, organization
	Tract C: general reasoning	Materials for general reasoning
	Tract D: visual–spatial	Visual–spatial manipulation sequential skills
	Tract E: visual–spatial and manipulation	
Observable Phenomena (Levine, 1993, 1994)	Educational evaluation	Psychoeducational testing, classroom observation and error analysis, identify "breakdown" points, history and interview
	Behavioral and affective evaluation	Assess affective-mood patterns, questionnaires, interviews, personality tests, observation
	Cognitive and developmental	Intelligence tests, neurodevelopmental tests, questionnaires of present and past neurodevelopmental functions and styles

TABLE 1. (*Continued*).

Models	Stages	Description
	Environmental assessment	Interview to identify factors in home, consider culture, peer, and community issues
	Medical assessment	Review medical history, physical examination, neurological examination

[a]Adapted with permission from Teeter Ellison and Semrud-Clikeman (2007).
[b]Multistage neuropsychological model (Teeter Ellison & Semrud-Clikeman, 2007).
[c]Developmental Neuropsychological Remediation/Rehabilitation Model (Rourke, 1994).
[d]Reitan Evaluation of Hemispheric Abilities and Brain Improvement Training (Reitan & Wolfson, 1992).

to neuropsychological evaluation and neuro-diagnostic examination immediately (Teeter Ellison & Semrud-Clikeman, 2007).

The eight-stage assessment–intervention model requires expertise from various educational, clinical, and medical professionals. School psychologists and educational professionals typically conduct Stages 1 through 4 assessment–intervention, whereas Stages 5 and 6 are usually conducted by clinical child neuropsychologists outside the school setting (Teeter Ellison & Semrud-Clikeman, 2007). Pediatric neurologists, neuroradiologists, and pediatricians are usually involved in Stage 7 assessment; and interventions appropriate for Stage 8 may require short-term hospitalization.

Systematic monitoring and modification of intervention plans are required at each stage of the MNM, and accurate diagnosis or problem identification is critical for designing specific intervention strategies (Teeter Ellison & Semrud-Clikeman, 2007). Periodic evaluation of the treatment plan is essential. This reduces the possibility of continuing to utilize strategies that are not effective. Thus, current assessment of the child's progress is part of effective intervention. (See Teeter Ellison & Semrud-Clikeman, 2007, for an in-depth discussion of the MNM.)

In summary, the MNM provides guidelines for linking multiple stages of evaluation into intervention plans. Rourke (1994) has also developed a multistage neuropsychological remediation model for children with LD. This model is briefly reviewed next.

Developmental Neuropsychological Remediation/Rehabilitation Model

The Developmental Neuropsychological Remediation/Rehabilitation Model (DNRR) was designed to address problems experienced by children with LD (Rourke, 1994). However, Rourke's DNRR paradigm provides a useful framework for designing remedial/rehabilitation plans for children with other brain-related childhood disorders (Teeter Ellison & Semrud-Clikeman, 2007). The DNRR was first described by Rourke et al. (1983) and Rourke, Fisk, and Strang (1986).

The DNRR is composed of seven major steps (Rourke, 1994). In Step 1, the clinician assesses the interactions among neuropsychological assets/deficits, LD, academic learning, and psychosocial functioning. Neuropsychological assessment is conducted within an ecological framework. Developmental considerations are investigated at this stage. Step 2 includes assessment of the demands of the environment. The functional status of the child (i.e., neuropsychological) is related to developmental challenges (i.e., behavioral, academic, and psychosocial) and the ecological context of the child (e.g., classroom, social, cultural) (Rourke, 1994).

In Step 3 short- and long-term behavioral predictions are generated. A determination of which deficits are expected to decrease without intervention and which strategies will be implemented for the other deficits is made. Resources (e.g., family, psychosocial, community) are also assessed during this step. Step 4 involves determining "ideal" short- and long-term remedial plans using information gathered in earlier steps. Ongoing monitoring and modification of the intervention plan is suggested on an "as needed" basis. In Step 5 the availability of remedial resources is assessed, and therapeutic goals, length of intervention, and prognosis of outcome are specified. Clear and specific recommendations at this step may reduce overlap and costs incurred when integrating efforts of the neuropsychologist with those initiated by school

professionals. Step 6 requires development of a realistic remedial plan by comparing recommendations developed in Steps 4 and 5. Finally, in Step 7 ongoing neuropsychological assessment is used to modify or clarify intervention plans (Rourke, 1994).

In summary, the DNRR offers an integrated paradigm for the assessment and remediation of LD in children. Further, the DNRR provides a framework for identifying critical factors that should be considered when designing interventions for other disorders as well. Reitan has also described remediation procedures for children with brain-related disorders.

The Reitan Evaluation of Hemispheric Abilities and Brain Improvement Training (REHABIT)

REHABIT was developed for rehabilitating brain-related deficits (Reitan, 1980). REHABIT includes assessment with the Halstead–Reitan test batteries, training with Halstead–Reitan test items, and rehabilitation with special REHABIT materials (Teeter, 1989). The Halstead–Reitan neuropsychological test batteries are used in both the assessment and remediation stages of this program. Neuropsychological evaluations are conducted, and interventions are designed to remediate the child's weaknesses, including abstract, concept formation, and reasoning deficits (Teeter Ellison & Semrud-Clikeman, 2007).

The REHABIT program includes tracts for training verbal–language deficits, abstract reasoning and logical deficits, visual–spatial problems, and right–left hemisphere deficits (Reitan & Wolfson, 1992). The child's neuropsychological profile is used to design individualized remedial programs (Teeter Ellison & Semrud-Clikeman, 2007). Difficulty levels can be manipulated, and systematic evaluation is important to monitor the child's progress throughout the remediation program.

More recently, Levine has described a model for addressing learning difficulties in children. The model is reviewed next.

Phenomenological Model for Educational Interventions

Levine (1993, 1994) developed a model based on observing and describing phenomena

that are known to interfere with learning and the academic performance of children. The model utilizes neurodevelopmental theory and acknowledges that both the child's brain and his/her environment (i.e., school and home) change over time "in terms of the level and complexity of demands placed on children" (Levine, 1994, p. 2). Levine (1993, 1994) describes 26 observable phenomena that affect a child's performance in the classroom. This model places an emphasis on "observable phenomena," that is, phenomena that are clearly observable when one watches the child perform. For example, it is possible to observe that a child has trouble remembering information when studying for a test or that the child has trouble organizing and planning study time. These phenomena are thus fully described and form the basis for determining intervention strategies.

Although many "observable phenomena" may be neurodevelopmental in nature, resulting from neurochemical/metabolic abnormalities, abnormal or uneven brain growth patterns, or synaptic abnormalities in specific brain regions, not all phenomena result from neurodevelopmental factors (Levine, 1994). Other environmental (e.g., exposure, teaching) or psychosocial factors may account for performance problems. Rather than stressing an investigation into the causes of learning problems, Levine emphasizes recognition and intervention of learning problem(s). Thus, evaluation includes assessment of educational, behavioral/affective, cognitive development, environmental, and medical factors that might affect performance. Levine (1993, 1994) advocates for a descriptive versus a labeling approach when evaluating children. Child assessment may have several levels: parent/teacher informal observation and discussion; consultation with a clinician; multidisciplinary evaluation; and/or further specialized neuropsychological assessment.

Once a thorough and comprehensive evaluation has been conducted, the educator and/or clinician can develop a detailed intervention program that specifically addresses the needs of the child. Levine (1993, 1994) describes components of a management plan, involving both parents and teachers, as (1) demystification; (2) bypass strategies; (3) direct remediation of dysfunctions; (4) direct remediation of skill areas; (5) medical interventions; (6) protection from

psychological harm/humiliation and develop-
ment of pride; and (7) long-term monitoring
and child advocacy. These components are
briefly described as follows.

Demystification is a process whereby edu-
cators and/or clinicians help the child to under-
stand the nature of his/her problems. By helping
the child to understand his/her strengths and
weaknesses more accurately, fears, frustrations,
and negative self-attributions can be modified.
Bypass strategies are employed in the classroom
to circumvent a child's problems (Levine, 1994).
These strategies may include modifying the
amount of time given to take tests; reducing the
amount of work that is required; reducing
the complexity of information; changing the
production/output format (i.e., oral versus
examination); changing the evaluation/grading
system; and/or using aids (e.g., calculators or
word processors). (See Levine, 1994, for more
details.)

Direct instruction of observable phenom-
ena is also incorporated into intervention plans.
Levine (1993, 1994) provides numerous strate-
gies for attentional, language, memory, produc-
tion, reasoning, motor, social, and specific
academic functions. Techniques that strengthen
weaknesses and enhance academic skills are
recommended. Medications may also be part of
some intervention plans, and when adminis-
tered, children should be advised of the implica-
tions, benefits, and potential side effects. Finally,
Levine (1994) describes ways to preserve the
child's pride in himself/herself, to protect the
child from humiliation, and to facilitate the
emergence of healthy self-esteem. Specific inter-
vention strategies are delivered within a colla-
borative process, where home, school, and
physicians work together for the benefit of the
child. A long-term commitment is necessary,
with ongoing monitoring and advocacy by pro-
fessionals and parents.

The models described above provide a
structure for the assessment, intervention,
and management of various childhood disor-
ders. In the following sections, selected
neuropsychological, neurocognitive, and neu-
robehavioral approaches for intervention are
described. Aspects of these approaches can be
incorporated into assessment–intervention
plans for children with various brain-related
disorders.

Neuropsychological Orientations for Remediation

Neuropsychological/neurobehavioral inter-
vention orientations are often classified in one of
three ways depending on whether the focus is on
improving the child's neurocognitive deficits,
accessing the child's neurocognitive strengths/
assets, or a combination approach addressing
both neurocognitive assets and deficits (Teeter,
1989). These three intervention orientations will
be briefly reviewed.

Attacking Neurocognitive Deficits

Psycholinguistic training, sensory integra-
tion, perceptual-motor training, and modality
training were historically used to strengthen the
child's weaknesses (Teeter Ellison & Semrud-
Clikeman, 2007). In general, little improvement
in the child's academic performance has been
demonstrated with these techniques; however,
modest success has been observed in some chil-
dren with specific problems/disorders. Specifi-
cally, Kavale (1990) reported that children with
reading disabilities do improve when given expli-
cit instruction in verbal comprehension and
auditory-perceptual skills. Training in phonolo-
gical awareness has also proven effective for
children with phonological core deficits (Cun-
ningham, 1990). So, in some instances remedia-
tion of a child's weakness may be warranted;
however, these methods typically utilize
approaches where specific processes are taught
within the context of reading instruction, and
not in isolation.

Teaching to Neurocognitive Strengths

Intervention programs have been designed
to access the child's unique neurocognitive
strengths and to avoid his/her deficits/weak-
nesses (Teeter Ellison & Semrud-Clikeman,
2007). Strength approaches make sense for chil-
dren with motivational problems (Rourke et al.,
1983). Gaddes and Edgell (1994) also cite cases
where teaching to the child's intact brain systems
might be helpful. For example, interventions
accessing intact right hemisphere systems can
be successful in improving reading skills in chil-
dren with bilateral cerebral dysfunction,

cognitive retardation, and/or language deficits (Teeter Ellison & Semrud-Clikeman, 2007).

Combined Treatment Programs

Intervention approaches that address the child's unique neuropsychological assets and deficits and are primarily compensatory in nature have been advocated by Rourke (1994). Rourke indicates that the age of the child may also help clinicians to determine which orientation should be instituted first. For example, young children with developmental disorders involving the white matter (see discussion on NLD) may improve with intervention methods that attack the child's deficits (Teeter Ellison & Semrud-Clikeman, 2007). Early intervention in these instances focuses on stimulating intact cortical regions and facilitating gray matter connections (Teeter Ellison & Semrud-Clikeman, 2007). Conversely, older children with persistent disorders (e.g., NLD) may benefit from compensatory strategies.

Levine (1994) describes a combined intervention model that includes both bypass strategies and methods for improving cognitive processing, attentional, language, and poor output and adaptational dysfunctions in children. Bypass strategies "circumvent or work around a student's dysfunctions...allow the child to continue to acquire skill, knowledge, and a sense of competency" and are "techniques that must be part of the management of every child with significant learning problems" (Levine, 1994, p. 260). However, Levine also describes numerous strategies for remediating or improving specific deficiencies as well. A combined intervention approach seems to provide mechanisms for increasing motivation, self-esteem, and engagement in the learning process, while decreasing the chances of the child falling precipitously below grade level, thus decreasing the probability of school drop-out in later grades.

There is a continued need for conducting research on specific strategies/programs to demonstrate the efficacy of specific intervention approaches. The following sections describe techniques that have been found useful for remediating cognitive–intellectual, academic, and psychosocial problems. The clinician may select specific strategies depending on the child's particular pattern of neurocognitive strengths and weaknesses. First, a number of common childhood disorders are briefly discussed.

Disorders of Childhood: Implications for Remediation

Selected childhood disorders will be briefly reviewed including reading disabilities, NLD, ADD, pervasive developmental delays, seizure disorders, TBI, and childhood brain tumors. Implications for interventions are discussed. Each disorder typically has primary deficits/characteristics (e.g., cognitive, attentional, memory), as well as associated deficits (e.g., academic and psychosocial) that need to be considered when designing intervention programs.

The following discussion highlights major features of each disorder that may need to be targeted for intervention. In later sections, other techniques (e.g., self-management, social skills) will be reviewed.

Reading Disabilities: Phonological Core Deficits

Numerous studies show that phonological awareness deficits are a primary cause of reading deficits (Liberman & Shankweiler, 1985; Mann, 1986; Stanovich, 1986; Wagner & Torgesen, 1987). Phonological awareness is the ability to use the phonemic segments of speech (Tunmer & Rohl, 1991), including the awareness and use of the sound structure of language (Mattingly, 1972). Children with phonological awareness deficits may also demonstrate other language-related deficiencies that appear related to phoneme awareness deficits, including difficulties with speech perception when listening; naming and vocabulary ability; and short-term memory involving phonetic representations in linguistic tasks (Mann, 1991).

Children with phonological reading disorders (PRD) exhibit a variety of disorders that may be associated with their linguistic problems (Teeter Ellison & Semrud-Clikeman, 2007). Various studies have shown that linguistic and phonological coding problems are linked to genetic (Olson, Fosberg, Wise, & Rack, 1994) as well as developmental anomalies in the left temporal regions (Semrud-Clikeman, Hynd, Novey, & Eliopulos, 1991). Semrud-Clikeman et al. found that slight morphological variations in the left temporal region were related to other

language-related deficits including word attack, comprehension, and naming abilities. Table 2 summarizes selected research findings on children with PRD.

Although not every child with PRD demonstrates all of the associated features presented, evidence of an interaction among specific neuropsychological, cognitive, perceptual, memory,

TABLE 2. A Summary of Specific Deficits Associated with Reading Disabilities: Phonological Core Deficits (PRD)[a,b]

Biogenetic factors	Environmental factors/prenatal/postnatal
40% variance in word recognition is genetic	Orthographic deficits related to exposure to print and learning opportunities
$h2\,g = 0.62$ phonology/reading deficits	Development of speech and vocabulary related to language acquisition and reading
$h2\,g = 0.22$ orthographic/reading deficits	Growth spurt in phonemic awareness at 6 years related to reading efforts
	Despite strong heritability of phonological awareness, deficits can be modified

Temperament	Birth complications
No known correlates	No known correlates

CNS factors
  White matter dysfunction
  Left temporal anomalies
  Larger plana in right hemisphere
  Symmetrical R/L temporal lobes
  Symmetrical or reversed parieto-occipital regions
  Abnormal asymmetry (R > L) in prefrontal regions
  Abnormal asymmetry in parietal regions

Neuropsychological factors
  Rapid naming
  Abnormal hemispheric lateralization
  Attentional activation of RH interferes with LH verbal processing
  Attentional control mechanisms between hemispheres
  Phonemic hearing, segmenting, and blending

Intellectual	Perceptual	Memory	Attentional
Verbal weaknesses	Phonemic	Digit span	Strong comorbidity of reading problems and ADHD
Vocabulary knowledge	Speech	Speech sounds	Attention to phonemes
Verbal associations		Word series	
Word similarities		Letter strings	
Verbal fluency		Phonetic strategies	
Receptive language			
Expressive language			
Verbal IQ			
Comprehension			

Academic/behavioral	Psychosocial	Family
Motivational problems	Research is sparse	Research is sparse on PRD
Chronic reading problems	RD in general show internalized disorders (i.e., depression)	Prenatal and postnatal risk factors related to general learning and behavioral problems
Disengaged in learning		"Disorganized" and/or poverty, environment more important with age
Spends less time reading		
Reading and spelling		

[a]Adapted with permission from Teeter Ellison and Semrud-Clikeman (2007).
[b]PRD, phonological reading disabilities; L and LH, left hemisphere; R and RH, right hemisphere; RD, reading disabilities.

academic, and psychosocial problems that accompany reading disabilities is accumulating (Teeter Ellison & Semrud-Clikeman, 2007).

Intervention Strategies

Remedial techniques that specifically address phonological core deficits are effective for students who are at risk for reading problems and for children with PRD (Byrne & Fielding-Barnsley, 1993; Cunningham, 1990; Iversen & Tunmer, 1993; Molter, 1993; Vellutino & Scanlon, 1987). Reading abilities are significantly increased when phonological awareness training is paired with metacognitive techniques, particularly when contextualized within the child's reading curriculum (Cunningham, 1990).

Motivational and psychosocial disturbances that often occur in children with chronic academic failure may be alleviated with early identification and remediation (Wise & Olson, 1991). Scruggs and Wong (1990) and Wong (1991) provide extensive guidelines for implementing strategy instruction, mnemonic instruction, social skills enhancement, problem-solving processes, and self-recording skills. Thus, intervention techniques for children with PRD should specifically include phonological awareness training within contextualized reading instruction to increase reading skills. Intervention plans may also include other strategy instruction (e.g., mnemonic, social), based on the child's individual profile.

The extent to which children with PRD require interventions across cognitive, as well as psychosocial, domains depends on the individual child. However, these features should be considered when designing treatment programs.

Nonverbal Learning Disabilities

Children with NLD have relatively intact language, reading, and spelling skills and show the most difficulty in the areas of mathematics reasoning and calculation, problem-solving, and basic social–emotional problems (Rourke, 1989). Table 3 presents an overview of the associated features of NLD. The complex set of problems associated with NLD appear related to a pattern of right hemisphere weaknesses (e.g., tactile and visual perception, concept formation, novelty, and complex psychomotor skills), with relative strengths in left hemisphere

activities (e.g., phonological skills, verbal abilities, reading, spelling, verbatim memory) (Rourke, 1994). Rourke advocates intervention programs that target both neurocognitive strengths and weaknesses.

Intervention Strategies

Extensive remedial techniques to improve the academic and psychosocial problems experienced by children with NLD are available (Rourke, 1989; Rourke et al., 1983; Rourke, Del Dotto, Rourke, & Casey, 1990; Rourke & Fuerst, 1991). According to Rourke (1994), children with the unique pattern of right hemisphere weaknesses and left hemisphere strengths display a tendency to engage in perseverative or stereotypic responding because they overrely on information they have previously learned (Teeter Ellison & Semrud-Clikeman, 2007). Children with NLD often have trouble developing problem-solving strategies and alternative solutions when strategies are ineffective. Typically children with NLD develop verbal compensatory skills, and they actively avoid novel situations. Further, children with NLD do not actively explore their environment because of tactile deficits and delays in early psychomotor skills.

For young children, intensive physiotherapy with sensorimotor integration is necessary to "stimulate the functioning of remaining white matter to the maximum" (Rourke, 1989, p. 130). Compensatory strategies, relying on verbal–language skills, may be considered if intervention is not effective or if it occurs later in childhood. Intervention should focus on academic as well as psychosocial deficits and should involve the parent. Techniques for increasing social awareness, teaching problem-solving strategies, encouraging generalization of strategies, and improving verbal skills are often included in the intervention plan for children with NLD (Teeter Ellison & Semrud-Clikeman, 2007). Concrete teaching aids, self-evaluation techniques, and life skills are also used. Methods for improving visual–spatial weaknesses, interpreting competing stimuli, teaching nonverbal behaviors, and providing structure for exploration are described in detail by Rourke (1989).

Further, Rourke (1989) describes techniques for increasing problem-solving skills, generalization of strategies and concepts, appropriate

TABLE 3. A Summary of Specific Deficits Associated with Nonverbal Learning Disabilities[a]

Biogenetic factors	Environmental factors/prenatal/postnatal
No known correlates	NLD appear at or soon after birth
	Neurodevelopmental disorder or may be caused by traumatic injury
	Few details on environmental impact

Temperament	Birth complications
No known correlates	No known correlates

CNS factors
  White matter dysfunction
  Intermodal integration (callosal fibers)
  Right hemisphere involvement
Neuropsychological factors
  Bilateral tactile deficits (pronounced on left side)
  Visual–spatial–organizational deficits
  Complex psychomotor deficits
  Oral–motor apraxia
  Concept formation and problem-solving deficits

Intellectual	Perceptual	Memory	Attentional
Concept formation	Visual discrimination	Tactile	Tactile
Strategy generation	Visual detail	Nonverbal	Visual attention
Hypothesis testing	Visual relation	Complex information	Attends to simple, repetitive verbal material
Cause–effect relations			
Little speech prosody			
Formal operational thought			

Academic/behavioral	Psychosocial		Family
Reading comprehension	Adapting		Research is sparse
Mechanical arithmetic	Overreliance on rote behaviors		
Mathematical reasoning	Externalized disorders (i.e., conduct, acting out)		
Science	Social perception and judgment		
	Social interactions skills		
	Social withdrawal or isolation		
	May develop internalized disorders (e.g., depression, anxiety)		

[a]Adapted with permission from Teeter Ellison and Semrud-Clikeman (2007).

nonverbal skills, accurate self-evaluation, and life skills—preparing for adult life. Because of the very serious psychosocial limitations inherent in the NLD syndrome, Rourke stresses the need for social problem-solving skills, social awareness, structured peer interactions, and parent involvement in the treatment plan. Techniques are also developed to increase the child's exploratory behaviors and interactions with the environment. Rourke's (1989) methods emphasize the need for a step-by-step problem-solving approach, where feedback is provided in a supportive manner. Children are encouraged to "lead with their strong suit" and are also taught more appropriate ways to utilize their relative strengths (i.e., verbal–language skills).

Despite positive findings using single-subject investigations, Rourke (1994) indicates that more systematic research is needed on interventions developed from neuropsychological findings. Studies should specifically address whether interventions should be deficit driven or compensatory in nature. The age of the child also seems to be a critical factor when deciding whether interventions should be deficit driven or compensatory in nature. When deficits result from early white matter disease or dysfunction, Rourke (1994) suggests that remediation might focus on attacking the deficit. However, if the child's problems are identified later in childhood or if NLD persists, compensatory strategies might be the best approach (Teeter Ellison & Semrud-Clikeman, 2007).

Attention-Deficit Hyperactivity Disorder

Children may be identified with primarily hyperactive–impulsive problems, attentional problems, or a combination of the two according to DSM-IV criteria (American Psychiatric Association, 1994). The manner in which these characteristics affect academic, behavioral, and psychosocial adjustment has been thoroughly described in numerous publications (see Barkley, 1990; Weiss & Hechtman, 1993). Table 4 summarizes major features and associated characteristics of ADHD.

ADHD appears to have strong genetic linkages (Weiss & Hechtman, 1993), and evidence suggests CNS variation in frontal lobe, corpus callosal, and right hemisphere regions (Teeter & Semrud-Clikeman, 1995). The extent to which

TABLE 4. A Summary of Specific Deficits Associated with Attention-Deficit Hyperactivity Disorder[a]

Biogenetic factors
  59–84% MZ
  29–33% DZ
  Independent genetic code differs from reading
  Familial ADD transmitted by single gene
  Single gene has not been isolated, probably dopamine receptor
    gene

Environmental factors/prenatal/postnatal
  Multifactorial, polygenetic, cultural, and
    environmental transmission seems unlikely
  Poverty, overcrowding, chaotic family style,
    pollution, food additives account for very little
    variance
  Common environmental factors: 0–30% variance

Temperament
  Genetic linkage
  Activity level
  Distractibility
  Psychomotor activity
  Attentional problems, school competence, and behavioral
    problems

Birth complications
  No known correlates

CNS factors
  Underactivated frontal lobe
  Bilaterally smaller anterior cortex
  Reversed asymmetry of anterior cortex (right < left)
  Reversed asymmetry of caudate nucleus (left < right)
  Reduced metabolic activity in right caudate region
  Smaller left caudate nucleus
  Right hemisphere deficits (disinhibition of left
    hemisphere)
  Left hemisphere underactivation (Zametkin)
  Genu (corpus callosum) smaller
  Rostrum and rostral bodies are smaller

Intellectual	Perceptual	Memory	Attentional
Range of IQ		Low verbal	Sustained
Low coding		Less efficient	Selective
			Alternating/divided

Reasoning
  Response inhibition
  Sustained effort
  Complex problem-solving
  Executive functions
  Organization skills

Academic/behavioral	Psychosocial	Family
Motivational problems	Rejected	Disorder exacerbates
Underachievers	Ignored	Parental psychopathology related to CD/ADHD
Comorbid LD	Comorbid INT/EXT	
Work completion	Comorbid aggression	

[a]Adapted with permission from Teeter Ellison and Semrud-Clikeman (2007).

these biogenetic factors relate to associated deficits, including executive functions, disinhibition, attentional controls, and self-regulation, is of interest to neuropsychologists (Teeter Ellison & Semrud-Clikeman, 2007).

This model suggests the need to develop strategies addressing broad domains of academic, behavioral, psychosocial, and family systems interventions.

Intervention Strategies

Intervention programs are typically multifaceted in nature and may include pharmacotherapy, behavioral management, cognitive/academic strategies, social skills building, and parenting and/or family interventions (Barkley, 1990; Teeter Ellison & Semrud-Clikeman, 1995). Even when medication is administered, children with ADHD usually require other academic, behavioral, and psychosocial interventions. Studies suggest that attention training (Semrud-Clikeman, 1995), peer tutoring (DuPaul & Stoner, 1994), and contingency management (Barkley, 1990) can be effective intervention strategies for children with ADHD.

It is important to note that a majority of children with ADHD also have comorbid disorders (e.g., oppositional defiant, conduct disorder, LD). When comorbid disorders are present, these problems also need to be addressed in the intervention program. (For detailed information on more specific strategies for children with ADHD, see Barkley, 1990; Teeter, 1998; Teeter Ellison & Semrud-Clikeman, 1995; and Weiss & Hechtman, 1993.)

Pervasive Developmental Disorders

Autism and pervasive developmental disorders are characterized by deficits in social reciprocity, communication, and cognition (Cook & Leventhal, 1992).

Intervention Strategies

Children with autism often respond to interventions that are similar to strategies used with cognitively delayed children (Teeter Ellison & Semrud-Clikeman, 2007). Behavioral techniques for reducing stereotypic behaviors and improving communication skills are recommended (Cook & Leventhal, 1992). Fluoxetine and clomipramine are often prescribed to control anxiety and compulsive behaviors in children with autism (Teeter Ellison & Semrud-Clikeman, 2007). Although behavioral intervention techniques are effective, the long-term prognosis for children with autism remains guarded.

Seizure Disorders

Epilepsy is defined as a chronic disturbance in brain functions that affects perceptions, movements, consciousness, and other behaviors; the term *seizures* refers to individual episodes (Bennett & Krein, 1989). Numerous associated features may be present in children with seizure disorders including cognitive disabilities (Cook & Leventhal, 1992); psychiatric disturbance (Cook & Leventhal, 1992); academic problems (Pazzaglia & Frank-Pazzaglia, 1976); and social stress related to chronic medical problems (Neppe, 1985). Thus, intervention planning incorporates medical as well as psychosocial techniques.

Intervention Strategies

Anticonvulsant medications (i.e., phenobarbital) are frequently prescribed for children with nonfebrile seizure disorders (Cook & Leventhal, 1992) and require careful monitoring. Side effects (e.g., sedation) may decrease academic performance (Cook & Leventhal, 1992) or increase hyperactivity (Vining, Mellits, Dorsen, et al., 1987) and depression (Brent, Crumrine, Varma, Allan, & Allman, 1987).

In children with intractable seizures, surgical removal of involved brain tissue may be necessary (Teeter Ellison & Semrud-Clikeman, 2007). In these rare cases, studies demonstrate the resiliency of the developing brain following surgery, wherein intact brain regions compensate for damaged regions. No significant decline in IQ scores was found in children who had undergone surgical removal of the dominant temporal lobes, including the hippocampus and amygdala (Meyer, Marsh, Laws, & Sharbrough, 1986). In another case, Smith, Walker, and Myers (1988) reported that a 6-year-old with perinatal epileptogenic seizures that spread across the hemispheres made remarkable recovery following surgical removal of the right hemisphere. Postsurgical test scores showed average to low-average intellectual abilities. The degree

to which cognitive development is affected depends on a number of factors, including the age of the child and the location of the lesion. However, once intact brain regions are freed from the abnormal influences of the lesioned regions, intellectual and cognitive abilities may improve following surgery (Teeter Ellison & Semrud-Clikeman, 2007).

Traumatic Brain Injury

TBI occurs frequently in childhood (Berg, 1986), because children are at risk for sustaining head injuries from accidents (Hynd & Willis, 1988; Spreen, Tupper, Risser, Tuokko, & Edgell, 1984). (See Bigler, 1990, for an in-depth discussion of the nature and associated features of TBI.) The site of injury, the severity of injury, and the age of the child impact on the types of problems that accompany TBI in children. (See Teeter Ellison & Semrud-Clikeman, 2007, for an in-depth review of recovery of functions following TBI.) Interventions should be designed to address the specific assets and deficits individual children display following injury.

Intervention Strategies

Child characteristics (i.e., cognitive and personality), family resources, marital stability, and socioeconomic status impact on the child's recovery following TBI (Teeter Ellison & Semrud-Clikeman, 2007). Developmental history and an assessment of the child's environment must be carefully considered when designing intervention plans (Goldstein & Levin, 1990). Preexisting disorders (e.g., impulsivity–hyperactivity, attentional deficits, social interaction problems, and academic failure) may be ascertained from teacher reports and a review of educational history (Craft, Shaw, & Cartlidge, 1972). Further, postinjury deficits may reflect premorbid problems, rather than the brain trauma itself (Rutter, 1981). Children with premorbid disorders, including impulsivity and hyperactivity, may have higher injury rates as a result of risk-taking behaviors sometimes associated with these problems (Rutter, 1981).

Guidelines for Educational Services for Students with Traumatic Brain Injury were developed by the Virginia Department of Education (1992), which include intervention plans for developing home–school partnerships. The needs of families and children are addressed in this program (Teeter Ellison & Semrud-Clikeman, 2007). Assessments, placement decisions, individual educational plans (IEPs) or 504 plans, and strategies for improving the behavioral and academic problems in the classroom should be included in the intervention plan.

Brain Tumors

Brain tumors comprise approximately 20% of malignancies of childhood and are most frequently diagnosed in children between the ages of 3 and 9 years (Carpentieri & Mulhern, 1993). Treatment protocols often include whole-brain radiation, chemotherapy, and/or surgical interventions in the medical treatment protocol of children with brain tumors. About 50–60% of children remain cancer free after 5 years (Carpentieri & Mulhern, 1993). Intervention typically addresses medical, education, and psychosocial domains.

Intervention Strategies

Medical procedures, including surgery, radiation, and chemotherapy, are often employed to reduce the size of the child's brain tumor (Price, Goetz, & Lovell, 1992). Cognitive and neuropsychological symptoms may be relieved once cranial pressure is reduced (Teeter Ellison & Semrud-Clikeman, 2007). Although medical techniques can produce positive outcomes, pharmacotherapy, psychosocial (i.e., individual and family therapy), and academic support are usually initiated after the child's medical status is stabilized (Teeter Ellison & Semrud-Clikeman, 2007).

Depending on the nature and type of brain-related disorder, children may require interventions for a variety of problems, including academic, executive functions, and psychosocial adjustment. The following selected strategies and intervention approaches may be employed in individual cases following a comprehensive assessment of the child's assets/deficits. Careful, ongoing monitoring for the effectiveness of these strategies must be included in the intervention plan. Selective classroom and behavioral management techniques are also described.

Interventions for Associated Cognitive–Academic, Psychosocial, Executive Function, and Attentional Problems

Selected strategies for addressing cognitive, academic, executive control, and attentional problems may be utilized for children with various brain-related disorders depending on their individual needs. Careful neuropsychological evaluation, with measures of cognitive, academic, and social–emotional functioning, helps to isolate the child's specific intervention needs. Also, a review of specific techniques that have been previously employed by the teacher or parent should be investigated to determine which strategies have been effective and which have been less successful in individual cases. For those strategies that have proven ineffective, it is important to make sure that the techniques were properly employed and were not prematurely abandoned.

Strategies for Cognitive and Academic Difficulties

Techniques for improving reading, written language, and arithmetic disorders are often employed in remediation programs for children. Strategies for teaching study/organizational skills and social skills training are also sometimes needed. Table 5 reviews selected strategies for addressing these problems.

Depending on the child's pattern of neuropsychological, cognitive, and psychosocial functioning, the clinician may want to consider the specific strategies outlined. Table 5 is not offered as a "one size fits all" approach, because specific techniques should be carefully selected based on results from a comprehensive evaluation and a clear understanding of the child's neuropsychological assets and deficits and his/her developmental, cognitive, academic, and social–emotional needs (Teeter Ellison & Semrud-Clikeman, 2007). Prior to initiating an intervention program, the clinician is advised to conduct a review of the child's educational records and interview the child's teacher. These efforts may reduce the possibility of repeating techniques or strategies that may have failed in the past. Further, it may

inform the clinician of pitfalls or behaviors to look out for when attempting certain techniques. Careful observation of the child's performance is also recommended. (See Levine, 1993, 1994, for details on conducting neurobehavioral observations and ratings for children with learning problems.)

Strategies for Reading Disorders

A number of techniques for addressing reading disorders are described, including phonemic awareness training, comprehension strategies, synthesized computer speech, and whole language methods. (See Teeter Ellison & Semrud-Clikeman, 2007, for a more in-depth review of these techniques.)

Phonological Awareness Training

Phonological coding deficits have been shown to be the strongest predictor of reading disabilities (Wise & Olson, 1991). The following studies report positive effects for teaching children phonemic awareness skills, including segmenting, blending, and analyzing sounds (Fox & Routh, 1976; Tunmer & Nesdale, 1985; Williams, 1980); preventing phonological awareness deficits in preschool children (Byrne & Fielding-Barnsley, 1993; Lundberg, Frost, & Petersen, 1988); using common sound elements in word families (Iversen & Tunmer, 1993); using words taken from classroom reading lessons (Cunningham, 1989); and incorporating metacognitive techniques showing children how and when to use strategies (Cunningham, 1990; Duffy et al., 1987; Gaskins et al., 1988; Iversen & Tunmer, 1993). Further, grapheme–phoneme correspondences are integrated during reading instruction.

Comprehension Strategies

"Reciprocal teaching" methods have been used to incre ase comprehension by teaching predicting, questioning, and clarifying strategies (Palinscar, Brown, & Martin, 1987). Maintenance and generalization were demonstrated with these methods (see Wise & Olson, 1991, for a review). "Interactive learning strategies" increase comprehension and vocabulary

TABLE 5. Selected Strategies for Addressing Cognitive, Academic, Psychosocial, and Attentional Problems in Children and Adolescents

Disorders	Strategies	References
Reading		
Phonemic awareness	Segmenting, blending, and analyzing sounds	Fox and Routh (1976)
	Phonological recoding, translating letters and letter patterns into phonemes	Iversen and Tunmer (1993)
	Grapheme–phoneme correspondences in word families (e.g., "ight") to teach generalizations	
	Phonemic awareness is contextualized in regular reading lessons	Cunningham (1989)
	Metacognitive strategies	Iversen and Tunmer (1993) Cunningham (1989)
Comprehension	"Reciprocal teaching" using predicting, questioning, and clarifying	Palinscar et al. (1987)
	"Interactive learning" accesses and links prior knowledge, "clue lists," and predicts relationships	Bos and Van Reusen (1991)
Computer and speech feedback	Speech synthesizer	Wise et al. (1989)
Whole language	Strength approach utilizing word recognition with metacognition	Wise and Olson (1991)
	Language activities (reading–writing) linked and literature freely used	
Written language	Cognitive and metacognitive strategies	Bos and Van Reusen (1991)
	Plan, organize, write, edit, and revise "Cognitive Strategy Instruction"	Englert (1990)
	"Self-Instructional Strategy Training"	Graham and Harris (1989)
Mathematics	Cognitive and metacognitive approaches understand the problem, plan solution, carry out solution, and assess accuracy	Montague and Bos 1986)
	Verbal elaboration, written cue cards with rules for problem-solving, and concrete aids	Strang and Rourke 91985)
	Step-by-step problem-solving with feedback	Rourke (1989)
Study and organization	Strategies Intervention Model	Ellis and Lenz (1991)
	Setting priorities, how can task be accomplished, analyzing task, setting goals, monitoring and checking on accomplishments	Ellis and Friend (1991)
Social skills	ACCESS program	Walker, McConnell, et al. (1988)
	ACCEPTS program	Walker, Holmes, et al. (1988)

knowledge utilizing the following steps: (1) identifying the child's prior knowledge about a topic; (2) linking prior knowledge to new information; (3) scanning reading material, to develop "clue lists," "relationship maps," or charts; and (4) predicting relationships across concepts (Bos & Van Reusen, 1991). Teacher–student relationships are a central feature of this program, wherein both work together to enhance and facilitate student learning.

Computer and Speech Feedback

A computerized speech synthesizer (i.e., DECtalk) has been successful in improving phonological coding and word recognition skills for children with reading problems (Olson, Foltz, & Wise, 1986). Segmented feedback is presented when the child is unable to read a particular word. The computer highlights and simultaneously "says" the word with the child.

Comprehension questions and corrective feed-back are also available in this software (Olson et al., 1994; Wise & Olson, 1991).

Whole Language Programs

Whole language incorporates reading into language activities, wherein reading and writing are taught together using the child's literature for reading activities (Teeter Ellison & Semrud-Clikeman, 2007). Word recognition and meta-cognitive techniques can also be included in whole language programs (Wise & Olson, 1991). Although still somewhat controversial, some suggest that word decoding can also be incorporated into a whole language curriculum for children who need it (Wise & Olson, 1991).

Strategies for Written Language Disorders

Techniques for written language problems frequently employ metacognitive strategies (Bos & Van Reusen, 1991) to teach students how to plan, organize, write, edit, and revise writing samples (Englert, 1990). Structured cur-ricular programs are available, including the Cognitive Strategy Instruction Writing (Raphael, Kirschner, & Englert, 1986) and Self-Instructional Strategy Training (Graham & Harris, 1987, 1989). Students are taught to iden-tify the main character, where the story takes place, and how the story ends. Self-regulation and self-monitoring techniques are usually stressed, although self-regulation training did not increase performance over the other strate-gies (Bos & Van Reusen, 1991).

Strategies for Math Disorders

Deficits in math problem-solving have not been viewed as an educational priority until recently (Bos & Van Reusen, 1991). Reasoning ability, metacognitive processing skills, and reading proficiency appear related to deficits in solving word problems (Bos & Van Reusen, 1991). Cognitive and metacognitive approaches, wherein students are taught to understand the nature of the problem, plan a solution, carry out the solution, and assess the accuracy of the solu-tion, have been designed to reduce math problem-solving deficits in children (Teeter Ellison & Semrud-Clikeman, 2007). Strategy instruction has been shown to be effective for math-related difficulties (Montague & Bos, 1986; Smith & Alley, 1981).

Few studies on math LD describe the neu-ropsychological characteristics of the subjects or the cognitive strategies employed (Fleischner, 1994). In this regard, Fleischner suggests using the Test of Early Mathematics Ability (TEMA-2) or the Diagnostic Test of Arithmetic Strategies to determine information about which strategies might be useful. Further, Rourke (1989) developed a model for describing the neu-ropsychological characteristics of children with specific deficits in the math area and developed a comprehensive intervention program (Teeter Ellison & Semrud-Clikeman, 2007). (See Rourke, 1989, for specific details to increase problem-solving and reasoning skills in children with math-related problems.)

Strategies for Deficits in Executive Functions: Planning and Organizational Skills

The Strategies Intervention Model (SIM), developed by the University of Kansas Institute for Research on Learning Disabilities, provides systematic strategy instruction for high school students (Ellis & Lenz, 1991). The SIM program teaches students learning strategies to acquire and store knowledge and to demonstrate this knowledge (Ellis & Friend, 1991). Effective strategies must be useful, efficient, and memor-able and often include: setting priorities; reflect-ing on how a task can be attacked and accomplished; and analyzing the task, setting goals, monitoring, and checking to see if goals were accomplished (Ellis & Friend, 1991).

Skills for Success is a structured curriculum to teach students (grades 3–6) study and organi-zation skills (Archer & Gleason, 1989). Reading, organizing and summarizing information, test taking, anticipating test content, how to study, and responding to various test formats are fea-tured (DuPaul & Stoner, 1994). DuPaul and Stoner provide guidelines for organizing materi-als, using assignment calendars, and steps to organizing and completing a paper. Initial evidence suggests that study and organizational skills are effective procedures for youth with LD (Ellis & Friend, 1991) and warrant further research for children with disorders such as ADHD (DuPaul & Stoner, 1994).

Teachers often comment that organizational, planning, and study skills often impede the performance of children with learning problems. Thus, techniques to increase these academic survival skills may need to be considered to increase the likelihood of school success. Children with various neurodevelopmental or acquired brain-related disorders often evidence problems with social interaction and emotional adjustment. Strategies for addressing these deficits are explored next.

Strategies for Social Skills Deficits

Social skills deficits have been linked to LD (Semrud-Clikeman & Hynd, 1991); school dropout, delinquency, and emotional disturbance (Barclay, 1966); and ADD (Carlson, Lahey, Frame, Walker, & Hynd, 1987). Further, peer rejection resulting from aggression predicts criminal activity in adulthood (Parker & Asher, 1987). This research has prompted the inclusion of social skills deficits in proposed definitions of LD (Bryan & Lee, 1990; Gaddes & Edgell, 1994; Lerner, 1993). (Bryan 1991) and Rourke (1994) suggest that intervention plans that focus solely on academic gains and ignore the impact of social skills deficits will limit remediation efforts for many children with LD. The importance of social skills as well as academic competencies is stressed in multifaceted intervention plans.

Bryan (1991) suggests that self-efficacy, self-esteem, attributional thinking, social cognition, comprehension of nonverbal cues and social mores, moral development, social problem-solving, communication skills, and behaviors in the classroom are related to social skills difficulties. These factors have been related to various neuropsychological syndromes associated with right or left hemisphere deficiencies (Semrud-Clikeman & Hynd, 1991). LD children with right hemisphere dysfunction display a variety of problems, including math weaknesses, visual–spatial and social imperception; motor weaknesses on the left side; verbal reasoning deficits; and social gesturing and communication/language problems (Denkla, 1978), 1983). Conversely, children with abnormal right hemisphere functioning, based on CT scans, EEGs, and neuropsychological measures, had trouble interpreting the emotions of others and expressing appropriate emotions (Voeller, 1986). Increased attentional and hypermotoric behaviors were also found in children with signs of right hemisphere dysfunction.

A number of structured social skills training programs are available, including the ACCEPTS program for elementary children (Walker, McConnell, et al., 1988) and the ACCESS program for adolescents (Walker, Holmes, Todis, & Horton, 1988). These social skills programs have been shown to be effective for a variety of children with mild to moderate learning and behavior problems (Teeter Ellison & Semrud-Clikeman, 2007). Further, behavior management is used outside structured sessions to increase generalization of trained skills.

Research investigating the effectiveness of social skills training shows mixed and sometimes disappointing results (Vaghn, McIntosh, & Hogan, 1990). Even when children do show behavioral changes in social interaction skills problems, these improvements are not readily acknowledged or perceived by peers or teachers (Northcutt, 1987). Issues related to generalization of "trained" social skills often do not occur in natural settings.

Vaghn et al. (1990) indicate that programs for students with learning problems have been shown to be effective when (1) LD students obtain part-time versus full-time LD services; (2) LD students are in elementary or high school (middle school students show fewer positive gains); (3) intervention programs include regular class students; (4) programs are individualized; (5) children receive training because of social skills deficits and not placement in LD classes alone; (6) training programs occur over an extended time (average 9 weeks, 23.3 h) and include follow-up sessions; (7) small groups or one-to-one instruction is utilized; and (8) coaching, modeling, corrective feedback, rehearsal, and strategy instruction are incorporated into the training program.

Intervention programs should address the broader social milieu of the child (La Greca, 1993) and should include high-status or nonproblem peers. La Greca recommends using multisystemic intervention models, prevention, peer-pairing and cooperative activities, avoiding cliques and child-picked teams, teacher monitoring, and parental involvement. Friendship building with one or two close friends might buffer the child who is not popular with the larger group (La Greca, 1993). A close friendship might further reduce anxiety, stress, depression, and

low self-esteem in children who have been excluded because of social skills problems.

In summary, broader goals should be considered in social skills training where the targeted child, peers, teachers, and parents are included in the social skills intervention plan (Teeter Ellison & Semrud-Clikeman, 2007).

Classroom and Behavior Management Strategies

Various behavioral management techniques have proven effective for numerous childhood problems (Shapiro, 1989). The literature demonstrating the strengths of behavioral principles is too extensive to review here. (See DuPaul & Stoner, 1994, and Witt, Elliott, & Gresham, 1988, for extensive reviews of token economies, contingency contracting, cost response, and time-out from positive reinforcement.) The following briefly reviews self-management, attention training, home-based contingencies, and peer tutoring.

Self-Management/Self-Control Techniques

Self-management techniques attempt to increase the child's ability to control his/her own behavior and to decrease dependency on the teacher. (Lloyd and Landrum 1990) describe the techniques for teaching self-assessment (i.e., observing one's own behavior), self-evaluation (i.e., comparing one's behavior to others), self-recording, and self-reinforcement. (See Table 6.) These techniques can target numerous behaviors, although attending to task has been of major interest (Teeter Ellison & Semrud-Clikeman, 2007).

Children with learning and behavior disorders from age 4 to adolescence have successfully utilized self-recording techniques to increase attention to task; decrease behavioral disruption; increase productivity and accuracy; and sustain and complete schoolwork (Lloyd & Landrum, 1990). Self-recording usually employs cuing (e.g., tape-recorded beeps at 1-, 2-, or 3-min intervals or kitchen timers that ring every 5 min) (Heins, Lloyd, & Hallahan, 1986) and fading of cues (Lloyd & Landrum, 1990).

Home-Based Contingencies

Home-based contingencies, employing daily or weekly teacher notes, reports, or ratings, often supplement school-based token systems (DuPaul & Stoner, 1994). Targeted behaviors may focus on increasing or improving attention, work/homework completion, compliance, and social interactions. Teachers provide written comments, the child takes the comments home, and the parent then discusses the child's performance in school and provides reinforcement depending on school behaviors. Home-based contingencies are increasingly used in schools and can be very effective (Teeter Ellison & Semrud-Clikeman, 2007).

Peer Tutoring

Greenwood, Maheady, and Carta (1991) developed peer tutoring techniques for various

TABLE 6. Selected Classroom and Behavior Management Strategies for Addressing Problems in Children and Adolescents

Strategies	Description	References
Self-management	Self-assessment, self-evaluation, self-recording, and self-reinforcement	Lloyd and Landrum (1990)
Attention training	Self-recording with taped cuing	Heins et al. (1986)
Home-based contingencies	Attention training with self-monitoring and strategic problem-solving	Semrud-Clikeman (1995)
Peer tutoring	Home–school weekly or daily notes target attention, work completion, compliance, and social interactions	DuPaul and Stoner (1994)
	Class Wide Peer Tutoring program dyads, tutor–tutee pairs with specified roles	Greenwood et al. (1988)

academic areas, including reading, spelling, and math activities. The class is organized into tutor–tutee pairs who work together on lessons and assignments (Shapiro, 1989). The Class Wide Peer Tutoring (CWPT) program provides systematic and detailed training guidelines for implementing this intervention technique (Greenwood, Delquardi, & Carta, 1988). Academic and behavioral gains for children who have been described as slow learners, learning disabled, and behavioral disordered have been documented (Shapiro, 1989). Recently these techniques were applied to a young child with ADHD and credited with less hyperactivity, increased on-task behavior, and academic gains in math (DuPaul & Henningson, 1993).

The selected techniques may be incorporated into intervention programs for children with various developmental, academic, behavioral, and social problems. Individual assessment and academic planning provides the mechanism for deciding which techniques should be employed (Teeter Ellison & Semrud-Clikeman, 2007). Intervention techniques are usually used in combination and must be carefully monitored to determine their impact. Intervention monitoring has been described by DuPaul and Stoner (1994), Shapiro (1989), and Shapiro and Kratochwill (1988).

Childhood disorders may require medical treatments, including psychopharmacology (Pelham, 1993a). The following section briefly reviews pharmacological interventions that are appropriate for a number of childhood and adolescent disorders.

Psychopharmacological Interventions

Although children and adolescents with neurodevelopmental or acquired brain-related disorders may require medication, intervention programs are usually multidimensional in nature. "Appropriate psychosocial and psychoeducational interventions should form a component of treatment for most children with these disorders—even those where pharmacotherapy is helpful" (Pelham, 1993a, p. 161). Medications for major depressive disorders, psychotic disorders, ADHD, Tourette's syndrome, and seizure disorders are briefly discussed. This is not meant to be an exhaustive list of medication options, but serves as an overview emphasizing potential benefits and side effects. Intervention programs for children receiving medication should specify how medications will be monitored and how teachers, physicians, and parents will communicate about medication efficacy.

Specific Classes of Medication

Green (1991) classified medications as stimulants, antipsychotics, tricyclic antidepressants or monoamine oxidase inhibitors, anxiolytics, and anticonvulsants, depending on their behavioral effects on the CNS. Selected medications for children and adolescents, with potential benefits and side effects, are shown in Table 7. (See Cook & Leventhal, 1992; Green, 1991; Teeter Ellison & Semrud-Clikeman, 2007, for in-depth discussions of the interactions among medications, neurotransmitter systems, and neuropsychiatric/neurodevelopmental disorders of childhood.)

Monitoring Medication

Determining whether medication should be administered typically includes comprehensive assessment and a review of the child's medical, educational, and psychosocial history (Teeter Ellison & Semrud-Clikeman, 2007). The nature and severity of the child's problem and the effectiveness of psychosocial and/or behavioral interventions should be considered. Nonmedical interventions for children with severe ADHD, depression, anxiety, and conduct disorders are generally attempted before medication is prescribed. If nonmedical interventions do not sufficiently improve the child's problems, controlled trials of medication may be initiated (Teeter Ellison & Semrud-Clikeman, 2007). Baseline data (e.g., ECG, EEG, urinalysis, liver, thyroid, and renal function tests, blood pressure, and serum blood levels) are generally gathered on children receiving antipsychotics, antiepileptics, and antidepressants (Green, 1991). Behavioral data (e.g., rating scales, questionnaires) are also used to measure the benefits/effects of medication.

Response rates to stimulant medications vary considerably from individual to individual (Barkley, 1990; DuPaul & Stoner, 1994; Pelham, 1993a). Thus, careful evaluation using rating scales or home–school notes is important (see Barkley, 1990; DuPaul & Stoner, 1994; Pelham, 1993b).

TABLE 7. Common Uses, Benefits, and Side Effects of Medications for Neuropsychiatric Disorders of Childhood[a]

Drugs	Common uses	Manifestations	Side effects
Stimulants			
Methylphenidate (Ritalin)	ADHD	75% of children are responders	Insomnia, appetite loss, nausea, vomiting, abdominal pains, thirst, headaches
		Decreased motor activity, impulsivity, and disruptive behaviors	
		Increased attention	Tachycardia, change in blood pressure
		Improved socialization	Irritability, moodiness
		Improved ratings (teacher, physician, parent)	Rebound effects
		Increased work completion and accuracy	Growth suppression (can be monitored)
		Improved test scores (mazes, PIQ, and visual memory)	Lower seizure threshold
			Exacerbate preexisting tics
Dextroamphetamine (D-amphetamine)	ADHD	Similar to methylphenidate	Similar to methylphenidate
		Subdued emotional response	Hallucinations, seizures, and drug-induced psychosis (rare occurrences)
		Increased reflectivity and ability to monitor self	
		Increased interest level	
		Improved school performance	
		Improved parent ratings (conduct, impulsivity, immaturity, antisocial, and hyperactivity)	
Magnesium pemoline (Cylert)	ADHD	Similar to methylphenidate	Similar to methylphenidate
		Improved teacher ratings (defiance, inattention, and hyperactivity)	
		Improved parent ratings (conduct, impulsivity, and antisocial behaviors)	
		Improved test scores (mazes, PIQ, visual memory)	
Antipsychotics			
Haloperidol (Haldol)	Psychosis	Reduces aggression, hostility, negativity, and hyperactivity	Behavioral toxicity with preexisting disorders
	Tourette's	Reduces psychotic symptoms	Dystonia (loss of tone in tongue and trunk)
	Autism	Reduces Tourette's symptoms	
	PDD	Reduces fixations, withdrawal stereotypies, anger, and fidgetiness in autism	Parkinsonian symptoms (tremors, mask face, and drooling)
	ADD with CD	Increases social responsivity and reality testing in PDD	Dyskinesis (mouth, tongue, and jaw)
			Dose reduction decreases motor side effects
			Intellectual dulling, disorganized thoughts
Chlorpromazine (Thorazine)	Psychosis	Reduces hyperactivity	Similar to haloperidol
	Severe aggression, explosiveness, and hyperexcitability in MR children	Reduces tantrums, aggression, self-injury	Dermatological problems
		Not effective for young autistics	Cardiovascular problems
			Lowers seizure threshold
			Endocrinological problems
			Ophthalmological problems
			Hematological problems

TABLE 7. (*Continued*).

Drugs	Common uses	Manifestations	Side effects
Thioridazine (Mellaril)	Psychosis Severe behavior disorders (extreme)	Reduces hyperactivity Improves schizophrenic symptoms Similar to Thorazine	Similar to haloperidol Sedation, cognitive dulling, and impaired arousal
Thiothixene (Navane)	Psychosis	Similar to Mellaril	Less sedating than Mellaril
Loxapine succinate (Loxitane)	Psychosis	Similar to Haldol	Similar to Haldol
Fluphenazine HCl (Prolixin, Permitil)	Psychosis		
Pimozide (Orap)	Psychosis Tourette's (resistant type)	Clinical improvement	High doses: death and seizures
Clozapine (Clozaril)	Severe psychosis (resistant type)	Clinical improvement	Life-threatening hypertension, tachycardia, and EEG changes Seizures
Tricyclic antidepressants			
Imipramine HCl (Tofranil)	Depression Enuresis ADHD School phobia	Improves depression (not severe) Inhibits bladder muscles Reduces hyperactivity Reduces separation anxiety	Potentially life-threatening cardiovascular problems CNS symptoms (EEG changes, confusion, lowers seizure threshold, incoordination, drowsiness, delusions, and psychosis) Improves sleep disorders Blurred vision, dry mouth, and constipation
Nortriptyline HCl (Pamelor)	Depression	Low rate of clinical improvement in children and adolescents	Withdrawal symptoms
Desipramine HCl (Norpramin)	ADHD ADHD with tics	Improved ratings (parents and teachers Conners) Clinical improvement	Dry mouth, decreased appetite, tiredness, dizziness, insomnia EEG changes at high doses
Clomipramine HCl (Anafranil)	Obsessive–compulsive disorders Severe ADHD Enuresis School phobia	Reduces obsessions Reduces school phobia/anxiety Reduces aggression, impulsivity, and depressive/affective symptoms	Withdrawal symptoms Seizures Somnolence, tremors, dizziness, headaches, sweating, sleep disorder, gastrointestinal problem, cardiovascular effects, anorexia, and fatigue
Monoamine oxidase inhibitors			
Fluoxetine HCl (Prozac)	Depression Obsessive–compulsive	Effective for adults Clinical improvement for OCD	Nausea, weight loss, anxiety, nervousness, sweating, sleep disorder
Bupropion (Wellbutrin)	Depression ADHD	Adolescents 18 + improve Improved global ratings not Conners	Seizures, agitation, dry mouth, insomnia, nausea, constipation, tremors
Anxiolytics			
Chlordiazepoxide (Librium)	Anxiety with hyperactivity and irritability School phobia	Clinical improvement Reduced hyperactivity, fears, enuresis, truancy, bizarreness Decreases emotional overload	Drowsiness, fatigue, muscle weakness, ataxia, anxiety, and depression with high doses

TABLE 7. (*Continued*).

Drugs	Common uses	Manifestations	Side effects
Diazepam (Valium)	Mixed psychiatric DX anxiety and sleep	Improved global ratings Better results for adolescents	Relatively low toxicity
Alprazolam (Xanax)	Anxiety Panic attacks Separation anxiety	Clinical improvements Responders (premorbid personality: shy, inhibited, nervous)	Mild drowsiness
Anticonvulsants			
Phenobarbital	Seizure disorders	Reduces seizures	Lethal at high doses Cognitive impairment, rigidity, and depression
Diphenylhydantoin sodium (Phenytoin)	Seizure disorders	Reduces tonic–clonic seizures	Cognitive impairment Drug toxicity
Carbamazepine	Seizure disorders Manic–depression	Reduces generalized and tonic–clonic seizures Psychotropic effects	Fewer adverse side effects than other drugs Less cognitive dulling, motoric, and affective
Sodium valproate	Seizure disorders	Reduces seizures Petit mal and tonic–clonic	Low cognitive symptoms Relatively nontoxic in adults Rare but potentially fatal hepatoxicity in children

[a]Adapted with permission from Teeter Ellison and Semrud-Clikeman (2007). Data from Dubovsky (1992), Green (1991), and Neppe and Tucker (1992).

Although a number of scales and procedures are described for children with ADHD, there are fewer scales available for other childhood disorders (Teeter Ellison & Semrud-Clikeman, 2007).

Ecologically valid behaviors in the classroom and in social situations should be assessed to determine the effects of stimulant medication (Pelham, 1993b). Daily report cards monitoring work completion/accuracy and compliance are helpful in this process (Pelham, 1993b). Ecologically valid assessment of medication effects for depression, anxiety, and conduct-related problems is needed. Specific targeted behaviors (e.g., sadness, panic attacks, or anger outbursts) would be more explicitly defined and monitored on a regular basis (Teeter Ellison & Semrud-Clikeman, 2007). Further medication monitoring should occur in the child's natural setting (e.g., home and school) and should not be based solely on clinic observations in the doctor's office (Teeter Ellison & Semrud-Clikeman, 2007). This necessarily increases the need for ongoing home–school– physician communication.

Pharmacological/Behavioral Interventions

Psychopharmacotherapy is rarely employed without other interventions (Teeter Ellison & Semrud-Clikeman, 2007). Most childhood and adolescent disorders affect multiple areas of adjustment (cognitive, academic, and psychosocial) which are not always improved by medication alone. Pharmacological is often combined with behavioral treatments (e.g., contingency management, home–school notes), individual or group therapy for the child or adolescent, parent training, and family therapy (Teeter Ellison & Semrud-Clikeman, 2007).

Pelham (1993b) said that "an important result of combined treatments may be that maximal improvement in behavior may be reached without resorting to high dosages of stimulant medication" which also lowers the adverse side effects of medication (p. 220). Carlson, Pelham, Milich, and Dixon (1992) also indicate that combined approaches (i.e., medication with behavioral interventions) complement the shortcomings of either treatment alone, whereas

Pelham (1993b) found that combined interventions add incremental effects not found when single interventions are used in isolation for children with ADHD.

Further research investigating combined intervention programs for various childhood disorders is needed. The need for ecologically based medication monitoring increases the need for home–school–physician partnerships. Children requiring medically based interventions need careful monitoring in school and at home. Thus, teachers and parents need to work closely with physicians to coordinate intervention programs and to monitor medication effectiveness. The following section briefly discusses collaborative partnerships.

Home–School–Physician Partnerships

There are numerous reasons why home–school– physician partnerships are important. Teeter Ellison and Semrud-Clikeman (2007) include the following reasons: (1) children often are seen by a number of different professionals so that coordination of interventions is required; (2) because of the high cost of medical and psychological services, duplication should be avoided if possible; (3) children on medication require monitoring of their behavior in a natural environment; (4) educational staff working with children with various brain-related diseases or disorders (e.g., brain tumors, TBI) must be knowledgeable about the child's medical, psychosocial, academic, and behavioral needs; and (5) parents and family members may require help from various professionals who must communicate with each other.

Confidentiality is of utmost importance and parental permission is required to obtain and share information (Teeter Ellison & Semrud-Clikeman, 2007). Further, it is important to have someone act as the coordinator of services when numerous professionals are involved in treatment plans. Parents are often forced into this role, and many are ill-equipped to deal with the demands of coordinator because of the day- to-day stress involved with raising children with significant medical, academic, and/or psychosocial needs. The case coordinator may vary depending on whether the child's problems are primarily educational and/or psychosocial (e.g., ADHD or LD) or medical (i.e., brain tumor or TBI); e.g., school staff may coordinate services in the first instance, and the physician or neuropsychologist may serve in the latter case. The role of case coordinator may also change as the child either improves, recovers, or deteriorates. Nonetheless, if parents are placed in this role by themselves, this may be an extra burden on an already overly taxed family.

Regular communication among all professionals is required, and a set schedule may be needed for initial assessment and intervention planning and for ongoing monitoring (Teeter Ellison & Semrud-Clikeman, 2007). Once the child shows improvement or stabilizes medically, follow-up may occur less frequently or at longer intervals (i.e., 6, 12, 18, and 24 months).

Summary and Conclusions

This chapter presented various strategies for developing intervention programs for children with various disorders. A transactional model was discussed, wherein neuropsychological, cognitive, behavioral, and psychosocial factors are considered in the evaluation–intervention process. Intervention strategies for children with neurodevelopmental and acquired brain-related disorders are usually multidimensional in nature. Intervention planning should follow comprehensive evaluation and accurate diagnosis of the child's problems and should address the full range of the child's neurocognitive, academic, behavioral, and psychosocial needs.

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20

Brain Injury Rehabilitation of Children and Youth: Neurodevelopmental Perspectives

H. DENNIS KADE AND ELAINE FLETCHER-JANZEN

Introduction

Traumatic brain injury (TBI) was coined, for many years, as the "silent epidemic" as its frequency and disabling effects were largely unrecognized by the professional community and the public (Ylvisaker, 1985). It was called the "silent epidemic" for two reasons: the public was unaware of its impact, and the cumulative data on incidence and prevalence did not include patients who sought medical attention from physicians' offices (Langlois, Marr, Mitchko, & Johnson, 2005). Today, TBI is not so silent. We know that of the 1.4 million who sustain a TBI every year in the United States, 50,000 die, 235,000 are hospitalized, and 1.1 million are treated and released from an emergency department. The male to female ratio is about 1.5 and the death rate is highest among African Americans (Langlois, Rutland-Brown, & Thomas, 2004). The latest incidence review from the Centers for Disease Control and Prevention (CDC) covers 2003 and reports somewhat similar results of 51,000 deaths, 290,000

hospitalizations, and 1.2 million emergency room visits for TBI (Rutland-Brown, Langlois, Thomas, & Xi, 2006). These statistics are more revealing when one considers that every 16 s someone in the United States sustains a head injury and every 12 min one of these people will die and another will become permanently disabled. Of those who survive each year, an estimated 80,000–90,000 people experience the onset of long-term disability associated with a TBI. An additional 2,000 will exist in a persistent vegetative state. Unfortunately brain injury kills more Americans under the age of 34 than all other causes combined and has claimed more lives since the turn of the century than all US wars combined (Hatch, 2007).

Studies show that 70–90% of treated brain injuries are mild (Semrud-Clikeman, Kutz, & Strassner, 2005). The incidence of mild TBI treated in the hospital is about 100–300 per 100,000 but population-based surveys of self-reported head injury suggest the mild TBI rate is actually above 600 per 100,000 because many do not seek treatment for concussions (Holm, Cassidy, Carroll, & Borg, 2005). Many of the individuals who do not seek treatment have sustained sports injuries. The etiological data category for being unintentionally struck by another person or object or immediately against an object has become the third largest cause of TBI; it includes

H. DENNIS KADE • Tidewater Child Development Services, Norfolk Department of Public Health. Norfolk, VA and Department of Psychology, Old Dominion University, Norfolk, VA. **ELAINE FLETCHER-JANZEN** • San Angelo, Texas 76901.

many sports injuries (Rutland-Brown, Langlois, Thomas, & Xi, 2006). A population-based medical record abstraction of 10 to 19-year olds seen in an emergency department, admitted to hospital, or who died from injury in the District of Columbia revealed that 5% had experienced at least one sports-related injury requiring medical attention during the 2-year period from June 1996 through June 1998. A significant proportion involved documented head and intracranial injuries: 37% of the baseball/softball injuries involved the head and 7% intracranial injuries, basketball had 17% head injures with 2% intracranial, bicycling had 29% with 9% intracranial, football had 16% with 5% intracranial, skating had 10% with 4% intracranial, and soccer had 22% with 10% intracranial (Cheng et al., 2000).

Sports and recreational activities alone produce about 300,000 TBI with loss of consciousness each year and a total of 1.6–3.8 million when those who seek no medical care are included. This may be an underestimate because the injury may go unrecognized and so unreported even in community surveys (Langlois, Rutland-Brown, & Wald, 2006):

> The "invisible disability" that persons with cognitive but not obvious physical problems experience poses unique problems for persons with TBI in accessing health services and maintaining a healthy lifestyle. Other barriers include lack of medical insurance and the limited awareness of TBI among some healthcare providers. Until these and other challenges are met, TBI will continue to exact an enormous toll. The lifetime costs of TBI in the United States, including medical costs and lost productivity, total an estimated $60 billion annually. This does not begin to address the indirect impact on friends, families, and caregivers and the community. (Langlois et al., 2006, p. 377)

The severity of the injury to the brain is not simply related to the severity of the injury to the head. Complications affecting outcome include anoxia, hypotension, and increased intracranial pressure as well as the secondary injury of brain's response (Ylvisaker et al., 2005). Mild TBI can have persistent sequelae, therefore, brain injury is one of the most disabling injuries; for example, productivity loss due to TBI is 14 times greater than spinal cord injury (Langlois et al., 2006). Estimates from the Centers for Disease Control and Prevention are that at least 5.3 million Americans have a long-term need for help with activities of daily living due to TBI (Thurman, Alverson, Dunn, Guerrero, & Sniezek, 1999). Needs for services are related to severity of injury. A survivor of severe TBI needs an average of 5–10 years of services; lifetime costs can exceed $4 million (Hatch, 2007).

Not all people are equally at risk. For example, up to 87% of incarcerated persons report prior head injury. To address gaps in the data the CDC has funded pilot studies of follow-up in Colorado and South Carolina and of the incidence of TBI in prisons and nursing homes (Langlois et al., 2005). Military personnel in Iraq and Afghanistan, first responders and civilian victims of terrorist attacks are at increased risk (Langlois et al., 2006). The publicity around the TBI Bob Woodruff sustained in Iraq has brought an increased public awareness to both the problems and the limitations in available rehabilitation services (Woodruff & Woodruff, 2007). In the United States, the age groups most at risk for TBI are 0- to 4- and 15- to 19-year olds (Langlois et al., 2004). The highest rate of emergency room visits for TBI across the age bands in 2003 was 1,091.2 per 100,000 for ages birth to 4 years (Rutland-Brown, Langlois, Thomas, & Xi, 2006). TBI causes an estimated 2,685 deaths, 37,000 hospitalizations, and 435,000 emergency visits each year among children aged 0–14 years (Langlois, et al., 2004).

TBI is a leading cause of death and disability in children and adolescents in the United States and it is the principal cause of brain damage in young adults (Brain Injury Association of America, 2007; Miller, 1992; National Information Center for Children and Youth with Disabilities [NICCYD], 1997). Across all ages, more than 1 million children sustain brain injuries annually, and approximately 165,000 require hospitalization, and more than 30,000 of these children have lifelong disabilities as a result (National Information Center for Children and Youth with Disabilities [NICCYD], 2006). Accidents continue to be the leading cause of death for ages 1–14 years in the United States; most of these are motor vehicle accidents over age 4; motor vehicle accidents rank behind other accidents from ages 1 to 4 (Miniño, Heron, & Smith, 2006). The prevalence is so high that a TBI has been sustained by 4 boys of every 100 and 2.5 girls of every 100 by age 16 (Schoenbrodt, 2001).

Between 30 and 50% of injuries are moderate, severe, or fatal (Begali, 1992). In addition to the incidence of TBI, 5,000 new cases of epilepsy caused by head trauma are reported each year (Miller, 1992). The incidence of TBI is not randomly distributed through the population. Males are about twice as likely as females to sustain a brain injury and their death rate from these injuries is four times that of females (Ball & Zinner, 1993). The most frequent causes of TBI are motor vehicle crashes (with alcohol involvement) (Ball & Zinner, 1993; Rusonis, 1990), falls, sports, and abuse/assault (Goldstein & Levin, 1990; NICCYD, 1997).

As the benefits of air evacuation of trauma victims in Vietnam began to be emulated in the United States in the late 1970 s and combined with advances in acute trauma care, rehabilitation services for survivors expanded dramatically in the 1980s (Ruff, 2005). Advances in medical science and technology such as increased effectiveness of hospital trauma units, availability of neurosurgeons, and developments in critical and acute care management have all contributed to the increased survival rates of severely brain-injured individuals (Bigler, 1990; Levin, 1990; Uomoto, 1989). Trauma survival has required the development of programs to meet the long-term needs of these individuals. The demand for services by patients and their families has preceded the development of theoretical models, and therefore, research evidence of efficacy, which is a common phenomenon in medical care (Kreutzer, 1991). Indeed, it is estimated that between 5 and 10 billion dollars is spent each year to provide medical care and rehabilitation to TBI survivors (Bigler, 1990; Burke, 1988).

The responsibility for advances in treatment of the neurocognitive impairments, functional and behavioral disabilities, and the chronic handicapping condition has come to rest with professionals who understand brain–behavior relationships. Neuropsychologists have played a critical role in documenting and evaluating brain injury for patients whose deficits were formerly misunderstood (Ball & Zinner, 1993; Crokett, Clark, & Klonoff, 1981). Before our current knowledge base existed, professionals had to either infer the degree and amount of structural brain damage or wait until a postmortem examination could be performed. Current technology allows a more accurate means of assessing structural damage, which, in turn, permits better understanding of brain injury mechanisms and the correlation between area of brain damage and related changes in behavior (Bigler, 1990; Provencal & Bigler, 2005). This has precipitated a shift in focus so that neuropsychological assessment is more related to functional evaluation and planning than lesion location (Provencal & Bigler, 2005; Darby & Walsh, 2005). However, it is only recently that patients with brain injury have received comprehensive treatment programs dealing with various cognitive and behavioral outcome deficits that accompany brain injury. Although there is a common scenario of frontal impact causing an acceleration/deceleration in closed head injury that produces associated posttraumatic deficits, each brain injury is unique. There is no single constellation of symptoms or unitary TBI syndrome for either children or adults. The recovery process also varies considerably. Therefore, reference to an average recovery curve would be of little use in predicting the course of a particular case in practice.

The focus of this chapter is the development of a pediatric brain injury rehabilitation program, based on a neurodevelopmental model and a neuropsychological paradigm of rehabilitation. The historical development of the treatment of brain injury will be reviewed and followed by an examination of the theoretical paradigms that have led to current models of service delivery in acute and inpatient facilities. In addition, differences between pediatric and adult programming and outcomes are addressed. The neurodevelopmental model of inpatient programming is based on the unique needs of the pediatric brain injury population and on holistic principles and is dedicated to a continuum of service delivery from acute to reentry to care by the family after discharge.

Historical Development of Clinical Neuropsychology and Brain Injury

The development of neuropsychological approaches to the rehabilitation of individuals with brain injury in the United States has been influenced by two main forces. The first is that of natural events in the world that have led to demands on the field of medicine to focus on

the brain, such as World War I and the return of soldiers with severe brain injuries. Although in World War I, brain injury casualties promoted the study of the functional aspects of brain anatomy, the institutionalized care of brain-injured soldiers in the United States did not occur until World War II (Boake, 1989). At that time, the first speech disorders unit affiliated with a military neurosurgical center was formulated in Fort Sam Houston, Texas, and by 1945, 13 speech units were in operation. Also included in the units were other professionals such as physical therapists, occupational therapists, and psychotherapists (Boake, 1989). A long lapse in treatment development then followed and did not reemerge until the late 1960s and early 1970s when, undoubtedly, the effects of motor vehicle accidents prompted the need for treatment (Sohlberg & Mateer, 1989). It was at this time that rehabilitation treatment units were developed that closely mirror those of today. Previously, the special team approach had primarily been used in spinal cord units. The first replications of this model were at Lowenstein Rehabilitation Hospital near Tel Aviv and the Rancho Los Amigos Hospital near Los Angeles where the guidelines for therapy with patients at different stages of recovery were established, and the efforts of latter facilities brought forth the Rancho Los Amigos Cognitive Scale that is in use today (Boake, 1989, 1991).

The treatment protocols generated for the different levels of coma reflected by the Rancho Los Amigos Scale began a field of cognitive rehabilitation (Rattok et al., 1992). At the same time, in 1973, the Yom Kippur War in Israel produced a sharp increase in brain-injured soldiers. This led to the development of a day treatment program that was under the joint direction of the Rehabilitation Department of the Israeli Ministry of Defense and the New York University Institute of Rehabilitation Medicine under the direction of the neuropsychologists Yehuda Ben-Yishay and Leonard Diller (Ben-Yishay & Gold, 1990; Boake, 1991). In the late 1970 s, day treatment centers were established in the United States and, simultaneously, residential treatment programs for post-acute head injury patients in Illinois, Texas, and Toronto, Canada. Although many treatment programs have since been established all over the United States, most have been based on program models developed before 1980 (Boake, 1989, 1991). Much of these treatment

models have the patient repeatedly attempt to do the things that are difficult to do in the hope that the patient and the therapist will discover new ways to accomplish the same neurocognitive task using areas of functioning that are relatively spared (Gronwall, Wrightson, & Waddell, 1990).

The second force that shaped the development of the present-day treatment programs for individuals with brain injury is that of the theoretical and sociopolitical factors associated with Western psychology, and in particular, the individualist/reductionistic interplay with psychometrics inherent in the United States. Although some would argue that, in the United States, psychological study of the individual organism is treatment of the individual "in vacuo," it may be viewed as a natural response to the sociopolitical emphasis on the study of the individual as opposed to the individual in a community or social context. This view was forwarded by such eminent Russian neuroscientists as L. S. Vygotsky, A. N. Leontev, and, perhaps the best known, A. R. Luria. Luria's development of a functional system(s) model of the brain became very well known and is still in full force today both in Russia and in the United States (Luria, 1973, 1980; Obrzut & Hynd, 1990). Many rehabilitation programs for individuals with brain injury use this model as the basis of the organized understanding of a patient's deficits (Schara, 1991).

Historically, primary foci of US neuropsychologists were the localization and documentation of structural damage and deficits associated with brain injury. There were no imaging machines to assist a physician's diagnosis and localization. The development of neuropsychological test batteries offering standardized and normative information was in response to a medical need. Not until the rapid advancement of diagnostic imaging technology did the entire field of neuropsychology in the United States shift from the assessment of brain structure to a combination of brain structure and brain function. It was realized by neuropsychologists that the goal was "to re-form the interrupted functional systems and those that have failed to develop" and efforts were made to "integrate the several facets of neurological, educational, and emotional functions" (Golden, 1979, p. 201). Thus, even neuropsychologists outside the field of TBI rehabilitation were increasingly

called on to establish the existence and magnitude of any cognitive deficits related to the brain insult, estimate the patient's ability to return to his/her previous lifestyle, and suggest remediation programs (Trexler, 1987).

Neuropsychology and Rehabilitation

The primary focus of traditional clinical neuropsychology was the diagnosis of generic cognitive deficits which were identified by responses to standardized tests (Ben-Yishay & Gold, 1990). The entrance of clinical neuropsychology into the rehabilitation arena precipitated requests to translate test scores and statements about mild, moderate, or severe impairment into more functional terms and to describe disabilities in terms of daily living that could be used for therapeutic goals (Ylvisaker, 1985). Diller (1987) proposes that the main difference between disciplines is that neuropsychology conducts studies to help elucidate and clarify the nature of impairments. Rehabilitation, on the other hand, is concerned with the remediation of impairments and teaching patients to manage their disabilities.

The natural forces that are currently operating in the field of neuropsychological rehabilitation of children and adolescents with brain injury continue to dramatically change. Advances in neuroscience are changing our understanding of brain–behavior relationships and neurodevelopment almost exponentially (Bigler, 1990; Casey, Tottenham, Liston, & Durston, 2005; Provencal & Bigler, 2005); Thomas, 2003). The expanding knowledge in neuroscience, cognitive psychology, and cognitive neuropsychology began to be integrated into clinical neuropsychology over a decade ago (Margolin, 1992; Semrud-Clikeman, Kutz, & Strassner, 2005). But the potential contribution of at least cognitive neuropsychology to the cognitive rehabilitation process has been questioned (Shallice, 2000).

With disability persisting over years and a persisting incidence of new brain injuries every year, the number of Americans with TBI increases every year. The pressures of cost containment for rehabilitation for individuals with brain injury are being controlled by the financial community rather than the clinical community. The average length of stay for adults in inpatient rehabilitation facilities shrunk from an average of 93 to 53 days over the 1980s (Gerring &

Carney, 1992). Comparing 1991–1994 with 1996–2002, the length of stay in one city's trauma center dropped from 36 to 26 days for patients with a serious TBI and their rehabilitation hospital admission from 46 to 25 days for an overall average of 31 fewer days of inpatient care within one decade, placing an increasing burden on outpatient services and families (Hawkins, Lewis, & Medeiros, 2005). As the insurance industry is often only interested in managing costs, the "managed care" concept of the 1990s continues to be something of a misnomer (Kade, 1994). Hospital management personnel became more focused on interest in increased efficiency and outcomes from the Continuous Quality Improvement movement. But at present it is the neuropsychologist and clinical personnel delivering care to patients with brain injury who are most interested in a model of care more likely to produce better efficiency and better outcomes than the pre-1980 models that continue to be used in many settings.

Biomedical Versus Service Neuropsychological Delivery Paradigms

Stanczak and Hutcherson (1992) have examined the differences in the neuropsychological and rehabilitative approaches to the treatment of brain injury. Giles and Fussey (1988) and Ylvisaker et al. (1990) observe that it is this absence of a fundamental, shared philosophy between the two disciplines that results in fragmented and disjointed delivery of rehabilitative services. For many years, rehabilitation professionals have worked within a biomedical paradigm. The latter paradigm has a fundamental notion of disease, and patients can be understood from a reductionistic examination of their constituent physical parts (Howard, 1991). Patient deficits are considered a deviation from biological norms and the disease process lies within the patient. From this perspective, neuropsychologists are looked to for a more holistic representation of the functional aspects of the patient, e.g., how the patient's brain functioning relates to the patient's behavior. It is interesting how the reductionistic versus dynamic theoretical antagonism is present not only between specialties but within specialties as well. Stanczak and Hutcherson (1992) assert that

the linear notion of a disease, with its demand of diagnosis and treatment, is no longer a viable one. Instead, the neuropsychological paradigm emphasizes the nonlinear notions of assessment and adaptation. Assessment is the identification and measurement of variables that affect the patient's performance. Adaptation is the systematic control of those variables to maximize the patient's functional autonomy. But assessment and adaptation are continuous processes that, in practice, occur concomitantly and repetitively. Instead of searching for "treatment" which effects change just within the head injury victim, rehabilitation specialists seek to maximize adaptation in two ways: (1) by altering the manner in which the patient interacts with his/her environment, and (2) by altering the way the environment affects the patient. Thus, within the neuropsychological paradigm, the range of possible "treatment" is limited only by the number of relevant variables identified and by the training and creativity of the health care provider. (p. 127)

It is essential that the differences between the biomedical and neuropsychological theoretical positions are understood by those who develop programs for patients with TBI in inpatient settings. The theoretical bias will determine which patient outcomes are considered important for treatment and the approaches to therapy and treatment. The Stanczak and Hutcherson (1992) comparison of the biomedical and neuropsychological paradigms of rehabilitation service delivery reproduced in Table 1 clearly documents the linear versus holistic methods of treatment.

What is not mentioned in the Stanczak and Hutcherson (1992) comparison, however, is the probable need for different foci at different stages of treatment. In terms of a continuum of care, the biomedical emphasis for brain injury takes its place in the initial acute phase of treatment and slowly gives way to neuropsychological emphasis as the patient's locus of control (in a medical and psychological sense) emerges. In other words, the paradigm should reflect patient need. In the acute stages of treatment, service delivery is primarily focused on the biomedical needs of the patient such as stabilization and maintenance while the patient is comatose. However, as the patient emerges from coma, interaction with the environment becomes a factor within the patient's control. At this point, the neuropsychological paradigm begins a dynamic assessment process that should help the patient

mediate his/her environment. The comatose patient is dependent on the biomedical response to his/her condition. As the patient's brain and body regain independent homeostasis, the acute period closes, the biomedical needs lessen, and the rehabilitative and neuropsychological needs increase (Grimm & Bleiberg, 1986). As the patient is discharged from a medical–surgical setting into a rehabilitation facility, the neuropsychological paradigm is in full force (except for those patients who continue to have major medical issues). Stanczak and Hutcherson (1992) state that programs that rely solely on one paradigm or the other probably do not exist. Most rehabilitative efforts are combinations of biomedical and neuropsychological interventions. However, it should be noted that unless a strong neuropsychology presence and a specific neuropsychological theoretical foundation exist in a brain injury rehabilitation program, that program is much more likely to reflect the supervision of the medical personnel involved. Reorientation of a biomedically managed program to a combination program that responds heavily to the neuropsychological needs of the patient is difficult and likely to deprive medical personnel of their considerable status and influence (Howard, 1991; Stanczak & Hutcherson, 1992). Therefore, the theoretical design of any brain injury rehabilitation program must be consciously held in the minds of the professionals involved and openly discussed and revised (Grimm & Bleiberg, 1986). A lack of theoretical perspective will reduce service delivery to reflecting the individual beliefs of the therapists or supervisors involved. The nature and complexity of brain injury rehabilitation demands cohesive and synergistic efforts from allied professionals and systems.

Models of Program Service Delivery

The neuropsychological rehabilitation programs that pioneered the methodology and designs of current programs were the Brain Injury Rehabilitation Unit of the Palo Alto Veteran's Administration Medical Center, the Neuropsychological Rehabilitation Program at Presbyterian Hospital of Oklahoma City, and the Cognitive Rehabilitation Program at the Robert Wood Johnson Jr. Lifestyle Institute. These programs were begun in the 1970s and

TABLE 1. A Comparison of the Biomedical and Neuropsychological Paradigms of Rehabilitation Service Delivery[a]

	Biomedical paradigm	Neuropsychological paradigm
Philosophy	Materialistic, reductionistic	Emergent, holistic
Primary model	Disease model	Dysfunctional model
	Linear diagnosis and treatment	Nonlinear assessment and adaptation
Theories	Little heuristic value	Proven heuristic value
	Brain viewed as internal organ	Brain viewed as organ of interface
	Presumes plasticity of neural tissue	Presumes learning occurs
Locus of dysfunction	Organismic	Is the interface between the individual and the environment
Role of provider	Healer	Consultant
Locus of power	Provider	Patient and family
	Patient blamed for lack of success	Treatment blamed for lack of success
Intrapsychic pathologizing	Accepted	Eschewed
Premorbid factors	Secondary importance	Primary importance
Role of patient	Passive recipient of services	Equal and active participant
Treatment options	Nil set	Unlimited
Behavioral disturbances	Viewed negatively	Viewed positively
	Treated by chemical restraints and behavioral treatment plans	Treated by environment modification plans and operant learning
Staff	Passive	Active
Meaning	For provider	For patient
Service delivery	Traditional static pyramidal model	Flexible systems model
	Authoritarian leadership	Authoritative leadership
	Vertical communication	Horizontal communication
	Leader decision-making and conflict resolution	Team decision-making and conflict resolution
	Focuses on tertiary and secondary interventions	Focuses on primary and secondary interventions
	Narrow scope	Broad scope
	Inefficient	Efficient
	Relatively inexpensive	Relatively expensive
	Architectural isolation	Architecture promotes resocialization
	Multidisciplinary	Transdisciplinary
	Fragmented treatment plans	Integrated treatment plans
	Staff competition	Staff collaboration
	Professional frustration	Professional autonomy
	Deficit management model	Health promotion model

[a]From Stanczak and Hutcherson (1992).

1980s and led the way for practical activities of daily living, psychotherapeutic interventions, and interventive cognitive neuropsychology to be included in programming for adults with TBI (Trexler, 1987).

Within the brain injury rehabilitation program, the focus of neuropsychological assessment has changed. Ben-Yishay and Gold (1990) have suggested that assessment should reflect psychometric, neurological, remedial, and functional perspectives. This holistic approach has received support (Prigatano, 1988, 1990, 1991a) and is probably a marriage of earlier efforts that were reductionistic and dynamic. Reductionistic approaches in neuropsychology focused on the diagnostic validity and reliability of specific tests and test batteries. Accuracy and prediction were the tenets of

assessment. Once a function was defined and measured, restoration of the deficits to some specific predetermined criteria was the practice and the goal. On the other hand, the dynamic thinking in neuropsychological rehabilitation placed emphasis on the therapist–patient relationship and a larger perspective of general adaptation in a variety of contextual situations.

As with others, Trexler 1987) proposed a model of treatment that included the reductionistic and dynamic approaches and described three basic dimensions for rehabilitation programming. The dimensions included the promotion of the patient being aware of his/her neuropsychological deficits, the treatment of general and specific deficits, and the promotion of generalization to the home or outpatient setting. This model may reflect the different views of the goals of rehabilitation. Neuropsychologists tend to focus on impairments reflecting brain–behavior relationships, whereas other rehabilitation professionals center their efforts on disability through readaptation at a functional level.

Other models that are currently in the forefront of programming for individuals with brain injury use multimodal approaches to cognitive rehabilitation and holistic approaches to team intervention. Embodied in the holistic conception of rehabilitation is the premise that patients allow themselves to be guided by clinicians. Individuals who were autonomous before the trauma learn to accept direction for their relearning (Ben-Yishay & Gold, 1990). Outcome studies of young adults with brain injury show that the best predictors of post-rehabilitation vocational attainments are improved self-awareness and acceptance. Ben-Yishay (1993) of the NYU brain injury program states,

> On one level the goal of neuropsychological rehabilitation is to ameliorate interferences with cognitive functions and aid in mastery of compensatory repertoires to improve functional competence. On another level the goal is to promote in TBI patients the necessary alteration of their sense of self or ego-identity so that in spite of the current limitations imposed by the brain injury they can reattain a minimum degree of self-esteem and self-worth. (p. 210)

The NYU Brain Injury Day Treatment Program is essentially a day treatment program for adults with brain injury. The program is divided into two main phases where the individual receives intensive assessment and remediation within a therapeutic community and then treatment progresses to supervision of the patient in an in vivo occupation work trial. Outcome studies for the cognitive remediation portion of the program indicated significant but modest improvement on test scores. Small-group therapy has been the more potent predictor of success in vocational attainment (Ben-Yishay & Gold, 1990). This program has flourished for decades, demonstrating clear outcomes such as returning patients to work, and continues essentially unchanged because of this success (Ben-Yishay & Daniels-Zide, 2000; Ben-Yishay & Gold, 1990; Ben-Yishay & Prigatano, 1990). Patients attend the Rusk Institute for 20-week cycles of treatment. The program provides day treatment for individuals between the ages of 18 and 55 who meet certain admission criteria (ability to tolerate extensive pretreatment neuropsychological testing, postinjury IQ above 80, a history of work or school attendance immediately before the brain injury, and lack of severe ambulatory and communication deficits, substance abuse, and physical aggression). After the initial assessment and evaluation period, remedial interventions begin within a small milieu including ten other patients. The day is organized around intensive group and individual activities with weekly counseling for the patient and family. Counseling sessions are often used to prepare the patient for an imminent group activity that is expected to be difficult for the patient. Periodically the patients prepare presentations that address the nature of the program and their individual problems and progress. The presentations sometimes resemble a 12-step program as the patient rises to address the assembly of peers, rehabilitation staff, and (sometimes) family, announces that he/she has a brain injury, and lists the impairments that result from the injury and the challenges of the neuropsychological rehabilitation program. Occupational trials and in vivo training end the cycle of treatment. Systematic bridging techniques are included to help the application of skills to functional daily living.

Perhaps the best way to represent the overall objective of the holistic program model is to describe the clinical challenges that the patient with brain injury must face. The NYU group (Ben-Yishay & Gold, 1990; Ben-Yishay &

Prigatano, 1990; Prigatano, 1990) developed a hierarchy of six stages of cognitive adjustment in the remedial program. The first is engagement, where the patient is encouraged to engage in the rehabilitation activities designed to optimize alertness, attention, and concentration. Awareness is the next stage. It is characterized by the patient beginning to focus on progressive awareness of his/her problems. The objective of this stage is to make sure that the patient has an understanding of the consequences of the brain injury and the commitment to undergo intensive rehabilitative efforts. The third and fourth stages of the program are the mastery and control, respectively, of compensatory strategies. These stages are also involved when the patient attempts to use compensatory techniques for daily problem-solving. The fifth stage, acceptance, is achieved when the patient attains a sense of realization that the limits of compensation for residual impairments have been met. According to Prigatano (1990), the latter is "never purely a cognitive act" (p. 297). The last stage concerns identity and refers to the culmination of the successful precedent stages. The patient established a new identity "hopefully with dignity and enthusiasm" (Prigatano, 1990, p. 287). At this point the patient achieves a perspective that the course of his/her life was permanently altered by the brain injury, but the new course is also a life worth living (Cossu, 1994).

Identity and acceptance of disability are key and related concepts in this model. Ben-Yishay used Erikson's concept of ego identity beginning as imitation in childhood, consolidating as a unique individual in adolescence, and then changing into a definition of self that, if transcendent, can reach beyond the limits of self, times, and culture. This identity is vulnerable; coherent memories of a stable self that endures over time are required (Ben-Yishay & Daniels-Zide, 2000). Thus, amnesia secondary to TBI could directly challenge this ego identity. Research with adults post-TBI shows their memory gaps are a direct challenge to identity (Nochi, 1997).

Ben-Yishay used the ideas of Kurt Goldstein on rehabilitation to provide structure to facilitate a healthy rather than a catastrophic response (severe anxiety from failure to cope with a threat to existence or identity) that might result from the inability to return to pre-injury functioning. Since this environment is not ordered by the patient, it limits personal

functional autonomy and lifestyle and so challenges the positive redefinition of identity and acceptance after TBI. The mourning of loss that accompanies acquiring a disability and feeling the loss of one's value in society can lead to a passive resignation without intervention:

> If the person persists in comparing himself or herself with who or what he or she was prior to the injury, self-acceptance is unlikely to occur. Nor would the person be able to view the results of rehabilitation as being very meaningful and emotionally satisfying. If, however, the person's value system shifts from a comparative perspective to an assets perspective (i.e., if the persons come to appreciate in themselves their preserved personality attributes and to value their current ability to make some meaningful contributions to either loved ones or to society), then the road to genuine acceptance is open. (Ben-Yishay & Daniels-Zide, 2000, p. 126)

Awareness and understanding of the nature and consequences of personal deficits leads to a voluntary choice to accept living with restrictions and thus to a feeling of health "without feeling victimized and ... feeling that life is worth living" (Ben-Yishay & Daniels-Zide, 2000, p. 116). More recent follow-up interviews related to identity and acceptance were completed with 24 patients who had worked without interruption since discharge. "We operationalize acceptance (of disability) as (a) a cessation of 'mourning' or agitation over the incurred losses, (b) morale, (c) satisfaction with the outcomes of one's rehabilitation, (d) capacity for enjoyment, and (e) improved self-esteem" (Ben-Yishay & Daniels-Zide, 2000: 120–121). The half who expressed a satisfying definition of self in their graduation speeches at the end of rehabilitation were rated more accepting of their disability at discharge and this was related to their vocational success at follow-up. Those who expressed a positive definition of self at graduation rated themselves at follow-up as having a more meaningful and productive life, feeling more at peace with oneself, and having a more satisfying social life and more ability to establish intimate relationships (Ben-Yishay & Daniels-Zide, 2000). Though only some symptoms are selected for remediation, outcomes are related to achieving goals related to identity and acceptance of disability. Psychotherapeutic interventions in which individuals with TBI can participate and

change are central to achieving these goals. Both cognitive and emotional functions are impaired in TBI, therefore, psychosocial interventions are part of a holistic neuropsychological rehabilitation program.

Psychosocial Aspects of Holistic Programs

The outcome of brain injury is affected by neuropathological, physical, functional, familial, vocational, and neuropsychological factors (Trexler, 1987). However, there is increasing recognition of the importance of psychosocial aspects. For example, the importance of psychosocial factors for functional outcome was used to explain why depth of lesion determined by SPGR MRI sequence was less related to outcome at 12 months than at 3 months post-TBI (Grados et al., 2001). Patients with TBI are much more seriously handicapped by emotional and personality disturbance than by their residual cognitive and physical disabilities (Divak, Herrle, & Scott, 1985; Lezak & O'Brien, 1990; McGuire & Sylvester, 1990). Also, cognitive deficits significantly influence the degree of disability and handicap associated with a physical impairment (Kaplan & Corrigan, 1994). The level of stress experienced by the family, the ultimate caregivers after rehabilitation has ended, varies with cognitive impairment and psychological adjustment to the brain injury (Allen, Linn, Guiterrez, & Willer, 1994; Semrud-Clikeman, Kutz, & Strassner, 2005). With the publication of the DSM-IV (American Psychiatric Association, 1994), the category of Personality Change Due to a Medical Condition has emerged as a diagnosis. In children, a deviation in development or change in behavior lasting for more than a year is substituted for personality change. Subtypes include labile affect, disinhibition, aggression, apathy, paranoia, and personality change associated with a seizure disorder. This category provides the first formal opportunity for psychological aspect of brain injury to be recognized by diagnosis. Postconcussional Disorder is now listed in Appendix B of DSM-IV-TR as worthy of further study, is more specific to brain injury, and is distinguishable from mild cognitive impairment (APA, 2000). In the holistic genre, psychotherapy is an integral part of rehabilitation because the physical and mental domains are not artificially separated. Thus, the

psychologist should be viewed as a rehabilitation therapist on the same footing as the physical, occupational, and speech language therapists. Psychotherapy provides a key ingredient through the process of teaching the patient to operate in his/her own best interest. Prigatano (1991a) states,

> at its core, psychotherapy is a teaching experience in which a socially sanctioned healer uses whatever learning techniques are culturally acceptable to the individual and society. These teaching techniques must "make sense" to the patient and to the therapist. They must reflect a method of interaction that considers the cognitive and personality characteristics of the individual being served. In post acute neurorehabilitation, the psychotherapist of TBI patients must demonstrate that the teaching methods are appropriate for a given patient and measure, directly or indirectly, the outcome to these interventions. (p. 3)

Many have argued that patients with a brain injury are not "psychologically minded" and are therefore not candidates for psychotherapy. However, a neuropsychological model of rehabilitation simply takes the psychotherapeutic goals for a given patient and addresses them from multiple perspectives. The goal is to assist the patient with psychosocial adjustment (Prigatano, 1988). Others (Deaton, 1990; Jackson & Gouvier, 1992) use cognitive behavioral interventions to help the patient comply with psychotherapy instructions or to provide psychotherapy reminders when fluctuations in motivational or emotional state are likely to occur. Cognitive behavioral therapy teaches the patient to become aware of the need for self-regulation and/or link the executive-intentional control of behavior with the motivational/emotional states.

Both the importance and relative neglect of psychosocial and family aspects of pediatric TBI rehabilitation have long been known by those working in the field (Ylvisaker, Wedel Sellars, & Edelman, 1998). Initial approaches were based on successful treatments of children with similar behaviors with no history of TBI (Kehle, Clark, & Jenson, 1996). This is no longer seen as adequate. Interventions to improve behavior should consider more than the child's need for behavioral support and address cognitive and executive functioning needs (Feeney & Ylvisaker, 2006). Thus, the psychosocial intervention is

itself more holistic. Similar to the decrease in problems behaviors in children with developmental difficulties that follow an increase in communication skills, there is evidence that behavior problems after TBI are reduced and quantity of completed work increased when positive behavior programming is accompanied by support for increased cognitive and executive function routine (Feeney & Ylvisaker, 2006).

Pediatric Versus Adult Programming for Individuals with Brain Injury

The traditional role of neuropsychologists in pediatric inpatient rehabilitation changed little through the 1980 s and focused on specialized assessments and treatment planning (Singer & Drotar, 1989) with little direct treatment of the child or family. There is little documentation of the benefits of rehabilitation treatment with brain-injured children and adolescents in the research literature (Deaton, 1990; Ewing-Cobbs & Fletcher, 1990; Lehr, 1990; Rourke, Bakker, Fisk, & Strang, 1983). Most research focuses on predicting status post-discharge based on some factor not related to the rehabilitation itself. The database that supports the Traumatic Brain Injury Model Systems Project funded by the National Institute on Disability and Rehabilitation Research includes only patients aged 16 or older (Dahmer, Shilling, Hamilton, Bontke, & Smith, 1993). A major reason given is the lack of appropriate outcome measures for children. The traditional neuropsychological approach to brain injury rehabilitation in children is based on the two pillars of cognitive rehabilitation (retraining, compensation, adapting the environment, and patient/family education) and behavioral approaches to emotional and behavioral sequelae (Thomson & Kerns, 2000). Unfortunately, there is limited empirical support for behavioral interventions to decrease externalizing and virtually none for treating internalizing symptoms (Warschausky, Kewman, & Kay, 1999).

Some research reports results with patients that include adolescents (and rarely children), but the pediatric cases are not analyzed separately. Reitan's REHABIT program for cognitive rehabilitation, described in Goldstein (1987), showed moderate to marked improvement in pre- and post-test scores for 23 of 26 patients aged 5–56 years with brain injuries (Brodsky, Brodsky, Lee, & Sever, 1986). However, they subsequently noted that the youngest patient, 7 years old at 25-month follow-up, had significant decline in verbal ability (Brodsky, 1988). The effectiveness of intervention for children with brain damage in general has been questioned, but the position of providers is that "the fields of rehabilitation medicine and developmental pediatrics are based on the principle that improving function, in spite of the permanence of handicap, is both desirable and possible" (Kaminer, 1986, p. 1101). Notwithstanding the staggering incidence of brain injury among the child and adolescent age group and the demands of Public Law 101-476 mandating services for students with brain injury in the public schools (Gerring & Carney, 1992), little is written about the specialized training and inpatient programming needed for these individuals. Gans, Mann, and Ylvisaker (1990) suggest that the two most important aspects of difference between adults and children with TBI are that "the child is a growing organism, and that functioning development is incomplete" (p. 593). In terms of inpatient treatment, the following general areas should be considered when describing a pediatric population and brain injury.

Age of Injury

The primary consideration of pediatric brain injury and long-term outcome is the age at which the injury occurred. It has become apparent that the extent of recovery following TBI in children and youth is determined by a variety of factors such as etiology, length of recovery interval, size of lesion, and lesion site (Ewing-Cobbs, Fletcher, & Levin, 1985; Lehr, 1990). A review of the literature on recovery notes that

> The most frequently postulated mechanisms [of recovery] have been resolution from oedema (swelling of the brain), or diaschisis (whereby lesions cause damage to other areas of the brain through shock), plasticity (change in the structure of the nervous system) and regeneration (regrowth of neural tissue). (Wilson, 1998, p. 281)

Much has been documented about the plasticity of the newly developing brain and will not be reiterated here. It was thought for sometime that "the earlier the insult the better the chance

of functional reorganization of the brain, or that plasticity of the young brain provided some measure of protection from the effects of the injury" (Sohlberg & Mateer, 1989, p. 388). This assumption was subsequently modified more to children over the age of 5, in that they may have substrates to provide the takeover of function. Younger children who sustain diffuse, widespread, or bilateral brain injury probably do not have the substrates necessary for domain specificity and may suffer serious compromises in the development of the basic cognitive structures that are necessary for psychoeducational and psychosocial functioning in later childhood and adolescence (Boll & Barth, 1981). More recent research (Lehr, 1990) suggests that short-term recovery from shifting functions to an area of the brain not yet specialized in function may result in compromise of later abilities to meet developmental milestones. The shift to new locations may make the child appear superficially intact but contribute to the slowing of reaction time, inefficient information processing, and ineffective memory for new learning that characterize much of postinjury functioning. Damage to immature areas of the brain may not have behavioral sequelae until neurodevelopment of functions associated with those structures fails to keep pace with environmental demands. Furthermore, there is an increased risk of hearing loss and seizure disorders that have extensive effects when combined with normal developmental demands (Sellers & Vegter, 1993). One possible pathway of the effects of a minor head trauma is subclinical posttraumatic seizures. Verduyn and colleagues studied 17 patients aged 11–56 who developed multiple, partial seizure-like symptoms after minor closed head trauma (Verduyn, Hilt, Roberts, & Roberts, 1992). Neuropsychological assessment in this study often suggested static and episodic cognitive impairment and most of the subjects benefited from treatment with anticonvulsant medication without fully returning to premorbid levels of social and vocational functioning. If seizures are uncontrolled, they continue to provide insults to the brain. In general, therefore, research concurs that children suffer greater effects of TBI than adults, and younger children suffer greater deficits than older children and adolescents (Mira, Tucker, & Tyler, 1992). The notion of plasticity suggesting greater recovery in those injured at younger ages has also not

born out in empirical studies of sensorimotor function (Kuhtz-Buschbeck et al., 2003). The Paediatric Brain Injury Rehabilitation Programme in Australia's routine follow-up through high school of all children hospitalized for brain injury has amassed outcome data arguing against plasticity (O'flaherty, 2004). The weight of what is known about recovery in young children after TBI argues against plasticity (Sellars, Vegter, & Flaig, 1997). Indeed, Stein (1988) offers a particularly succinct viewpoint:

> after an injury, the remaining nervous system should be considered as a new, reorganized structure and not just as a structure minus one part. In my view, the symptoms that follow brain damage do not stem from the missing or damaged part, but rather from the organism's attempt to adapt, cope, and survive. (p. 34)

This may account for the emergence of new problems in functioning or in development at follow-up. A study of 96 children 1 year after TBI divided into three different age groups (0–6 years; 7–13 years; 14–18 years) found younger patients show more internalizing problems such as withdrawal and older patients have more behavior problems like hyperactivity and aggressiveness (Geraldina et al., 2003). Johnson and Rose (2004) review traumatic brain injury in shaken infants and note that

> Recovery and outcome after brain damage are radically different matters, more so when the damage occurs to the immature brain. Recovery is a process to be inferred and is not directly measurable. In contrast, outcome is an end state, the cumulative result of injury, recovery, rehabilitation, education and development at any point in time.... If one considers development to be a continuous process, requiring the child to continually interact with changing environments, then it is self-evident that outcome after brain injury sustained in infancy cannot be determined at 5 months or 5 years or even 15 years of age. The child's level and type of dependence or independence cannot be determined prematurely in any but the most severe injury cases (pp. 187–188).

Large-scale follow-up studies of children have found that even milder injuries not admitted to the hospital can have needs for services, with only 87% being symptom-free at 10 months and 10% having problems with

attention and with low frustration tolerance (Hooper et al., 2004). Children show a recovery curve in academic skills after TBI, but those with more severe injuries continue to show greater deficits. Younger children show a decelerating growth curve in reading and math scores 2 years later regardless of severity but related to persistent cognitive deficits interfering with academic skill acquisition (Ewing-Cobbs et al., 2004; Semrud-Clikeman, Kutz, & Strassner, 2005). Long-term deficits are also apparent in social functioning. Few children (who do not receive neuropsychological rehabilitation) after TBI had four or more close friends at follow-up (38.9% for mild, 20% for moderate, and 14.3% for severe TBI) compared to 75% for children who had only orthopedic injuries (Prigatano & Gupta, 2006); the number of friends was related to higher academic performance regardless of TBI severity. This underscores the importance of a holistic approach to rehabilitation that targets more than one area of functioning.

In addition to differences based on age of injury, there may be gender differences (Donders & Hoffman, 2002). In light of the findings of significant impact of TBI on both present function and future development of children, worse with younger age and severity of injury, there is a need for comprehensive rehabilitation services encompassing inpatient and community settings (Gillett, 2004). The results of controlled studies of neuropsychological outcome after TBI in children are important to consider in rehabilitation planning:

> (1) standardized, office-bound cognitive assessments are often invalid predictors of real-world functioning and less useful than situational observation and hypothesis testing; (2) it is often executive control over cognitive processes (associated with the vulnerable frontal lobes), rather than the specific processes themselves (e.g., memory/learning, attention, organization), that is impaired and in need of rehabilitative attention; (3) there is substantial overlap between cognitive outcome after TBI and cognitive profiles of individuals with nominally different disabilities (e.g., attention deficit hyperactivity disorder, learning disability, autism, behavior disorders), mandating integration across disability boundaries; (4) cognitive impairments are typically tied to communication disorders (e.g., problems with disorganized discourse, slow and inefficient word retrieval, impulsive communication style), social/behavioral problems (e.g., impulsive and context-insensitive social interaction, anger and aggression, social withdrawal), and academic difficulties (e.g., problems with new learning and strategic learning, disorganized studying and writing, and the like); (5) young children often have a worse outcome than do adolescents with comparable injuries; and (6) furthermore, although general functioning can continue to improve for years after the injury, cognitive problems associated with impaired executive control often worsen over the child's developmental stages. (Ylvisaker et al., 2005: 98–99)

Assessment

The neuropsychological assessment of the child with brain injury goes far beyond the administration of a standardized set of test instruments (Ewing-Cobbs & Fletcher, 1990; Sohlberg & Mateer, 1989). Ylvisaker (1985) states that "traditional methods of assessment often require modification or flexibility in interpretation as a result of the particular combinations of cognitive, psychosocial, and motor problems that in many cases distinguish head injured children from those whose impairments are congenital" (p. 558). However, the procedure for assessment is similar for the pediatric and adult populations and, according to Sohlberg and Mateer (1989), includes (1) examination of the premorbid history, (2) review of the medical history, (3) interview and behavioral observations, (4) administration and scoring of neuropsychological tests, (5) drawing of conclusions describing the cognitive/behavioral strengths and weaknesses, (6) formulation of recommendations for a remedial plan, and (7) attempts at prognosis for recovery. What little scientific evidence there is regarding the ecological validity of neuropsychological testing following pediatric TBI shows only modest correlations with real world functioning (Silver, 2000).

Though premorbid conditions need to be considered in treatment and discharge planning, the milieu does not have to be different to achieve functional outcomes (Flood, Dumas, & Haley, 2005). Similarly, TBI complications may alter the individuals' rehabilitation plan based on assessment results. Evaluation and treatment of depression post-TBI can be successfully integrated into rehabilitation (Hassan, Turner-Stokes, Pierce, & Clegg, 2002). For example, those working with a child post-TBI should be aware of the possibility that an individual may

have suffered an anoxic brain injury after the original trauma since the recovery process and prognosis are different in some ways (Shah, Al-Adawi, Dorvlo, & Burke, 2004).

In the future, improvements in the early identification of patients most likely to benefit from rehabilitation may help direct resources. A study of 24 patients found the presence of organized sleep patterns on 24 –h polysomnographic recordings 7–14 days after severe TBI to be a better predictor of Glasgow Outcome Scale at 1 year than Glasgow Coma Scale or neuroradiological findings at admission, predicting a good outcome (full recovery/mild disability) with a sensitivity of 100% and specificity of 83% (Valente et al., 2002).

Neuropsychologists should be involved in early assessment of the patient through use of procedures developed for those still too impaired to respond to traditional psychological tests. In the acute phase of treatment, the depth of coma is tracked in a variety of ways, including the Glasgow Coma Scale, Coma Recovery Scale (CRS), Rancho Los Amigos (RLA) Level, and the Disability Rating Scale (DRS). The first two scales are based on a specific examination of the patient and the latter two scales are based on observations of what changes the patient has exhibited since the last rating. The Rancho Los Amigos Scales have been changed to fit pediatric assessment needs. Therefore, not only does the summary table of Levels of Consciousness reflect overall pediatric assessment, Records of Consciousness Levels focus on three separate pediatric groups: infant (6 months–2 years), pre-school (2–5 years), and school-age children (5 years and older) (Sellers & Vegter, 1993). Loss of consciousness (LOC) is tracked because the duration of unconsciousness is a gauge of the severity of the injury. However, as the coma gradually lightens, it can be difficult to agree on a precise time at which the coma ended because there is no consensual definition of coma boundaries. Posttraumatic amnesia (PTA) refers to how long the person remains confused, disoriented, and has trouble with memory. In a mild brain injury the person may not have been unconscious and patients can experience brain injury without head injury such as is seen in "occult brain injury" in spinal cord patients (Hinnant & Kade, 1992; Varney & Varney, 1995). Thus, it is not surprising that PTA is a better general gauge of how seriously the brain was injured than LOC and the better predictor of neurobehavioral outcome in children 1 year postinjury (McDonald et al., 1994).

Consensus on diagnostic criteria and evaluation protocols (Giacino, 2004) and related research now allows better specification of children's potential for recovery from coma (lacking both wakefulness and awareness), vegetative state (wakefulness without awareness), and minimally conscious state (MCS; minimal but definite behavioral evidence of self or environmental awareness) (Ashwal, 2004). Though "persistent" has been dropped from the term vegetative state, Borthwick and Crossley (2004) caution that we should also leave behind the assumptions of poor prognosis that have been associated with the term. The differentiation of the minimally conscious state allows distinctions to be made ranging from the neurophysiological level to the prognosis (Bernat, 2006).

There have been numerous neurobehavioral approaches to evaluating the patient with limited or no communication that make valuable contributions when carefully interpreted beyond what is learned from the commonly used Glasgow Coma Scale (Wilson, Graham, & Watson, 2005). In the future, neurophysiological and radiological techniques may assist in differentiating and further refining our definitions of these states (Laureys, 2004; Schoenle & Witzke, 2004; Shewmon, 2004). But even the newer behavioral scales available today are not routinely used in practice to help distinguish the minimally conscious state (Laureys, Perrin, Schnakers, Boly, & Majerus, 2005).

The role of the pediatric neuropsychologist at this stage is often largely confined to the neurobehavioral assessment of the patient's responsiveness and the education of the family. These activities can be combined by including family members in the assessment process. By becoming joined with the family at the patient's bedside, the neuropsychologist can begin a working relationship with them that sets the stage for eventually training the family to provide rehabilitation services to their child post-discharge. Family members have long been encouraged to participate in the treatment (Helwick, 1994; Semrud-Clikeman, Kutz, & Strassner, 2005) and even clinicians skeptical of the benefits to the patient may value the procedure as giving the family a way to feel they are contributing to the patient's care. As Tolle and Reimer (2003) point

out, patients still in a vegetative state for more than 6 months receive little active therapy beyond that provided by nurses and families.

Several assessment procedures are available that differentiate the minimally conscious state and some specifically seek family input. The Sensory Modality Assessment and Rehabilitation Technique (SMART) combines formal assessment with observations by family members and others over the course of the day (Gill-Thwaites & Munday, 1999, 2004). The revised JFK Coma Recovery Scale (CRS-R) adds new items that allow discrimination of the MCS (Kalmar & Giacino, 2005).

For the patient in a minimally conscious state, a neuropsychological assessment battery that allows the patient to respond with "yes" or "no" has been outlined (Neumann & Kotchoubey, 2004) once it is determined that their responses are reliable (Wilson et al., 2005). After a patient has progressed, neuropsychological assessment can provide useful results, even when completed early in the rehabilitation process. Neuropsychological testing completed in the acute rehabilitation setting once the child is oriented can be predictive of functioning 12–24 months later (Miller & Donders, 2003).

Telzrow (1990) has described and compared the different domains of assessment suggested by leading neuropsychologists in the field of pediatric neuropsychology. Most neuropsychological assessments address the following areas: intelligence, organizational skills, tactile perceptual, visual perceptual, auditory perceptual, memory, attention, problem-solving, abstract reasoning, manual dexterity, effects of feedback on performance, new learning ability, speech and language, personality, social skills, behavior, and family functioning. The domains are similar for adult and pediatric populations, but the latter group is more difficult to assess for a variety of reasons. The assessment is being conducted at a time when developmental processes are proceeding in the child. The processes vary from child to child and are subject to changes, spurts, and plateaus that complicate the establishment of valid measurements of neurocognitive function. Individuals at different ages may use different cognitive approaches to the same task (test) and possibly different areas of the brain as well (Hynd & Willis, 1988). The reliable and valid measurement of dynamic processes requires that tests reflect these developmental changes

(see Franzen, 1989, for a review of specific tests). Like the Wechsler intelligence scales, neuropsychological tests for children are largely downward extensions of adult measures. They may be validated for brain–behavior relationships but have inadequate developmental norms (Hynd & Willis, 1988; Spreen & Strauss, 1991). Conversely, cognitive measures with better developmental norms are not validated for brain–behavior relationships (Reitan, 1993). One attempt used the Woodcock–Johnson Revised Tests of Cognitive Ability (WJTCA) from the Woodcock–Johnson Psycho-Educational Battery-Revised with 39 patients aged 17–57 with closed head injury (Tupper, 1990). It found significant correlations between coma duration and performance on the Perceptual Speed and Memory clusters of the WJTCA, between Trail Making test performance and many WJTCA clusters, but no relationships with the Halstead Category test and any of the other Halstead–Reitan neuropsychological measures used. One attempt at the development of valid and functional assessment techniques that affects those reaching driving age involves fitness to drive. Galski and colleagues compared an off-road, predriving evaluation of skills regarded as important in driving and an on-road, behind-the-wheel evaluation of abilities needed to drive in actual traffic situations with patients who had a head injury or stroke. Only 4 out of 21 items on the predriving evaluation significantly predicted the outcome of the predriving evaluation and none predicted the outcome of the behind-the-wheel evaluation. Only 6 of the 26 tasks on the behind-the-wheel evaluation significantly predicted the outcome of the behind-the-wheel evaluation (Galski, Ehle, & Bruno, 1990, p. 709). A subsequent study of 106 patients aged 16–87 showed residual deficits in cognition less related than behavior in determining fitness, and when behavioral measures were included, off-road and on-road evaluation reached sensitivities of 90 and 92% (Galski, Bruno, & Ehle, 1993).

Arguments against the validity of inferences from neuropsychological tests are well known (Reschly & Gresham, 1989); however, little else is offered as a guideline for assessing children and adolescents with brain injury. Consensus has been reached on measures that discriminate the degree of brain injury and are sensitive to change over time (Kreutzer, Gordon, Rosenthal, &

Marwitz, 1993), but most of these lack adequate norms and similar validity data for children. The process of assessment of younger patients with brain injury is further clouded by the difficulty that clinicians and parents have distinguishing between neurobehavioral problems caused by the injury versus the emotional reactions to the trauma surrounding the event itself (Waaland & Raines, 1991). Nonetheless, neuropsychological assessment is helpful in determining the individual patient's initial status, establishing a comprehensive baseline for future comparison, identifying strengths and weaknesses, developing prescriptions for treatment, and assisting with prediction and determination of outcomes (Lynch, 1990). The pediatric neuropsychologist will need to be familiar with developmental as well as functional neuropsychological measures to be able to track progress and set appropriate goals (Long, Blackman, Farrell, Smolkin, & Conaway, 2005).

Developmental Stage

Notwithstanding the neurological aspects of brain development and brain injury, the developmental stage of psychosocial adjustment is also an important difference between pediatric and adult populations (Deaton, 1990). Preschool children have limited executive function. Traditional belief based on behavioral function was that supramodal or tertiary zones became functional between 5 and 8 years of age whereas prefrontal regions did not reach functional maturity until age 12 (Risser & Edgell, 1988). However, later neuro-science research suggests that prefrontal regions begin a process of maturation at 6–12 months of age and continue, perhaps in stages, to maturity (Casey et al., 2005 Pennington, 1991). In addition, there appears to be a correlation with neo-Piagetian stages of cognitive development. Thus, latency-aged children do not have the neuropsychological apparatus for the identity formation and executive functions that pubescent and adolescent individuals exhibit. Therefore, certain aspects of rehabilitation that would be addressed with adults would simply not be appropriate for adolescents and younger children. For example, the rehabilitation goal of acceptance and the formulation of a new identity that incorporates brain injury would not be a goal for an 8-year-old. The focus of acceptance of a new identity (or perhaps a different vision of the child as an adult) would be emphasized more with the family than with the patient in this case. With a patient who is 15 at the time of injury, the developmental stage would be the emergence of identity. The latter would be incorporated into the therapeutic goals because psychosocial adjustment in rehabilitation incorporates realistic appraisal of abilities and expectations in life. Adolescent needs do not essentially have a long-established sense of self-preinjury, as do those of adults (Lehr, 1990). Adolescents are in the process of individuation and emancipation from the family, and brain injury interrupts the natural unfolding of these events. Therefore, the adolescent's "identity development and independence striving can be significantly threatened or interrupted by injury" (Lehr, 1990, p. 4).

Stage of Recovery

Many pediatric rehabilitative programs use a three-phase structure for rehabilitation with individualized plans based on the child's stage of recovery, developmental age, and specific impairments (Henry, 1983; Ylvisaker, 1986). Although the benefit of treatment beyond nursing and nutritional care of the comatose patient is controversial, studies have shown that patients in coma can learn to do simple tasks such as removing a cloth from their face via backward chaining teaching technique (Sheil, Wilson, Horn, Watson, & Smith, 1993). Thus, a more reliable response to specific stimuli can be taught to a patient normally thought to be unresponsive. A study of 47 patients aged 14–55 with severe TBI has found a greater likelihood of functional change in those admitted to treatment less than 6 months postinjury. There was also a relationship between the amount of intervention provided and the level of functional change, suggesting some benefit to intervention even for those at a low level of functioning (Timmons, Gasquoine, & Scibak, 1987). Structured stimulation sessions for patients with limited or no awareness have been criticized for lack of empirical support and a Cochrane systematic review found none of the three studies available at the time provided useful and valid results that could be used to determine effectiveness for patients in coma or vegetative state (Lombardi, Taricco, De Tanti, Telaro, & Liberati, 2002). A subsequent review of a larger number of studies reached the

same conclusion (Rigaux & Kiefer, 2003). Despite such criticisms it continues to be practiced (Gerber, 2005) so commonly that, with few exceptions (Karma & Rawat, 2006), studies lack a no-treatment control group.

The goals of rehabilitation shift over the course of recovery as the patient emerges from coma and can reliably communicate, yet is still disoriented and experiencing PTA. Research suggests that in this second phase the patient can acquire skills (i.e., use procedural memory) during motor performance and pattern-analyzing tasks, but cannot recognize words they learn to read in mirror orientation or recall recent events (i.e., use declarative memory) (Ewert, Levin, Watson, & Kalisky, 1989).

In the third phase of rehabilitation, the patient has become oriented and PTA has ended. Formal assessment makes possible a delineation of the specific impairments that will become the foci of treatment. In this phase metacognitive and executive functions have received increasing attention of therapists from a variety of disciplines. For example, it is felt that "awareness, goal setting, planning, self-initiation, self-inhibition, self-monitoring, ability to change set, and strategic behavior" are necessary for completion of rehabilitation, community reentry, and social independence (Pollens, McBratnie, & Burton, 1988, p. 26). Ylvisaker and Szerkeres (1989) state that "metacognitive dysfunction involves deficits in both the knowledge base and executive system" with the latter involving "self-planning, self-directing, self-monitoring, and problem solving" (p. 34). Inclusion of these factors in treatment plans for speech–language therapy was seen as very important. Initial findings of limited functional improvements from interventions to improve memory resulted in additional interventions in executive functions to improve an adolescent patient's "ability" to identify a memory problem and to initiate a general plan for dealing with that problem (Lawson & Rice, 1989). Others have intervened in attentional processes with the logic that poor attention leads to poor encoding of information into memory (Mateer, 1993; Semrud-Clikeman, Kutz, & Strassner, 2005). However, studies of attentional deficits in 88 patients aged 16–45 with severe traumatic head injuries versus 59 age-matched, orthopedic rehabilitation patients provided no evidence of deficits of focused attention, sustained attention, or supervisory attentional control, but significant deficits in speed of information processing on tests such as the Symbol Digit Modalities Test, simple and choice reaction time tasks, and color naming and word reading scores on the Stroop (Ponsford & Kinsella, 1992). It has been suggested that treatment produces limited improvement in speed of information processing; therefore, patient and family education and supportive counseling are suggested (Lezak, 1994).

Psychosocial aspects are also dealt with in the third phase of rehabilitation. It is acknowledged that rehabilitation of a child with a condition such as cerebral palsy requires physical and occupational therapy, but a child with an acquired brain injury also requires psychological intervention and an intensive educational program (Russman, 1990). Self-esteem, self-image, and identity are key issues in brain injury rehabilitation. Garske and Thomas (1992) studied 47 individuals aged 16–35 with a history of severe closed head injury and found 55% mildly to severely depressed on the Beck Depression Inventory. Depression and lower self-esteem on the Rosenberg Self-Esteem Scale were significantly related to each other and to rehabilitation need satisfaction. McCabe and Green (1987) presented case reports of three 4- to 18-year-old boys who developed socially disinhibited behaviors following severe head injuries. Treatment helped them "to manage their maturational tasks of adolescence . . . including . . . identity issues" (p. 111).

Secondary changes in self-image have been studied and found significant. A study of eight patients aged 16–57 with head injuries found that both patients and their close relatives saw "significant changes on a semantic differential rating scale of the patient's present, past, and future self . . . [Patients] tended to see themselves in a more positive light than relatives regarding a present self. Both. . .anticipate a return to past self within a year" (McWilliams, 1991, p. 246).

Research with adults suggests that it is difficult, but possible for people to construct new self-images based on their experiences after the trauma. Retrograde amnesia for the trauma makes it difficult to readily comprehend the reasons for their present condition. More extensive loss of memory of their previous lives affects identity since memories are used to construct a self-narrative about who the individual is. Understanding of present capabilities can be

difficult for non-physical changes, but can be assisted by comprehensible personalized feedback from the neuropsychologist. Difficulties are also presented by comparing the post-TBI self-image with the recalled pre-trauma self-image or with the image of the individual presented by others, particularly when a negative image or label is used that communicates abnormality or powerlessness (Nochi, 1998a; Nochi, 1998b; Nochi, 2000). The adults in children's lives have an important influence:

> children, and especially adolescents, face a daunting task of integrating their evolving preinjury sense of self with new realities imposed on them by their injury. Parents and professionals play a crucial role in the difficult process of constructing a positive and organized identity. (Ylvisaker et al., 2005: 98–99)

Research on impaired awareness of deficit after TBI suggests deficits are influenced by number of lesions detected on CT or duration of posttraumatic amnesia (PTA) rather than on location of injury (Sherer, Hart, Whyte, Nick, & Yablon, 2005).

A review of the literature on impaired self-awareness after TBI shows evidence of a relationship to treatment outcome, length of stay, and treatment adherence (Prigatano, 2005). Family members' distress is correlated with their ratings of impairment in self-awareness in patients with TBI, dementia, or memory complaints (Prigatano, Borgaro, Baker, & Wethe, 2005). People from the general population overestimate social and intellectual abilities, partly because of an associated reduction in metacognitive ability to distinguish accuracy from error in themselves or others. Though not improved by exposure to a more accurate peer, direct instruction in the deficient intellectual ability results in more accurate self-awareness (Kruger & Dunning, 1999). The issues and interventions of this third phase of rehabilitation are the focus of much of this chapter because the differences in pediatric programming are most apparent once the patient is oriented.

Modalities of Treatment

Rehabilitation can be viewed at the level of the program or at the level of the therapeutic dyad of therapist and patient. Both levels of intervention must provide structure in the form of alteration between activity and rest (Gronwall et al., 1990). The comatose patient has difficulty regulating exposure to stimuli. The latter is usually evidenced in behaviors that represent frustration from overstimulation and fatigue. In addition, the level of regulation has an important influence on function and mood during the therapy sessions. Therefore, more (treatment) is not necessarily better (treatment). Later in the recovery process the patient's need for structure is balanced against an increasing need for self-control via shared decision-making. Of course, a child's ability to make decisions will vary by age and functioning level.

The obvious and well-established differences between child and adult therapies involve matching techniques to the developmental age of the child. These include such techniques as play therapy, the use of games and toys in speech, occupational, physical, and cognitive retraining therapies, and generally child-oriented materials and activities. The concept that play (and later school) is the work of the child takes on special meaning in rehabilitation because the traditional goal of adult rehabilitation is return to work: For the child it is return to play and to school. Play is intrinsically motivating to the child and an endeavor mediated by language with peers and more able models. Research studies have shown that "the proficiency of the therapist and his/her relationship with the patient proves to be the most significant variable related to the effectiveness of a therapy" (Rourke et al., 1983, p. 156). This therapeutic relationship may be determined, in part, by the presentation and interaction style of the therapist matching the neuropsychological strengths or weaknesses of the patient. For example, a patient with auditory processing deficits may have difficulty experiencing success with a therapist who favors highly verbal psychoeducational methods. A patient approaching a task greatly affected by his/her neuropsychological impairments and lacking in motivation and self-confidence may have limited success with a therapist providing emotional support but little structure. The amount of success the patient and therapist experience together will probably greatly affect the therapeutic relationship. Therefore, the link between neuropsychological assessment and therapist flexibility in terms of treatment modality and style is imperative for successful outcomes. Neuropsychological rehabilitation is not simply aimed at

restoring and facilitating the further development of higher mental functions, but works with child, family, other rehabilitation professionals, and school staff toward improvement in the child's quality of life (L. c. W. Braga, de Paz, Christensen, & Uzzell, 2000).

As Warschausky, Kewman, and Kay (1999) point out in their review of the literature, we have learned much more about the sequelae of pediatric TBI, including the importance of noncognitive psychosocial outcomes, than we have about how to successfully treat those psychosocial factors. The approach to psychosocial treatment has been almost exclusively behavioral interventions for acting out, rather than treatment of the emotional and social sequelae, with virtually no study of implementing psychosocial interventions within the multidisciplinary team.

Family Involvement

The obvious difference between family involvement with pediatric versus adult patients is that the family expectation on reentry for children is that the family will resume primary guidance and structure for the patient. In one way, this may reduce the amount of change for the family because they do not necessarily have to make the adjustment that a former autonomous adult is now a dependent adult, requiring a shift in family dynamics. The family of a pediatric patient expects to continue a guidance role when the child reenters. However, the adjustment for the idealized child to a child with special needs has its own set of emotional and psychosocial sequelae (Semrud-Clikeman, Kutz, & Strassner, 2005; Waaland & Raines, 1991). The adolescent patient may significantly interfere with the natural development of the family. The family may plunge from the developmental stage of family separation back into the school-aged developmental stage. Younger siblings at this time may resent the attention that the injured child receives. In addition, the greater need for supervision and structure sets the injured child apart from his/her siblings. The "birth order" among the siblings can be temporarily rearranged as an older child with an acute brain injury becomes more dependent on parents than younger siblings who may have to step into the "big brother or sister" role vacated by the patient. This can reverse with good recovery and then reverse again if the younger sibling later overtakes the patient whose development slows at later milestones. If the child is the survivor of an accident where other family members were killed, then special issues and difficulties may arise within the family (Mira et al., 1992). Patients who were premorbidly difficult children may precipitate the family's anger by becoming even more difficult after emerging from an initially docile postinjury phase (Miller, 1993). The family with a child who is brain injured is placed in a special situation:

> Related to the issue of dependency is that of protection. The child who has become disinhibited and socially fearless is now at increased risk for social and sexual exploitation, as well as for harming others, and the parents face the challenging dilemma of fostering independence and recovery, while at the same time providing control and structure to maintain safety. (Miller, 1993, p. 214)

Any assessment of the family should include assessment of the patient as a member of that family system and acknowledge individual differences within the system. Willer and colleagues used structured small-group discussions with 13 young men aged 14–25 with TBI, their mothers, and their siblings to document problems from each perspective (Willer, Allen, Durnan, & Ferry, 1990). Patients saw problems with peer relations, autonomy, and success at school. Mothers focused on problems with the service system and its accessibility. Siblings saw family stress as the biggest problem. Patients coped through accepting personal responsibilities for progress. Mother's acceptance of the patient was their most important means of coping. Siblings primarily coped by suppressing frustrations.

The stages in family adaptation when a child has sustained a TBI include shock, denial or disbelief, sorrow, anger, and adaptation (Martin, 1988). The "sudden and dramatic changes in the child's cognitive abilities and personality, ambiguity about recovery, . . . increased dependency and long term care needs" and the "lack of financial resources, lack of respite care, and lack of appropriate rehabilitation and educational programs in the community" are sources of family stress (Martin, 1988, p. 464). Clearly, the family must be prepared to accept the child's reentry into the home. It has been suggested that an Internet-based support network could provide contact with children's

family and friends at home (Verburg, Borthwick, Bennett, & Rumney, 2003). Experience with non-accidental TBI in shaken babies has also shown the importance of both rehabilitation and training caregivers to optimize outcome (Splaingard, 2001). In addition to the need for allocation of adequate resources to allow the professional to work collaboratively with the family in health care or educational settings, many of those professionals within the rehabilitation team lack a model for producing change that extends beyond the individual (Sohlberg, McLaughlin, Todis, Larsen, & Glang, 2001).

Reentry Issues

The field has made conceptual and practical advances in understanding and planning for post-discharge rehab in the community (DePompei & Tyler, 2004). A community-based program can serve as a transitional placement between hospital discharge and reentry to public school (Luiselli et al., 1998). Post-discharge planning must consider goals beyond the successful resumption of academic work at school and think in the broad goal of helping the child with the challenge of fitting back in, since children who do not are at risk for dropping out (Sharp, Bye, Llewellyn, & Cusick, 2006). As Dykeman (2003) points out, social functioning is a critical aspect after TBI and children need help with relearning old skills as well as learning new skills in order to make developmental progress.

Psychological distress, social dysfunction, and disrupted family functioning in family members 18 months after TBI in 144 adults were not due to the direct impacts of resulting impairments; the effects were mediated by the families' perceived level of support and the degree of community participation achieved by the person with TBI which also have direct effects on the families (Winstanley, Simpson, Tate, & Myles, 2006). "Clients with high levels of impairment were likely to experience low levels of community participation and, within this context, their relatives were more likely to perceive that their support needs were not being adequately met" (Winstanley, Simpson, Tate, & Myles, 2006: 462). The needs of children after they have returned home from inpatient rehabilitation also extend to psychosocial factors beyond the family (Lash, 2004). The challenge of providing rehabilitation to school-age children is incredibly complex because so many of the social, emotional, behavioral, and cognitive issues become evident at home and in school over time (Semrud-Clikeman, Kutz, & Strassner, 2005). Recent TBI outcome research has utilized caregiver reports of symptoms in children (Hooper et al., 2004). The development of measures of participation, environment, and child factors for children and youth with acquired brain injuries is an important contribution (Bedell, Haley, Coster, & Smith, 2002).

A community-based program can serve as a transitional placement between hospital discharge and reentry to public school (Luiselli et al., 1998). Group treatment can improve adolescents' pragmatic communication deficits secondary to acquired brain injury (ABI) and potentially ease school reentry, lessen social sequelae, and improve involvement in the community (Wiseman-Hakes, Stewart, Wasserman, & Schuller, 1998).

Case management and early discharge planning can effectively shorten hospital stays (Sakzewski, Ziviani, & Swanson, 1996). With or without planning, the practice of discontinuing funding for inpatient rehabilitation at the point the child becomes ambulatory creates an increasing emphasis on organized outpatient programs that go beyond sequential appointments with different disciplines and address the whole child. When 109 children with moderate or severe TBI were followed up to 4 years after injury, some recovered cognitive function during the first year, but then recovery reached a plateau and deficits persisted in cognitive skills (Yeates et al., 2002). The children showed little if any change in behavioral adjustment and academic performance. The latter problems were related to environmental factors in addition to TBI severity so a holistic approach that considers the child in context is required.

Even when comprehensive outpatient services are available, there are barriers to accessing outpatient services for many patients. In a study of people with fee-for-service Medicaid, 79% of those with brain injury had difficulty accessing services; 29% reported difficulty obtaining cognitive rehabilitation and 26% for other mental health problems (Shigaki, Hagglund, Clark, & Conforti, 2002). This discourages professionals from developing new services. Part of the difficulty in accessing comprehensive outpatient care

is that managed care organizations may shift responsibility to schools after the patient has returned home. But we cannot rely on schools to meet all the needs of children with TBI. When 42 children with severe TBI were followed up to 4 years after injury, it was found that less than 50% of those in special education were under the TBI classification; 21% of those who were in regular programs prior to injury were not in special education despite impaired functioning; rates of regular classroom accommodations were no different than matched children with only orthopedic injuries (Taylor et al., 2003). The same follow-up of 42 children with moderate TBI showed they were especially likely to not receive services when problems were not apparent in the first 12 months. Few in either group not in special education received remedial assistance and none of them received private interventions; none of the children received outside physical, occupational, or speech therapy.

Adult patients are rehabilitated to achieve a return to capacity and children are trained to develop capacity (Rourke et al., 1983). Adults and children relearn information in rehabilitation. However, children are in a constant state of maturation and new learning (Shapiro, 1987) and will return to an environment (i.e., school) where new learning is essential for success. Closed head injuries often involve the frontal and temporal lobes and therefore compromise problem-solving, higher-order processing, initiative, memory, and new learning (Levin, 1990). It is proposed (Lehr, 1990) that pediatric brain injury rehabilitation can be understood "as one process imposed on another" (p. 41).

Considering these specialized problems for children and adolescents reentering school, the lack of programming for youngsters with TBI in the public schools is surprising (Begali, 1992; Lash & Scarpino, 1993; Rourke et al., 1983; Ylvisaker, 1985). It is unfortunately usual that a child or adolescent will reenter school and interact with personnel who have little or no training in the special needs of youngsters with TBI. Although an influx of publications about TBI is emerging because of federal legislation, overall staff development for a low-incidence population is not economical, and therefore staff training is and will probably be done on a case-by-case method. This will obviously hamper any given student's progress with new learning or psychosocial adjustment because the staff

and student are learning about TBI reentry as they go along. This may also alter rehabilitation decisions as to reentry placement. If the pediatric patient is ready for community reentry and needs specific programming in the public schools, the rehabilitation team has the responsibility of making sure that the continuum of services available support the timing of reentry.

Savage and Carter (1988) present guidelines for rehabilitation professionals to use to contact school personnel, initiate school/hospital visits, conduct inservice training for educators, design appropriate education programming, and provide follow-up service. Although services are provided by public school systems, children with closed head injury differ from children traditionally served in special education programs and the burden is currently on rehabilitation professionals to facilitate reentry. Carney and Gerring (1990) present two cases that illustrate the necessity of cooperation between hospital and school to obtain the proper "assessment, environment, class size, teaching style, behavioral programs, instructional emphases, and integrated therapies" (p. 222). The informational needs of the school may dictate a different assessment. Specific elements of a functional assessment for adolescents who are reentering a classroom setting include visual processing, conversational processing, critical thinking, and skill integration (Milton, Scaglione, Flanagan, Cox, & Smith, 1991).

Even when these issues are satisfactorily resolved, access to services is problematic. Given briefer treatment in hospital and rehabilitation centers and reduced reimbursement for rehabilitative services, increasing emphasis is placed on services provided within schools; yet a total of fewer than 15,000 students receive special education services in the United States for TBI despite 20,000 entering school each year with persistent post-TBI disabilities (Ylvisaker et al., 2005).

Program Evaluation

TBI rehabilitation has limited empirical data supporting its efficacy or cost effectiveness, but fraud and abuses in the industry have brought further scrutiny (Ricker, 1998). The available research on efficacy of rehabilitation is perhaps most suggestive of a decreased length

of stay with more intensive rehabilitation or a "dose–response relationship" (Elliott & Walker, 2005). Follow-up studies of intensive rehabilitation are also supportive. Follow-up 2–10 years posttrauma of 353 children and adults after intensive inpatient rehabilitation found 76.5% of students were continuing with their studies or had progressed into work (Avesani, Salvi, Rigoli, & Gambini, 2005). Outcome differences were related to markers of TBI severity and length of stay (LOS), but higher success rates were achieved than might be expected given a very poor initial prognosis. A similar study was completed of 145 patients aged 0–25 years admitted in a vegetative state (VS) or minimally conscious state (MCS) after severe brain injury (72% traumatic) who received intensive rehabilitation until they reached consciousness or until it was concluded that no progress was achieved within 3 months (Eilander, Wijnen, Scheirs, de Kort, & Prevo, 2005). Almost two-thirds reached full consciousness, a more favorable outcome than earlier studies. Traumatic etiology was associated with a much better outcome, a finding replicated by others (Fragala, Haley, Dumas, & Rabin, 2002; Moorthi, Schneider, & Dombovy, 1999).

A follow-up study of 141 children and adults with TBI with up to 60 days of acute, transitional living, neurobehavioral and day treatment via multidisciplinary, programmatic rehabilitation found that 90% of patients were living at home and 88% functioning independently (Bryant, Sundance, Hobbs, & Jenkins, 1993). There were 29% fully employed, 5% employed part time, and 35% in school. Average length of stay and cost for acute rehabilitation were lowest at l9.4 days for $11,188.52.

More innovative therapies such as music therapy (Kennelly, Hamilton, & Cross, 2001) and therapeutic horseback riding (McCulloch, 2001) need to demonstrate effectiveness, but empirical backing for the traditional services does not set the bar too high. Literature on the effectiveness of discipline-specific rehabilitation services for children after TBI is generally lacking (Jones & Drummond, 2005).

Practices in measuring outcome in rehabilitation in general, and in brain injury programs in particular, have become increasingly important (Johnston, Keith, & Hinderer, 1992; Malkmus & Evans, 1992). Program evaluation proposed specifically for adults with brain injuries focuses on questions of whether the patient is still living at the same place and employed 1 year post-discharge. These measures have little meaning in pediatric rehabilitation because most children with brain injuries will still bet to school is legally mandated and therefore may artificially inflate simply defined success rates. The following research helps illustrate this point. A study of 93 patients aged 12–65 with severe head injuries found that at 6 months, 18% of former workers had returned to gainful employment and 62% of former students had returned to school (Ruff, Marshall, Crouch, Klauber, & Smith, 1993). Of the remaining patients, 31% of the former workers and 66% of the former students had returned by 12 months. "Age, length of coma, speed for both attending and motor movements, spatial integration, and intact vocabulary were all significantly related to returning to work or school" (Ruff et al., 1993, p. 101). The best predictors of return to work or school were verbal ability, speed of information processing, and age.

In many rehabilitation families the program evaluation methodology is often based on subjective assessments by the therapists who treated the patient. The potential for bias toward positive outcome in such an approach is obvious (Barber, 1976; Neale & Liebert, 1973), but unstudied. Furthermore, the new pediatric measures such as the Functional Independence Measure for Children or WeeFIM (Uniform Data System for Medical Rehabilitation, 1994) are downward extensions of adult measures with no specific procedures to adjust each measure to the developmental age of the individual patient. The alternative approach of calculating "percent of therapists' goals met by discharge date" has the effect of encouraging therapists to set lower goals to make outcomes appear most positive. Program evaluation for children with brain injuries is just beginning to develop measures that are adjusted to the child's specific age and include the behavioral, emotional, and social sequelae of prime importance to long-term outcome (Kade, 1994). In addition, many have documented the difficulty of determined outcomes with children because of the inherent problems that come with standardization of treatment in scientific investigations with children (Rourke et al., 1983).

Outcome Measurement

As the Glasgow Coma Scale predicts outcome, the Glasgow Outcome Scale measures outcome. The five areas of outcome are (1) death, (2) persistent vegetative state, (3) severe disability (conscious but disabled), (4) severe disability (disabled but independent), and (5) good recovery (Taylor, 1992). The latter category of the Glasgow Outcome Scale does not necessarily imply that there is an absence of persistent limitations for the patient. Only approximately one-third to one-half of all survivors of severe closed head injury can achieve good recovery (Begali, 1992). The Glasgow Outcome Scale may be popular because most patients have mild to moderate head injuries and these patients may simply be rated as "good recovery" at discharge from the acute medical–surgical hospital. The issue about the use of this scale with children, however, is that the term good recovery does not accurately reflect the academic and developmentally related criteria required for appropriate assessment of outcome. For example, good recovery of any injury sustained at age 4 may be the initial diagnostic impression until severe reading problems are discovered at age 8. Rourke et al. (1983) have stated that

> In the case of brain injury, the first and most obvious initial symptom (e.g., attentional deficiencies and impairment of motor functions) may represent only the "tip of the iceberg" with respect to the problems that the child will face over the span of a lifetime. For example, in cases in which the parietal region of the right cerebral hemisphere has been damaged, the child's social skills and awareness of self, particularly in relation to others, may prove to be one of the most outstanding and difficult areas to remediate. Although this may not be a prominent feature of the child's adaptive deficiencies during the first weeks or months following brain injury, one of the most important targets of remediation is to teach such children those skills that would help to alleviate their immediate and eventual difficulties in social responsiveness. (p. 157)

Therefore, Begali (1992) suggests that outcome scales with children and adolescents should be supplemented with formal and objective measures of "cognitive functioning, behavior, motor function, achievement, social skills, personality, and neuropsychological functioning" (p. 58). Research focusing on congenital malformations of the brain and early hydrocephalus from congenital or perinatal causes, but including childhood-acquired left hemisphere stroke and traumatic head injury, shows that these children exhibit deficits in word-finding, anomia, and verbal fluency, with impairments persisting in some 7 years after injury (Dennis, 1992). Although gross linguistic impairments in children with severe head injury are typically transient, more subtle problems such as work retrieval, verbal organization, comprehension, verbal learning, and effective conversation are common (Ylvisaker, 1986). Indeed, it has been felt that deficits in "attention, perception, organizing processes, and functional integrative performance" can influence functioning in these areas (Ylvisaker, 1986, p. 112). Thus, a comprehensive approach to neuropsychological functioning is needed.

The neuropsychological approach must be comprehensive enough to include psychological functioning. A study of 32 patients aged 16–55 with severe TBI found that initial assessments of medical factors were related to adaptive physical functioning at discharge (Torkelson, Jellinek, Malec, & Harvey, 1983). However, those who were minimally aware of their physical abilities and limitations at admission improved in their adaptive physical functioning during treatment. The psychological factors were related to relative improvement in adaptive physical functioning when change occurred. Both physical and psychological functioning were related to length of rehabilitation stay.

Psychosocial outcome is equally important. The adult (defined as over 18 years old) outcome of severe closed head injury sustained by 12 adolescents discharged home and returned to school was dependent on many areas of adult functioning when assessed from the perspective of the patient and a primary caregiver (Bergland & Thomas, 1991). A recent review concluded that

> Studies measuring psychosocial outcome in children and adolescents have shown that head injury leads to cognitive impairment that is directly related to the severity of injury in those with very severe head injury. Psychiatric disorders are also related to the severity of injury, but the relationship suggests that mediating factors are involved. No specific pattern of posttraumatic psychological/psychiatric dysfunction emerges from the studies, but it is clear that, as with adults,

psychosocial recovery lags behind physical. Head injury affects the functioning of the young person in the family, at school, and within the wider community, often resulting in a secondary handicap of low self-esteem. (Livingston & McCabe, 1990), p. 255)

A 6-month follow-up study of 25 (28.1% of 89) children and adolescents with TBI showed most (64–80%) of the children sustained the functional outcome levels achieved at hospital discharge from inpatient rehabilitation (Dumas, Haley, & Rabin, 2001). There were significant further gains over the 6 months in mobility and social function but not self-care on the Paediatric Evaluation of Disability Inventory.

Bedell (2004) developed a new survey to monitor needs and outcomes of children with acquired brain injuries including TBI and their families after discharge from pediatric inpatient rehabilitation. The assessment of participation in movement-related activities and participation in communication and school-based social activities is a welcome addition to the Pediatric Evaluation of Disability Inventory (PEDI) that measures functional activity in self-care, mobility, and social function. An initial study of 60 children found they were restricted in peer social-play, structured community activities, and managing daily routines (Bedell & Dumas, 2004). There is a need to develop outcome measures with less limited ceilings that prevent the detection of needs and gains in areas such as home and social integration (Hall, Mann, High, & Wright, 1996).

The Pediatric Rehabilitation Milieu

Diller and Gordon (1981) cite three types of environments that enter into rehabilitation: (a) physical (e.g., housing and transportation); (b) interpersonal (i.e., the immediate network of people around the patient); and (c) social (i.e., overt legal and covert norms and political/economic forces; for example, in a depressed economy, employment prospects for the disabled decline).

The interpersonal environment mentioned by Diller and Gordon could also be called the milieu. Much has been written about the social milieu of rehabilitation programs for individuals with TBI (Moore & Plovnik, 1991; Rattok et al., 1992). However, apart from the examination of the treatment team and its effectiveness within the social milieu with adult populations, formal manipulation of the sociotherapeutic environment for the pediatric populations has not been addressed. Prigatano and Ben-Yishay are probably credited with bringing milieu therapy per se into the neurorehabilitation arena with adults with brain injury, and it has long been recognized that an effective rehabilitation program should provide "individualized, round-the-clock service aimed at integrating therapeutic goals and objectives into day-to-day living so that the individual can achieve maximum independence" (Moore & Plovnik, 1991, p. 29).

Prigatano is perhaps the foremost proponent of using the psychotherapeutic milieu with individuals with brain injury. He extended the role of social work in rehabilitation from one of helping the patient and family adjust to brain injury and its sequelae to include an understanding of personality factors associated with successful outcomes. Prigatano (1988) also addressed the clinical understanding of the interplay between psychopathology and brain injury. In addition, small cohesive groups provide peer feedback about social skill deficits, a factor that provides therapeutic leverage (Grimm & Bleiberg, 1986; Rattok et al., 1992). Therefore, Prigatano's definition of the milieu (or holistic) approach to neurological rehabilitation is basically a program that "incorporates cognitive retraining activities with psychotherapy activities within the context of day treatment program" (Prigatano, 1990, p. 297).

The effectiveness of milieu therapy, especially with adolescents, has long been established by those who work in pediatric psychiatric setting (Abrahms, 1969; Bettleheim, 1969; Schwartz, Myers, & Astrachan, 1973). It is also well known to professionals in mental health rehabilitation who acknowledge that an appropriately structured rehabilitation milieu provides a nurturing, organizing, and generally helpful world for head-injured patients (Haarbauer-Krupa, Henry, Szekeres, & Ylvisaker, 1985; Rattok et al., 1992). The growth in the last decade of pediatric rehabilitation settings that are designed for chronic and/or residential needs has prompted the establishment of planned therapeutic communities. The rehabilitation milieu provides a "…'proving ground' gradually approximating a more naturalistic

uncontrolled environment for patients to refine and experiment with their developing skills, hopefully without the tragic and negative consequences characteristic of highly demanding everyday life" (Grimm & Bleiberg, 1986, p. 526). Romano (1984) summarizes Kelman's three processes of influence at work in a rehabilitation milieu: (1) compliance, when a patient is influenced to behave in a certain way in order to obtain rewards or punishments without regard to the content at hand; (2) identification, when the patient's behavior is influenced because he/she wants to establish or maintain a relationship with the group; and (3) internalization, when a patient accepts behavior because it is inherently rewarding and congruent with a value system.

In terms of structure, a milieu provides the patients with "stimulation, which can either confuse them further or contribute to cognitive recovery" (Haarbauer-Krupa, Moser, Smith, Sullivan, & Szekeres, 1985, p. 287). The rehabilitation team assists patients in making sense of the new environment and manipulates the programmatic structures within the milieu to reflect the patients' neuropsychological needs. Haarbauer-Krupa, Henry, Szekeres, and Ylvisaker (1985) propose seven principles of milieu treatment that describe the structure of rehabilitation milieu. The principles focus on the analysis of the complexity, relation, and duration of stimuli in the patient's external environment; coordination of family and staff approaches; predictability and familiarity of the physical setting; routines and repetition of events such as meals; use of a journal by the patient; and communication between the team members. A 6- to 39-month follow-up study of 24 patients with severe brain injury (aged 13–62 at admission) who had posttraumatic behavior disorders that had prevented rehabilitation in a more common setting showed lasting improvement from a token economy (Eames & Wood, 1985). It is impossible not to have a milieu in a treatment program because an environment or milieu exists wherever individuals gather. On the other hand, it is a different question altogether as to whether the milieu is planned or unplanned. The proponents of interdisciplinary versus multidisciplinary teaming in rehabilitation settings have long considered the consequences of unplanned communities or milieu.

Interdisciplinary Versus Multidisciplinary Rehabilitation Treatment Teams

Historically, the ideology of the team treating the individual with brain injury was aligned with the biomedical model. That team was made up of a neuropsychologist, clinical psychologist, medical social worker, dietitian, physical therapist, occupational therapist, speech–language pathologist, educational therapist, and other consultants as needed. Cognitive rehabilitation was provided by the neuropsychologist, occupational therapist, or speech–language pathologist. The individual leading the team was the primary care physician or appropriate medical–surgical specialist in a model derived from medical–surgical care and codified in standards of the JCAHO (Joint Commission on Accreditation of Healthcare Organizations, 1993).

Essentially, the multidisciplinary model presupposes that the individual disciplines work on their separate treatment goals and report to the team leader (usually the attending physician) at regular intervals (Howard, 1991). In some models of rehabilitation treatment, the clinical psychologist and social work personnel are not included in the team. Sometimes the neuropsychologist is limited in role to that of consultant or diagnostician rather than rehabilitation therapist. Indeed, for many years rehabilitation has been viewed as the domain of physical, occupational, speech, recreation, and vocational therapists along with nursing staff. The multidisciplinary team is essentially a set of somewhat related disciplines brought together by one or two individuals. The patient's environment is essentially the living space that he/she shares with other patients interrupted by clinicians taking the patient from the unit to designated therapy rooms. This is not a milieu designed to view the patient as a whole. It is a planned milieu in that the program design reflects the needs of the biomedical model. However, the biomedical model does not plan a holistic view or treatment of the patient, and in this sense, it is a non-therapeutic milieu. Thus, it is not surprising that Ben-Yishay has suggested using such programs as the "control group" treatment to contrast with the results of a planned, holistic, neuropsychological milieu (Ben-Yishay, 1992).

The interdisciplinary team approach, although made up of the same disciplines, demands that team members work collaboratively on treatment goals, and the general themes of neuropsychological and functional rehabilitation are woven into all aspects of treatment (Campbell, 1981). This idea is not new to pediatric rehabilitation. Henry described an interdisciplinary cognitive rehabilitation therapy for school-age children with head injuries that emphasized strategies to compensate for deficits (Henry, 1983). In the current formulation of this model for rehabilitation, the physician and neuropsychologist work closely to facilitate the team's decisions about selection and assessment of treatment goals, but decisions are team centered rather than physician centered. The clinicians are a part of the patient's milieu at all times. Each clinician understands the individual goals of his/her discipline and the connection of each goal to the whole team and whole patient. The key premise behind the interdisciplinary process is that "the group produces a resultant quality of health care to patients that is greater than the sum of the care they would produce if working separately" (Schultz & Texidor, 1991, p. 2).

Interdisciplinary intervention has produced significant gains using a neurodevelopmental model with infants and children. It produced similar general progress and recovery patterns beyond maturation effects in infants and preschool children with acquired and congenital brain injuries (Bagnato & Mayes, 1986). Progress in this age group was measured in terms of developmental quotients, neurodevelopmental and neurobehavioral skills, and rhythmic behavior patterns (Bagnato & Neisworth, 1986). The measures used to set and prioritize goals, track progress, and assess outcome reflect the conceptual model of the therapists. Bagnato's group uses two levels of appraisal (administrative and clinical child) and three bases of assessment (normative, adaptive curriculum, and clinical judgment) (Bagnato, Mayes, Nichter, Domoto, & Smith, 1988). A 2-year follow-up of 14 of the 17 original cases was conducted (Bagnato & Neisworth, 1989). The average age at follow-up was 6 years 3 months. It was found that children with congenital impairments made better progress than those with acquired brain insult. Patient progress was related to number of days enrolled in early childhood education programming, frequency of therapy services, and parental involvement. The size of the study is very small. However, it is exemplary in being a rehabilitation treatment outcome study with children published in referred journals. In addition, the findings support the importance of rehabilitation rather than relying on the traditional belief in the power of spontaneous recovery in children.

The purpose of the model proposed in this chapter is to take the interdisciplinary, holistic, and neurodevelopmental program models and include inpatient psychotherapy with school-age populations into the design. If the milieu becomes the true focus of the program, then every clinician is working on the whole patient with good lateral communication between clinicians. Lateral communication with nursing staff extends the effects throughout the milieu, beyond the bounds of the therapy room. Thus, cost effectiveness is achieved through replication of clinical effects throughout the milieu. This is a living and breathing program design that constantly fluctuates with the input of new learning and interchange between clinicians and the ever-changing nature of the patients involved.

The Neurodevelopmental Model of Pediatric Brain Injury Rehabilitation

The synthesis of successful elements of brain injury rehabilitation into a working paradigm is probably best illustrated by Ben-Yishay and the NYU group at the Rusk Institute in New York. A large part of the model presented in this chapter utilizes and adapts the clinical stages of the NYU program to a pediatric population that has an ongoing post-acute inpatient milieu. In addition, the model represents an interdisciplinary clinical paradigm for the treatment of children and adolescents with brain injury that lends itself to successful functional outcomes through the mechanism of holism and respect for the developmental autonomy of the patient, hence the term neurodevelopmental rehabilitation model.

The differences between the biomedical and neuropsychological paradigms of service delivery are clearly described in Table 1. Neither of these models, however, addresses the developmental concerns of the pediatric population. The neurodevelopmental model extends the elements of the neuropsychological paradigm by reflecting the status of the child within the

environment, the fluid nature of pediatric development, and the responsibility of the team toward a minor individual. The specific extensions are outlined in Table 2.

The neurodevelopmental model was formulated to (1) utilize the proven heuristic value of the clinical/cognitive stages originated by the NYU group, (2) extend the neuropsychological model to include pediatric concerns, (3) incorporate psychotherapeutic milieu elements into the rehabilitation treatment paradigm, and (4) sustain the interdisciplinary team as an effective component of rehabilitation treatment. The neurodevelopmental model is designed for the patient who has emerged from coma, become medically stable, and may or may not have returned home before admission to a post-acute rehabilitation setting. The program is characterized by the NYU cognitive adjustment stages

that have been adapted to represent clinical stages of neurorehabilitation. Each stage marks the clinical task for the patient and team, allows for ongoing assessment of progress toward outcome, and is useful for program evaluation. The process of rehabilitation (as opposed to the content) is the central focus at all times.

In the neurodevelopmental model, the first meeting of the pediatric interdisciplinary team marks the beginning of the synthesis of treatment. Each discipline is aware of the stages of clinical adjustment and translates their assessment and treatment recommendations through the language of these stages. In order for a large team of professionals to understand each other and work on the same goals, there must be a common language and a consensus about treatment approach that speaks to all disciplines at once without compromising the integrity of those disciplines.

TABLE 2. The Extension of the Neuropsychological Paradigm to the Neurodevelopmental Paradigm of Rehabilitation Service Delivery[a]

	Neuropsychological paradigm	Neurodevelopmental paradigm
Philosophy	Emergent, holistic	and dynamic, adaptive
Primary mode	Dysfunctional model	and functional/adaptive model
	Nonlinear assessment	and age-appropriate comparisons
Theories	Brain viewed as organ of interface presumes learning occurs	and developmental level
Locus of dysfunction	In the interface between the individual and the environment	and as defined by authority figures
Role of provider	Consultant	and authority figure
	Treatment blamed for lack of success	and developmental level (ceiling)
Intrapsychic pathologizing	Eschewed	unless in familial framework
Premorbid factors	Primary importance	plus prediction of future performance
Role of patient	Equal and active participant	and subject to authority
Treatment options	Unlimited	and matched to developmental stage
Behavioral disturbances	Viewed positively	and developmentally with peer support
Staff	Active	and authority figures
Meaning	For patient	and family/peers
Service delivery	Flexible systems model	with family/peer/milieu/direction
	Authoritative leadership	and consultants to family
	Team decision-making and conflict resolution	with family input and treatment continuation
	Staff collaboration	and family representation
	Health promotion model	and strength model of remediation
	Integrated treatment plans	tied to school reintegration and programming

[a] From Stanczak and Hutcherson (1992).

Hence, a speech pathologist and social worker can be working with the same patient, with their respective discipline-specific goals and yet be synchronous. If the team is to work consistently within a given paradigm, the central principles of the paradigm must be ones that can be easily remembered, understood, and translated. These central principles must be stated in a common language that is efficient and elegant. The following stages of rehabilitation treatment are adapted from the cognitive adjustment stages devised by Ben-Yishay and his colleagues. They can provide a universal language for the interdisciplinary team that is concise and simple to remember. At the first treatment team meeting, the team will describe the patient's initial status in terms of the six stages of clinical adjustment.

Stage 1: Engagement

Engagement is the patient's minimum level of investment in the rehabilitation program. It is possible for a patient to be admitted into the hospital and for a variety of reasons refuse to mediate the environment. Many times, this entry for adolescents is not essentially voluntary. The patient has become medically stable but is far from functional independence, and the continuation of treatment is a disappointing and frustrating detour from the initial hopes of returning home. The adolescent does not essentially have a legal or medical say in the decision for inpatient rehabilitation, and the involuntary nature of admission may result in the patient denying any need for treatment, grieving the lack of ability to return home, and refusing to engage. Therefore, after perhaps months of challenging circumstances in the acute care hospital, the patient and family face a new set of rules, expectations, and information.

The team members assess the patient's level of cognitive and affective engagement in treatment. This can be done by answering an assortment of questions that translate directly to treatment goals. An example of questions used for assessment and documentation of progress through this process is shown in Table 3. The patient's adjustment is observed in the milieu. The questions that must be addressed include "Does the patient acknowledge that he or she has a reason for being in the hospital?" "Does the patient acknowledge the therapist's expertise and authority?" "Does the patient attend therapies willingly?" "Does the patient understand the milieu/unit rules and expectations?" All disciplines may measure engagement by documenting such instances as number of therapies refused, frequency of agitation and oppositional behaviors at initiation of therapy times, and instances when the patient denies knowledge of milieu rules (not accounted for by memory impairment). Documenting observable instances of non-engagement and engagement will assist the team in (1) determining what level of engagement is necessary or acceptable for individual patients and (2) developing specific treatment goals related to facilitating transition to the next step of adjustment.

The patient who is unengaged may be so for many reasons. This could simply be a time of orientation and initial adjustment. The patient may need some time to reserve judgment as to whether the program is an appropriate placement for him/her. Entry could also be hampered by typical neuropsychological deficits associated with brain injury such as memory difficulties, lack of impulse control, unawareness of prominent features of brain injury, separation from family, and general disruption in surroundings. The team must be wary of producing oppositional behavior by overcontrolling the patient under the guise of providing structure or by using a schedule that perpetuates fatigue.

In most cases, if a patient is not engaged in therapy, it will be reported by most or all team members. This, then, becomes the focal point for the group and the point of treatment entry for the patient. The manner in which the team assists the patient with engagement is a key interdisciplinary goal for the whole team. Each discipline has specific goals to target engagement within a specific period of time (e.g., 2 weeks) until a reevaluation can be made by the team. For example, the team may decide that engagement is best facilitated by each therapist allowing the patient to choose a "fun" activity for therapy after they have engaged in "work" for a specified number of minutes. The "work" time can be extended as the patient achieves compliance and rapport with the therapists. In other cases of non-engagement the team may simply want to allow rapport to naturally build between the patient and the team. In some cases, peer modeling of engagement can be very powerful and is developed simply by observation of the milieu. The child who is able to acknowledge

TABLE 3. Example of Patient Progress Summary of the Milestones in Cognitive Adjustment to Brain Injury

I	I	I	I	I	I
Engagement	Awareness	Mastery	Control	Acceptance	Identity
Stage 1: Engagement				Date demonstrated	
Acknowledges at least one sequela as a reason for being in the hospital					
Separates from his/her family to attend therapy					
Understands the milieu/unit rules and expectations (may be shown by trying to find "loopholes")					
Understands the rules and expectations of individual and group therapies					
Attends a majority of therapies willingly					
Cooperates with a majority of therapist requests					
Stage 2: Awareness				Date demonstrated	
Acknowledges sequelae beyond concrete (such as inability to walk or speak clearly) symptoms					
Attributes impairments to brain injury and functional disabilities that result from impairments					
Can discuss his/her brain injury directly rather than use terms such as "the accident" or "my head injury"					
Accepts/agrees with at least some treatment goals beyond concrete symptoms					
Stage 3: Mastery				Date demonstrated	
Exhibits understanding of concept of the compensatory strategies					
Exhibits engagement in learning compensatory strategies					
Contributes suggestions (by work or deed) as to how to compensate for disabilities					
Exhibits consistent advancement in content knowledge of strategies					
Stage 4: Control				Date demonstrated	
Spontaneously demonstrates compensatory strategies for therapists					
Uses compensatory strategies in the milieu when coached through the process					
Uses compensatory strategies in the milieu when told which strategy to use					
Uses compensatory strategies in the milieu when simply cued to "stop and think"					
Spontaneously demonstrates compensatory strategies in the milieu					
Demonstrates compensatory strategies in different environments					
Remarks on inappropriate behaviors of peers					
Stage 5: Acceptance				Date demonstrated	
Acknowledges present and future need for compensatory strategies					
Refers to his/her rehabilitation as a necessary process that is nearing completion					
Takes on role model status in groups and milieu (for example, recommends same compensatory strategies to peers)					
Incorporates compensatory strategies into planning for future events such as reentry					
Stage 6: Identity				Date demonstrated	
Initiates changes in design/content of compensatory strategies (within his/her ability)					
Takes an active part in discharge planning					
Exhibits goals for reentry as realistic as expected for age					
Refers to himself/herself as a person who has worked through trauma or risen to the challenge of the injury					
Possesses a sense of personal dignity and positive self-worth and sees the course of his/her life as altered but worth living					

verbal communication may benefit from empathic statements by therapists about how hard it is for someone of the patient's age to accept help from adults outside the family (or if the patient is an adolescent, help from any adult) balanced by statements about how that help is necessary because of the brain injury. Any intervention is designed by the team after an extensive evaluation and is tailored to each patient. If the patient does not have difficulties engaging in

therapy and the treatment process, then this area is acknowledged but not addressed.

There may be instances where a patient in treatment is engaged and then becomes disengaged because of frustration, family issues, and the like. At this time, the team may wish to revisit this stage and problem-solve the cause of the disengagement and strategies for reengagement. In the event that some team members report engagement and other team members do not, then this is an ideal time for the team to problem-solve the strong and weak areas of both programming and individual therapist and strategies for assisting individual therapist and strategies for assisting individual team members or disciplines. From a psychosocial viewpoint, non-engagement could be a simple lack of adjustment to a new and highly structured environment. A psychotherapeutic view of non-engagement may be that rapport has not been established with the patient. Physical therapists may interpret a lack of engagement as avoidance of physical pain. Each discipline can tap into the issue of non-engagement and develop discipline-specific and team goals to solve the problem. It should be stressed that engagement, regardless of discipline interpretation, is fundamental to the course of rehabilitation treatment. If engagement is not established with the team, then successes in different therapies will appear seldom and random. The superficially compliant but unengaged patient may demonstrate more functional behavior in the context of the therapy room, but fail to later show change in other environments. The latter is symptomatic of fragmented services that service discipline-specific goals at the expense of therapeutic movement for the patient as a whole. It is all too easy for multidisciplinary therapists to proceed with discipline-specific goals for an unengaged patient and then attempt to explain the predictable lack of progress with labels such as "unmotivated" or references to the patient's premorbid personality characteristics. Much of the psychological and psychiatric consultation in a multidisciplinary model is for teams trying to treat an unengaged patient as if the patient were engaged in therapy. A conscious and planned system of interdisciplinary intervention should produce general therapeutic movement. Though not validated on youth under 17 years of age, a scale has been developed to quantify patient engagement in rehabilitation (Lequerica et al., 2006).

Stage 2: Awareness

Anosognosia (a lack of knowledge about a recognition deficit) was formally recognized as long ago as 1914 by Babinski (Kilstrom & Tobias, 1991; Prigatano & Schacter, 1991). According to Kilstrom and Tobias, Babinski defined unawareness as the patient being unaware of any problems in memory, language, perception, or voluntary movement. Unawareness could be evidenced by (1) the patient not acknowledging that there is anything wrong, (2) the patient acknowledging difficulty but attributing it to some source other than the known cause, or (3) the patient actively denying any difficulty at all. In addition, Prigatano and Klonoff (1991) argue that a deficit in self-awareness is the most limiting factor in the psychotherapeutic treatment of individuals with TBI and therefore results in a negative impact on long-term outcome. Schacter and Prigatano (1991) believe that "describing patients as 'aware' or 'unaware' of their deficits does not do full justice to the subtleties of awareness disturbances" (p. 261). They make distinctions between defensive denial of deficits versus neural bases of unawareness and note a lack of formal or objective measures of unawareness in brain-injured individuals. Prigatano (1991b) states that an understanding of individual awareness deficits is important not only to assist the patient in the process of self-appraisal but because

> self awareness emerges primarily in the areas of the brain deemed heteromodal cortex. This region is important for integrating what might broadly be called "cognitive" and "affective" components of experience. Learning any new behavior, as well as attempts at relearning "old" behaviors, might well require involvement from these structures. That is, awareness of various components of the self (or higher cerebral mediated activities) is by definition important for relearning necessary in neurorehabilitation. (p. 123)

It is important for the team treating pediatric patients to distinguish yet a third possible factor associated with unawareness and that is the cognitive and/or developmental level of the patient. Is it reasonable to expect a 12-year-old with severe TBI to ever be aware of his/her specific cognitive and psychosocial deficits and the long-term impact of those deficits? If so, to what extent? Would the impact of brain injury at

latency age permanently alter a child's ability to develop awareness? Is it developmentally appropriate for adolescents with brain injury to exhibit moderate amounts of defensive denial/unawareness? All of these questions must be posed with each pediatric patient. The developmental expectations for the patient will determine awareness goals, and in some cases the reverse may be true.

Awareness, then, is a process for the pediatric patient with brain injury. It is a progression of understanding about his/her residual or anticipatory neurobehavioral deficits that result from the injury. The patient is aware that there are specific sequelae from the brain injury that affect everyday functioning. In addition, this awareness includes "optimum responsiveness to treatments and the ability and willingness to modify one's maladaptive behaviors" (Ben-Yishay & Gold, 1990, p. 197). The compensatory strategies that are patient specific are usually domain specific and are introduced to the patient by the individual therapist. The unaware patient is introduced to assessments made about his/her psychosocial and neuropsychological strengths and weaknesses. In addition, assessment results are tied to interventions and specific therapy goals. Many times in rehabilitation, the introduction of compensatory strategies and techniques for the adolescent with brain injury occurs via the rules of the program. The patients "learn by doing in the clinical environment" (Moore & Plovnik, 1991, p. 501). For example, all patients may use a memory notebook or journal. It is expected of all patients, and therefore the individual becomes aware of a milieu-based strategy simply because it is the rule. Staff members are knowledgeable of the benefits of memory books and reiterate the usage and benefits on a daily basis in the milieu. In this way, many patients become aware of one of the common sequelae to brain injury.

Impaired self-awareness negatively impacts perceived life satisfaction at discharge from inpatient rehabilitation in adolescents and adults, independent of the patient's level of functioning (Evans, Sherer, Nick, Nakase-Richardson, & Yablon, 2005). A review of 12 longitudinal group outcome studies published between 1980 and 2006 empirical studies found four showing those with greater awareness of deficits achieve more favorable rehabilitation outcomes, six give partial support, and two

studies failed to support this relationship (Ownsworth & Clare, 2006). This variability in findings may be due to complex underlying relationships. Reduced self-awareness and unrealistic goals are associated with decreased productive activity and employment, but increased self-awareness and motivation to achieve goals may be linked to emotional distress or dysfunction that, especially when occurring within the first 6 months, is linked to poor employment outcome (Ownsworth, Desbois, Grant, Fleming, & Strong, 2006).

Increased awareness of dysfunction can increase negative mood with irritability, anger, or depression. The neuropsychologist can help the patient, family, and other rehabilitation staff view this as progress. Researchers at a VA Medical Center (VAMC) Rehabilitation Unit found that 14 patients given 3 h long sessions of personalized information based on their medical records and neuropsychological test showed higher levels of participation in physical therapy, improvement in cognitive functioning and functional independence, satisfaction with the information they received, and satisfaction with their communication with staff, personal involvement in treatment, and overall rehabilitation progress than 14 who received an equal amount of general information about head injuries and rehabilitation (Pegg et al., 2005).

The study of self-awareness in adults often includes older adolescents in the same sample (Port, Willmott, & Charlton, 2002), but measures appropriate for children are needed. The Subjective Awareness of Neuropsychological Deficits Questionnaire for Children (SAND-C) measures 9- to 16-year olds' awareness of strengths and weaknesses in psychomotor, attention, executive functioning, learning and memory, language, and visual–spatial functioning, though the preteens' ratings seem to reflect only one dimension (Hufford & Fastenau, 2005). Limited awareness of neuropsychological deficits may be the direct result of neuroanatomical damage, but research has focused on adults and the capacity to take an objective perspective of self changes with age.

Awareness is the conscious extension of the engagement stage. The patient is cooperative in therapies for the most part and exhibits membership in the milieu. The team evaluates awareness by addressing obvious questions about patient performance. "How does the patient respond to

assessment results given by the team?" "Does the patient express interest in his/her individual progress?" "Does the patient exhibit community awareness in the milieu?" "Does the patient participate in the milieu and therapies?" "Does the patient acknowledge that he/she has deficits associated with his/her medical condition and/or brain injury?" "Does the patient understand the consequences of the deficits?" "Does the patient understand specific treatment goals targeted in the treatment plan?" "Does the patient accept/ agree with treatment goals?" (See Table 3.)

The awareness stage of treatment may be very difficult for adolescents because emotional lability and behavior problems are inherently severe for this age group (McGuire & Sylvester, 1990). Becoming aware of severe and long-term sequelae is not a pleasant process and many adolescents will typically resist limits and authority (Barin, Hanchett, Jacob, & Scott, 1985). The usual education that assists normalization with regard to adjustment to injury for adults is not as reassuring for adolescents. The life experience for adolescents is short, and they have fewer overlearned coping skills premorbidly on which to draw for assistance (Haarbauer-Krupa, Moser, Smith, Sullivan, & Szekeres, 1985). It is difficult to normalize experiences that have to be synchronized with the separation and individuation tasks of the adolescent. Hence, the team must satisfy the need of the adolescent patient to feel that his/ her adjustment to the brain injury is appropriate and yet he/she can remain or become an independent entity. Although an adult's self-confidence can be bolstered by accessing memories of previous success at becoming independent after passing through adolescence, the adolescent has nothing to access other than the normal facade or feigning of not needing help from an adult. The milieu must make up for this by providing more support and structure to the adolescent than the adult patient would need.

Stage 3: Mastery

This is the stage where the patient is in the process of mastering compensatory techniques for the deficits identified by the interdisciplinary team. For most patients, a repertoire of skills must be learned that focus on functional or cognitive deficits. Haarbauer-Krupa, Henry, Szekeres, and Ylvisaker (1985) provide a detailed list of variables to consider in the selection and training of compensatory strategies. The variables range from the consideration of developmental factors to type and extent of brain injury. The list provides a comprehensive framework for the team when the mastery stage is negotiated. This stage is, perhaps, the easiest to assess because treatment goals are distinct and measurable. For example, learning a selection of cognitive behavioral techniques to reduce physical aggression is a common task set for an adolescent patient. The techniques can be taught in the milieu, community groups, individual and group therapies, or essentially anywhere in the rehabilitation setting. The individual counselor or psychotherapist may be the person responsible for the direct teaching of the strategies but the team is responsible for incorporating and/or facilitating generalization of training.

In terms of assessment, the patient receives the information and demonstrates retention of the information. Questions that would be appropriate for this stage may be "Does the patient exhibit understanding of the concept of the compensatory strategies?" "Does the patient exhibit engagement in learning compensatory strategies?" "Does the patient exhibit consistent advancement in content knowledge of strategies?" "Does the patient effectively use compensatory strategies when prompted?" "Does the patient exhibit at least 90% mastery of strategies?" For each brain injury patient, the team develops a list of specific goals that are presented to the patient for mastery. Knowledge of a compensatory strategy and spontaneous use of a strategy, however, are two different things.

Stage 4: Control

Control is represented by the patient demonstrating mastery of a compensatory strategy and also demonstrating spontaneous employment of that strategy in the milieu. In the case of the first example above, a patient would demonstrate understanding and knowledge of compensatory strategies to extinguish physical aggression and then would demonstrate use of one or more of the strategies to extinguish physical aggression and then would demonstrate use of one or more of the strategies when confronted with a situation that would normally evoke physical aggression. The patient may, for example, start a verbal altercation with a peer in

the milieu and instead of escalating to aggression, the patient requests staff to assist him/her in a self-imposed time-out to cool down. The strategy is initiated spontaneously by the patient and the results or consequences of the employment of the strategy are immediate (i.e., the patient is positively reinforced for choosing the strategy).

The team assesses this stage by observing the patient spontaneously using compensatory strategies in the milieu. It may be the observation that the patient is using a memory notebook on a consistent basis, is refraining from entering the personal space of peers, or is utilizing social skills (e.g., introductions, eye contact, non-verbal cues). The latter examples are measurable and dependent on the clinicians being aware of the patient not only in specific therapies but in the general milieu as well. Questions that the team may ask at this stage could be "Does the patient spontaneously demonstrate compensatory strategies in the milieu?" "Does the patient demonstrate compensatory strategies in different environments?" "Does the patient remark on inappropriate behaviors of peers?" "Does the patient need significantly less cues to use compensatory techniques?"

This completion of the control stage is critical if the patient is able to live outside an institution or at least a constantly supervised setting. If the patient cannot control the compensatory strategies in the inpatient milieu, then the chances for generalization on reentry are slim. Laments of patients being successful in the rehabilitation setting and failures in real life are replete in the rehabilitation literature (Ben-Yishay & Prigatano, 1990; Bruce, 1990; Cicerone & Tupper, 1991; Grimm & Bleiberg, 1986). The essence of control, therefore, is the emergence of generalization.

With regard to the patient who does not demonstrate control of any compensatory strategies, the team must revisit the initial goals for mastery and assess if the level of mastery is sufficient for generalization. It may be that in some cases the nature (deficits in executive functioning or metacognition) or severity of the brain injury may preclude a desirable level of control. For the "patient with a brain injury," it is a difficult process to recognize when a problem is developing or exists, inhibit an initial and perhaps "emotional" response, imagine a desired outcome, consider multiple possible responses based on

matching previous experiences with the present problem in context, and then choose a response based on predictions of the likelihood of success. Yet to be efficient, the patient must also sometimes allow the quick overlearned response to occur without conscious, verbal mediation. For the team, it is easy to have assumed that the patient needed a program of instruction in coping skills when more careful assessment may reveal the patient has more coping skills than are used because of metacognitive and executive deficits. Brain injury rehabilitation borrowed self-instructional training (literally teaching the patient how to think himself/herself through solving a problem) from clinical psychology where it became popular in the treatment of impulsive children with attention-deficit hyperactivity disorder (ADHD) (Haarbauer-Krupa, Henry, Szekeres, & Ylvisaker, 1985; Szerkeres, Ylvisaker, & Holland, 1985). Unfortunately, after 20 years of research there is still a lack of scientific evidence that this approach leads to mastery outside the therapy room for impulsive children (Abikoff, 1985, 1991). Without scientific evidence, there is no reason to persist in using the same techniques for brain-injured children in the hope that they will somehow achieve generalization and mastery through that approach.

If the patient with brain injury does not master use of compensatory strategies, then discharge planning is facilitated by the fact that the patient has reached a level of independence and will require a given level of structure in the next placement. For example, a patient may be able to master the memory notebook in the milieu with staff assistance and cues. Whether the patient moves to self-sufficiency regarding the memory notebook or remains dependent on external cues to use the book is the fundamental difference between mastery and control. The difference will have far-reaching effects for independent living on patient reentry.

Stage 5: Acceptance

Acceptance is related to control in that now the patient incorporates the changes in his/her life while consciously accepting personal deficits. The patient and team have an ongoing verbal discourse at this time that has been predicated on the patient learning new aspects of the self that have been transformed into measurable and successful tasks. This stage is characterized by the

patient taking pride in his/her accomplishments and demonstrating generalization of training. In addition, many times the patient becomes a role model for other patients and is an active member of the milieu. For adolescents, membership in the milieu includes an acceptance of the authority and expertise of staff as well as acceptance from peers as an experienced patient. In terms of the example given above, a patient would spontaneously use compensatory strategies to solve problems on a regular basis. In terms of team assessment, the frequency of use of compensatory strategies would be higher than in the mastery and/or control stages. In addition, the team would observe the patient identifying deficits in peers and offering advice to those peers as to how to use compensatory strategies to avoid physical aggression, for example. Peer-to-peer redirection is a powerful intervention in the adolescent milieu (Grimm & Bleiberg, 1986) and is only evidenced when more experienced and successful patients achieve acceptance and serve as guides to patients who have not yet achieved control of compensatory strategies. Therefore, assessment of this stage would be characterized by questions such as "Does the patient consistently use compensatory strategies in therapy?" "Does the patient consistently use compensatory strategies across environments?" "Does the patient refer to himself/herself as a patient retrospectively?" "Does the patient consistently take on role model status in groups and milieu?" "Does the patient incorporate compensatory strategies into reentry planning?" (See Table 3.)

Stage 6: Identity

Identity is the last stage of clinical adjustment in the neurodevelopmental model. It consists of the patient becoming temporarily aware of his/her progress through the former stages. This stage, as with the others, is interpreted within a developmental context. It is not appropriate for a 13-year-old to exhibit the formulation of identity that we would expect with an 18-year-old. The latter has a component of emancipation from the family that is developmentally desirable and predictable. The 13-year-old, on the other hand, is not ready for emancipation and identity formation. Indeed, the goal for this age group is to exhibit age-appropriate movement toward identity formation. The successful patient, in the identity stage, exhibits developmentally appropriate understanding of the events surrounding the injury, the residual deficits, and the mastery and control of compensatory strategies. Developmental issues are critical in assessing the identity stage. It is the reintegration of the patient at an age-specific period and is assessed with questions such as "Does the patient initiate changes in design/content of compensatory strategies?" "Does the patient take an active part in discharge planning?" "Does the patient exhibit realistic goals for reentry?" "Does the patient refer to himself/herself as a person who has worked through trauma?"

The patient is consciously aware of the progress made in treatment and is cognizant of the realistic implications of the brain injury. The patient also exhibits age-appropriate levels of identity formation. At all times, the emphasis is on the patient making choices for the future that are as realistic as would be expected for his/her age. The team's focus is on the appropriateness of placement at discharge and an accumulation of in vivo experiences that assist the maintenance of skills developed in treatment at this stage. Hence, discharge planning and reentry issues are the focus of treatment. Many times, the level of synthesis needed for this stage may be precluded by the severity of brain injury and/or level of maturity. In addition, the duration of stay in many facilities does not allow patients the time necessary to accomplish the goals of the identity stage or even earlier stages with patients who are unengaged in the rehabilitation process at admission. This places additional pressure on reentry into school or the services that bridge the gap between the rehabilitation hospital and the school.

Family-Centered Treatment in the Community

There are many arguments for the central role of the family in the child's transition to home and to school (Conoley & Sheridan, 1996; DePompei & Williams, 1994; Farmer, Clippard, Luehr-Wiemann, Wright, & Owings, 1996). Ultimately, the family can be the provider of rehabilitation after professional services have ended. Poor outcomes after TBI result from shortened length of stays in both inpatient and outpatient medical settings; insurance coverage

denials for rehabilitative treatment; and inadequate funding for public services (Brain Injury Association, 2007). Training the family to facilitate a good outcome should be part of the professionals' duties. The more detailed information we can provide parents about the likely persistence of deficits such as attention and memory, the better they will be able to help children cope with them (Shelton, 2004).

Preliminary study of level of 41 people providing care for people with ABI found that a community intervention was superior to traditional outpatient service in terms of the caregivers' ratings of met family needs, family dysfunction, and caregiver emotional acceptance (Smith et al., 2006). But community-based treatment is often provided in-home and is more ecologically valid than traditional outpatient treatment, it is more expensive. Involving the family as treatment providers is potentially more cost-effective.

Guides that assist parents in helping themselves and their children with psychological issues such as denial, grief, frustration, and limited awareness of their deficits are available (Schoenbrodt, 2001). Somewhat surprisingly L. W. Braga, Da Paz Júnior, and Ylvisaker (2005) showed that children aged 5–12 years in the chronic phase of their recovery receiving intensive services for 1 year made statistically and clinically significant improvements in physical and cognitive functioning through family-supported interventions and supports within the context of everyday routines of the child's life at home, but not through services directly delivered by clinicians.

Online training in family problem-solving can improve child adjustment after moderate to severe TBI, particularly in older children and children of lower SES (Wade, Carey, & Wolfe, 2006; Wade, Wolfe, Brown, & Pestian, 2005). Conoley and Sheridan (1996) describe the adjustment process of families following a child's brain injury in terms of emotions ending in reorganization. Most parents are not prepared for their child's continued needs 1 year post-discharge and many report decreased family functioning (Tomlin, Clarke, Robinson, & Roach, 2002). Evaluations of the family of a person with a TBI have focused on stress in the patient and the primary caregiver; a better model would include all family members, the variety of tasks facing families after TBI, an accumulation of stressors over time, stress appraisal, a thorough analysis of family coping behavior and a range extending to both positive and negative adaptation to stress (Perlesz, Kinsella, & Crowe, 1999).

Though the development of new technologies and smart devices holds promise, the reality for children is that the most common memory and organization strategy is "someone does it for me" (Gillette & DePompei, 2004).

Families are apt to be less forgiving of social mistakes made by the child with TBI and better able to include typical peers in interactions to build on social understanding (Turkstra, Dixon, & Baker, 2004). Families will also be present years after professional treatment has ceased because problems persist and new ones develop.

Follow-up of adolescents and adults after moderate to severe TBI at 7–24 years postinjury shows the continued functional limitations in this population (Colantonio et al., 2004). At the time of injury 22.6% were attending school, 18.6% full time; 77.1% were employed outside the home, 64% full time, and 3% described themselves as homemakers; only 1% were retired. At follow-up 5.6% were attending school, only 1% full time. There were 43.4% employed, 31% full time, and 2.6% homemakers; 19% of those not employed were looking for work. There were 11.1% retired, but most had retired because of their brain injury. Follow-up at 1–2 years of 21 patients not receiving rehabilitation showed 24% with clinically significant improvement on the Community Integration Questionnaire but an equal percentage declined (Cicerone, 2004). In the same follow-up of 998 patients in the NIDRR Traumatic Brain Injury Model System (TBIMS) database, 22.7% demonstrated clinically significant improvement from 1 to 2 years and 15.7% showed a clinically significant decline. Though TBI rehabilitation may be preventing some decline in community functioning, there is clearly room for improved outcomes. As Cicerone (2004) notes, satisfaction with cognitive functioning is strongly related to community integration, similar to the relationship between perceived self-efficacy and the performance of community-based activities. Despite their importance, "improvements in social participation and quality of life . . . have only just begun to be addressed in studies of rehabilitation effectiveness" (Cicerone, 2004, p. 500).

Summary and Conclusions

This chapter has focused on the history of brain injury treatment as it pertains to the development and gradual definition of the role of neuropsychology in rehabilitation. Neuropsychology has played an important part in assisting the medical profession in the diagnosis and localization of brain damage. With the increase in objective medical technology and the advancement of the field of rehabilitation, neuropsychology has come to serve in the areas of assessment and treatment of cognitive and neurobehavioral strengths and weaknesses associated with brain injury. The shift from localization to function has been reflected in the development of theoretical paradigms that are holistic versus reductionistic. Holistic programs represent neuropsychological principles whereas reductionistic programs serve the biomedical position.

While the biomedical and neuropsychological paradigms have a large research base with adult populations, little has been written about pediatric groups. The differences between adult and pediatric programming are substantial and essentially entail the problem of assessing and predicting outcomes for individuals who are in the process of developing. Issues surrounding family involvement must be handled differently within the educational and inclusion approach of interdisciplinary rehabilitation. Determining appropriate school placement is difficult, given that most teacher training in TBI is sparse and brief (Sohlberg & Mateer, 1989). Reentry is challenging for children and it is compounded by decreasing lengths of stay which are financially rather than clinically determined.

The neurodevelopmental model was formulated to (1) utilize the proven heuristic value of the clinical/cognitive stages originated by the NYU group, (2) extend the neuropsychological model to include pediatric concerns, (3) incorporate psychotherapeutic milieu elements into the rehabilitation treatment paradigm, and (4) sustain the interdisciplinary team as an effective component of rehabilitation treatment. The neurodevelopmental model aligns the interdisciplinary team with a framework of assisting the patient through six clinical stages of rehabilitation. The first two stages, engagement and awareness, seek to orient the patient to the difficult task at hand, set limits and expectations, and mark the beginning of a partnership between the patient and team. The next two stages, mastery and control, involve the learning of compensatory strategies that are individualized for each patient and the beginning of generalization of those strategies in the milieu. The last two stages, acceptance and identity, focus on patients incorporating their experiences (both positive and negative) into their self-concept and rehearsing reentry and discharge decisions and actions. The clinical stages are the unifying elements that allow different disciplines to communicate and accurately assess patient progress at any time. At any given stage, the team can assess patient progress and task analyze problems in progression. In essence, most patients will enter treatment unengaged and leave treatment with a synthesis of what and how treatment has affected them. In addition, the team may predict the stage at discharge that is appropriate for the patient and recommend placements that are commensurate with mastery and control. Program evaluation is essential and must include this six-step linear model of patient progress.

The neurodevelopmental model is concrete and therefore provides a means for quantifiable evaluation of its effectiveness and basis for further empirical studies that are important in the development of effective pediatric rehabilitation programs. In addition, the model becomes an effective teaching tool for patients, families, and staff. The framework allows for anyone in the milieu to be aware of the patient's immediate rehabilitation and milieu needs, and it allows those individuals to have a basic means of assessment of patient progress. Families are much more likely to participate in treatment and feel a part of the team if they understand and use the same language to describe their experience. The families, after all, are the individuals who carry the pediatric patient from one setting to another. Most often, the patient makes the transition from facility to home and, notwithstanding the best of discharge planning, the family members shoulder much (or all) of the responsibility for supporting the continuum of care and ultimately are the caregivers after formal rehabilitation is finished. It is up to the rehabilitation treatment team, then, to support the pediatric patient and family with treatment that transcends discipline and setting.

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21

The Neuropsychology of Pediatric Epilepsy and Antiepileptic Drugs

THOMAS L. BENNETT AND MAILE R. HO

Epilepsy is a nervous system disturbance that abruptly interferes with ongoing behavior, perception, movement, consciousness, or other brain functions. Individual attacks are called seizures, and when the problem is consistent it is called either a seizure disorder or epilepsy. Seizures are relatively common among infants, children, and adolescents with Hauser (1994) estimating 30,000 newly diagnosed cases of epilepsy in children in the United States for 1990 alone. Probably 8 of every 1000 children experience some sort of seizure activity, even if it is only a single occurrence of a febrile seizure (Lechtenberg, 1984). Occasionally, a seizure disorder will disappear as a child matures, but in a majority of cases, epilepsy persists into adulthood, and in 80% of adults with epilepsy, this condition developed when they were children. The purpose of this chapter is to describe the neuropsychology of pediatric epilepsy, and the emphasis will be to discuss the emotional/behavioral and cognitive concomitants of epilepsy and antiepileptic drugs (AEDs). We use the term *concomitants* to underscore the fact that epilepsy is a complex phenomenon, and the behavioral and cognitive events associated with it are the product of a complex interaction among neurological, medication, and psychosocial variables (Hermann & Whitman, 1986).

The apparent association between cognitive impairment and epilepsy has been observed for at least several centuries. For example, in his seventeenth century Oxford Lectures, Thomas Willis remarked, "It often happens that epileptic patients, during their paroxysm and afterward, suffer a severe loss of memory, intellect, and phantasy" (Dewhurst, 1980). This view of epilepsy pervaded the thinking of physicians through the nineteenth century as clinicians continued to note a high frequency of cognitive impairment in patients with epilepsy (e.g., Turner, 1907).

A significant limitation of the early observations was that they were typically confined to investigating patients in institutions. Thus, even when IQ began to be used as an index of intellectual ability (e.g., Fox, 1924), the results were biased by sampling error. Since the 1950s, the trend has been to sample the population more generally and to investigate intellectual functions in noninstitutionalized individuals. As these latter studies were published, it soon became quite evident that epilepsy and cognitive impairment were not highly correlated. Lack of cognitive impairment began to be stressed (e.g., Keating, 1960; Lennox & Lennox, 1960). In a study of 1905 individuals with epilepsy, Lennox and Lennox concluded that fully two-thirds of their patients were intellectually normal, and only one-seventh were clearly impaired.

Many problems were encountered in the early studies of cognitive impairment in epilepsy. Major factors known to affect cognitive

THOMAS L. BENNETT AND MAILE R. HO • Department of Psychology, Colorada State University, Ft. Collins, Colorado 80523.

processes in patients with epilepsy were not controlled, and indeed, this remains a major problem for research conducted on this topic today. These factors include age at onset and duration of the seizure disorder, seizure type, seizure frequency, medication variables, and whether the seizures are idiopathic or symptomatic. These variables are discussed later in this chapter.

A second major problem deals with the assessment of epilepsy. Early studies that employed objective measures used IQ testing. However, although IQ testing is in general a good measure of a person's biological level of adaptive functioning, it is nevertheless highly dependent on achievement. Furthermore, having not been developed originally to evaluate cerebral dysfunction, IQ tests are not particularly sensitive to the types of cognitive problems that people with brain injury experience. Neuropsychologists use IQ scores along with other information to estimate premorbid functioning in brain-injured individuals because of the IQ's resistance to brain injury.

Rather than using IQ as a measure of cognitive functions, recent research has used a cognitive process approach in evaluating cognitive abilities in epileptic populations. The cognitive processes investigated have included sensory processes, attention and sustained concentration, learning and memory, language skills, perceptual abilities, conceptualization and reasoning, and motor abilities. The majority of studies do not investigate all of these processes, and within a given process such as attention, one is struck by the fact that few investigators use the same task. Another problem is that a test may not evaluate what it purports to evaluate. Thus, a test of memory may actually be a test of attention, or it might be failed because of impaired attention, language, or conceptualization processes.

This latter difficulty can potentially be circumvented by utilizing a battery approach in assessment, an example of which is the Halstead–Reitan Neuropsychological Test Battery (Reitan & Wolfson, 1993). Reitan (1974) believed that this approach would be sensitive to the aggregate of cognitive impairments that might characterize a particular type of epilepsy under investigation.

Although generally in agreement with Reitan's view, Carl Dodrill has further refined the battery approach in the assessment of

individuals with epilepsy (e.g., Dodrill, 1978, 1981). He has modified and/or extended the Halstead–Reitan Battery to optimally assess cognitive deficits associated with epilepsy. His battery uses 16 measures of performance. Ten of these are from the Halstead–Reitan Battery [Category Test, Tactual Performance Test, total time, memory, and localization scores; Seashore Rhythm Test; Finger Tapping, total; Trails B; Aphasia Screening Test errors; Constructional Dyspraxia; Sensory/Perceptual exam; and Name Writing, total (letter/second)]. To this core, he added the following: Seashore Tonal Memory; Stroop Test; and the logical and visual reproduction portions of the Wechsler Memory Scale. Norms that reliably distinguished performance of patients with epilepsy from that of closely matched control subjects were established. The two groups were matched according to sex, age, education, occupational status, and race.

The sensitivity to cognitive deficits associated with epilepsy that Dodrill attempted to achieve was apparently realized as illustrated in a study by Dodrill and Troupin (1977). This study investigated the effects of phenytoin and carbamazepine on cognitive function. Use of the standardized Halstead–Reitan Battery yielded no statistically significant findings. However, several important differences emerged when Dodrill's Epilepsy Battery was employed. The application of neuropsychological test batteries to evaluate the cognitive effects of epilepsy and Dodrill's development of a battery specific to epilepsy represent advances. Unfortunately, the most common approach still remains narrow, and the majority of inquiries on this topic have continued to focus on a single, or only a few, cognitive abilities.

Four major topics are discussed in this chapter. First to be considered are the effects of epilepsy on cognitive processes such as attention, memory, and reasoning ability. That section is introduced by a model of the brain's functions in neuropsychological processes. Neural factors underlying cognitive deficits are discussed next. These include such factors as the age of onset and duration of the seizure disorder, seizure type, seizure frequency, and whether the seizures are idiopathic or symptomatic. Third, the influence of AEDs on cognitive processes is considered. Finally, alternative treatment options (nonmedication) are considered.

Epilepsy and Cognitive Processes

Because patients with epilepsy frequently present with a variety of cognitive and psychomotor deficits, as will be described in this chapter, neuropsychological assessment can be a valuable aid in establishing the severity of these impairments and monitoring the effects of treatments on these deficits. Specifically, neuropsychological evaluation before and after treatment is begun, and before and after major medication changes, should be used to determine if such changes produced positive effects for the patient; the evaluations could help determine an AED regimen that would strike an optimal balance between seizure control and adverse cognitive effects (Trimble & Thompson, 1986). Finally, knowledge of the nature and extent of neuropsychological deficits may be of help in devising remedial programs or compensatory strategies to alleviate these deficits.

The neuropsychologist can provide a direct role in treatment through traditional group and individual psychotherapy. The neuropsychologist can be an educational source for the child and his or her family about the nature of epilepsy, can help the child deal with psychosocial stressors associated with the disorder, and can help the family or teachers of the child to devise methods to manage objectionable behavior. As indicated, remedial or compensatory strategies can be devised to alleviate cognitive deficits. The neuropsychologist may also be involved in stress management and/or biofeedback training whose goal it is to reduce seizure frequency. Behavioral approaches to the treatment of epilepsy will be described later in this chapter.

This section of the chapter discusses the effects of epilepsy on cognitive processes. We discuss this against a model of neuropsychological function, which is described following a brief discussion of the effects of epilepsy on general intelligence.

Epilepsy and General Intelligence

While the vast majority of children with epilepsy fall within the normal limits of intelligence, the distribution for children with epilepsy is skewed toward the low-normal range of scores because of the underlying mechanisms/pathophysiology of the epilepsy, and not the epilepsy itself. Intelligence and the difficulties that will be discussed apply to all children, regardless of whether or not they have epilepsy, but are more frequently seen in children with epilepsy.

The importance of understanding a child's intelligence capabilities is key to being able to decipher underlying causes of poor academic performance. Material beyond a child's difficulty level or boredom with material beneath his or her level can both lead to poor academic performance. Frustration with these academic difficulties and misplaced parental and teacher expectations can lead the child to behave in improper manners during school and thus to be classified as a behaviorally problematic child. Pressures to perform at unrealistic levels by parents and teachers may be alleviated early in the child's academic career by recognizing the contributions and appropriateness of intelligence testing to academic placement and performance. Learning problems caused by interrupted auditory or visual information processing secondary to the seizure activity are common. Lack of concentration and distractibility are also more common to children with epilepsy than children without such conditions. Particular care must be taken to evaluate the possible influences of AEDs on learning and attentional deficiencies as they can all cause problems (Freeman, Vining, & Pillas, 1990). Such sequelae are common causes of academic difficulties in children with epilepsy and careful evaluation of the causes of academic problems must be made.

Neuropsychological Model of Brain Functioning

To appreciate fully the effects of epilepsy on cognitive processes, it is helpful to consider these processes within a theoretical or conceptual model of the behavioral correlates of brain functioning. In our own conceptualizations, we have found it helpful to expand on and modify the model presented by Reitan and Wolfson (1993), which denotes six categories of brain–behavior relationships. Bennett (1988) has expanded the number of categories to seven to separate attention from memory and to emphasize the dependence of memory on attention and concentration. He expanded on their level of logical analysis and renamed it "executive functions." Note that this is a process model and not

an anatomical model. With the exceptions of language skills and visuospatial, visuoconstructive, and manipulospatial skills, which are more represented, respectively, in the left and right hemispheres, these processes are bilaterally represented. This model is diagrammed in Figure 1 (from Bennett, 1988).

According to this model, the first level of neuropsychological processing is input to the brain via one of the sensory systems. It should be remembered that input could also arise endogenously from within the brain. The input must be attended to or concentrated on for information processing to occur and for the significance of the input to be ascertained (second level). Determining the significance of the stimulus or remembering it for later reference requires involvement of the memory system (third level).

The interdependence of attention and memory illustrates the fact that this neural system is dynamic, with activity flowing in both directions. In general, if information is to be remembered, it must be attended to, although, on the other hand, attention is no guarantee for memory. Similarly, attention is dependent on memory in terms of attentional processes being involved in such activities as habituation and filtering of gated-out nonrelevant information.

Input material that is verbal in nature requires the processing activities of a fourth neuropsychological category, language skills. Nonverbal material similarly requires processing mechanisms of a fifth category, visuospatial, visuoconstructive, and manipulospatial skills.

Executive functions represent the highest level of information processing. These activities
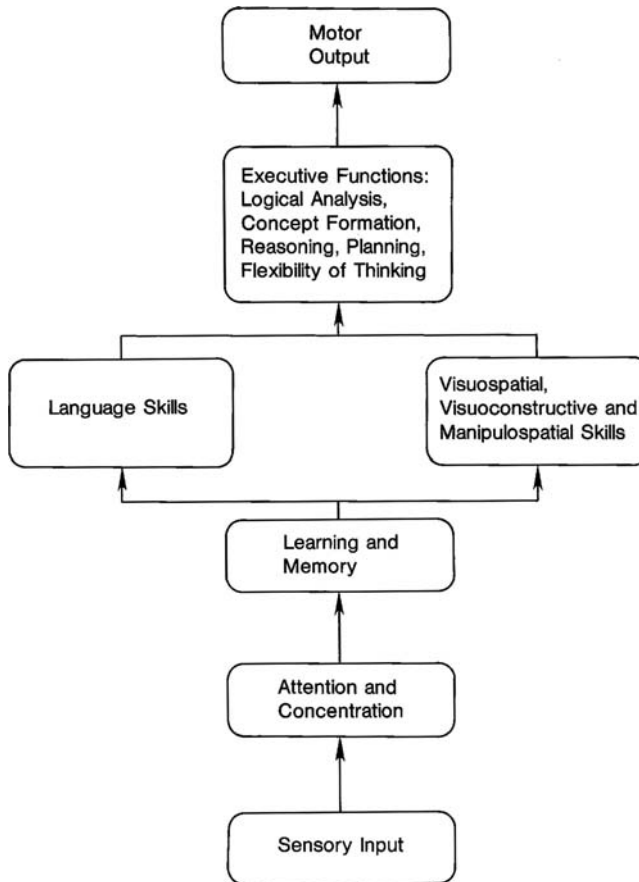
FIGURE 1. Conceptual model of the behavioral correlates of brain functioning (after Reitan & Wolfson, 1993; modified by Bennett, 1988).

are involved in logical analysis, conceptualization, planning, self-monitoring, and flexibility of thinking. Poor performance on tests of executive functions can result from a primary deficit to those functions themselves, or it can result from a primary deficit to one of the lower levels of processing on which executive functions depend. Executive functions quickly become quite impaired in the person who is distractible, forgetful, language impaired, or who cannot perform higher-level perceptual processes.

Motor functions are the basis for responding and represent the final common path of the neuropsychological processes. They reflect the output capabilities of the system. This is the rationale for placing motor output at the top of Figure 1. With this neuropsychological model as a backdrop, the effects of epilepsy on specific cognitive processes can be discussed.

Effects of Epilepsy on Specific Cognitive Processes

Sensory Input

Both impairment and exaggeration of sensory input can be said to result from seizures. Absence or petit mal attacks are generalized nonconvulsive seizures that occur particularly in children. They are characterized by brief episodes of loss of consciousness lasting approximately 5–15s. During these episodes, the child seems to be unaware of his or her surroundings and stares with a vacant expression. Sensory input occurring during these periods is neither attended to nor registered.

Complex partial seizures, on the other hand, may be manifested as sensory misperceptions and/or hallucinations. Misperceptions are often visual and complex. They typically involve distortions in depth perception or size. Size misperceptions can result in objects being perceived as much smaller (micropsia) or larger (macropsia) than they are. Visual misperceptions reflect a posterior temporal lobe seizure focus. For example, they were observed to occur in a patient of ours prior to discovery of a right temporal lobe astrocytoma, and they diminished following its removal.

Misperception of voices results from a focal discharge of the anterior temporal lobe neocortex, especially from the left hemisphere. Voices will be perceived as too high or too low in pitch or as being too loud or too soft. The patient might complain that the voices around him or her sound like they are coming out of a tunnel.

Hallucinations or auras that are experienced by patients with complex partial seizures are typically simple. In general, olfactory–gustatory sensations, which are often quite displeasing, result from a focal discharge in the uncus of the hippocampus. Our patients who experience these auras most typically report salty or bitter taste sensations and/or olfactory sensations best described as burning flesh or putrid. One patient, whose seizures were particularly refractory to anticonvulsant therapy and who experienced secondary generalized seizures correlated with menstruation, was anosmic except when she experienced olfactory auras just prior to and during menstruation each month.

Abdominal and epigastric sensations typically arise from an amygdala focus. Simple auditory phenomena, such as buzzing, ringing, and hissing sounds, are produced by focal activity on the surface of the temporal lobe, especially the primary auditory reception area. Complex visual hallucinations, although uncommon, arise from the temporoparieto-occipital junction (Rodin, 1984).

Cephalgic auras reflect discharge originating in the central regions of the temporal lobes. They consist of severe, sharp, stabbing knifelike head pains that are often associated with the head feeling too big, too small, or off the body. Cephalgic auras will occasionally be misdiagnosed as migraine headaches and subsequently incorrectly medicated.

An important feature of auras is that they are passive experiences. The patient feels like an observer to these ictal (seizure) events, dissociated from the actual experience. This is different from the schizophrenic who firmly believes his or her hallucinations are "real" experiences. The ictal events are unrelated to the environment, except for rare seizures triggered by specific stimuli (e.g., musicogenic seizures, sexual seizures). We once had a patient whose seizures were reliably triggered whenever he played the arcade game Foosball! More typically for the complex partial seizure patient, the ictal events begin spontaneously with an arrest of all activity, and the aura and/or psychomotor responses follow. Finally, while attention is usually paid

to the most salient attribute of the epileptic patient's aura, the dreamlike quality of the epileptic aura will often encompass many experiences. For example, a patient of ours regularly experienced a series of events including epigastric sensations, time distortion, detachment from her surroundings, and olfactory sensations as components of her seizure episodes.

Attention and Concentration

Impairment of attention and concentration, in the absence of overt clinical seizures, has been documented by several writers. For example, Holdsworth and Whitmore (1974) reported that 42% of their population of children with epilepsy were rated by their teachers as being markedly inattentive, and other writers have noted the detrimental effects of epilepsy-associated inattention on school success (e.g., Stores, 1973). In adults, Mirsky and Van Buren (1965) noted that the presence of epileptic spike waves was associated with decreased attention and concentration that was particularly apparent just prior to onset and following spike wave activity.

Attention difficulties in epilepsy are related to seizure type. Patients with generalized seizures are more impaired on measures of sustained attention than are patients with focal seizures (Lansdell & Mirsky, 1964; Mirsky et al., 1960). Mirsky and his colleagues argue that this occurs because generalized seizures are more likely than focal seizures to affect central subcortical structures that are responsible for maintaining attention.

In contrast, it appears that patients with focal seizures are more impaired on selective attention than are patients with generalized seizures (Loiseau, Signoret, & Strube, 1984; Stores, 1973). Loiseau et al. (1984) demonstrated that individuals with focal seizures and those with generalized seizures performed significantly worse on a test of selective attention than nonepileptic individuals. The worst performance was seen in the group with focal seizures. Stores interpreted this phenomenon as indicating that subcortical structures are important in determining what to pay attention to (selective attention). Focal seizures in the cortex thus produce inattentiveness by disrupting selective attention.

Learning and Memory

Memory deficits in association with epilepsy have been documented for over 100 years. Evidence has accumulated associating these deficits with temporal lobe epilepsy foci. In an early study that compared cognitive abilities in patients with generalized seizures versus those with focal complex partial seizures of temporal lobe origin, Quadfasel and Pruyser (1955) found that memory impairment was significant only in the focal group.

It should be noted, however, that most studies have been based on investigations of patients who were surgical candidates for intractable epilepsy. Little attention has been directed toward patients with complex partial seizures who were not candidates for surgical intervention. In addition, the findings from existing studies have not been entirely consistent.

When present, the memory deficit seen in individuals with complex partial seizures can exist in isolation. For example, when a complex partial seizure patient was initially evaluated using the Halstead–Reitan Battery, he showed a severe memory deficit that was more pronounced when he attempted to learn verbal material than when he attempted to learn nonverbal material (patterns). His Full-Scale WAIS-R IQ score was in the high average range, and his performance on all of the tests of the Halstead–Reitan Battery was within the normal range. Unfortunately, he showed a more global disruption of cognitive ability when tested a year later. Although his overall intellectual ability, as evaluated by the WAIS-R, had not significantly changed, he showed, in addition to his memory deficits, impairments in word-finding (dysnomia), psychomotor speed, and attention and sustained concentration. His conceptualization and logical analysis abilities remained unimpaired, but his memory deficits were even more pronounced than they had been in the initial evaluation.

The pattern of the neuropsychological deficits may prove to be an aid in determining the laterality of a temporal lobe focus, just as it is in determining the laterality of dysfunction after brain damage. One discrepancy worth noting is a difference in the severity of a deficit in processing, consolidating, and recalling verbal versus nonverbal information. It is well established that left temporal lobe dysfunction yields greater

verbal than nonverbal deficit, and the opposite pattern is obtained with right temporal lobe dysfunction (Jarvis & Barth, 1984; Milner, 1975). An analogous phenomenon occurs in patients with left versus right temporal lobe foci. For example, the patient we described who had a greater deficit in verbal memory than in nonverbal memory apparently had a left temporal lobe focus, as indicated by his EEG evaluations.

Although clinical evidence that memory disorders exist in complex partial seizures in longstanding, few carefully designed experiments on this topic have been carried out, and verbal memory has been studied more often than nonverbal memory. Studies of verbal memory in complex partial seizure patients indicate that those individuals with a left temporal lobe focus perform worse on tests of verbal memory than those with a right temporal lobe focus (Masui et al., 1984; Mayeux, Brandt, Rosen, & Benson, 1980).

Fedio and Mirsky (1969) studied verbal and nonverbal memory in children with right versus left seizure foci. Although no differences on short-term memory were found, recall of verbal material after a 5 min delay was significantly poorer in the left-focus group. In contrast, delayed recall of nonverbal material was significantly poorer in the right-focus children. Glowinski (1973) confirmed the direction of these laterality differences in adults, but the magnitude of these differences was not significant.

Since these initial studies were conducted, methodology for categorizing and matching patients has improved, and the basic findings have been confirmed, with long-term memory more significantly affected than short-term memory. For example, Lavadas, Umitta, and Provinciali (1979) investigated patients with epileptic foci in either the left or right temporal lobe who had no evidence of structural lesion on their CT scans. Short- and long-term memories were assessed. No difference in short-term memory was observed. On the other hand, patients with a left temporal lobe focus were more impaired on verbal long-term memory tasks. Delaney, Rosen, Mattson, and Novelly (1980) reported similar findings in right- and left-temporal-lobe-focus patients matched for age of onset, duration of epilepsy, and seizure frequency.

Taken together, these studies suggest a significant impairment of memory functions in patients with complex partial seizures of temporal lobe origin. A word of caution comes from Mayeux et al. (1980), who reported findings indicating that dysnomia contributes greatly to the interictal memory impairment seen in patients with complex partial seizures. Impairment on memory testing was highly correlated with deficits on the Boston Naming Test. They wrote that "the relative anomia demonstrated in temporal lobe epilepsy patients may have been interpreted by these patients and their relatives as poor memory" (p. 123). The authors further suggested that the verbosity and circumstantiality observed in some patients with complex partial seizures (e.g., Bear & Fedio, 1977; Bennett, 1987) may be the expression of a compensatory mechanism for dysnomia. This research points to the difficulty in attempting to evaluate deficits in specific cognitive processes for patients with epilepsy.

Language Skills

Both experimental inquiry and clinical observation indicate that epilepsy may adversely affect language skills. As indicated earlier, Mayeux et al. (1980) demonstrated that dysnomia was prominent in their complex partial seizure patients who had a left temporal lobe focus as indexed by scores on the Boston Naming Test. They also suggested that dysnomia contributed to the verbosity and circumstantial speech that are often observed in these individuals.

Circumstantiality is seen in both their spoken and written communication. Their communications are often overinclusive and include excessive background detailing, precise times, clarifications, and other nonessentials (Bear, Freeman, & Greenberg, 1984) and can prevent conversations from reaching a normal end. This interpersonal communication style can lead to such patients being shunned.

Hypergraphia is also often seen in patients with complex partial seizures. Hypergraphia refers to a tendency toward excessive and compulsive writing, and it was first well documented in these patients by Waxman and Geschwind (1984). It is often characterized by verbosity and circumstantiality, but it facilitated the writing of complex partial seizure victim and legendary author Fyodor Dostoyievski (Geschwind, 1984).

Impaired language skills as a consequence of epilepsy are also suggested by studies indicating that children with epilepsy have difficulty learning to read. Tizard, Rutter, and Whitmore (1969), for example, reported that 25% of their sample of children with epilepsy who were 9- to 12-years old were more than 28 months behind in reading and comprehension versus only 4% of the general population. In their Isle of Wight study, Rutter and his colleagues found that children with epilepsy showed a 12-month lag in reading ability compared with their chronological age (Rutter, Graham, & Yule, 1970). Bagley (1971) and Long and Moore (1979) have reported similar findings.

Perceptual–Motor Skills

There has not been a great deal of research investigating the effects of epilepsy on perceptual–motor skills, but the following has been reported. As was noted earlier, Dodrill (1978, 1981) found that total time, memory, and localization scores from the Tactual Performance Test were sensitive measures of the effects of epilepsy on cognitive processes. The total time score is a measure of perceptual–motor (manipulospatial) ability. A deficit in spatial memory can be evaluated via the localization score if a significant discrepancy exists between the localization score and the memory score from this task.

Several studies using the Bender–Gestalt test have indicated that children with epilepsy perform more poorly than control subjects (e.g., Schwartz & Dennerll, 1970; Tymchuk, 1974). Tymchuk found that a score that combined errors with reproduction time reliably distinguished between children with epilepsy and children with school/behavioral problems and borderline to mildly retarded children without epilepsy. No attempt was made to distinguish differential effects according to seizure type in these studies. Regarding this last factor, Morgan and Groh (1980) reported greater impairment on the Frostig Test of Developmental Visual Perception in children with focal seizures than in those with generalized seizures.

Executive Functions

Because of their dependence on lower-level neuropsychological functions, executive functions of the brain involved in such processes as conceptualization, logical analysis, reasoning, planning, sequential thinking, flexibility of thinking, and self-monitoring are especially sensitive to dysfunction, including that associated with epilepsy. As indicated earlier in this chapter, executive functions will typically be impaired in the person who is distractible, has a poor memory, is language impaired, or who has difficulty with perceptual–motor skills. In a general sense, executive functions are the basis for a person's ability to effectively meet the demands of his or her environment. Although these impairments may be easily overlooked, they are commonly seen in individuals with epilepsy as indicated by performance on such tests as the Trail Making Tests, the Wisconsin Card Sorting Test, and the Category Test. Trails B and the Category Test from the Halstead–Reitan Battery are components of Dodrill's Epilepsy Battery, and both Reitan (1974) and Dodrill (1981) stress the use of tests of executive functions in evaluating cognitive function in patients with epilepsy.

An interesting study by Hermann, Wyler, and Richey (1988) investigated Wisconsin Card Sorting Test performance (a test of frontal lobe functions) in patients with complex partial seizures of temporal lobe origin. Performance was studied in individuals whose seizures arose from the dominant versus nondominant temporal lobe as well as in an epilepsy control group composed mainly of patients with primarily generalized seizures. Thirty-seven percent of the dominant hemisphere-focus group and 79% of nondominant-temporal-lobe groups were impaired on this task, suggesting frontal lobe involvement. Only 17% of the epilepsy controls were impaired. It was suggested that these findings reflected dysfunction of the frontal lobes because of epileptic discharge ("neural noise") being propagated from a temporal lobe/hippocampal epileptic focus. Pathways that could transmit such temporal–frontal discharges are well known. After partial resection of the epileptogenic temporal lobe, Wisconsin Card Sorting Test performance improved, presumably because of a significant diminution of neural noise. A similar explanation was used to account for the finding by Novelly et al. (1984) that patients who underwent unilateral temporal lobectomy experienced a postoperative improvement in material-specific memory mediated by the hemisphere contralateral to the resection.

Motor Output

Decreased reaction time and psychomotor speed are common difficulties for individuals with epilepsy. Thus, McGuckin (1980) proposed that lack of speed is one of four main barriers to competitive employment faced by individuals with epilepsy. Using subjects with absence seizures, Goode, Penry, and Dreifuss (1970) reported that the presence of spike wave activity was accompanied by disruption of attention, increased reaction time, and impaired movement on tasks of motor performance, thereby producing more errors. Errors further increased when spike waves were present for more than 3s. Bruhm and Parsons (1977) also showed that slowed reaction time was common in patients with epilepsy.

Neural Factors Underlying Cognitive Deficits

Cognitive and behavioral changes associated with epilepsy are commonly attributed to neurophysiological dysfunction associated with ictal (seizure) events or long-term alterations in the central nervous system associated with repeated discharge. An example of the latter would be the kindling phenomena (e.g., see Post, 1983) or Bear's (1979) hypothesis that personality changes associated with complex partial seizures reflect a hyperconnectivity or a hyperexcitability of the limbic system. A number of variables, as reviewed by Hermann and Whitman (1986), have been posited as determining the magnitude of behavioral changes. In general, more significant effects are thought to result if the seizure disorder starts at an early age, in patients with poor seizure control, in individuals who have had the disorder for a relatively long period of time, and if the person exhibits multiple seizure types. Complex partial seizures, particularly those of temporal lobe origin, are typically believed to produce more obvious cognitive and behavioral changes than most seizure types.

This section of the chapter briefly considers some of the neural variables that must be considered in evaluating the effects of epilepsy on cognitive processes. The following factors are discussed: etiology of the seizure disorder, seizure type and frequency, and age at onset and duration of the seizure disorder.

Etiology of the Seizure Disorder

Of the intellectual correlates associated with epilepsy and the variables that alter them, the most predictable is that of etiology and its relationship to IQ. In his review of research concerned with intellectual and adaptive functioning in epilepsy, Tarter (1972) summarized studies in which etiological factors were considered. IQ scores of individuals whose seizures were idiopathic ranged from 4 to 11 points higher than scores attained by patients whose seizures were secondary to other etiology in both institutionalized and noninstitutionalized children and adults.

Etiology can significantly confound attempts to study neuropsychological processes in persons with epilepsy. For example, Fowler, Richards, Berent, and Boll (1987) conducted a study, utilizing a modified Halstead–Reitan Neuropsychological Test Battery, to assess cognitive impairments in persons with epilepsy and to investigate correlations between deficits on these tests and EEG indices of focus localization. They were able to demonstrate cognitive impairments on most of the measures employed and, where applicable, correlate these findings with EEG localization. For example, persons scoring low on tests of verbal comprehension usually had a left temporal lobe focus. However, approximately half of the subjects in this study knew the origin of their seizure disorder. Etiologies included head injury, infectious disease (e.g., encephalitis), intracranial tumors, and cerebrovascular disease (e.g., stroke). Given that brain damage alone can severely impair cognitive functioning and that the Halstead–Reitan Neuropsychological Test Battery is highly sensitive to the effects of these conditions, it would seem impossible to sort out the cognitive impairments related to epilepsy from those related to the disorder underlying the epilepsy in this inquiry.

Dikmen and Reitan's (1978) results would support this view. They have demonstrated that, when coupled with head injury with or without persistent focal cortical signs, persons with post-traumatic epilepsy demonstrate impaired performance on the Halstead–Reitan Neuropsychological Test Battery. It is not surprising that such impairments are seen in persons with persistent focal cortical signs since there are obvious signs of brain pathology. It is their contention that it is not possible to tell if the impairments

seen in persons without persistent cortical signs are related to the epilepsy or to the effects of the head injury. They argue, however, that they are most likely the result of the residual effects of the head injury picked up by a neuropsychological test sensitive to these effects.

Recent research in our laboratory by Sandra Haynes took great care to rule out prior history of head injury or neurological disease in her study of the cognitive effects of epilepsy in adults with clear evidence of focal left versus right temporal lobe seizures (Haynes & Bennett, 1991). Subjects with epilepsy were closely matched to a normal group on sex, age, IQ, and education. The test battery administered included the WAIS-R, Lateral Dominance Exam, Seashore Rhythm Test, Speech Sounds Perception Test, Seashore Tonal Memory Test, Rey–Osterreith Figure Memory Test, Story Memory Test, Boston Naming Test, Trail Making Tests, Category Test, Finger Oscillation Test, and the Grooved Pegboard Test.

The number of experimental subjects was small (four in each group), but in the absence of prior head injury or neurological disease, there were no lateralized deficits observed. The only trend found was that the subjects with epilepsy as a group exhibited generalized deficits in the areas of psychomotor speed, selective attention, and reasoning ability. This study emphasizes the importance of ruling out underlying cerebral pathology related to head injury or other neurological disease in studying cognitive processes in persons with epilepsy per se.

Seizure Type and Frequency

In addition to etiological factors, type and frequency of seizures constitute important variables influencing the nature and extent of intellectual and cognitive dysfunction. A number of studies have shown generalized tonic–clonic seizures to be associated with greater intellectual and cognitive impairment than other types of seizures. An early study by Zimmerman, Burgemeister, and Putnam (1951) investigated intellectual ability in children and adults using the Stanford Binet, Wechsler–Bellevue, and Merrill–Palmer Performance Tests. Mean IQ measured in children and adults with idiopathic absence seizures ranged from 10 to 14 points higher than in patients with tonic–clonic seizures. Using the WAIS and the Halstead–Reitan

Battery, Matthews and Kløve (1967) found that adult patients who experienced generalized seizures demonstrated greater overall intellectual–cognitive impairment than patients with other types of seizures regardless of whether the seizures were idiopathic or symptomatic. Wilkus and Dodrill (1976) also observed poorer performance by adults with EEG evidence of generalized discharged versus a focal seizure group. In addition, they noted that more frequent seizures were associated with greater deficits. This negative correlation between cognitive ability and frequency of seizures was also reported by Dikmen and Matthews (1977) in a study of 72 adults with tonic–clonic seizures of known and unknown etiology.

A similar relationship between seizure frequency and intellectual–cognitive impairment has been reported in children. In an early study, Keith, Ewert, Green, and Gage (1955) reviewed medical records of 296 children and found a regular increasing progression in percentage of retarded children as frequency of seizures increased. This relationship was consistent across all seizure types considered. Also, cases on which the seizures were symptomatic showed a greater incidence of retardation (73%) than those on which the cause of seizures could not be attributed to organic abnormality (22.2%).

Farwell, Dodrill, and Batzel (1985) evaluated a large group of children whose ages ranged from 6 to 15 years. Within each seizure type studied, lower seizure frequency was associated with higher scores on the WISC-R. In addition, seizure type was found to be a discriminating factor when both IQ and neuropsychological functions were evaluated. The minor motor and atypical absence groups showed statistically significant lower IQ scores than all other groups. However, children with partial or generalized tonic–clonic seizures demonstrated proportions of Full-Scale IQ scores comparable to those observed in the control group. When considered together, children with epilepsy showed significantly greater neuropsychological impairment than controls as measured by the age-appropriate Halstead–Reitan Battery. Overall, neuropsychological impairment was found to differentiate between seizure types with greater sensitivity than did Full-Scale IQ (WISC-R). Children with minor motor or atypical absence seizures demonstrated no detectable neuropsychological impairment, but when seizure types

were mixed (classical absence plus generalized tonic–clonic), impairment was again evident.

Seizure type has been found to affect selected cognitive functions differentially. Quadfasel and Pruyser (1955) compared cognitive abilities in adult male patients with generalized seizures versus complex partial seizures and found that memory was impaired only in the partial seizure group. Fedio and Mirsky (1969) assessed the performance of outpatient groups of children (6- to 14-years old) who had left temporal lobe epileptic focus, right temporal focus, or centrencephalic epilepsy (generalized seizures). Children were evaluated using measures of attention, verbal and nonverbal learning and memory, and IQ. Regardless of seizure type, the performance of children with epilepsy was below that of the epileptic control group. Of greater interest, however, was the pattern of deficits observed between seizure types and within the temporal lobe seizures groups. Children with left temporal lobe focus showed learning and memory deficits on measures that required delayed recall of verbal material whereas children with right temporal lobe focus had greater difficulty with recall tasks involving visuospatial abilities. Significant differences between performance on measures of short-term memory were not evident between groups. Further, children whose seizures were centrencephalic in nature performed at a significantly lower level on tasks of sustained attention than did the temporal lobe groups, but they did not demonstrate either short- or long-term memory impairment.

Patterns of intellectual performance on the Wechsler Intelligence Scales (WAIS or WISC-R) that varied with seizure type were observed by Giordani et al. (1985). Adults and children with partial seizures performed better on Digit Span, Digit Symbol (or Coding), Block Design, and Object Assembly than did patients with either generalized or partial secondarily generalized seizures although significant differences between groups on Full-Scale IQ scores were not present.

In contrast, some studies have not shown a clear relationship between seizure type and cognitive impairment (Arieff & Yacorzynski, 1942; Scott, Moffett, Matthews, & Ettlinger, 1967) or frequency of seizures and greater intellectual impairment (Delaney et al., 1980; Loiseau et al., 1980; Scott et al., 1967). O'Leary et al. (1983) found only one variable that showed a significant difference in performance between groups of children with differing seizure disorders. Children with partial seizures performed significantly better on the Tactual Performance Test (TPT-total time) than children with generalized seizures. The partial seizure group in this study, however, was composed of simple partial, complex partial, and partially secondarily generalized seizure types, and this wide variation of seizure types within one group may have accounted for the limited differences seen when groups were compared.

Because seizure classifications and their inclusion criteria have not been consistent, particularly in the earlier studies, and populations tested have not been uniform across investigations (institutionalized versus noninstitutionalized), direct comparisons between studies are not always possible. The study of seizure type and frequency and its effect on intellectual and cognitive function is further complicated by the severity of seizures and the levels of antiepileptic medications necessary to achieve adequate seizure control. It is also possible that in some cases, the association between observed cognitive deficits and frequency of seizures is related to the extent of cerebral damage which is responsible for both. When considered as a whole, however, current studies suggest that the extent of intellectual and cognitive dysfunction in epilepsy varies with type of seizure and increases with greater seizure frequency.

Age at Onset and Duration of Disorder

More than a century ago, Gowers recognized the relationship between early onset of seizure disorder and poor prognosis for mental functioning (Browne & Reynolds, 1981). In general, current research supports this observation. Studies of intellectual and neuropsychological functions in children with epilepsy, regardless of seizure type, indicate that onset of seizures early in life and a consequently long duration of seizure disorder places children at higher risk for cognitive dysfunction. It should be noted that in studies of children, long duration of seizure disorder is necessarily associated with early onset. Many studies of the effect of age of onset in the past have considered only major motor (generalized tonic–clonic seizures). Dikmen, Matthews, and Harley (1977) found that adult patients with early onset of major motor seizures (0–5 years of age) achieved significantly lower

Verbal, Performance, and Full-Scale IQ scores (WAIS) than a group of patients with later onset of seizures (10–15 years of age). Both seizure groups showed impaired neuropsychological functions (Halstead–Reitan) relative to a nonepileptic control group. However, differences in performance between the early and late-onset epileptic groups were not significant. On the other hand, Matthews and Kløve (1967) found that early onset of generalized tonic–clonic seizures resulted in greater impairment of both intellectual and neuropsychological abilities. This difference was observed in both idiopathic seizures and seizures secondary to known pathology (symptomatic seizures).

O'Leary et al. (1983) studied the effects of early onset of epilepsy in children 9–15 years of age with partial versus generalized seizures. Results indicated that both groups of children with early seizure onset performed more poorly on measures of neuropsychological abilities than children whose seizures began at a later age. These findings remain consistent with observations of the effect of seizure onset by Farwell et al. (1985), who studied a variety of seizure types, and Scarpa and Carassini (1982) in their study of children with partial seizures.

As in studies of seizure frequency, investigation of the effects of age at onset is complicated by AEDs. These have been found to affect cognitive performance in both children and adults (Browne & Reynolds, 1981; Trimble, 1981). In cases of early seizure onset, the effects of AEDs on the developing brain become an important consideration as does the subsequent long-term drug therapy that must follow.

Intellectual and Cognitive Effects of AEDs

AEDs or anticonvulsant medications have been implicated in producing negative cognitive and emotional effects in patients with seizure disorders. As a general rule, toxic blood serum levels of all AEDs adversely affect behavior and cognition (Reynolds, 1983; Wyllie, 1993), but adverse behavioral effects are sometimes associated with serum levels of AEDs that are within the therapeutic range (Thompson, Huppert, & Trimble, 1981). Polypharmacy increases the risk of epilepsy patients developing cognitive and emotional disorders with reductions in polytherapy resulting in improved cognition

(Duncan, Shorvon, & Trimble, 1990; Thompson & Trimble, 1982). Generally, phenobarbital and primidone (20% of which is metabolized into phenobarbital) are thought to produce the most significant effects, but phenytoin has also been implicated. In a double-blind study of polytherapy reduction, removal of phenytoin from drug therapy resulted in significant improvements in motor speed and in attention and concentration. Discontinuation of sodium valproate and carbamazepine in polytherapy has also resulted in increases in motor speed but no improvement in attention and concentration (Duncan et al., 1990). Generally, AEDs can magnify behavioral and cognitive changes produced by the seizure disorder itself, but in contrast, carbamazepine and sodium valproate have been argued to produce positive psychotropic effects.

Intellectual and cognitive impairments in people with epilepsy, especially memory deficits, were observed and noted in the literature over 100 years ago, long before current AEDs were utilized (Trimble & Thompson, 1981). Unfortunately, there is increasing evidence not only that cognitive deficits occur as a direct result of seizures themselves but also that many, if not most, AEDs affect cognitive abilities. As a result, AEDs may thereby compound the cognitive difficulties and behavioral problem seen in persons with epilepsy (American Academy of Pediatrics, 1985; Bellur & Hermann, 1984; Blumer & Benson, 1982; Committee on Drugs, 1985; Corbett, Trimble, & Nichol, 1985; Himmelhock, 1984; Reynolds & Trimble, 1985; Walker & Blumer, 1984; Wilson, Petty, Perry, & Rose, 1983). Therefore, the disentangling of medication effects from seizure effects represents a formidable challenge to researchers.

For most AEDs, favorable reports, usually based on subjective impressions, have been noted immediately after the drugs have been introduced for general use. With widespread use and experimental inquiry into their neuropsychological influence, adverse effects soon have emerged for most AEDs. Toxic doses of virtually all AEDs can affect mental functioning. It is, however, the possibility of cognitive impairment resulting from serum concentrations of AEDs within therapeutic ranges that is of most concern in the long-term treatment of epilepsy.

For example, Reynolds and Travers (1974) studied a group of 57 outpatients some of whom

were experiencing intellectual deterioration, psychiatric illness, personality change, or psychomotor slowing. Those who were experiencing these difficulties had significantly higher blood levels of phenytoin or phenobarbital than those without such changes even though these individuals all had blood levels of these drugs that were within the optimum or therapeutic range. Patients with overt drug toxicity, detectable cerebral lesions, or psychiatric illness that preceded the onset of epilepsy had been excluded from the study. These observations were also not simply related to seizure frequency. Similar findings were reported by Trimble and Corbett (1980) in a study of 312 children in a residential hospital school. Children who experienced a decline in IQ of between 10 and 40 points over a 1-year interval had significantly higher levels of phenytoin and primidone, with a similar trend for phenobarbital, than those who did not. Farwell et al. (1990) found that children receiving phenobarbital after at least once febrile seizure and who were at risk for further seizures scored an average of 8.4 IQ points lower than those receiving placebos. Again, blood levels of these AEDs were within the therapeutic range for both studies.

The nature and extent of these deficits vary with the drug or combination of drugs administered, as well as the serum concentration of the drug. As would be expected, polytherapy (administration of more than one AED) has been found to result in greater deficits than monotherapy (MacLeod, Dekaban, & Hunt, 1978; Shorvon & Reynolds, 1979; Thompson & Trimble, 1982). Shorvon and Reynolds (1979) were able to reduce polytherapy to monotherapy in 29 of 40 outpatients studied. In over half of the patients reduced to monotherapy, improvements in alertness, concentration, drive, mood, and sociability were observed. This was especially noted in association with withdrawal of phenobarbital or primidone. Similarly, Fischbacher (1982) reported that reduction of at least one AED in institutionalized patients improved alertness, psychomotor performance, and behavior. Most investigations of AEDs have been conducted with adults. However, there is no evidence suggesting that the pathophysiological mechanisms or properties of anticonvulsant medications in childhood (partial) epilepsy differ from adult partial epilepsy (Pellock, 1994). The body of a child, however, utilizes the medications quite differently than adults and, further, each child will metabolize and eliminate the AED differently (Dodson & Pellock, 1993). While the cognitive effects of the older AEDs on children have been investigated quite extensively, the cognitive effects of the newer AEDs on children remain to be established. Many reports of the mechanisms of action of the new AEDs have been published (e.g., Fisher, 1993; Kalviainen, Keranen, & Riekkinen, 1993; Vajda, 1992) and more specific information in children will follow suit as was the case with previous AEDs. To date, the known cognitive effects produced by commonly prescribed AEDs include the following.

Phenobarbital

Early studies investigating the cognitive effects of phenobarbital led to the conclusion that, despite its sedative properties, the drug had no adverse effects on cognitive ability (Grinker, 1929; Lennox, 1942; Somerfield-Ziskind & Ziskind, 1940). However, with the development of more sensitive neuropsychological tests and the medical technology necessary to accurately monitor serum anticonvulsant levels, intellectual and cognitive dysfunction associated with phenobarbital soon became apparent. For example, Hutt, Jackson, Belsham, and Higgins (1968) tested phenobarbital on nonepileptic volunteers and found that it impaired sustained attention and psychomotor performance.

Hyperactivity is often a paradoxical side effect of phenobarbital therapy (McGowan, Neville, & Reynolds, 1983; Painter & Gaus, 1993; Wolf & Forsythe, 1978). In a comparative study of monotherapy with four major anticonvulsants in previously untreated children with epilepsy, McGowan et al. (1983) found that 5 of the 10 children assigned to the phenobarbital group developed hyperactivity or aggressive behavior or difficulty coping with school-work. This necessitated withdrawal of the drug from the patients and discontinuing its use in the study.

Primidone

Primidone (Mysoline) is a barbiturate analogue that is metabolized to phenobarbital and phenylethylmalonamide (PEMA) whose actions may be synergistic. There is little direct

experimental evidence with respect to the effects of primidone on cognitive ability in children, but it is generally believed that the effects closely parallel those produced by phenobarbital.

Phenytoin

When phenytoin (Dilantin) was initially introduced as an AED, it was thought to improve alertness (Trimble, 1981). Past research has indicated that phenytoin has adverse effects on psychomotor performance (Idestrom, Schelling, Carlquist, & Sjoquist, 1972; Thompson & Trimble, 1982), concentration (Andrewes, Tomlinson, Elwes, & Reynolds, 1984; Dodrill & Troupin, 1977), memory (Andrewes et al., 1984; Thompson & Trimble, 1982), and problem-solving (Dodrill & Troupin, 1977). However, the most recent indications are that the negative cognitive effects associated with phenytoin (and phenobarbital) were not large in psychometric magnitude and that conflicting results in previous studies may be related to problems in patient selection, study design, and serum concentration levels (Dodrill & Troupin, 1991; Duncan et al., 1990; Meador, Loring, Huh, Gallagher, & King, 1990). Meador et al. (1990) found no evidence of adverse cognitive effects of phenytoin at moderate doses.

A reversible phenytoin-induced encephalopathy, observed without other clear neurological evidence of toxicity such as nystagmus or ataxia and characterized by intellectual and memory impairment, has been reported (Trimble & Reynolds, 1976). This encephalopathy can occur in adults, but is most often seen in children and especially those with preexisting mental retardation or brain damage. The deterioration of intellectual functioning in the absence of classical signs of toxicity may result in a misinterpretation of the reversible encephalopathy as a progressive neurological disease.

Ethosuximide

Browne et al. (1975) studied the effects of ethosuximide on psychometric performance and noted an improvement in 17 of 37 children. Blood levels of ethosuximide were monitored and remained within therapeutic ranges over the 8-week duration of the study. These findings were inconsistent with earlier reports (Guey, Charles, Coquery, Roger, & Soulayrol, 1967).

However, 15 of 25 children studied by Guey et al. (1967) were mentally retarded and taking other drugs in addition to ethosuximide. Nevertheless, there have been additional reports of psychosis or encephalopathy resulting from ethosuximide administration (Roger, Grangeon, Guey, & Lob, 1968).

Valproic Acid (Sodium Valproate)

Trimble and Thompson (1984) reported minimal adverse side effects associated with the administration of valproic acid on neuropsychological test performance. Barnes and Bower (1975) had previously suggested that sodium valproate improved alertness and school performance. On the negative side, there have been several reports of sodium valproate-induced encephalopathy, similar to that described for phenytoin (Davidson, 1983; Reynolds, 1985). Dean (1993) suggests that when at-risk populations are correctly identified, sodium valproate clearly remains the drug of choice for most forms of generalized epilepsy because of its effectiveness, broad spectrum of activity, and relative lack of CNS side effects. Dean (1993) further points out that sodium valproate exhibits lower cognitive dulling and behavioral disturbances when compared to phenytoin, phenobarbital, primidone, and the benzodiazepines.

Carbamazepine

Carbamazepine (Tegretol), like sodium valproate, appears to produce minimal adverse side effects on cognitive processes. Dalby (1975) reported the occurrence of behavioral alterations associated with complex partial seizures of temporal lobe origin. Specifically, decreases in speed of information processing, interpersonal viscosity, emotional lability, and increased aggressivity all improved with carbamazepine in approximately 50% of his patients.

An interesting study by Schain, Ward, and Guthrie (1977) evaluated the cognitive consequences of replacing phenobarbital and primidone with carbamazepine in the treatment of children with tonic–clonic and complex partial seizure disorders. A battery of neuropsychological tests intended to assess general intelligence, problem-solving ability, and inattentiveness was administered. Substantial improvement in problem-solving measures were noted with

carbamazepine drug therapy. In addition, the children appeared to be more alert and attentive than when they were treated with phenobarbital or primidone. Carbamazepine control of seizures remained adequate. Thompson and Trimble (1982), using adults, also found carbamazepine to have a less detrimental effect on cognitive functioning than did phenobarbital or primidone.

Overall, carbamazepine appears to be a promising AED that is most effective as monotherapy but also effective as polytherapy, with seizure reduction shown for focal, generalized tonic–clonic (primary and secondary), and some types of symptomatic generalized seizures. Its efficacy appears to be comparable to phenytoin, phenobarbital, primidone, and valproate with some positive psychotropic effects observed with a controlled release (Sillanpää, 1993).

Felbamate

Of the current and new antiepileptic medications, initial investigation indicated that felbamate (Felbatol) was effective both in monotherapy and in polytherapy treatment of complex partial seizures with the added benefit of low toxicity. The speculated mechanism of action is that felbamate appears to prevent the spread of seizures by increasing the seizure threshold (Graves & Leppick, 1991; Wagner, 1994) but its specific mechanism of action remains unclear (Ramsay & Slater, 1993).

However, felbamate can and does have complex interactions with other AEDs (see Ramsay & Slater, 1993, for a complete reporting). A double-blind safety and efficacy trial of felbamate in polytherapy, sponsored by the National Institutes of Health (NIH), indicated significant changes in serum levels of phenytoin and carbamazepine. These pharmacokinetic changes necessitated a redistribution of relative doses of phenytoin and carbamazepine to alleviate toxicity (Graves & Leppick, 1991). It is suggested that polytherapy with felbamate be carefully titrated and that doses of felbamate and concurrent AEDs be adjusted accordingly. Most adverse effects associated with felbamate are observed in polytherapy (Wagner, 1994). Initial clinical trials indicate that phenytoin and valproic acid doses were routinely reduced by 20% following administration of felbamate. It should be noted that while felbamate has been found to significantly alter serum levels of phenytoin and carbamazepine, the latter have likewise been found to alter serum levels of felbamate. Additionally, felbamate has not been linked to any neurotoxic effects independent of phenytoin and carbamazepine (Graves & Leppick, 1991).

During the summer of 1994, the manufacturers of felbamate recommended discontinuation of therapy utilizing felbamate due to reports of its adverse effects on the liver and incidents of aplastic anemia (Trimble, 1994). Felbamate usage was resumed shortly thereafter, but it continues to be underutilized because of the 1 in 10,000 incidence rate of aplastic anemia. Frequent monitoring of complete blood counts is recommended with current felbamate usage.

Gabapentin

Early studies of gabapentin indicate that it is moderately to highly effective in the treatment of partial and tonic–clonic seizures (Crawford, Ghadiel, Lane, Blumhardt, & Chadwick, 1987). A double-blind, add-on study by Sivenius, Kalviainen, Ylinen, and Riekkinen (1991) showed that patients who received 1200 mg/day gabapentin for 3 months reduced their partial seizure frequency by 57% whereas patients receiving 900 mg/day and patients in the placebo group experienced no significant reduction in seizure frequency. Transient mild to moderate somnolence was the only consistent adverse effect reported in gabapentin add-on use. Despite the encouraging early figures touting gabapentin as an interaction-free AED (Schmidt, 1989), more recent polytherapy efficacy reports for gabapentin doses have been conflicting. As of 1993, nearly 800 patients with refractory partial seizures have been followed by Browne (1993). Of these, 15% of the patients administered 900 mg/day and 19% of the patients administered 1200 mg/day dropped out of the study because they had no decreases in seizure frequency by 12 and 18 months. The remaining patients experienced decreases in seizure frequencies of 45 and 46% at 12 and 18 months, respectively, after beginning polytreatment with gabapentin. Some patients with generalized tonic–clonic and absence seizures have shown some benefit from gabapentin (Abou-Khalil, Shellenberger, & Anhut, 1992; Bauer, Bechinger, Castell, Deisenhammer, &

Egli, 1989). Clinical safety and efficacy trials continue to show support for gabapentin's utility as an AED (see Graves & Leppick, 1991; Ramsay & Slater, 1993) and variations reported should take into account the lack of well-defined therapeutic range of gabapentin dosage.

Monotherapy utilizing 1200 mg/day of gabapentin reduced seizures in 50% of the test population but was less effective than the same dose of carbamazepine or polytherapy with gabapentin and carbamazepine (Wilensky, Temkin, Ojeman, Rischer, & Holubkov, 1992). Of 127 patients with refractory partial epilepsy administered either 1.2 g/day gabapentin or a placebo in a double-blind parallel design, 26% of the patients exhibited a greater than 50% reduction in seizure frequency versus 10% of those receiving the placebo (Graves & Leppick, 1991). A similar study by Schmidt (1989) produced like findings for patients receiving comparable doses of gabapentin and additionally reported best responses by generalized tonic–clonic and absence seizure types.

Dodrill, Wilensky, Ojeman, Temkin, and Shellenberger (1992) compared neuropsychological performances of monotherapy gabapentin and carbamazepine patients after treatment for 4–8 months. Results indicate no significant performance differences between the two groups. Interestingly, after patient reports of a general improvement in feelings of well-being, a 1986 study of 10 healthy volunteers by Saletu, Grunberger, and Linzmayer showed that improvements in concentration, alphabetical reaction tests, and numerical memory were observed after 200 mg and again after 400 mg doses of gabapentin (in Ramsay & Slater, 1993).

Lamotrigine

Lamotrigine was recently developed as an AED whose mechanism of action is postsynaptic and has a profile similar to phenytoin. Lamotrigine's efficacy has been extensively studied with an exhaustive overview by Richens and Yuen (1991) reporting 27–30% of subjects from various studies and populations achieving at least 50% reduction in total seizures (Vajda, 1992).

Although studies of lamotrigine safety are ongoing, initial results from an adult population of over 1000 subjects indicate a low incidence of adverse reactions. This double-blind design with lamotrigine as an add-on to existing antiepileptic medications resulted in no higher than 14% of the population reporting mild adverse experiences including dizziness, diplopia, somnolence, headache, ataxia, and asthenia (Betts, Goodwin, Withers, & Yuen, 1991). Similar rates of adverse effects were reported by Gram (1989). See Ramsay and Slater (1993) for a comprehensive report of seven efficacy trials that suggest an overall result profile of lamotrigine as an effective AED in add-on polytherapy in partial seizure disorders and possibly in primary generalized seizures with relatively minor adverse effects.

Of 36 pediatric subjects exposed to lamotrigine for over 12 weeks, add-on results indicate similar results with up to 50% reductions in seizures previously resistant to AEDs. Myoclonic jerks, myoclonic absences, and tonic and atonic seizures responded best to lamotrigine (Dulac, Withers, & Yuen, 1991). Recent studies in pediatric epilepsy have indicated that lamotrigine is well tolerated and exhibits best results in absence epilepsy, Lennox–Gastaut syndrome, and other symptomatic generalized epilepsy (Schlumberger et al., 1994; Wallace, 1990).

While lamotrigine appears to operate without altering serum levels of concurrently administered AEDs, the reverse is not true. Lamotrigine pharmacokinetics are significantly altered by valproic acid (Gram, 1989) and may have significant interactions with other AEDs (Graves & Leppick, 1991).

Vigabatrin

The study of the role of GABA inhibition in the reduction of seizure activity has led to the development of vigabatrin (Sabril), whose mechanism of antiepileptic action is tied to its ability to increase GABA levels in the brain (Beyers, 1993). Patients with chronic refractory epilepsy receiving predominately polytherapy showed significant reductions in seizure activity. Ring, Heller, Farr, and Reynolds (1990) found that the addition of vigabatrin was associated with a 48% reduction in seizure frequency. Adverse side effects including headache, depression, increased lability of mood, dizziness, and confusion led to the withdrawal of 7 of the original 51 subjects. Six other subjects were withdrawn because they failed to achieve a 50% reduction in seizures. A 1991 study by Reynolds,

Ring, Farr, Heller, and Elwes showed even greater promise for the utility of vigabatrin with a third of their sample showing greater than 75% reductions in seizures. Two of their subjects became seizure free and adverse side effects were similar to other AEDs in nature and frequency. Such results have led to vigabatrin's consideration as one of the most promising new AEDs available. Despite the fact that vigabatrin is well documented to significantly reduce serum levels of phenytoin as well as primidone and phenobarbital concentrations, the number of efficacy and safety studies in support of it has not been surpassed. Ben-Menachem et al. (1989) report favorable and comparable efficacy between adults and children treated with vigabatrin. In children, both controlled and open clinical efficacy studies indicate that vigabatrin is a safe and effective AED in the treatment of partial seizures (Gillham, Blacklaw, McKee, & Brodie, 1993; Grant & Heel, 1991; Herranz et al., 1991; Livingston, Beaumont, Arzimanoglou, & Aicardi, 1989; McGuire, Duncan, & Trimble, 1992; Mumford, Beaumont, & Gisselbrecht, 1990). Adding to vigabatrin's appeal is the apparent lack of tolerance to the medication following long-term use (Browne et al., 1989; Tartara et al., 1989).

When collectively considered, these studies indicate that some AEDs can have negative effects on cognitive functions. These findings allow us to conclude that some of the neuropsychological changes that are observed in children with epilepsy occur as a result of anticonvulsant therapy rather than a consequence of the many variables, reviewed earlier, that can themselves alter cognitive ability in these individuals. This is an important consideration in prescribing these agents. Although these subtle, yet significant, cognitive effects may easily be overlooked without careful neuropsychological monitoring, they may be a large price to pay for seizure control or, quite commonly, inadequate seizure control. This is especially true for children and others in academic pursuits (Stores, 1981) and for adults whose occupations require psychomotor speed, sustained concentration, and high levels of information processing. Studies of the efficacy and cognitive effects of the newer AEDs continue, however, and show promise in the treatment of certain refractory childhood epilepsy syndromes.

In addition to the specific effects of AEDs on cognitive functioning, one should also take into account the 1994 study by Austin, Smith, Risinger, and McNelis examining the quality of life for children with epilepsy versus those with asthma. While a reduction in seizure activity is certainly an improvement in one's quality of life, their results indicate that children with epilepsy still have a greater degree of compromised quality of life in terms of psychological, social, and school domains than children with a comparable chronic illness. The role of psychosocial problems in the lives of adolescents with epilepsy has been recognized by the development of the Adolescent Psychosocial Seizure Inventory (APSI). The APSI is an objective assessment tool covering eight areas of psychosocial adjustment (Batzel et al., 1991).

Nonmedication Alternative Treatments

Surgical Treatment

Of the 150,000 people who develop epilepsy each year, 10–20% are deemed to have intractable seizure disorders that fail to be controlled by AEDs (NIH, 1990). Advances in neuroimaging technique have improved the accuracy of locating epileptogeneses, thus minimizing the possible adverse effects of surgical intervention. With these advances in surgical management and localization of seizures, investigators estimate that "2000–5000 new patients in the United States might be suitable for operations each year, compared with the present annual rate of about 500" (NIH, 1990). Surgical success rates of up to 75% have been reported with patients remaining seizure free for 5 years postoperatively. When deemed appropriate, surgical therapy may prevent the development of long-term AED-related toxicity, psychosocial, educational, and vocational problems (Graves & Leppick, 1993).

Guldvog, Løyning, Hauglie-Hanssen, Flood, and Bjørnaes (1991) compared surgical and medical treatment outcomes in a retrospective parallel longitudinal cohort study in Norway that spanned the years 1949–1988. Subjects were closely matched on appropriate demographics. Results indicated that partial seizure frequency is better controlled by surgical treatment but that neurological deficits may be more

frequent in surgically treated than in medically treated patients. Recent advances have been made in the definitive diagnosis and identification of potential surgical candidates most likely to benefit from epilepsy surgery. However, careful consideration of the trade-off between seizure frequency reduction and neurological deficit must be made.

Surgical therapy is not without its risks and precise and exhaustive evaluation of candidates is necessary. The NIH Consensus Development Conference on Surgery for Epilepsy (1990) has recommended that a specialized epilepsy center with comprehensive evaluation and treatment services for intractable epilepsy lead the surgical candidacy evaluation. They further espouse that such a center should include epilepsy-specific trained neurologists, neurosurgeons, neuropsychologists, and neurodiagnostic personnel. Personnel trained to deal with social, psychological, and psychiatric problems as well as educational and vocational rehabilitation should also participate in the holistic evaluation and ensuing treatment. A minimum of electroencephalographic (EEG), magnetic resonance imaging (MRI), and neuropsychological testing facilities should also be available in an effective and comprehensive epilepsy center.

Behavioral Treatment

Following an initially serendipitous discovery, Sterman and his colleagues have found consistently over the past 20 years, a reliable correspondence between 12 and 15 Hz activity and resistance to seizure activity (see Sterman, 1993). In his initial findings, cats trained to maintain the 12 to 14 Hz frequency were more resistant to drug-induced seizures than when the 12 to 14 Hz frequency range was not maintained (Wyrwicka & Sterman, 1968). He has termed this frequency of activity the *sensorimotor rhythm* (SMR) and, since his first case study described in 1972 (Sterman & Friar, 1972), has found success in training epileptic patients in maintaining the frequency and thus enhancing normal thalamocortical regulation which, Sterman proposes, acts to increase seizure thresholds. The scalp-recorded SMR has been shown to correlate quite well with subcortical thalamocortical firing (Sterman & Bloomfield, 1987), whose abnormality in firing has been established as a factor in epileptogenesis.

In his most recent work, Sterman (1993) reported two cases in which successful SMR training has enabled reductions in both monotherapy and polytherapy antiepileptic medication regimens in high-functioning females. Lantz and Sterman (1992) demonstrated that subjects who were most successful in acquiring the SMR response exhibited greater improvements on neuropsychological test performance than did less successful subjects. Sterman warns, however, that SMR training is not effective in all individuals and that factors such as education and motivation play integral roles in successful training.

Dietary Treatment

Prior to the 1920's development and widespread use of AEDs, a common technique in the treatment of epilepsy was nutritionally based mimicking, originally based on the observation of a faith healer who successfully demonstrated that fasting and prayer reduced seizures. Further medical investigation revealed that when one fasts, the body first uses glucose in the bloodstream for energy but that when glucose is depleted, the body switches to burning fat deposits. This is the ketogenic state in which there results the release of ketone bodies. The presence of ketone bodies in urinary sampling has been shown to be very important in indicating the physiological state of fasting. The onset of ketosis, clinical improvement, and prognosis have been correlated with the normalization of EEG for more than 20 years (Nellhaus, 1971). Obviously, fasting indefinitely may reduce seizures indefinitely, but is inherently dangerous and impractical.

The ketogenic diet is based on mimicking of the fasting state through the massive intake of fats in proportion to daily caloric intake (80–90%). Minimal intake of proteins and carbohydrates are allowed—just exactly enough to maintain the child's weight. Virtually no glucose is allowed. Extra carbohydrates, protein, and all forms of glucose become primary energy sources (versus the stored energy in fat) and would take the body out of the ketogenic state. The diet must be followed exactly as prescribed, with absolutely no deviation, and monitored continually to ensure maintenance of the ketogenic state. Even slight deviations in the diet (e.g., 2 g of extra protein or a child not finishing his or her

meal completely) can result in the child leaving the ketogenic state and have been accompanied by the reoccurrence of seizure activity (Schwartz, Boyes, & Aynsley-Green, 1989; Schwartz, Eaton, Bower, & Aynsley-Green, 1989). If the child remains seizure free for 2 years, the diet is usually discontinued and deemed a success (Hendricks, 1995). With renewed public interest in the ketogenic diet, Kinsman, Vining, Quaskey, Mellits, and Freeman (1992) reported the actuarial results of 58 children started on the diet between 1980 and 1985. These were among the most refractory pediatric epilepsy cases and all children were having a minimum of three seizures a day despite proper maintenance of multiple medications. Of the 58 children, 88% were in polytherapy and 80% had multiple seizure types. Improvement in seizure control was generally noted within the first 2 weeks of being on the diet. Improvement was defined as a 50% or more reduction in seizure frequency for a minimum of 4 weeks. Of the 67% of the children who exhibited improved seizure control, 28% exhibited *complete* seizure control. That is, 16 of the 58 children had complete cessation of seizures while on and after completion of the strict dietary regimen. Of the 58 children, 64% were able to reduce one or more AEDs while 28% were able to reduce two or more AEDs and 10% were able to completely discontinue use of AEDs. Note again that these results are particularly striking when one considers that this population consisted of the most resistant cases of pediatric epilepsy seen at Johns Hopkins. Additional benefits of the diet noted in the Kinsman et al. (1992) study included improvements in alertness, behavior, and cognition. These effects can most likely be attributed to the benefits in reducing AEDs, whose cognitive effects have been discussed throughout this chapter.

Schwartz, Eaton, et al. (1989) suspect the beneficial effect of the ketogenic state to be a decreased neuronal excitation due to an alteration in nerve-cell lipid membranes. However, despite 70 years of study and use, the specific mechanisms of action that make the classical ketogenic diet (and other modified versions) so successful remain unclear (Hendricks, 1995; Schwartz, Boyes, & Aynsley-Green, 1989). Its absolute strict guidelines and 2-year length of adherence for long-term benefit make it impractical for controlled experimental study. The classical diet's efficacy, however, remains clearly demonstrated (Kinsman et al., 1992; Schwartz, Eaton, et al., 1989) and as its reputation spreads, increasing numbers of patients as well as less severe cases continue to consider the diet, and the waiting lists for the dozen centers that administer the diet grow (Hendricks, 1995).

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22

Neuropsychological Effects of Stimulant Medication on Children's Learning and Behavior

RONALD T. BROWN AND BRIAN P. DALY

Historical Overview and Evolving Research

Stimulants are psychotropic drugs that produce excitation of the central nervous system (CNS). Stimulants have been used in the management of children and adolescents since the 1930s when Dr Charles Bradley first used Benzedrine to treat children with behavioral disturbances (Bradley, 1937). Bradley studied the effects of Benzedrine with children at a therapeutic day school and found that children's disruptive behaviors decreased and their academic performance improved when they were managed with this stimulant. Bradley et al.'s research was primarily clinical and lacked the rigorous methodology associated with empirical efforts. Therefore, following the reports by Bradley, research efforts were subsequently conducted in the 1960s that demonstrated reductions in overactivity and oppositional behavior by boys identified as conduct disordered (Eisenberg et al., 1961). In the late 1960s, improvements in the target symptoms of intention and overactivity were shown as a function of stimulant drug therapy (Conners et al., 1967).

Research on the effects of the stimulants has proliferated since the 1960s (Swanson, 1993). The majority of these studies have investigated several different aspects of stimulants, including short-term efficacy of the stimulants; atypical drug response (typically examining stimulant drug response in symptomatic and nonsymptomatic populations); organic etiologies of attention-deficit hyperactivity disorder (ADHD) and response to stimulants; predictors of stimulant drug response; long-term outcome of stimulant treatment; adverse side effects associated with both short-term and long-term stimulant drug therapy; and the use of alternative and adjunctive therapeutic modalities to the stimulants (Jacobvitz et al., 1990). The short-term efficacy studies have included randomized, double-blind, placebo-controlled trials; the use of the stimulants and their effects in various settings (e.g., laboratory, school, home); the effects of the stimulants on cognition, learning, achievement, and social skills; and dose–response relationships of stimulants.

Research studies also have attempted to clarify the etiology of symptoms associated with ADHD (e.g., genetic and environmental factors) and the mechanisms underlying stimulant drug response. Empirical efforts recently have focused on testable genetic differences in predicting positive drug response to the stimulants (e.g., Stein et al., 2005). Studies that

RONALD T. BROWN AND BRIAN P. DALY • College of Health Professions, Professor of Public Health, Psychology, Pediatrics, Psychiatry and Behavioral Sciences, Temple University, Health Sciences Center, Jones Hall, 3307 N. Broad Street, Philadelphia, PA 19140–0000.

investigated the long-term outcome of treatment with stimulants over the course of several years have examined variables including cognitive functioning (including performance on higher order tasks of memory and attention), academic performance, peer relations, and functional behaviors across a number of settings (e.g., home, school). Studies also have examined the safety and physical adverse side effects of stimulants. Finally, recent investigations have systematically compared stimulant drug treatment to other forms of nonsomatic therapies such as behavioral therapies.

Collaborative interdisciplinary research and practice efforts of clinical child psychologists, cognitive neuroscientists, cognitive psychologists, neurologists, neuropsychologists, molecular geneticists, pediatricians, and child psychiatrists have advanced our knowledge and understanding of the actions of stimulants on children's learning and behavior. Fortunately, new radiographic advances in assessing brain functioning, including computerized tomography (CT) and magnetic resonance imaging (MRI), will extend our knowledge of the effects of stimulants on neurological functioning and the role of stimulants in the management of learning and behavior.

Prevalence

Stimulant use in children and adolescents has been the most widely investigated and frequently used psychotropic medication in behavioral pediatrics and child and adolescent psychiatry (see Brown, Dingle, & Dreelin, 1997). Stimulants represent the class of psychotropic agents most commonly prescribed for school-age children and adolescents (Jensen et al., 1999; Teitelbaum et al., 2001; Zito et al., 2003). There also is evidence to indicate a dramatic increase in the use of stimulants since 1980 (Safer & Krager, 1988), particularly for preschoolers (Rappley et al., 1999; Zito et al., 2000). Approximately 80% of children receiving pharmacological agents for the management of ADHD are prescribed the stimulants, and hence these agents represent the class of medication employed by primary care physicians for the management of ADHD and its associated symptoms (Wolraich et al., 1990). More than 1.5 million children in the United States receive stimulants, the most common of which is methylphenidate (MPH [Ritalin]) (Robison et al., 1999; Safer, Zito, & Fine, 1996). Recent data indicate that from 1990 to 1995, rates of MPH prescriptions for the management of ADHD increased 2.5 times (Safer, Zito, & Fine, 1996). During the early 1990s, MPH production in the United States increased from 1,784 to 5,110 kg/year; in 1996 over 10 million prescriptions for Ritalin were written by providers (Vitiello & Jensen, 1997). ADHD-related outpatient visits to primary care physicians increased from 1.6 to 4.2 million per year during the years 1990–1993 (Swanson et al., 1995), and recent epidemiological surveys have estimated a 12-month stimulant prescription rate of 6% in Baltimore (Safer et al., 1996) and 7.3% in rural North Carolina (Angold et al., 2000).

Although greater experimental evidence supports the safety, dosing, and efficacy of stimulants than any other psychotropic agent for pediatric populations (Greenhill et al., 2002), there continue to be concerns associated with the increased prevalence of use among school-age children (Safer, Zito, & Fine, 1996; Zito et al., 2000), possible adverse side effects, and uncertainty pertaining to the implications of long-term stimulant use among children (Richters et al., 1995). This is especially true in the lay press where news reports related to concerns about overmedicating children and adolescents with stimulants appear almost daily. The lay press and public often voice concerns regarding the abuse potential of stimulants and the supposed overmedication of children and adolescents with psychotropic agents, including the stimulants. Given that many children and adolescents with learning or behavioral problems are frequently managed with stimulant agents, it is imperative that pediatric neuropsychologists obtain a working knowledge of the literature in this area, including both the safety and efficacy of these agents and limitations regarding safety and efficacy.

Pharmacology

Action Mechanism

The most commonly prescribed stimulants include MPH, dextroamphetamine, *d*- and 1-amphetamine racemic mixture, and pemoline.

Medications in which MPH is an ingredient include brand-name drugs such as Concerta, Metadate CD, Methylin, Ritalin, Ritalin-SR, and Ritalin LA. Dexmethylphenidate hydrochloride, the active ingredient of Focalin, also is found in MPH. The action mechanism for MPH involves increasing extracellular dopamine levels by selective binding of the presynaptic dopamine transporter in the CNS (prefrontal and striatal areas) (Solanto, Arnsten, & Castellanos, 2001). Because dextroamphetamine selectively binds to the dopamine transporter, there is a resulting increase in extracellular synaptic dopamine. Volkow et al. (2002) employed positron emission tomography (PET) to investigate the action mechanism of MPH in the human brain and found that therapeutic doses of MPH block more than 50% of the dopamine transporters and significantly enhance extracellular dopamine in the basal ganglia. Brand names that include dextroamphetamine are Dexedrine, Dexedrine Spansules, and Dextrostat. Dextroamphetamine, unlike MPH, has an affinity to the presynaptic neurons and induces the release of dopamine into the synapses; there is also norepinephrine reuptake inhibition (Solanto et al., 2001). Pemoline (Cylert) is a stimulant that is not a MPH- or amphetamine derivative and is structurally dissimilar from both, but possesses pharmacological activity similar to that of other known stimulants; it is believed to have minimal sympathomimetic effects and primarily influences dopamine neurotransmission (Barkley, DuPaul, & Costello, 1993).

Despite evidence that dopamine and norepinephrine play a central role in problems associated with attention and behavioral problems of children and adolescents with ADHD, the mechanism by which stimulants produce behavioral and cognitive effects in children and adolescents remains unclear. Because each medication has its own specific actions on individual neurotransmitters, the ability to accurately predict the best clinical response for a particular individual has yet to be realized (American Academy of Child & Adolescent Psychiatry [AACAP], 2002; Solanto, 1998; Solanto et al., 2001).

Types of Stimulants

The most common stimulants employed with pediatric populations are MPH, dextroamphetamine, amphetamines, and pemoline. They have similar adverse side effects and may be grouped according to their approximate duration of action: short-acting (effects lasting 3–4 h); intermediate-acting (effects lasting 6–8 h); and long-acting (effects lasting 8–12 h) (Wolraich, 2003). New stimulant formulations were developed to control the rate of dose delivery to optimize the effect for longer intervals than immediate-release medication (Adesman, 2002). Immediate-release or short-acting versions include MPH (Ritalin, Methylin, Focalin) and dextroamphetamine (Dexedrine, Dextrostat). Intermediate-acting stimulants include MPH (Ritalin-SR, Methylin ER, Metadate ER) and amphetamine salts (Adderall tablets). Long-acting formulations are available only for MPH (Concerta, Metadate CD) and amphetamine salts (Adderall XR).

Stimulants are characterized by rapid absorption from the gastrointestinal tract, low plasma protein binding, and rapid extracellular metabolism (Patrick et al., 1987). They are eliminated from the body within 24 h (Barkley et al., 1993). Short-acting stimulants are administered orally several times a day whereas intermediate-acting stimulants were developed to reduce dosing to a maximum of twice a day. Long-acting stimulants are administered once a day in the morning, with the onset of action within 2 h after administration, and typically last 12 h. Smooth, consistent release of medication throughout the day avoids rebound effects (when severe inattention and overactivity begin to occur upon cessation of the medication) that can occur with short-acting stimulants. Additional advantages of single daily dosing include the child not being stigmatized by needing to take a pill at school on a twice-daily basis, improved adherence with prescribed medication, and reductions in rebound effect that may occur with short-acting mediation.

Methylphenidate (MPH)

MPH is available in both immediate-release and sustained-release versions. The immediate-release (short-acting) preparations include Ritalin, generic MPH (Methylin), and the *d*-isomer of MPH (Focalin). Immediate-release MPH is rapidly and extensively absorbed (Canadian Pharmacists Association, 1999) and begins working almost immediately (within about 20–30 min) and lasts 3–4 h. MPH is eliminated

from the plasma with a mean half-life of 2.4 h in children (Brown et al., 1997) and the drug is entirely metabolized within 12–24 h (Barkley et al., 1993). The time to peak serum concentration in children has been reported to be approximately 2 h (range 0.3–4.4 h) (Brown et al., 1997). Recent literature has been equivocal as to whether or not the stimulants are inactivated or delayed in action if ingested with food. However, administering stimulants with meals or snacks has been shown to help minimize adverse gastrointestinal side effects. Following oral administration of MPH, 78–97% of the dose is excreted in the urine and 1–3% in the feces in the form of metabolites within 48–96 h (Brown et al., 1997).

Methylin is a branded generic MPH preparation that is lactose- and dye-free. Focalin is a refined formulation of Ritalin (*d*,1-methylphenidate HCl) that contains only the more active *d*-isomer of MPH. The 1-isomer, essentially inert, is left out. Because of this special formulation, Focalin is twice as potent as MPH; thus the usual dose of Focalin is half that of the MPH dose. Focalin begins working immediately and lasts 3–4 h after ingestion. The mean plasma elimination half-life of Focalin is approximately 2.2 h and it is metabolized primarily in the liver and eliminated in the urine.

The intermediate-acting preparations of MPH include Ritalin SR, Methylin ER, and Metadate ER. The Ritalin-SR brand of MPH extended-release tablets has a time to peak serum concentration of 4.7 h (range 1.3–8.2 h) in children and a duration of action of approximately 8 h (Kollins, Rush, Pazzaglia, & Ali, 1998). In order to achieve efficacy, the tablets may not be crushed and must be swallowed whole. Metadate ER, the extended-release form of MPH, has a duration of action of approximately 8 h. Methylin ER is an extended-release formulation of Methylin. It uses a dual-acting hydrophilic polymer release technology, where the release of MPH occurs by diffusion and erosion. Methylin ER is thought to have a duration of action of 8 h.

The long-acting preparations of MPH include Concerta, Metadate CD, and Ritalin LA. Concerta is a capsular version of MPH and employs the osmotic release oral system (OROS). The advantage of Concerta over other extended-release and long-acting stimulant delivery systems is that it distributes a unique pattern of medication throughout the day and early evening hours. Initially, only 22% of the medication is released upon ingestion because the first dose of medicine is released via the surface of the Concerta capsule, which is coated with immediate-release MPH. About 1 h later, after the outer coat has dissolved, the OROS delivery system uses osmotic pressure to pump MPH out of the capsule over the course of the day resulting in the remaining 69% of the medication being released over 8–12 h (the MPH in OROS is 91% bio-available) (Modi, Lindemuler, & Gupta, 2000). MPH is able to be pumped out because the tablet shell allows water into the tablet and the active ingredient pushes out through the hole in the shell as water is absorbed. Overall, the active medication is released evenly, resulting in a steady stream of active medication being absorbed throughout the day, regardless of food intake (Modi et al., 2000). Due to the presence of the pump inside the capsule, the medicine should not be broken or chewed. The pump is not digested; it is excreted in the stool. Concerta has a plasma half-life of approximately 3.5 h. The initial maximum peak of MPH occurs 1–2 h after administration, followed by a gradual increase over 6–8 h (Sonuga-Barke et al., 2004).

Metadate CD preparations are extended-release capsules that comprise both immediate-release and extended-release beads. This medication uses a unique method of controlled drug delivery called Diffucaps, which employs beads inside the capsules so that nearly one-third of the dose of medication from the beads is provided by the immediate-release component, whereas the other 70% is provided as extended release of the active medication. This ratio is designed so that increased blood levels occur later in the day to help overcome acute tolerance and provide an evenly distributed affect of the medication across 8 h (Steinhoff, 2004). The plasma half-life of Metadate CD is approximately 6.8 h, which is more than double that of traditional MPH, with the first peak concentration reached in 1.5 h after dosing and a second peak occurring in 4.5 h after dosing (Sonuga-Barke et al., 2004).

Ritalin LA is an extended-release formulation of MPH that employs a bimodal release system and uses proprietary Spheroidal Oral Drug Absorption System (SODAS) technology. Bimodal release of the active medication is achieved through each bead-filled capsule containing half the dose as immediate-release beads and the other

half as enteric-coated, delayed-release beads. The immediate dose of MPH occurs upon ingestion of the medication, thereby inducing a relatively large initial effect, with the second dose being released approximately 4 h later. Thus, the medication is similar to Metadate CD because there are two distinct peak plasma concentrations; however, these peak plasma concentrations occur 4 h apart in Ritalin LA, with a duration of effect of 8 h (Wolraich & Doffing, 2004).

Dextroamphetamine

Peak plasma concentration for immediate-release dextroamphetamine (e.g., Dexedrine and Dextrostat) is achieved in 3 h with an elimination half-life of 10–13 h. Dextroamphetamine is metabolized primarily by the liver and is renally excreted. It is recommended that dextroamphetamine be administered with breakfast or lunch. Barkley et al. (1993) reported that behavioral effects following administration of dextroamphetamine are observable within 30–60 min, peak 1–2 h following administration, and often dissipate within 4–6 h following ingestion (Brown et al., 1997).

Dexedrine Spansules are the extended-release formulation of dextroamphetamine; the medication may be administered once daily in the morning and lasts approximately 4–8 h.

Amphetamine (d- and 1-Amphetamine Racemic Mixture)

Adderall is an immediate-release formulation of the amphetamine salts that consists of d-amphetamine and 1-amphetamine. Peak plasma concentrations for Adderall have been reported to be 3 h, with an elimination half-life of 9 h for d-amphetamine, and 11 h for 1-amphetamine in children. Behavioral effects often are observable within 45 min.

The sustained-release formulation of the amphetamine salts, Adderall XR, also contains d-amphetamine and 1-amphetamine and has a duration of effect of 10.5 h in lower doses and a 12-h effect in higher doses.

Pemoline

Cylert (pemoline) is structurally unrelated to amphetamines or MPH. Because of its potential for serious adverse side effects affecting the liver, pemoline should not be considered a first-line drug therapy for children and adolescents with attentional problems (Pliszka et al., 2000), and is recommended as an alternative treatment only after a child has failed three or more stimulant trials (AACAP, 2002). Additionally, patients and their families must be informed of this serious adverse effect, must provide written informed consent, and patients must be placed on a strict protocol for follow-up, including ongoing monitoring of liver functioning (Greenhill et al., 2002). Due to the aforementioned risks, some recent psychopharmacology algorithms do not even include pemoline as a treatment option (AACAP, 2002). Pemoline is rapidly absorbed from the gastrointestinal tract. Its half-life is 7–8 h in children; peak serum levels occur within 2–4 h following ingestion. Pemoline is metabolized by the liver and is excreted primarily by the kidneys. Contrary to previous suggestions that pemoline takes several weeks to work, recent studies have shown it to be effective immediately following the first dose (Pelham et al., 1995).

Other Stimulant Agents

The wake-promoting agent Modafinil, a novel cognitive enhancer, has a clinical profile similar to conventional stimulants and is prescribed in off-label therapy for ADHD (Rugino & Samsock, 2003). Finally, new technology for the delivery system for MPH and other stimulants continues to evolve (e.g., the development of a transdermal patch formulation of MPH [MethyPatch] for the treatment of ADHD [Sane & McGough, 2002]).

Comparative Clinical Trials

Controlled clinical trials comparing the efficacy of MPH, amphetamines, and dextroamphetamine have failed to demonstrate group differences in efficacy and safety (Arnold, 2000; Brown et al., 2005). For example, in a double-blind, crossover controlled clinical trial, the comparative efficacy of MPH and dextroamphetamine was examined for children with ADHD (Efron, Jarman, & Barker, 1997). Findings revealed significant improvements from baseline on all measures for both agents: 68.8% of children medicated with dextroamphetamine and 72% of children medicated with MPH were rated by parents and teachers as improved.

Regarding prevalence and severity of adverse side effects from both MPH and dextroamphetamine, problems falling asleep were rated higher for dextroamphetamine whereas poor appetite was observed for both agents (Efron et al., 1997). A retrospective review that compared Adderall and MPH found no statistically significant differences between the two stimulants in efficacy, safety, or adverse effects (Grcevich et al., 2001).

Short- and long-term-acting medications have shown comparable safety and efficacy. For example, one large randomized controlled trial showed that Concerta was as effective as traditional short-acting MPH when MPH was administered in the standard three-times-daily regimen (Wolraich et al., 2001). Although children may vary in their clinical response to various stimulants and to different doses of the same stimulant (Elia et al., 1991), fortunately most children who do not respond to one of these stimulants are likely to respond to another stimulant (Sharp et al., 1999). Because of the favorable safety profile of the stimulants, if one agent does not prove effective, the practitioner may take comfort in attempting a trial of another stimulant.

Administration and Dose Response

Schedule. As noted previously, dosing schedules vary depending on the type of stimulant used, duration of action, and the target behaviors in need of change (e.g., attention, behavior). Short-acting stimulants are administered on a twice-daily schedule; however, three-times-per-day dosing schedules have been used when clinically appropriate or when there are specific target behaviors in the late afternoon, with the third dose being administered in the late afternoon. The schedule for intermediate-acting stimulants is twice a day, whereas long-acting stimulants are administered once a day in the morning (see Table 1).

Dose response. Research on the relationship between dose and symptom management with stimulants gained considerable interest in the

TABLE 1. Current Pharmacological Treatments for Attention-Deficit/ Hyperactivity Disorder

Generic class and brand name	Duration of action (h)	Dosage
Stimulants		
Methylphenidate		
Short-acting		
Ritalin, Metadate, Methylin	3–5	5–20 mg BID to TID
Focalin		2.5–10 mg BID to TID
Intermediate-acting		
Ritalin LA, Ritalin SR, Metadate ER, Methylin ER	3–8	20–40 mg QD
Long-acting		
Concerta	8–12	18–54 mg QD
Metadate CD		20–60 mg QD
Dextroamphetamine		
Short-acting		
Dexedrine	4–6	5–40 mg BID to TID
Dextrostat		
Intermediate-acting		
Dexedrine Spansules	4–8	10–30 mg QD
Amphetamine		
Short-acting		
Adderall	4–6	10–30 mg QD to TID
Long-acting		
Adderall XR	8–12	10–30 mg QD

Note: BID = twice a day; QD = four times a day; TID = three times a day.

1970s following published studies that investigated dose response with stimulants employing cognition and behavior as dependent variables. Specifically, a lower weight-adjusted dose (0.3 mg/kg) compared to a higher weighted dose (1.0 mg/kg) was associated with optimal cognitive performance on paper and pencil tests, whereas higher doses (1.0 mg/kg) were associated with optimal behavioral response (Brown & Sleator, 1979; Sprague & Sleator, 1977). However, the notion of specific dose–response relationships has been challenged since the publication of the seminal studies (Rapport & Kelly, 1991), with few studies replicating the previous data demonstrating a differential effect of high and low doses on cognition and behavior. Moreover, some experts have argued that there is no compelling evidence that bodyweight or stimulant dose predicts response (Rapport, DuPaul, & Kelly, 1989). Dose–response studies of stimulants with larger groups of children than those published by Brown and Sleator (1979) and Sprague and Sleator (1977) have failed to demonstrate significant differences between MPH, dextroamphetamines, or amphetamines (Arnold, 2000; see Brown et al., 2005). Moreover, Rapport et al. (1989) have suggested there is compelling evidence to indicate large individual differences in response to various stimulants and doses of these stimulants (Elia et al., 1991). Thus, although group effects of stimulants may be of interest, behavioral and cognitive responses to dosages show significant variability across children, with some children evidencing best response to low doses, whereas other children evidence optimal response to higher doses.

Recent research demonstrates an association between stimulant dose response and differential symptom improvement for specific subtypes of ADHD. Stein et al. (2003) reported that higher doses of stimulants were associated with greater improvement of inattention and overactivity for children with the combined subtype of ADHD. However, lower doses proved more beneficial for children diagnosed with the inattentive subtype of ADHD. In support of a differential dose response as a function of specific subtype, Barkley, DuPaul, and McMurray (1991) found that children with ADD without hyperactivity (based on DSM-III criteria) were more likely to perform well on lower doses of MPH, whereas children with ADD with hyperactivity are apt to require higher dosages of the stimulant for target symptoms of overactivity and inattention. Barkley et al.'s findings (1991) also revealed more non-responders among children without hyperactivity (35%) than for those with ADHD with overactivity (25%). It should be noted that dose response according to ADHD subtype is not definitive. For example, De Quiros et al. (1994) studied several subtypes of children with ADHD and their findings did not support the notion that children diagnosed with the inattentive subtype of ADHD responded differentially to medication or to various doses of medication.

Although of theoretical interest, more research in this area needs to be conducted prior to drawing definitive conclusions regarding ADHD subtype and stimulant drug dose response. Recent research provides compelling evidence for cognitive improvement with linear dose responses on measures of cognition, including speed and accuracy of processing, attention, flexible thinking, problem solving and persistence, and working memory (Douglas et al., 1995; Tannock, Ickowicz & Schachar, 1995a). These findings suggest that children failing to respond to lower doses have a high probability of responding to higher doses of stimulants in both the areas of cognition and behavior (Rapport et al., 1994). Of course, the clinician must weigh enhanced cognitive performance and behavioral functioning against associated adverse side effects that may be associated with the stimulants (e.g., appetite suppression, sleep disturbances, irritability, rebound). Unfortunately, it is impossible to predict the optimal dose of a stimulant for any pediatric patient due to the variables associated with stimulant drug response and adverse effects. For example, dose of medication, duration of drug effect, individual differences, diagnosis and subtype, task and performance characteristics, and prevailing social and psychiatric conditions and comorbidities may interact to influence a child's response to stimulants.

Therapeutic application. Stimulants are the most widely prescribed psychotropic medications for children and adolescents and carry Food and Drug Administration (FDA) indications for the treatment of ADHD and narcolepsy (Greenhill et al., 2002). Although stimulants are used in the treatment of narcolepsy, they are primarily employed in the clinical management of ADHD. Fortunately, the stimulants have been

the most thoroughly researched psychotropics for the management of children with ADHD. Research has shown that stimulants are an effective treatment for symptoms associated with ADHD, including inattention, impulsivity, and overactivity, which occur in the classroom, the home, and in social settings or situations involving peers. Moreover, there has been an increase of both open and controlled trials—as well as case studies—examining the safety and efficacy of stimulants for a variety of other disorders, both psychiatric (e.g., autism, mental retardation) and physical (e.g., cancer) (Brown et al., 1997). Recent studies also have focused on the combination of stimulants and other psychotropic agents in the treatment of comorbid conditions, including autism and problems associated with attention and concentration, mental retardation when it is accompanied by attentional problems, and the comorbidity of conduct disorder and ADHD (Greenhill et al., 2002).

Attention-Deficit Hyperactivity Disorder

ADHD is a neurobehavioral disorder that may interfere with a child's capacity to stay on a task and exercise age-appropriate inhibition in behavioral settings or on cognitive tasks. ADHD is the most commonly diagnosed behavioral disorder of childhood and is estimated to affect anywhere from 3 to 5% of school-age children in the United States. The syndrome is characterized by symptoms that may include, but are not limited to, inattention, failure to listen to instructions, inability to organize oneself and school work, fidgeting with hands and feet, talking too much, leaving projects, chores, and homework unfinished, and having trouble paying attention to and responding to details (American Psychiatric Association [APA], 2000[1]).

Action mechanisms. Although stimulants are the first-line treatment for the management of ADHD and related symptoms, the precise action mechanism is not completely understood. Early reports of the mode of action of stimulants on children with ADHD suggested a paradoxical effect (e.g., motor activity is reduced in hyperactive children) (see Brown et al., 1997). This common misconception originated due to the belief that stimulants have a different effect on individuals with ADHD than they do on the general population. Brown et al. (1997) reviewed the literature in this area and concluded that normally developing children and adults have similar cognitive and behavioral responses to stimulants as do children with ADHD. For example, findings from one study (Peloquin & Klorman, 1986) showed that children without ADHD respond to low doses of stimulants in a similar manner as children with ADHD, thereby casting doubt on the paradoxical nature of stimulants for children and adolescents with ADHD. Current thinking regarding the action mechanism of stimulants in children with ADHD is that stimulants are believed to exert their action through the enhancement of dopamine and norepinephrine neurotransmission and the level of the synapse (Brown & La Rosa, 2002). Moreover, research also suggests that the action mechanisms for amphetamines and MPH differ slightly (Solanto et al., 2001). For example, MPH is posited to block the dopamine transporter in the synaptic cleft, which amplifies the release of dopamine, thereby enhancing attention and focus in individuals who have weak dopamine signals, such as individuals with ADHD.

Amphetamines also are sympathomimetic agents that block the reuptake of dopamine at the synapse, although the amphetamines appear to promote the release of newly synthesized dopamine more selectively (Wender, 2001). These findings are supported by neuroimaging studies demonstrating that cortical–subcortical pathways, which are primarily mediated by dopamine, are directly affected by stimulant compounds (Ernst et al., 1997). Although the specific mechanism regarding the mode of action of stimulants in children with ADHD needs more research, specific evidence that establishes the mechanism whereby MPH, amphetamines, or dextroamphetamines produce mental and behavioral effects in children is not entirely certain. Recent technological advances of neuroimaging techniques have advanced our knowledge on the action mechanism of the stimulants, although they have no current role in the identification or diagnosis of ADHD. Furthermore, there continue to be individual differences regarding the variation in response to stimulants in children with ADHD. It is certain, however, that the actions of the stimulants are not specific to associated symptoms of the ADHD disorder. The use of behavioral psychopharmacology has been of most interest to

clinicians and scientists studying the disorder whereby it is recognized that the behavioral actions of the stimulants are of primary interest rather than the physiological or biochemical actions of the medication.

Treatment prevalence. Epidemiological surveys estimate prevalence rates for ADHD to range from 4 to 12% in the population of 6- to 12-year-olds, and there is overwhelming evidence that stimulants are the treatment of choice for these children. Safer, Zito, and Fine (1996) suggest that the increase in the number of children receiving stimulant drug treatment may be attributed in part to children being better managed on stimulants for longer periods of time, a greater frequency of children with learning disabilities and ADHD (primarily the inattentive type) receiving stimulant drug therapy, a larger number of girls both being diagnosed with ADHD and hence receiving stimulants, and the prescribing of stimulants during the summer months. However, epidemiological surveys have not always provided definitive answers as to whether children are appropriately medicated with stimulants. For example, one survey in four different communities found that only one-eighth of children diagnosed with ADHD were being treated with stimulants (Jensen et al., 1999), whereas another survey conducted in rural areas in North Carolina found that approximately one-third of the school-age children who were receiving stimulants did not meet diagnostic criteria for ADHD (Angold & Costello, 1997).

Brown and Sammons (2003) concluded that children from low socioeconomic backgrounds were no more likely to receive stimulants than their peers from more affluent homes. However, epidemiological studies note disparate rates of stimulant prescription among Latino/a or African-American youth as compared to their Caucasian counterparts, with minority children being less likely to receive treatment with the stimulants (Fox, Foster, & Zito, 2000; Zito, dosReis, Safer, & Riddle, 1998). Although the stimulants are among the most studied medications in child psychiatry, concerns persist about whether stimulants are overused by professionals. Moreover, although there are compelling data to suggest the safety of the stimulants at least in the short term, controlled clinical trials examining the safety of the stimulants over the course of many years are difficult to conduct,

leaving some to question the long-term safety of these agents (Pelham, 2000).

Despite publicity about ADHD and the use of stimulants in the lay press, there is little empirical evidence of widespread overdiagnosis or overtreatment of ADHD. For example, one epidemiological survey concludes that, despite public perceptions, the stimulants such as MPH are likely under-prescribed rather than over-prescribed for children with ADHD across communities (Jensen et al., 1999). However, the jury regarding the pharmacoepidemiology of the stimulants is still out. For example, in the absence of specific safety data over the long term, coupled with the dearth of epidemiological data, some experts suggest the need to be judicious in prescribing stimulants and cautious about dismissing concerns about ADHD overdiagnosis (LeFever, Arcona, & Antonuccio, 2003).

Cognitive effects. Studies of the cognitive effects of stimulants have indicated that they exert a positive effect on laboratory measures of specific cognitive tasks such as indices of executive function (see Brown & Sammons, 2003; Brown & Sawyer, 1998; Rapport & Kelly, 1991). For example, studies have shown that stimulants significantly enhance cognition on various tasks associated with vigilance, reaction time, short-term memory, and learning of verbal and nonverbal material. Stimulants also have been shown to improve performance laboratory measures of attention and distractibility, inhibitory control, and perceptual-motor function. For example, MPH has been shown to enhance the cognitive performance of children diagnosed with ADHD (Kempton et al., 1999; Riordan et al., 1999), including significant effects on classroom measures of attention and academic efficiency (DuPaul & Rapport, 1993), decreasing response variability and impulsive responding on cognitive tasks (Tannock, Schachar, & Logan, 1995b), and improving reaction time and computation. A relatively low dose of MPH (0.5 mg/kg) administered in an acute trial also showed improved spatial working memory, attentional-set shifting, and visual-search task performance in 14 boys who met criteria for ADHD (Mehta, Goodyer, Sahakian, 2004). Moreover, studies of the cognitive effects of MPH for children diagnosed with ADHD have shown significant improvements in performance on measures of attention (e.g., Test of Everyday Attention for Children) compared to

placebo controls (Hood, Rankin, & Isaacs, 2005), as well improved selective inhibition (Claude-Bedard et al., 2003).

Similar to MPH, laboratory studies of the cognitive effects of amphetamines on various tasks suggest improved memory consolidation and long-term retention when administered after a learning session (Soetens, Casaer, D'Hooge, & Hueting, 1995). Additional studies have reported increases in overall speed and accuracy on choice reaction time and target-detection tasks as a function of amphetamines (Denney & Rapport, 2001; Douglas, 1999; Klorman, Brumaghim, Fitzpatrick, & Borgstedt, 1991). Additional data also suggest enhanced sustained attention, attentional allocation, as well as the speed and organization of the motor response processes and motor inhibitory control (Konrad, Gunther, Hanisch, & Herpertz-Dahlmann, 2004). As a result of these findings, the investigators conclude that amphetamines in moderate doses enhance learning, memory, impulsivity, cognitive flexibility, and performance on academic tasks.

Recent theories have posited that the orbital-frontal cortex for those diagnosed with ADHD, which is responsible for executive functions, relative to normally developing children is not as active in children with ADHD (Barkley, 1997). Studies that examined stimulants and executive function in children with ADHD suggested that stimulants are effective in improving cognitive performance on most executive function tasks. For example, Kempton et al. (1999) studied executive function in medicated and unmedicated children with ADHD, and concluded that unmedicated children with ADHD displayed specific cognitive impairments on executive function tasks of spatial short-term memory, spatial working memory, set-shifting ability, and planning ability. Impairments also were noted on tasks of spatial recognition memory and delayed matching to sample tasks, although pattern recognition memory remained intact. In contrast, the children receiving stimulants did not demonstrate impairment on any executive function tasks except for deficits in spatial recognition memory. Moreover, Barnett et al. (2001) report deficits in executive functions related to spatial working memory for unmedicated children with ADHD, but did not provide evidence for similar deficits in children who were receiving stimulants.

Academic achievement. Measuring the influence of pharmacologic intervention for children and adolescents with ADHD on academic functioning is important because of the preponderance of research demonstrating that children with ADHD suffer significant academic impairments. Therefore, the question of whether stimulants improve academic achievement and learning has received significant attention in the literature. The data indicate that although stimulants improve short-term gains in academic efficiency, the long-term efficacy of the stimulants on academic achievement has yet to be confirmed (Bennett et al., 1999). The review by Bennett et al. has been supported by the results from a meta-analysis conducted by Jadad et al. (1999) that reported on 77 randomized controlled studies associated with the treatment of ADHD. Jadad et al. note that academic performance over time was not enhanced by treatment with stimulants. McCormick (2003) examined the effect of stimulant drug therapy for children with predominantly inattentive ADHD who also suffer from academic impairment and found that neither MPH nor dextroamphetamine significantly improved the primary outcome measure of grade-point averages after 1 year of stimulant treatment. Frankenberger and Cannon (1999) found that after 4 years of stimulant drug management, children did not evidence improvement in specific or broad areas of academic achievement. In fact, children seemed to fall further behind academically.

Results of the Multimodal Treatment of Attention-Deficit Disorder (MTA) study (MTA Cooperative Group, 1999a) found that combined treatment (stimulants and behavioral therapy) was superior to medication alone in improving academic performance, as assessed by standardized testing. However, there has been one investigation that fails to support the superiority of combined treatment for academic achievement. Hechtman et al. (2004) compared long-term use of MPH and multimodal psychosocial treatment on the academic achievement of children with ADHD. Academic achievement was assessed by means of standardized testing and parent ratings of homework problems. The investigators found no advantages on any measure of academic performance for the combined treatment over MPH alone and MPH in combination with an attention control group. Hechtman et al. noted significant improvements

across all treatments and the maintenance of these improvements over the course of 2 years.

Given that there are few studies providing data to support the long-term benefits on academic achievement as a function of stimulants for ADHD, it has been suggested that stimulants exert their effects primarily on academic efficiency and productivity, rather than on achievement as measured by standardized assessment instruments (Brown et al., 1997). One explanation to explain the disappointing finding of enhanced academic functioning has been the criticism of using standardized achievement tests as dependent measures in clinical trials with stimulants. Specifically, these standardized achievement tests may be less sensitive to the short-term change that may be induced by stimulants during an acute clinical trial. Although further evidence is needed, studies demonstrating that stimulants enhance classroom productivity and teacher reports of behavior, attention, seatwork, homework, and grades suggest that stimulants work well in managing symptoms (e.g., attention, impulsivity, overactivity), although they are less effective in enhancing functional behaviors (e.g., academic skills, social skills) (Pelham et al., 1993; Runnheim et al., 1996). Chacko et al. (2005) conducted an acute 6-week trial of MPH on young children with ADHD. Significant effects were observed in teacher ratings of children's following classroom rules and amount of seatwork completed, but not for accuracy on problems completed during seatwork. Additional investigations suggested that stimulants enhance academic productivity (Carlson et al., 1992; Pelham et al., 1985; Tannock et al., 1989), increase compliance with academic demands in the classroom setting (Benedetto-Nasho & Tannock, 1999; Jacobvitz et al., 1990), and improve reading and arithmetical problem solving (Pelham & Hoza, 1987).

A recent question is whether the longer-acting stimulants produce the same effects as the short-acting stimulants. To address this question, James et al. (2001), in a double-blind, placebo-controlled study, compared the efficacy and time course of immediate- and sustained-release dexamphetamine (Dexedrine Spansules) and Adderall on several dependent measures, including academic achievement scores. All stimulant treatments were significantly superior to placebo at improving academic achievement. However, only the sustained-release dexamphetamine had a prolonged effect in improving mathematics problem-solving ability. Future investigations are needed to examine the differential effects on academic achievement and learning as a function of immediate- and sustained-release versions. Some experts have recommended additional study of the relationship between dose response and academic productivity across various age groups (Chacko et al., 2005) with caution on employing measures of academic achievement as the sole dependent measure given that these measures may not be sufficiently sensitive to assess the effects of the stimulants on academic achievement.

Behavioral and motoric effects. Because two of the core symptoms of ADHD, impulsivity and hyperactivity, involve behavioral and motoric effects, much research has investigated the influence of stimulants on the behavioral and motor activity of children diagnosed with ADHD. The majority of these studies have been conducted in laboratory, classroom, home, or naturalistic (e.g., playground) settings. Dependent measures in the studies typically have included teacher and parent ratings of behavior and direct observations of behavior. Many of the studies have been double-blind controlled trials. Overall, much of this work has shown that MPH, dextroamphetamine, and pemoline are equally effective in reducing overactivity and impulsivity in children diagnosed with ADHD. Moreover, the stimulants have beneficial influences on interactions between parent and child and between the child and his or her siblings (Barkley, 1995), disruptive behavior (Bukstein & Kolko, 1998), activity and inattention (Teicher et al., 2003), physical aggression (Hinshaw, 1991), and antisocial behaviors, such as conduct problems and negative verbalizations (Pelham et al., 1999).

Immediate-release MPH and Concerta were found to improve children's behavior in regular school settings and in laboratory settings (Pelham et al., 2001). Specifically, improved behavior in the traditional classroom setting was demonstrated by both stimulants as measured by teacher ratings and individual target behaviors. In the laboratory setting, both pharmacotherapies enhanced productivity and accuracy on arithmetic seatwork assignments, decreased disruptive behavior and increased on-task behavior, and increased compliance to following classroom rules. Among children

diagnosed with ADHD, the stimulants also have been shown to increase attention and reduce noncompliance with rules in the classroom setting (Barkley, 1990; Carlson, Pelham, Milich, & Dixon, 1992). Rapport, Denney, DuPaul, and Gardner (1994) investigated MPH effects on classroom behavior in children diagnosed with ADHD. The effect sizes also were examined and the results provided interesting data to suggest that large proportions of treated children exhibited significantly improved or even normalized classroom functioning. Positive effects of MPH also have been shown for adolescents on classroom behaviors including note-taking, quiz performance, written language, and study hall assignments (Evans et al., 2001). However, studies with adolescents suggest that behavioral ratings in the classroom are discordant with ratings of home behavior. For example, some studies have found that although MPH improved behavior in the classroom as rated by teachers, parent ratings did not attest to the same behavioral improvement at home (Bukstein & Kolko, 1998; Schachar, Tannock, Cunningham, & Corkum, 1997).

Pelham et al. (1990) evaluated the efficacy of MPH on children's attention while playing baseball. Findings revealed that children were on task twice as often when medicated, although their baseball skills did not improve. Similarly, Reitman et al. (2001) evaluated the influence of MPH on attention and disruptive behaviors during sports activities in three children diagnosed with ADHD and findings supported those of Pelham et al. Specifically, MPH was found to have a positive impact on children's attention while also reducing disruptive behavior. Another interesting investigation conducted in a recreation setting found that stimulants had little influence on sportsmanlike behavior during kickball games (Hupp, Reitman, Northup, O'Callaghan, & LeBlanc, 2002). Finally, in response to concerns that stimulants may reduce appropriate levels of activity by children in naturalistic settings, Swanson et al. (2002) evaluated the effect of MPH on children's activity level in the classroom and on the playground. Swanson et al. reported significant reductions in activity and inappropriate behavior in the classroom and conclude that the effects of MPH were situationally dependent and exerted less effect on the playground than in the classroom setting. These findings suggest that MPH does not interfere with children's ability to engage in high-energy play outside of the classroom setting.

Recently, there has been interest in examining the differential duration of the stimulants on children's behavior. Pliszka, Browne, Olvera, and Wynee (2000) examined the impact of MPH and Adderall in the treatment of ADHD and found that both drugs reduced oppositional behavior, although the behavioral effects of Adderall persisted longer than did those of MPH. Furthermore investigation is needed to understand the duration of action of immediate- versus extended-release stimulants on behavior for children with ADHD.

Studies have shown that children with ADHD have difficulties with motor control, inhibition of motor responses, motor flexibility, and motor preparedness (Ben-Pazi, Gross-Tsur, Bergman, & Shalev, 2003). As a result, there is considerable interest in the psychopharmacology for motoric activities for children with ADHD. The results of studies with the stimulants have shown improvements in sequential motor functioning (Sheppard et al., 2000), executive motor timing (Rubia et al., 2003), and motor planning and response inhibition among boys diagnosed with either ADHD combined type or ADHD predominantly inattentive type (O'Driscoll et al., 2005). Finally, several studies have found that MPH exerts positive effects on fine motor skills and handwriting (Lerer & Lerer, 1976; Lerer, Artner, & Lerer, 1979; Peeples et al., 1995; Tirosh et al., 1993).

Aggression. Children with ADHD tend to be more gregarious, risk-taking, impulsive, argumentative, and aggressive than their peers and are often rejected by their peers for these reasons (Hodgens, Cole, & Boldizar, 2000). There has been considerable interest in psychopharmacological interventions for problems associated with aggression and peer relations among children and adolescents with ADHD (see Whalen et al., 1989). Hinshaw (1991) provides a review of the role of stimulants and aggression among children with ADHD. Conclusions by Hinshaw, Heller, and McHale (1992) indicate that the stimulants have not been overwhelmingly effective in reducing aggression among children with ADHD. Studies have shown that stimulants can decrease aggressive behaviors in the short term (see Brown & Sawyer, 1998; Phelps, Brown, & Power, 2002) and often

attenuate impulsive aggression (Wilens & Spencer, 2000). Positive effects of the stimulants include the reduction of overactivity (Butte et al., 1999), impulsive, oppositional (Schachar, Tannock, Cunningham, & Corkum, 1997), and antisocial behaviors (Smith et al., 1998). Moreover, some research has suggested a dose–response effect on antisocial behaviors including stealing and property damage (Hinshaw, Heller, & McHale, 1992).

Bukstein and Kolko (1998) evaluated the efficacy of MPH in a clinical population of aggressive children diagnosed with ADHD. Staff ratings of the children's behavior in the program and the classroom revealed significant improvements in aggressive behavior with low and high doses of MPH. The data support the findings of other investigations conducted within naturalistic settings as to the efficacy of MPH (see, Brown et al., 1997).

Do stimulants affect aggressive responding in a laboratory-based setting? There has been little evidence to suggest significant stimulant effects on aggression in the laboratory environment (see Brown et al., 1997). Despite these disappointing findings, Casat et al. (1996) have provided evidence that MPH decreased aggressive responses on a computerized analog of aggression in a laboratory setting for six boys diagnosed with ADHD. Given the small number of participants in this investigation, however, the data must be interpreted cautiously. As Brown and Sawyer (1998) observed, the discrepancy in findings between laboratory and naturalistic settings may be due to specific assessment strategies and doses of stimulants that differed within both laboratory and naturalistic settings.

Several studies have shown that dextroamphetamine may be efficacious in reducing aggression in children. For example, Winsberg et al. (1974) found significant effects of dextroamphetamine (20 mg twice daily) on aggression in children identified with hyperactivity. Similarly, Amery et al. (1984), using 15–30 mg of dextroamphetamine daily, reported that the stimulant decreased aggressive behaviors in boys with hyperactivity. Thus, there is some evidence to suggest that there may be a differential effect of stimulants on aggression with dextroamphetamine demonstrating greater effects than MPH.

Connor et al. (2002) recently completed a meta-analysis of stimulant effects on variations of aggressive behavior, including overt/covert aggression-related behaviors in children diagnosed with ADHD. The investigators defined "overt aggression-related behaviors" as aggression resulting in a direct confrontation with others. In contrast, "covert aggression-related behaviors" were defined as aggression that is furtive and hidden from others. A major finding from this meta-analysis is that the stimulants exert significant effects on aggressive behaviors occurring in the context of ADHD separate from their effects on the core symptoms of ADHD. The overall weighted mean effect size was 0.84 for overt and 0.69 for covert aggression-related behaviors in ADHD.

It should be noted, however, that several studies have provided nonsignificant findings for the effects of stimulants on aggressive behaviors. Hinshaw, Henker, and Whalen (1984) found no significant effects of 0.3 mg/kg of MPH on anger and verbal or physical aggression in children with ADHD. Similarly, Matier et al. (1992) noted no changes in impulsive behaviors in aggressive or in nonaggressive children with ADHD.

Because there is a fairly high comorbidity for ADHD with disruptive behavior disorders, such as oppositional defiant disorder (30–40%) and conduct disorder (30–50%) (Biederman, Faraone, & Lahey, 1992), some investigators have evaluated the efficacy of stimulants for aggression with these comorbid disorders. The studies have suggested that children with ADHD and aggression, oppositional defiant disorder (ODD), or conduct disorder (CD) do not differ in their response to stimulants on the core symptoms of ADHD relative to nonaggressive children with ADHD (Barkley et al., 1989; Greenhill et al., 2001; Vitiello et al., 2001). Moreover, Klein et al. (1997) investigated the efficacy of MPH in children with conduct disorder (CD) with and without ADHD and reported that children who met criteria for CD and ADHD responded to MPH (up to 60 mg per day) for the 5-week trial. Findings also revealed that a diagnosis of ADHD did not necessarily need to be present for a therapeutic effect of MPH on symptoms associated with conduct disorder. Finally, it has been suggested that given the frequent presence of aggression and disruptive behaviors with ADHD, coupled with the favorable side-effect profile of the stimulants, the stimulants should be considered as the drug of choice for managing aggressive behavior and disruptive behavior disorders frequently

co-occurring among children and adolescents with ADHD (Turgay, 2004).

Because the available evidence suggests that stimulants can decrease aggressive behaviors only in the short term, further research on the long-term effects of stimulant drug therapy on aggression in children diagnosed with ADHD is needed. Continued research that examines the effects of stimulants on specific types of aggression, including overt and covert aggression, also is needed.

Social relations and peer status. It is well known that most children with ADHD often have difficulties in developing and sustaining peer relationships (Milch & Landau, 1982; Nangle & Erdley, 2001; Whalen & Henker, 1991). Specifically, children with ADHD evidence a number of impairments in peer relationships compared to their peers due to the symptoms associated with their disorder, including hyperactivity and impulsivity (frequently annoying, bossy, immature, boastful, intrusive, overbearing, and physically and verbally aggressive) (Pelham, Fabiano, & Massetti, 2005). These behaviors are considered by their peers as impolite and offensive. Similarly, difficulties in sustaining attention and effort to various tasks and activities may be interpreted by some as being either indifferent or uncaring (Barkley, 1997). For many of these reasons, children with ADHD may experience rejection by peers (Hoza et al., 2005; Moser & Bober, 2002). Studies have documented these impairments across settings (Cunningham & Siegel, 1987; Hinshaw & Melnick, 1995). For example, children are apt to reject other children who are impulsive and blurt out answers in the classroom and who fail to take turns while playing rule-governed games. Moreover, deficits in peer relationships and social functioning have been shown to continue well into adolescence and even adulthood (e.g., Barkley, Fischer, Smallish, & Fletcher, 2004). In fact, social relationships with peers are considered to be some of the strongest predictors and mediators of negative adult outcomes (Coie & Dodge, 1998; Huesmann, Lagerspetz, & Eron, 1984).

Some studies have shown that stimulants often improve social interactions (Wilens & Spencer, 2000), communication, and responsiveness (Hinshaw, Heller, & McHale, 1992), as well as peer relationships (see Brown & Sawyer, 1998). A review of studies investigating the efficacy of MPH in the management of symptoms associated with ADHD suggests improved functioning for observable social and classroom behaviors (effect sizes ranging from 0.63 to 0.85, with a mean effect size of 0.81) (Miller, Koplewicz, & Klein, 1997). The stimulants also have been shown to improve, although not necessarily normalize, peer appraisal of children with ADHD (Whalen et al., 1989). Moreover, there is evidence to suggest that stimulant treatment reduces negative social behaviors (Gadow, Sverd, Sprafkin, Nolan, & Ezor, 1995; Gillberg et al., 1997; Hinshaw et al., 1989; Klein & Abikoff, 1997; Whalen et al., 1987).

Some controlled trials of children with ADHD have compared stimulants to placebos on functional indices of behavior, including social behavior. In a trial that examined stimulant effects in a summer treatment program for children with ADHD, low and high doses of MPH produced improvement on all social behaviors that were assessed (following activity rules, noncompliance, conduct problems, negative verbalizations) (Chacko et al., 2005). Similar findings regarding enhanced social behaviors were found for adolescents treated with MPH in a summer treatment program (Smith et al., 1998).

Although the aforementioned findings are encouraging, it should be noted that not all findings of stimulant therapy for children's social behavior have been positive. In one controlled trial, children who received stimulants compared to placebo doses displayed muted social behavior, decreased social engagement, and increased dysphoria relative to those receiving placebo doses. Conversely, children who did not receive active medication were more socially engaged, used more aversive leadership techniques, and were rated as less likable by peers (Buhrmester et al., 1992). These findings are of concern because they suggest that stimulants may exert a "depressive" effect on children whereby they become isolated and less socially engaged with peers. Whether these data may be associated with the dose is unclear. Jacobvitz et al. (1990) suggested that lower levels of prosocial behavior may be associated with relatively high doses of stimulants.

It has been suggested that the effective use of stimulants to increase prosocial behaviors may require the simultaneous use of adjunctive therapies, such as behavioral management (Bennett, Brown, Craver, & Anderson, 1999). In fact, in a review of the literature, Jensen

(2001) found that for social skills, combined treatments, including stimulants and behavior therapy or social skills training, offer some modest advantages over single treatment approaches. However, one investigation that investigated the differential effects of various treatment approaches on children's social functioning provided disparate results. For example, the Multimodal Treatment of Attention-Deficit Hyperactivity Disorder (MTA) study tested whether MPH, combined with intensive multimodal psychosocial intervention, including social skills training and behavior modification, significantly enhanced social functioning in children diagnosed with ADHD compared to MPH alone or MPH combined with a nonspecific psychosocial treatment (attention control). Findings suggested that no advantage was revealed on any measure of social functioning for the combined treatment group over the MPH employed alone or MPH combined attention control group (Abikoff et al., 2004). Analyses of the data from the MTA study suggest that although little evidence was found for superiority for any of the treatments as to peer-assessed outcomes, the available evidence favors treatments involving medication management (Hoza et al., 2005). It is important to note that significant improvement did occur across all treatments and continued over the course of 2 years. The MTA study is important as it suggests that, for young children with ADHD, there may be little support for clinic-based social skills training as part of a typical treatment program to manage social difficulties (Abikoff et al., 2004).

Some researchers have examined whether stimulant treatment is able to normalize social functioning in children diagnosed with ADHD. DuPaul and Rapport (1993), in their studies of children with ADHD, have observed normalized social functioning in the majority of children receiving MPH. However, the consensus is that although stimulants often are associated with improved social functioning, they rarely normalize the behavior of ADHD children to that of their peers (Pfiffner, Calzada, & McBurnett, 2000). Additional evidence for this conclusion comes from the MTA study, which found that children from all four treatment groups did not achieve normal peer relationships and remained significantly impaired in their peer relationships compared to randomly selected classmates (Hoza et al., 2005). More long-term, controlled prospective studies of social skills of children with ADHD who are treated with stimulants are needed, particularly of children being treated with longer-acting agents and in combination with other nonsomatic treatment modalities (including social skills training).

Learning Disabilities

"Learning disabilities" is a category used to describe a heterogeneous group of children who evidence a discrepancy between achievement and intellectual functioning in a variety of academic skill areas, including reading, arithmetic, language, writing, and motor skills (APA, 1994). Deficiencies in specific neurocognitive skills, including attention, memory, and reasoning, have been observed in this population (Douglas & Peters, 1979). Few researchers have studied the effects of stimulants on children with specific learning disabilities. Research conducted in this area has focused on children with reading disabilities. The literature indicates that there is little or no improvement for children with reading disorders who are treated with stimulants (Aman & Werry, 1982; Ballinger, Varley, & Nolen, 1984; Cooter, 1988; Gittleman, Klein, & Feingold, 1983). Moreover, there is no compelling evidence to suggest that stimulants improve basic learning disabilities or enhance academic achievement (Alto & Frankenberger, 1994; Barkley & Cunningham, 1978; Weber, Frankenberger, & Heilman, 1992), although some data suggest that stimulants enhance academic efficiency or completion of academic tasks (Barkley, 2005).

Because a significant number of children with ADHD also have learning disabilities (Barkley, 1990), researchers have focused on the effects of stimulants on children with comorbidities, including children with ADHD and learning disabilities. Brown et al. (1997) suggest that stimulants exert little specific influence on learning disabilities. Rather, it is likely that stimulants may attenuate symptoms associated with ADHD, such as attention and concentration deficits, thereby assisting the child in participating in the learning environment and leading to an increase in completion of school work (Elia et al., 1993). Thus, although stimulants may play an adjunct role in the treatment of children with learning disabilities who also suffer from attentional problems, the most promising treatment

for learning disabilities is either special education and/or remedial assistance tailored to the individual child with a specific learning impairment.

Conduct Disorders

Conduct disorder is characterized by a number of persistent problematic behaviors, including oppositional and defiant behaviors and antisocial activities (e.g., lying, stealing, running away, physical violence, sexually coercive behaviors), that violate societal norms (Gadow, 1992). *Oppositional defiant disorder* includes disruptive behaviors such as noncompliance, temper tantrums, arguing, and mild aggression (Farley, Adams, Lutton, & Scoville, 2005). Given the comorbidity of ADHD and conduct disorders coupled with the fact that both disorders are indicated under the nosology of disruptive behavior disorders of childhood (APA, 1994), of interest is whether children with conduct disorders and oppositional defiant disorder respond to stimulants in a similar way to their peers with ADHD. However, few studies have examined the effects of stimulants on children with conduct disorder or oppositional defiant disorder when these disorders occur without ADHD. There is some encouraging support for the effects of stimulants on disruptive and aggressive behaviors, the core symptoms found in youth with conduct disorders (Connor et al., 2002; Pelham & Murphy, 1986). For example, some studies have shown that antisocial behaviors in school-age children—such as stealing and fighting—can be reduced by stimulant treatment (Hinshaw et al., 1992; Klein et al., 1997). Gerardin Cohen, Mazet, and Flament (2002) reported that treatment with MPH improved some conduct disorder symptoms, even in the absence of ADHD. Klein et al. (1997) investigated the effects of stimulants on conduct disorder in children. The participants were administered MPH (up to a total of 60 mg/day) or a placebo for a period of 5 weeks. Parent, teacher, and clinician ratings were employed as dependent measures as well as direct observations of classroom behavior. Two-thirds of the participants also met criteria for ADHD. Thus, the majority of the sample had comorbidity. Findings revealed that ratings of antisocial behaviors specific to conduct disorder (e.g., obscene language, attacks others, destroys property,

deliberately cruel) were significantly diminished with the use of MPH treatment. Moreover, the magnitude of the MPH effect suggested meaningful clinical benefits, including diminished symptoms of oppositional defiant behavior and conduct disorder (e.g., less aggression). The investigators conclude that MPH has a positive effect, albeit short term, on children and adolescents with conduct disorder. Although the majority of the sample had comorbidity of ADHD, because of the improvements in conduct-related symptoms the investigators suggest that the effects of the MPH are independent of ADHD symptom severity.

Similar to the research related to the management of learning disabilities with stimulants, much of the literature on the use of stimulants to treat conduct disorder has occurred in the context of children with comorbid ADHD. Indeed, research has found a high degree of comorbidity between ADHD and conduct disorders (Biederman et al., 1991). Connor et al. (2002) completed a meta-analysis that identified 28 studies of children ranging in age from 7 to 15 years. Specifically, the meta-analysis addressed oppositional/aggression-related behaviors within the context of ADHD. Findings revealed that children who meet full diagnostic criteria for conduct disorder or oppositional defiant disorder plus ADHD (American Psychiatric Association, 1994) showed significant improvements in aggressive behaviors when treated with stimulants. The National Institute of Mental Health (NIMH), Multimodal Treatment Study of ADHD (MTA), also found that ADHD children who were comorbid with other disruptive behavior disorders, such as conduct disorder or oppositional defiant disorder, evidenced favorable response to stimulants (MTA Cooperative Group, 1999a). Children in the MTA study with conduct disorder or oppositional defiant disorder who were treated with stimulants showed a greater response rate than the group that received behavior treatment alone. It should be noted, however, that participants with ADHD in the MTA study who had comorbidity of conduct disorder or oppositional defiant disorder responded best to a combination of behavioral and medication treatments (MTA Cooperative Group, 1999a). Thus, the addition of behavior therapy was particularly helpful for symptoms of oppositional defiant disorder (Jensen et al., 2001a). More important,

the combined treatment of behavior therapy and stimulants prevented the development of other disruptive behaviors (Jensen, 2001).

Stimulants have been shown to be effective in reducing aggression, primarily in children with conduct disorder when comorbid with ADHD. However, there is little research on children with disruptive behavior disorders without ADHD (i.e., without comorbidity) when compared with placebo. In fact, no psychotropic medications have been approved specifically for the treatment of oppositional defiant disorder (Kaplan et al., 2004). Moreover, stimulants have yet to show significant effects on covert antisocial behaviors such as lying and cheating (Gilligan & Lee, 2004). Therefore, it has been suggested that for pure conduct or oppositional defiant disorders, the first-line treatment for these disorders should be behavioral and psychosocial interventions, with pharmacotherapy considered as an augmentation only when aggression and/or impulsivity are marked and persistent (Kutcher et al., 2004). Conversely, for children with ADHD with comorbid conduct disorder, evidence suggests that psychosocial intervention combined with pharmacotherapy is the treatment of choice (Kutcher et al., 2004).

Related to the entire notion of externalizing behavior disorders and stimulants is the issue of the potential positive association between stimulant treatment and potential substance abuse, especially in the long term. Given that the potential for drug abuse is high among adolescents with impulsivity and poor school achievement, this raises the question as to whether ADHD children and adolescents who share similar symptoms and are treated with stimulants are at greater risk for abuse of substances. Of greater concern is whether children and adolescents who have comorbidity of conduct disorder or oppositional defiant disorder and ADHD and who are managed with stimulants are at greater risk for substance abuse than if they were not managed with stimulant drug therapy (Disney, Elkins, McGue, & Iacono, 1999; Elliott, 1988). There is also the concern among practitioners and the lay public that stimulants could be misused, especially if youths are treated with stimulants in adolescence. Fortunately, some studies suggest that stimulant treatment among children with ADHD is associated with a *reduction* in the risk for subsequent drug and alcohol use disorders during early adulthood (Milberger et al., 1997;

Wilens, Faraone, Biederman, & Gunawardene, 2003). Moreover, Barkley et al. (2003), in their longitudinal follow-up study of young children who were treated with stimulants and later evaluated as young adults, found no evidence to suggest that stimulant treatment of children with ADHD resulted in an increased risk for substance experimentation, dependence, or drug abuse during young adulthood (see also Hechtman, Weiss, Pearlman, & Amsel, 1984). In fact, one study demonstrated that adolescents treated with stimulants reduced their chance of later substance abuse by 85% (Biederman et al., 1999). However, it should be noted that no studies can be located that have evaluated the long-term impact of stimulant treatment on later substance abuse for youth with conduct disorder. More important, there are no studies that have focused on youth with comorbidities who have been treated with stimulants and potential substance abuse. Obviously, it will be necessary to examine patterns of later substance abuse among specific subtypes of children with ADHD, including comorbid groups of ADHD children with other disruptive behavioral disorders (e.g., oppositional defiant disorder, conduct disorder). Until additional studies are forthcoming, the practitioner should be judicious in prescribing stimulants to children with ADHD, particularly when there is comorbidity of any other disruptive behavior disorder.

Mental Retardation

Mental retardation (MR) is a heterogeneous condition defined by significantly subaverage intellectual and adaptive functioning, with an onset prior to age 18 (Szymanski & King, 1999). Children who are mentally retarded frequently also have co-occurring symptoms consistent with ADHD. Reported rates of MR comorbid with ADHD range from approximately 7 to 18% (Gillberg et al., 1986). Stimulants have been commonly prescribed for children with both comorbid conditions (Gadow, 1985). There have been few controlled clinical trials that directly assessed the effects of stimulants for individuals presenting with both ADHD and MR (see Brown et al., 1997). Evidence from studies conducted with this population suggests improvements in ADHD symptoms with the use of stimulants in children with sub-average intellectual functioning (Filho

et al., 2005). The majority of evidence from placebo-controlled trials suggests that children with mild-to-moderate MR and behaviors associated with overactivity and inattention respond to stimulants in a manner similar to their peers with normal intelligence and ADHD (Aman et al, 1991; Handen, Breaux, Gosling, Ploof, & Feldman, 1990; Handen et al., 1992; Pearson et al., 2003). Aman, Buican, and Arnold (2003), however, indicated that the beneficial response to MPH appears to be well below that of children with at least average intellectual functioning and that the response is more variable. Taken together, the available evidence suggests that the degree of improvement from stimulants for children with MR is directly associated with their degree of cognitive impairment, with MPH efficacy being greater among children with higher intellectual functioning (i.e., intellectual functioning greater than 45) (Aman et al., 1991; Gadow, 1985). Moreover, there have been a number of studies that suggest a dose–response effect for stimulants in children with MR who have comorbid ADHD; higher MPH doses have been shown to be associated with greater improvements in behavioral response (e.g., declines in hyperactivity, conduct problems, antisocial behavior, and improved attention) and even some gains in cognitive functioning (Pearson et al., 2003, 2004).

In an investigation of 24 children with ADHD and either mild or moderate MR, Pearson et al. (2004) examined the efficacy of various doses of MPH versus placebo. Findings revealed that most children showed some degree of behavioral and cognitive improvement with MPH treatment, with the highest dose of MPH (0.60 mg/kg) being on average the most effective of all doses. Specifically, over half of the children receiving the highest dose of MPH showed substantial behavioral gains and nearly half of the sample made substantial gains in cognitive task performance. It is worth noting that the investigators found substantial independence between changes in behavior and cognitive task performance. This finding is important because it suggests that improvements in one functional domain (e.g., behavior) do not necessarily predict similar improvement in another functional area (e.g., cognition) for children with MR when comorbid with ADHD (Pearson et al., 2004). In a parallel-group design trial of MPH and risperidone (an atypical neuroleptic agent) in children

and adolescents with moderate MR and ADHD, children receiving both psychotropics showed reduced ADHD symptoms (Filho et al., 2005). However, risperidone was found to exert a more marked effect in reducing overall ADHD symptoms in this population.

In a controlled trial of MPH, fenfluramine, and a placebo in children with borderline MR (Aman et al., 1997), MPH was found to reduce errors on the Continuous Performance Test and reduce seat movements. Teacher ratings revealed improvements in conduct problems, hyperactivity, and distractibility with both psychotropics, with MPH showing the greatest improvement in the area of attention. Moreover, parent ratings indicated improvements in hyperactivity and conduct problems for both agents. In one of the few studies of stimulant treatment with preschool children with borderline MR and ADHD, 8 of 11 children showed improvements (as rated by teacher and parent ratings of hyperactivity and impulsivity), although only small effects were shown on laboratory tasks of cognitive performance (Handen et al., 1999).

For the purpose of assessing the effectiveness of MPH on disruptive behavior and task engagement, a single-subject experimental design study was conducted with three children with severe to profound MR. Findings confirmed that a high dose of MPH (0.6 mg/kg) decreased disruptive behavior and improved engagement with the task for two of the three children. For the two children that showed clinically significant effects, the higher dose (0.6 mg/kg) of MPH was found to be more efficacious than the lower dose (0.2 mg/kg) (Blum, Mauk, McComas, & Mace, 1996). In another case study, Johnson et al. (1994) studied three children with mild MR and reported additive effects of MPH and a behavioral intervention as assessed by measures of task accuracy, but not for measures of activity or disruptive behaviors. Conversely, in a group study with children who evidenced intellectual functioning of less than 45, almost no beneficial response to MPH was shown (Aman, Kern, McGhee, & Arnold, 1993). Thus, research suggests the efficacy of stimulant drug treatment when MR is comorbid with ADHD, with more optimal response inversely related to the degree of MR.

The evidence is equivocal as to whether children with MR are at greater risk for more frequent and severe adverse side effects from

MPH therapy. For example, Handen et al. (1991) reported a greater number of adverse side effects associated with stimulants among children with MR and ADHD than had been reported among school-age children without MR. Specifically, MPH treatment was discontinued for nearly one-fourth of the children, primarily because of motor tics and social withdrawal at unacceptable levels. In another placebo-controlled trial of MPH in preschool children, 5 out of 11 children showed significant adverse effects, including severe social withdrawal (Handen et al., 1999). However, Filho et al. (2005) suggest that the side-effect profile for MPH that they report in a trial of children and adolescents with moderate MR and ADHD was similar to that found in typically developing patients treated with MPH (e.g., insomnia, decreased appetite, and weight loss) (Barkley et al., 1990). Thus, the literature on the use of stimulants in children with MR comorbid with ADHD suggests some beneficial effects with more adverse effects noted among preschoolers and those with more profound retardation.

The literature indicates similar efficacy of stimulants for children with intellectual functioning between 45 and 75 and children with ADHD without MR. In general, the most significant improvements have been found for behaviors such as impulsivity, hyperactivity, and attention deficits. Evidence indicates a significant association between intellectual functioning and positive stimulant response. Specifically, higher functioning children show better responses to stimulant than children with more profound retardation (i.e., intellectual functioning below 45). Researchers need to examine large cohorts of children with a wide range of intellectual functioning to clarify the association between dose–response, intellectual functioning, and long-term efficacy, as well as adverse side effects associated with MPH therapy. Finally, additional research is needed to examine the effects of MPH combined with behavioral management or parent-training sessions with children who have a comorbidity of MR and ADHD (Weber & Lutschg, 2002).

Acquired Neurological Conditions

Research in the area of neuropsychological, social, and emotional sequelae of acquired brain injuries in pediatric patients has revealed characteristic deficits such as cognitive, academic, and behavioral disturbances (see Brown et al., 1997). The neurocognitive functions most vulnerable to acquired brain injuries are attention, memory, and problem-solving abilities (Brown et al., 1997). Thus, children with acquired brain injuries share some similarities to their peers with ADHD; in fact, ADHD places many children at risk for acquired brain injuries (Rutter, 1983). Unfortunately, however, there are few studies of the effectiveness of stimulants for attentional problems among children evidencing various forms of brain injury (Butler & Mulhern, 2005); most studies of stimulants have focused on adult populations with traumatic brain injuries. Moreover, studies examining the efficacy of MPH on attentional disorders that are associated with traumatic brain injury have yielded equivocal data (Butler & Mulhern, 2005). Nevertheless, clinical research has supported the use of MPH for patients with traumatic brain injury and stroke because of stimulants' affinity for cognitive, attentional, and behavioral problems (Kajs-Wyllie, 2002).

Hornyak, Nelson, and Hurvitz (1997) completed one of the few studies that examined the effect of MPH on cognitive functions in a pediatric population with closed head injuries. A longitudinal design was used to evaluate the effect of MPH on 10 children with traumatic brain injuries for the management of attentional problems and arousal deficits. MPH showed a beneficial response for behavior as rated by parents, teachers, and the day-treatment team. Similarly, in a controlled clinical trial of 14 children who had sustained mild-to-severe brain injury with acquired attentional deficits, participants were treated with MPH between 1 and 60 months after having sustained the trauma (Mahalick et al., 1998). Findings revealed significant differences between MPH and the placebo on tasks of attention and concentration. However, these data were not replicated in a subsequent investigation (Williams, Douglas, Ayyangar, Scheft, & Berch, 1998). Siddall (2005) conducted a review of the literature regarding the effectiveness of MPH in the management of the cognitive and behavioral changes observed following traumatic brain injury (TBI). Specifically, 10 clinical trials evaluating the efficacy and safety of MPH in pediatric and adult patients with TBI were reviewed. The results of these studies indicated

that MPH is likely to improve memory, attention, concentration, and mental processing in children with TBI.

There have been a number of studies demonstrating that children who survive various types of cancer, including acute lymphocytic leukemia (ALL), lymphoma, and brain tumors, also suffer from cognitive impairments including attentional problems. These impairments or cancer *late effects* are typically the result of prophylactic treatments administered to the CNS to prevent cancer cells from entering the brain (see Butler & Mulhern, 2005; Morris et al., 2000; Waber & Mullenix, 2000). Moleski (2000) concluded that a majority of children treated for ALL experienced declines in intellectual functioning, neurocognitive functioning, and delays in academic achievement. The core neurocognitive deficits in survivors of ALL and malignant brain tumors typically included deficits in attention/concentration and nonverbal memory (Butler & Mulhern, 2005). For example, children surviving ALL and malignant brain tumors (BTs) have shown deficits in attention and academic achievement when compared to their healthy peers (Brown, Mulhern, & Simonian, 2002; Mulhern et al., 2004). Butler and Mulhern (2005) have suggested that because children who survive ALL and malignant brain tumors exhibit behavioral symptoms similar to those of children with ADHD, particularly symptoms of the primarily inattentive type of ADHD, stimulant drug treatment may prove effective in ameliorating the attentional and behavioral symptoms in these children, especially during the late effects period (i.e., 1 year following completion of treatment). In the first controlled parallel-group design of childhood cancer survivors (MPH compared to a placebo) (Thompson et al., 2001), the group receiving MPH showed significantly greater improvement on errors of omission and the overall index on the CPT (a measure of focused or sustained attention). However, significant differences were not revealed for reaction time or errors of commission on the CPT, the overall score on the California Verbal Learning Test—Children's (a measure of short-term and long-term memory via recall and recognition tasks), or the Visual-Auditory Learning Test on the Woodcock-Johnson Cognitive Battery. The lack of findings suggested that MPH exerts its primary therapeutic effect on attention and concentration rather than on more complex cognitive tasks. In another double-blind controlled clinical trial of MPH among 83 long-term survivors of leukemia and brain tumors who were identified as having attentional deficits and problems with academic achievement (Mulhern et al., 2004), significant improvements were revealed for attentional problems and social skills deficits as rated by parents and teachers when compared to placebo. Specifically, ratings from teachers and parents revealed reductions in attentional problems, whereas only teacher ratings yielded reductions in social skills deficits among childhood survivors of leukemia and brain tumors. Interestingly, the investigators did not observe any advantages of a moderate dose (0.6 mg/kg) of MPH relative to a lower dose (0.3 mg/kg).

Two investigations examined whether children with learning problems (presumably due to cancer treatment) improve with stimulant drug treatment. The first investigation included 12 children who survived malignant brain tumors or ALL and were treated with MPH for 6 months to 6 years (median period of treatment was 23 months) (DeLong et al., 1992). Results revealed that eight children had a "good" response, two had a "fair" response, and two had a "poor" response to medication, although no dosing information was provided. In only one child, who had a poor response, MPH was discontinued because of marked appetite loss. Researchers concluded that MPH response seems to be especially poor for children who receive the most intensive radiation therapy and chemotherapy. The findings are important because they suggest that for children who suffer from severe neural tissue damage caused by either the illness itself or its associated treatment, stimulants (i.e., MPH) may not be especially efficacious or may even produce greater adverse side effects than for healthy peers. The second investigation consisted of a small sample of six children who had received radiation therapy 3–12 years earlier for malignant brain tumors (Torres et al., 1996). Findings revealed no significant immediate or delayed benefits associated with MPH treatment, although the small sample size indicates that these data must be interpreted with caution.

Deficits in attention and concentration also are frequently associated with pediatric seizure disorders (Williams, Griebel, & Dykman, 1998). However, questions remain as to whether

deficits in attention have their etiology in seizure disorders or whether they are exacerbated by the anticonvulsant agents. Another possibility is that a combination of factors, including comorbidity of ADHD or iatrogenic effects of anticonvulsant agents, plays a role in neurocognitive deficits (Weber & Lutschg, 2002). In a double-blind crossover study of 10 children with a variety of seizure disorders, MPH was examined as a measure of ameliorating attentional problems in this small sample. Findings revealed improvements in attention capacity based on teacher ratings of attention in the classroom and neuropsychological measures of attention and concentration (Feldman et al., 1989). It is also important that there were no increases in seizure activity as a function of MPH therapy, refuting the common clinical lore that stimulants lower seizure threshold. Gross-Tsur et al. (1997), in a double-blind, placebo-controlled crossover study, examined the safety and efficacy of MPH in 30 children with various types of seizure disorders. Of the sample, 70% showed improvements in the area of attention and concentration as rated by parents. Moreover, improvement also was revealed for a laboratory measure of attention. Loss of appetite was reported to be the only persistent adverse side effect. Finally, a study by Finck et al. (1995) revealed similar results where MPH was found to enhance attention. Few adverse side effects and no increase in frequency of seizures were reported. Weber and Lutschg (2002) have suggested that for children with seizure disorders, adverse side effects from MPH therapy are minimal if the children are seizure-free, but caution that close monitoring is necessary if seizure activity is continuous.

The data regarding the neuropsychological outcome of bacterial or viral meningitis or encephalitis in children are equivocal (Weber & Lutschg, 2002). For example, no significant difference in attention was found between children 12 years of age following bacterial meningitis when compared with controls (Grimwood et al., 2000). However, Anderson and Taylor (1999) conducted a review of patients with pediatric meningitis and reported that children post-meningitis displayed more deficits in attention on various tests of executive functions relative to comparison controls. Nonetheless, no studies of the effects of stimulants can be found for children who have sustained either meningitis or encephalitis. Given the frequent presence of cognitive and learning impairments among this population, controlled trials examining the efficacy of stimulants on learning, behavior, and cognition may prove fruitful.

Although recent data have been encouraging as to the use of stimulants for children with acquired brain injuries, cancer late effects, seizure disorders, and meningitis or encephalitis, more research is needed regarding safety and efficacy prior to endorsing the use of stimulants for children who have sustained these disorders. Siddall (2005) has suggested the need for large sample, double-blind, placebo-controlled studies of stimulants in treating traumatic brain injury to identify optimal doses, choose the specific phase of recovery to commence treatment, determine length of treatment, and ensure long-term safety for patients with mild, moderate, and severe TBI. Research is also needed to determine whether stimulants can enhance academic achievement among childhood cancer survivors who have sustained attentional problems as a function of cancer treatment (i.e., radiation, chemotherapy). Longitudinal studies of stimulant treatment for attention problems in pediatric seizure disorders are warranted, as well as investigations of the effects of dose on the safety and efficacy of stimulants with this population. Research is needed to examine the efficacy and safety of stimulants in children with attentional deficits resulting from meningitis or encephalitis.

Tourette's Syndrome

Tourette syndrome (TS) is a hereditary neurological disorder characterized by repetitive involuntary movements and vocalizations called *tics*. Many children with TS experience additional neurobehavioral problems including inattention, overactivity and impulsivity; tic disorders and TS are frequently accompanied by other conditions; the most frequent comorbid condition is ADHD (about 50% of patients with TS have accompanying ADHD) (Burd, 1995).

Treatment of comorbid ADHD has been controversial because of reports that stimulants hasten the onset or exacerbate the severity of tics in some patients (Golden, 1988; Kurlan, 1997; Sverd et al., 1992). Given this concern, greater efforts have been undertaken to examine the effects of stimulants in ADHD children with comorbid tic disorders.

Gadow et al. (1999) conducted a prospective, follow-up open-trial that examined the effects of long-term treatment with MPH therapy for ADHD symptoms and motor and vocal tics among prepubertal children with ADHD and chronic multiple tic disorder (the majority of children qualified for a diagnosis of TS). Children included in this study had participated in an earlier 8-week, double-blind, placebo-controlled MPH trial. Dependent measures for this investigation included direct observations of child behavior in a simulated (clinic-based) classroom and behavior ratings completed by parents and the study physician. Findings from group data provided no evidence to support the notion that motor or vocal tics changed in frequency or severity during MPH maintenance therapy compared with diagnostic or initial double-blind placebo evaluations. Moreover, behavioral improvements demonstrated during the acute drug trial were sustained during the follow-up evaluations. Gadow et al. (1999) suggest that long-term treatment with MPH seems to be safe and effective for the management of ADHD behaviors in many (but not necessarily all) children with mild-to-moderate tic disorder. However, Gadow et al. (1999) caution that clinical monitoring should always be standard of care so as to rule out the possibility of drug-induced tic exacerbation in children with comorbid ADHD.

Castellanos et al. (1997) examined the effects of stimulants (MPH or dextroamphetamine) and dose response on tic severity for the management of boys with ADHD and comorbid TS. Results indicated that a substantial minority of the comorbid participants had consistent exacerbation of tics on stimulants. Despite this concern, however, it should be noted that the majority of boys evidenced improvement in symptoms associated with ADHD with no real exacerbation of tics. Overall, treatment with MPH was better tolerated than dextroamphetamine therapy in children with TS. This investigation is important as it is one of the few studies to compare types of stimulants in a controlled clinical trial for children with TS.

The Tourette's Syndrome Study Group (2002) conducted a randomized double-blind, placebo-controlled trial with a 16-week follow-up period on the effects of clonidine and MPH for the treatment of 136 children with ADHD. MPH compared to placebo resulted in beneficial effects for ADHD symptoms as assessed by teacher ratings of ADHD symptoms; however, the greatest benefit was observed with combined clonidine and MPH. Results also revealed that the combined treatment of clonidine and MPH was most effective in diminishing tic severity (75% of the children showed improvement) and enhancing overall global functioning. Findings also revealed that MPH alone was effective in diminishing tic severity and decreasing functional impairments. Tics were not found to be substantially worse in the active medication group versus the placebo group; however, the study failed to address the relationship between dose of MPH and the emergence of tics (Goldberg, 2002). Findings from this study and those of Law and Schacher's (1999) are potentially important as clinicians may take comfort in the fact that treatment with MPH is not a sufficient condition to cause or exacerbate tics (Tourette's Syndrome Study Group, 2002). Nonetheless, studies are needed to examine dose–response associations between specific doses of stimulants (e.g., high versus low doses) and the emergence of tics.

Palumbo et al. (2004) reexamined the data from five studies to evaluate the impact of once-daily MPH (Concerta) administration on the emergence of tics in children with ADHD. Results from the analyses again suggest that MPH-based therapy does not significantly induce or exacerbate tics in children with ADHD. Similar conclusions were reached in another comprehensive review of seven studies that compared stimulants with placebo or with other medications where no increase in tics was revealed for children treated with stimulants (Jadad et al., 1999). Kurlan (2003) concludes that the most frequently prescribed stimulants, particularly MPH and dextroamphetamine, are safe and efficacious in the management of ADHD. Kurlan also suggested that some children may in fact experience improvement in tic symptoms while receiving stimulants. Product labeling for stimulants currently contraindicates the use of these psychotropics in children with tics, full TS, or children with a family history of tics. Nonetheless, the recent literature has suggested that a comorbid tic disorder should not be considered a serious contraindication to the use of stimulants for treatment of ADHD (Kurlan, 2003). However, clinicians must be cautioned that each patient should be considered

individually and carefully. The astute practitioner must monitor responses to stimulant drug therapy, including the possible emergence of tics and TS.

In summary, recent studies have suggested that stimulants are an effective and safe intervention for children with ADHD who have comorbid tic disorders. However, if, after assessment, the practitioner elects a trial of stimulants, caution should be the standard, together with ongoing monitoring regarding adverse effects, including the emergence or exacerbation of tics. Additional studies are needed to examine the risks and benefits of stimulants in children and adolescents with TS or a family history of TS, as well as dose–response relationships that could delineate the emergence of tics to specific stimulant doses.

Depression in Medically Ill Groups

The treatment of depression in chronically ill groups, particularly where the medical management includes palliative care, presents multiple challenges. Many individuals with a chronic debilitating disease frequently develop depressive symptoms that may be exacerbated by their functional impairments as well as the guarded prognosis of the disease. For example, for some chronic illnesses where there may be cardiac or liver dysfunction, tricyclic antidepressant drugs may not be the pharmacotherapy of choice. Moreover, the 2- to 3-week delay between initiation of antidepressant therapy (e.g., tricyclics or specific serotonin reuptake inhibitors) and dissipation of target symptoms casts doubt on the use of these agents with individuals who may lack energy or even evidence depressive symptoms (Frierson, Wey, & Tabler, 1991). Thus, for some chronic illness groups, it has been suggested that the use of stimulants be considered due to their rapid onset of action coupled with their safety and generally favorable side-effect profile (Satel & Nelson, 1989). Researchers, however, have almost exclusively focused on stimulant treatment of depression in adult and geriatric populations. Indeed, the literature reveals only one case report using MPH in a depressed adolescent with HIV/AIDS (Walling & Pfefferbaum, 1990). After the youngster experienced adverse effects from a traditional antidepressant agent, MPH therapy was initiated and the patient showed improved

mood, energy level, and appetite (Walling & Pfefferbaum, 1990). However, controlled clinical trials examining stimulant treatment for depression in medically ill children and adolescents are needed before we can draw definitive conclusions about the safety and efficacy of this treatment.

Developmental Issues

Developmentally inappropriate degrees of hyperactivity, inattention, and impulsivity are common symptoms in childhood; therefore, stimulants have been used primarily in the elementary school-age population. However, there is increasing recognition that attentional and behavioral problems (both social and cognitive) affect individuals throughout the lifespan. Stimulants have been shown to be a viable treatment modality across age groups.

Preschoolers

The use of stimulants for preschool children has received widespread attention, particularly among the lay press, and the practice has been controversial. Diagnosing ADHD in this age group is especially difficult because a high activity level, impulsivity, and a short attention span are considered by many to be age-appropriate characteristics for most preschool children (Blackman, 1999). Moreover, professionals and the public alike have expressed concerns about the administration of psychotropic medication to very young children. This concern has been especially heightened considering that the use of stimulants in children aged 2–4 years tripled between 1991 and 1995 (Zito et al., 2000). MPH is among the three most commonly prescribed medications for children under the age of 6 years (Zito et al., 2000). In fact, Michigan Medicaid found 60% of children aged 3 years or younger diagnosed with ADHD are prescribed stimulants (Coyle, 2000).

Although the clinical use of stimulants for preschool children diagnosed with ADHD is becoming more common (Connor, 2002), there are few studies in the literature that have systematically examined the safety and efficacy of stimulants with preschoolers. Results from a computerized literature search that extended back to 1970 identified nine controlled studies of stimulant treatment and two

controlled trials examining stimulant side effects among preschool children diagnosed with ADHD (Connor, 2002). Findings indicate that there may be a greater variability of stimulant response in ADHD preschoolers when compared with their school-age peers who exhibit similar symptoms. However, improvements have been noted in cognition, interpersonal interactions, and hyperactive-impulsive behavior. Results from the studies reviewed also found that although adverse side effects for preschool children are reported to be mild, these children may experience a higher frequency and a different quality of stimulant-induced adverse side effects compared with their older counterparts. Connor (2002) concludes that, based on the review, stimulants meet evidence-based criteria as both beneficial and safe for preschool children diagnosed with ADHD aged 3 years and older. However, Connor has cautioned that there needs to be more research assessing stimulant effects on very young children and the developing brain.

In one clinical trial of preschoolers, Musten et al. (1997) studied 31 children in whom ADHD had been diagnosed ranging in age from 4 to 6 years. The investigators found that preschoolers' symptoms responded to both 0.3 mg/kg (a relatively lower dose) and 0.5 mg/kg (a relatively higher dose) in a fashion similar to that of school-age children. Adverse side effects were relatively mild (Firestone et al., 1998). In another clinical trial, Short et al. (2004) examined the efficacy and adverse side effects for MPH and mixed amphetamine salts (Adderall) in a sample of preschoolers in a naturalistic setting. Findings revealed clinically significant changes in behavioral ratings of preschoolers in response to stimulants. No differences were found regarding efficacy and adverse side effects as a function of the two stimulants. Finally, Chacko et al. (2005) examined the effectiveness of stimulants on multiple domains of functioning in 36 young (5–6 years) children diagnosed with ADHD. Results revealed that MPH had a marked effect on social behaviors and resulted in improvements in two of the three areas of academic functioning.

The literature guiding the clinical safety and efficacy in the use of stimulants for preschool children is limited. Nonetheless, results from recent randomized, controlled, clinical trials indicate that stimulants may be safe and effective for use in this population. Notwithstanding, in these results, behavioral treatments should be considered the first-line treatment option for preschool children with attentional and behavioral problems. If stimulants are administered to preschool children, it is important that the children be monitored for adverse side effects.

Adolescents

Until the mid-1980s, it was commonly believed that children with ADHD outgrew their condition by the time that they reached puberty. Since that time, it has been recognized that ADHD no longer results in a benign prognosis. Although many adolescents may become less restless and overactive, inattention and impulsivity often persist into adolescence (Klorman, 1986). For example, Cuffe et al. (2001) found that more than 80% of adolescents with ADHD continued to display evidence of impairment that first appeared during childhood. Given that some ADHD symptoms persist well into adolescence and that stimulants have been shown to be effective in the management of inattention and impulsivity in childhood, recent research has examined the pharmacology of stimulants in adolescents diagnosed with ADHD.

Evans and colleagues (2001) tested the effects of MPH on 45 (predominantly male) adolescents diagnosed with ADHD enrolled in a summer treatment program. Findings revealed that MPH, in combination with behavior management, resulted in improved performance on a range of academic tasks, including note-taking, daily assignments, and quiz scores. No major adverse side effects were reported. Specifically, between 78 and 91% of the participants displayed a beneficial effect, depending on the index examined.

In another multicenter, randomized, double-blind, placebo-controlled study, Stein and Greenhill (2002) examined the safety and efficacy of the long-acting MPH formulation (Concerta) in a group of 264 adolescents ranging in age from 13 to 17 years. Caregivers rated treatment as "good or excellent" in 84% of participants after 3 months of MPH therapy. After 6 months of therapy caregivers continued to rate treatments as "good or excellent" for 97% of the participants. Interestingly, caregiver satisfaction with medication was noted to be high; specifically, 87% of parents reported being satisfied

with treatment after 3 months and some of the caregivers reported being very satisfied. Only 6.8% of the patients withdrew from the study due to adverse side effects. Consistent with the aforementioned studies, Greenhill's (2002) multicenter, randomized, double-blind, placebo-controlled study of long-acting MPH (Concerta) in 175 adolescents with ADHD (aged 13–18 years) also provided important data that demonstrated significant benefits of stimulants for this age group.

Finally, reviews and meta-analyses have confirmed the effectiveness of MPH, at least in the short term in the treatment of adolescents with ADHD (Klassen et al., 1999; Schachar et al., 2002; Schachter et al., 2001). Another comprehensive review examined data from eight crossover trials with adolescents. Each study included in the review revealed significant improvements on symptoms associated with ADHD, as well as functional outcomes, including social behavior and academic performance as a result of MPH therapy (Smith et al., 2000). Finally, AACAP supports the use of MPH in the management of adolescents with ADHD in their treatment guidelines (Greenhill et al., 2002). In summary, data on adolescents diagnosed as ADHD parallel that obtained from their younger counterparts. There is compelling evidence that stimulants improve cognitive performance, impulse control, academic efficiency, and diminished aggression in adolescents diagnosed with ADHD. Areas needed to be investigated in the adolescent stimulant drug literature include optimal dosing, adverse side effects, and the long-term effects of stimulants in this population. Until such data are forthcoming, clinicians are advised to be judicious in the use stimulants as a treatment modality for adolescents. Also, given the increased risk of substance abuse among adolescents, and the fact that stimulants are a controlled substance, the practitioner should proceed with caution in prescribing these agents.

Adults

ADHD persists into adulthood and there has been considerable interest in executing controlled trials to further examine the effects of stimulants in treating this population. Although a discussion of the spectrum of stimulant effects in adults is not within the scope of this chapter, double-blind, placebo-controlled trials have generally indicated that adults with ADHD evidence response to stimulant medication (Weiss & Murray, 2003; Wender, 1995) similar to their younger counterparts.

Issues of Assessment

Physiological Correlates

There has been growing interest in the anatomical, biochemical, and physiological processes of the CNS, and more specifically the brain of children with ADHD. Although recent reviews of the neurobiology of ADHD have concluded that there is no single pathophysiological profile underlying this disorder (di Michele et al., 2005), the effects of stimulants on the central and autonomic nervous system remain a significant area of interest in the scientific and clinical literatures.

Central and autonomic nervous system variables. It has been suggested that the effectiveness of psychostimulants rests in their ability to enhance levels of arousal in the CNS and autonomic nervous system. Earlier clinical "folklore" suggested that children with ADHD are typically underaroused (see Satterfield & Cantwell, 1974; Sergeant et al., 1999). Essentially, the effects of stimulants had been associated with a normalizing of several CNS regulations (Brown & Borden, 1989), although this theoretical model has since been refined.

The best-researched CNS measure of brain function is the event-related potential (ERP), which measures changes in the electrical activity of the brain that occurs when specific tasks are undertaken. ERP testing is important because it provides objective evidence of the inefficiencies in the brain that may be associated with ADHD (Selikowitz, 2004). Abnormalities have been found in children with ADHD relative to their normally developing peers, especially during tasks requiring sustained attention (Brown et al., 1997). For example, studies that have examined tasks of sustained attention reveal a smaller amplitude of the N200 and P300 components, and a longer latency of the P300 component in unmedicated study participants with ADHD versus comparison controls without ADHD (Kilpelainen et al., 1999; Oades et al., 1996; Satterfield, 1990); Satterfield et al., 1994).

Moreover, some studies suggest that MPH therapy may improve or even normalize the P300 amplitude for children with ADHD (Seifert et al., 2003; Zillessen et al., 2001). Broyd et al. (2005) also examined the effect of MPH on response inhibition among children with ADHD. ERPs and skin conductance level (SCL) were recorded from 18 boys with ADHD and 18 comparison controls while they performed a cued "Go/NoGo" task with 70% "Go" probability. Findings revealed that although the children with ADHD showed lower SCLs than comparison controls prior to pharmacotherapy, this difference was not found following the administration of MPH. The children with ADHD evidenced a greater frequency of overall errors (omission and commission) prior to pharmacotherapy on a task of sustained attention and continued to make more omission errors than children in the comparison control group post-medication. However, it should be noted that the groups were soon indistinguishable on the number of commission errors. The data suggest that MPH results in a cessation of deficits associated with response inhibition. Finally, the N1 and P2 amplitudes were enhanced in children with ADHD, whereas the N2 amplitudes were reduced relative to comparison controls. The investigators conclude that the differences were not significant post-medication due in part to the action of MPH.

Unfortunately, there have been few studies investigating the effects of stimulants on autonomic nervous system measures of arousal in children with ADHD. One exception is an investigation conducted by Lawrence et al. (2005). In a naturalistic open-trial, Lawrence et al. examined the effects of MPH on central and autonomic nervous system measures in children with ADHD during a continuous performance task. Errors of omission and commission as well as reaction time were recorded as measures of cognitive performance, electrodermal activity as an autonomic nervous system measure, and finally, ERPs as an index of CNS activity. Findings indicated that although children with ADHD made more errors than comparison controls in the first session, no group differences were found after administration of MPH. Moreover, no significant differences were revealed in reaction time for children with ADHD and their typically developing peers. However, results did reveal that the SCL was lower in children with ADHD than for comparison controls. More

importantly, differences did emerge following administration of MPH. These findings are important because they indicate that MPH has the potential of ameliorating some of the dysfunctions in children with ADHD that are based on behavioral and ERP measures. The researchers conclude that their data, in combination with differences in electrodermal activity, support a hypo-arousal model of ADHD, which they have interpreted to support the actions of stimulant agents including MPH in these children.

Electroencephalograph (EEG) methods also have been employed to monitor neurological activity to learn more about the functional capacities of the brain. Several studies have provided important data to suggest various abnormalities in the EEGs of children with ADHD (Clarke et al., 2002; Clarke et al., 1998; Mann et al., 1992). Moreover, Chabot et al. (1999) employed behavioral and quantitative EEG techniques to evaluate treatment response to stimulant therapy in children with ADHD. Findings revealed significant quantitative EEG differences between children with ADHD and their typically developing peers. Specifically, quantitative EEG abnormalities involved increased theta or alpha power and were greatest in the frontal lobe regions of the brain. The findings underscore the importance of frontal lobe morphology in children. It is worth noting, however, that alterations in the theta and alpha waves of the EEG tended to dissipate commensurate with stimulant treatment in these children.

MEG and MRI. Neuroimaging studies conducted with children and adults with ADHD have reported anatomical and functional abnormalities, particularly in frontostriatal circuitry (Casey et al., 1997; Castellanos, 2002; Hesslinger et al., 2002; Kates et al., 2002; Mostofsky et al., 2002; Overmeyer et al., 2001; Sowell et al., 2003). Giedd et al. (2001) reported that anatomic MRI studies have revealed anomalies in total cerebral volume, corpus callosum, basal ganglia, and cerebellum in children with ADHD. In an investigation of possible frontal lobe dysfunction in children with ADHD, Mulas et al. (2006) employed magnetoencephalography to measure event-related brain activity during a simplified version of the Wisconsin Card Sorting Test (a frequently used measure in the studies of children with ADHD) of children with ADHD combined type or predominantly inattentive type and in age- and

intellectually matched comparison control children. Findings revealed that children with ADHD evidenced lower degrees of activation in the medial temporal lobe of the brain when compared to their typically developing peers. Moreover, children with ADHD showed early activity in the left inferior parietal lobe and posterior superior temporal gyrus regions of the brain, which were barely activated in comparison to control children without ADHD. The results were interpreted to support theories of frontal lobe dysfunction in children with ADHD. The data are important because they also suggest that deficits in higher level functions may be secondary to disruptions in earlier limbic processes.

In a review of the literature on MRI studies of the brain anatomy of children and adults with ADHD, Castellanos and Acosta (2004) conclude that most studies have focused on frontal striatal regions and have tended to find smaller volumes in children with ADHD relative to their normally developing peers. Additional studies have reported that ADHD is associated with a significant global reduction in brain volume (34%) for both males and females. Castellanos and Acosta point out that specific regional differences have been found in many studies of the basal ganglia, with the most prominent differences in the cerebellum. Moreover, Castellanos et al. (2003), employing MRI scans of monozygotic twins discordant for ADHD, found that affected twins had significantly smaller caudate volumes than their unaffected co-twins. The investigators concluded that their results provided further support for models of ADHD that implicate prefrontal-striatal circuitry. Castellanos et al. (2002) also employed MRI scans to investigate regional brain volumes in patients with ADHD and healthy controls for the purpose of determining the effect of prior stimulant drug exposure on anatomic abnormalities for participants with ADHD. MRI scans were conducted initially and their change over time was measured both for medicated and previously unmedicated participants with ADHD and healthy controls. The investigators reported that abnormal brain development in the participants with ADHD, which manifested in decreased brain volumes in both white and gray matter compartments, was not associated with stimulant drug therapy.

Positron emission tomography (PET) and functional magnetic resonance imaging procedure

(fMRI). Geidd et al. (2005) suggests that for children with ADHD, functional imaging studies, including those employing PET scans and functional MRI, implicate dysfunction in neural circuitry involving the frontal lobes, striatum, and cerebellum. Because some studies have implicated a primary role of the dopaminergic system in the neuropathophysiology of ADHD, PET scans have been employed for the purpose of examining the integrity of presynaptic dopaminergic function in children with ADHD (Ernst et al., 1999). Results from the PET scan showed that the accumulation of [18F]DOPA in the right midbrain was nearly 50% higher in children with ADHD than for their normally developing peers. Conclusions from this investigation are that dopaminergic dysfunction occurs at the level of the dopaminergic nuclei for children with ADHD. Moreover, Volkow et al. (2005) reported that PET scans revealing dopaminergic effects of MPH in the human brain indicate that MPH blocks the dopamine transporters. The investigators suggest that the therapeutic effects of MPH are due in part to the ability of this agent to enhance the magnitude of dopamine increases.

Teicher et al. (2000) assessed the basal ganglia of six boys with ADHD employing a functional magnetic resonance imaging procedure (fMRI). The daily use of MPH enhanced blood flow significantly in the putamen. Conversely, for boys with ADHD that were not "objectively hyperactive," MPH decreased greater blood flow in the putamen. The investigators believe this indicates that children who are objectively hyperactive may receive the greatest benefit from treatment with MPH. Additional studies that have employed fMRIs to investigate the effects of MPH in children have concluded that MPH affects striatal activation differentially in children with ADHD than for their healthy counterparts (Shafritz et al., 2004; Vaidya, Austin, & Kirkorian, 1998).

Recent advances in technology present opportunities to study the electrophysiological and radiographic correlates of the clinical effectiveness of stimulants on attention and impulsivity in children with ADHD (Seifert et al., 2003). This research has allowed us to study brain–behavior relationships as well as changes in the CNS (i.e., the brain) as a function of pharmacotherapy. Although event-related potentials primarily have been used in these investigations,

other biochemical and physiological processes show the potential to be good barometric indicators of CNS response to stimulants (see Brown et al., 1997).

Learning

Although stimulants improve academic efficiency and productivity (Bennett et al., 1999; Carlson et al., 1992), no studies have provided data to support the long-term benefits of this pharmacotherapy on learning and academic achievement for children and adolescents with ADHD (Swanson et al., 1991). Previous research failed to support the effect of stimulants on state-dependent learning (see Brown & Borden, 1989). Nonetheless, it is incumbent upon practitioners to closely monitor their patient's academic performance following initiation, continuation, and cessation of stimulant therapy.

Behavioral Correlates

Because children with ADHD typically exhibit inattention, impulsivity, and/or hyperactivity, behavioral assessment represents the primary means by which children are evaluated for stimulants and by which they are monitored as to efficacy and adverse side effects (see Brown et al., 1997). The techniques that have been used to assess behaviors include the use of direct observations of behavior, rating scales of behavior that may be completed by caregivers and teachers, and sociometric ratings completed by peers. It has been suggested that direct observations and rating scales are the best methods to evaluate the effects of stimulant drug trials particularly on children's behavior (DuPaul, Barkley & McMurray, 1991). Direct observations typically entail observations of children's behavior in a laboratory setting, playroom, or classroom setting. Direct observations have proven especially valuable when documenting stimulant effects and distinguishing active medication effects from placebo (Gadow, Nolan, Sprafkin, & Sverd, 1995). In addition, the empirical evidence indicates that direct observations of specific target behaviors are especially sensitive to the effects of stimulants (Kollins, 2004).

Behavior rating scales are widely used in clinical diagnosis of children with various types of psychopathology including ADHD and are of established value for the purpose of monitoring

the efficacy of stimulant treatment effects. Standardized rating scales are typically administered to teachers, parents, and, in the case of adolescents, the patient himself/herself. The primary advantages in using rating scales include simplicity in administration and scoring, cost-effectiveness, and reduced subjectivity (see Brown et al., 1997). Moreover, rating scale factor scores have shown sensitivity to medication effects across various psychotropic agents, raters, and doses of medication (Kollins, 2004). Parent and teacher rating scales are particularly valuable for assessing behaviors of children with ADHD and also for monitoring the effectiveness of treatment. This is due, in part, to the fact that rating scales provide avenues for assessing similar symptoms across several settings (i.e., school and home) and at different times of the day. Results from the Multimodal Treatment of Attention-Deficit Hyperactivity Disorder (MTA) study (MTA Cooperative Group, 1999a) provide evidence for the successful use of standardized rating scales when evaluating children's response to stimulants compared to a standard community care condition. Overall, behavioral assessment of stimulant effects is most complete when the evaluation involves repeated assessments of children's behaviors across doses, including placebo, for the purpose of having a basis of comparison (or, more specifically, a baseline evaluation). The most commonly used rating scales for stimulant evaluation are the Conners Parent and Teacher Rating Scales (Conners, 1997), the IOWA Conners Rating Scale (Loney & Milich, 1982), and the Swanson Nolan Abikoff and Pelham Rating Scale [SNAP] (Swanson, 1992). While many other rating scales are available (see DuPaul & Stoner, 1999), these aforementioned rating scales have been employed most frequently in the contemporary empirical literature.

Finally, it has been recommended that the use of a multivariate approach including both direct observations of behavior and rating scales, each of which are gathered in multiple settings, is a best-practice approach to assessing drug response in children with ADHD (Atkins & Pelham, 1991; Kollins, 2004). These ratings should come from multiple sources, including teachers, parents, peers, and the children themselves across a variety of settings and situations, because each of these informants provides a unique perspective and hence important

information about response to medication (Brown et al., 1997).

Psychological Testing

Psychological tests include written, visual, or verbal evaluations administered to assess primarily the cognitive and emotional functioning of children. Psychological tests also may prove useful in screening deficits associated with attention and concentration for the purpose of identifying specific target behaviors that may be responsive to stimulants. Given that children and adolescents who suffer from attention and concentration difficulties are often evaluated for a trial of stimulants, instruments that assess these indices are valuable when attempting to differentiate stimulant drug response from placebo. Although a discussion of the instruments available for assessing attention and concentration is not possible within the space constraints of this chapter, the most commonly utilized measures to evaluate drug response include computerized performance tests that assess a child's ability to maintain vigilance, refrain from responding impulsively, and sustain focused attention. Typically, the computer-based serial performance tasks involve the repetitious presentation of specific target stimuli over time. The instruments assess stimuli missed (omission), false positives (commissions), and the amount of time to respond (impulsivity). Results from studies employing these computer tasks have shown that such tasks are sensitive to placebo and active doses of stimulants (see Brown et al., 1997).

Neuropsychological evaluation. Neuropsychological instruments designed to identify children with impairments in attention and concentration are increasingly employed to monitor response to placebo and stimulants. Hood et al. (2005) employed a neuropsychological battery (Test of Everyday Attention for Children) designed to tap different aspects of cognitive attention for the purpose of evaluating the immediate effects of MPH on cognitive attentional processes in children with ADHD. Findings have revealed that following administration of MPH, the children with ADHD showed significant improvements on their performance of measures of attention compared to their typically developing peers. Another examination also investigated the effects of MPH on

various attentional functions in children with ADHD (Konrad et al., 2004). Results indicate that various components of attention are influenced differentially by MPH. Specifically, the investigators report that the intensity dimensions of attention are best influenced by higher doses of MPH, executive functions by moderate doses, and selectivity dimensions of attention by variable doses. Konrad et al. suggest that a more comprehensive assessment of attention may help to identify optimal doses of stimulant drug therapy for the treatment of attentional dysfunctions for children with ADHD. Hanisch et al. (2004) investigated the effect of MPH in preschool and grade-school children diagnosed with ADHD. Children in the two age groups were compared on tasks of attention. Participants were administered both active MPH and placebo and dependent measures included tasks of alertness, sustained attention, focused attention, divided attention, and a cognitive conflict task. For both age groups, findings revealed positive effects of MPH relative to placebo for tasks of sustained attention. Thus, performance on computerized tasks of attention was especially improved by MPH therapy for children who showed objective attentional deficits. Findings are interpreted to suggest that specific neuropsychological testing may prove useful for the purpose of optimizing treatment outcome.

Previous studies also have shown that MPH improves maintenance of attention (Van der Meere et al., 1999), accuracy (Jonkman et al., 1999), working memory (Tannock et al. 1995a), visual-spatial memory (Bedard et al., 2004), and inhibition (Scheres et al., 2003; Tannock et al., 1995b) in children diagnosed with ADHD. In contrast, other studies that have examined the effects of stimulants (MPH) on cognitive and behavior functions for children with ADHD have found no MPH effects on the Stroop interference task (Jonkman et al., 1999), Go/NoGo-tasks (Van der Meere et al., 1999), or a divided attention task (De Sonneville et al., 1994).

One study of stimulant drug effects that examined the impact of pharmacotherapy on intellectual functioning (as measured by the Wechsler Intelligence Scale for Children-III [WISC-III], a standardized intelligence test) for children with ADHD provided findings to indicate that children receiving medication had evidenced significant increases on scores of intellectual functioning; no changes were revealed for

children not receiving stimulants (Gimpel et al., 2005). Thus, recent evidence has emerged to suggest that neuropsychological instruments provide value when examining for cognitive effects following treatment with stimulants.

Clinical evaluation. Despite the recent proliferation in diagnostic instruments for children and adolescents, clinical evaluation remains the hallmark for the diagnosis of attentional problems and prediction of stimulant response. The clinician should gather information including historical data and behavioral observations from multiple sources (teachers, caregivers, peers) and direct observations of the child in the classroom setting. Data should be collected across settings (classroom, home environment, peer interaction, clinical setting) (see Brown et al., 1997). After a comprehensive assessment, if a trial of stimulants is indeed warranted, collaboration with parents, the child, and school personnel is particularly valuable in assessing response to pharmacotherapy. It is recommended that clinicians adhere to consistent data-based procedures that evaluate the impact of stimulate therapy for designated target outcomes.

Predicting response. The consensus in the literature is that specific tasks of attention or neurocognitive functioning do not predict response to stimulants. However, the most exciting line of research for predicting stimulant drug response comes from the area of psychopharmacogenetics, which involves the study of how individual genetic information may aid in understanding and predicting the effects of psychopharmacologic medications. In a recent study, Stein et al. (2005) tested 47 children with ADHD, aged 5–16 years, in a 4-week, double-blinded, crossover trial with forced weekly dosage changes. The investigators sought to determine which variant of the dopamine transporter gene the participants carried, focusing on two specific variants—9R and 10R—of the transporter gene. The investigators evaluated how varying doses of MPH would affect ADHD symptoms, impairment, and adverse side effects of stimulants. Findings indicated that the majority of the patients had one or two copies of the 10R variant. Of the children, nearly 60% had an excellent response to the highest dose of stimulant (54 mg). In contrast, of the patients with two copies of the 9R variant, none of the patients displayed such dramatic improvement.

Two studies were conducted that examined the dopamine transporter gene and response to MPH: in African-American boys with ADHD (Winsberg & Comings, 1999) and Brazilian boys with ADHD (Roman et al., 2002). Results from each investigation support an association between homozygosity for the 10-repeat allele at dopamine transporter gene locus and poor response to MPH. Finally, Hamarman et al. (2004) investigated whether the 48 base pair VNTR polymorphism (7- repeat allele) of dopamine receptor gene DRD4 predicts MPH responsiveness in children with ADHD. Findings indicate children with ADHD possessing the DRD4 7R allele required higher doses of MPH for symptom improvement and normalization. The data are important because they demonstrate that the 7-repeat allele of the DRD4 gene VNTR polymorphism is associated with stimulant treatment outcomes for children with ADHD. Although the field of psychopharmacogenetics still is in its infancy, results from recent investigations are promising for predicting stimulant drug response in children with ADHD particularly for specific subtypes of the disorder.

Limitations of Stimulants

Iatrogenic and Emanative Effects

Physical. The most frequently reported adverse effects of stimulant drug therapy are decreased appetite, headaches, abdominal discomfort, problems falling asleep, irritability, motor tics, nausea, fatigue, and social withdrawal (McMaster University Evidence-Based Practice Center, 1999; Pliszka, 2000). It has been suggested that many of the adverse side effects associated with stimulants in the school-age population appear to be relatively mild, short lived, and responsive to dosing or timing adjustments (McMaster University Evidence-Based Practice Center, 1999). Severe adverse side effects occur in 4–10% of children treated with stimulants, with the most common manifestations being delayed sleep onset, reduced appetite, stomachache, and headache (Santosh & Taylor, 2000).

The development of longer-acting stimulants has led to studies that compare the safety profiles of these new agents versus traditional stimulants. Fitzpatrick et al. (1992) evaluated 19 children with ADHD in a double-blind

clinical trial consisting of four 2-week phases: sustained-release MPH; standard MPH; a combination of standard and sustained-release MPH; and placebo. Disturbances in sleep and appetite were similar between sustained-release and standard MPH therapy. In another comparison trial, no significant differences in adverse effects were found between sustained-release MPH and immediate-release MPH administered three times daily (Swanson et al., 2003). In contrast, results from another clinical trial comparing the various MPH formulations revealed that sleep and appetite problems were more pronounced with the longer-acting stimulants (Pelham et al., 1990).

A 24-month study evaluating the tolerability of extended-release mixed amphetamine salts (MAS XR; Adderall XR) in children with ADHD reported that stimulant treatment was well tolerated, with most adverse effects being mild (McGough, 2005). The most frequently reported stimulant related adverse effects were anorexia, insomnia, and headache. Moreover, the incidence of drug-related adverse effects increased proportionally to increasing extended-release mixed amphetamine doses, leading the investigators to conclude that there is a dose–;response curve with a greater frequency of adverse effects being linearly related to increasing dose. Another 24-month long-term study evaluated the safety of sustained-release MPH in children with ADHD (Wilens et al., 2003). Results indicated minimal effects of sustained-release MPH on growth, tics, vital signs, or laboratory test values. In an investigation for children with ADHD that evaluated the adverse effects of stimulant treatment over 5 years, Charach et al. (2004) found that stimulants resulted in adverse effects for up to 5 years, but they were generally mild and of little health concern. The investigators indicated that many of the physiological adverse effects seemed to be tolerated over time, as many children who experienced such effects continued to take medication regardless of the effects.

There has been concern, particularly among the media and lay public, that stimulant treatment retards children's natural growth. Hechtman and Greenfield (2003) reported that long-term adverse effects from stimulant treatment in childhood—specifically adult height or future substance abuse—have not been substantiated by extant studies. Moreover, Poulton (2005) completed a meta-analysis of 29 studies that examined the issue of height attenuation among children with ADHD treated with stimulants. Findings revealed that the height deficit amounted to approximately 1 cm/year during the first 1–3 years of stimulant treatment. Therefore, although ongoing use of MPH does decrease growth, the long-term effects on weight and height are not considered to be significant, thereby leading some experts to suggest that there is a rebound effect of height and weight, particularly when there is a medication holiday (e.g., during the summer).

One adverse effect, particularly noted with shorter-acting stimulants, has been the behavioral rebound phenomenon, typically described as "behavioral deterioration" (e.g., increased hyperactivity and bad moods), which may occur when the beneficial effects of stimulants begin to dissipate. Carlson and Kelley (2003) examined the rates and implications of stimulant-induced rebound in 149 psychiatrically hospitalized children treated with short-acting stimulants. Behavioral deterioration was observed in nearly one-third of children on at least one dose of stimulants but was serious enough to discontinue treatment in 8.7% of treated children. The investigators concluded that although rebound does exist, it occurs in less than 10% of psychiatrically hospitalized children with ADHD and does not appear to have specific diagnostic significance. Similarly, Johnston et al. (1988) found limited evidence for behavioral rebound effects for nonpsychiatrically hospitalized children with ADHD receiving MPH during the day. Furthermore, no consistent reports of behavioral rebound have been found in controlled trials (Spencer et al., 1996). One suggested strategy to avoid rebound effect is to add a third dose of a short-acting stimulant in the late afternoon (Greenhill et al., 1996).

Finally, although rare, there have been chart reviews and clinical reports that document the serious side effects of psychosis following stimulant treatment. Cherland and Fitzpatrick (1999) conducted a chart review of children receiving stimulant treatment for ADHD and found that 6% of 98 children treated with MPH developed psychotic symptoms during treatment. A recent case report also documented acute psychosis associated with the therapeutic use of dextroamphetamine in a 7-year-old boy diagnosed with ADHD (Calello & Osterhoudt, 2004).

Overall, adverse effects are similar for all stimulants, and are transient and linearly related to dose, with higher doses associated with a greater frequency of adverse effects (Santosh & Taylor, 2000). It is likely that decreasing the dose will reduce or possibly eliminate common side effects associated with stimulant treatment (Santosh & Taylor, 2000). Although stimulants are safe and effective in the majority of treated children, it is important for the practitioner to monitor patients receiving these medications as well as evaluate the associated benefits with potential adverse effects.

Psychosocial Attitudes and Beliefs About Medication

Stimulants have been the most meticulously studied psychotropic medication in the field of child psychiatry. Nonetheless, there continues to be controversy in the lay press about their use. Moreover, there are differences in attitudes and beliefs regarding treatment acceptability and satisfaction with all psychotropic medication. We review this literature briefly, particularly as it pertains to children, families, and other professional groups (teachers, physicians, and peers).

Child and peer attitudes. Doherty, Frankenberger, Fuhrer, and Snider (2000) examined children's and peers' attitude about the effects of stimulants. They investigated the self-reported positive and negative physical, academic, and social effects of stimulants on middle/junior high school and high school students diagnosed with ADHD. Other students' attitudes toward those diagnosed with ADHD and receiving stimulants also were examined. Students with ADHD reported that stimulants helped them perform well in school, stay more organized at school, sustain attention during the day, and reduce impulsivity and overactivity. Moreover, students not receiving medication reported that teachers did not treat students receiving stimulants any differently from those receiving medication. Finally, students not receiving stimulants did not endorse being different from other students. Despite these positive findings, nearly one-half of the students reported that they wanted to cease taking the medication immediately. The data from this investigation are in contrast to the results from a similar study with children in which only 11% of children wished to discontinue the use of MPH (Bowen et al., 1991). Moreover, Efron, Jarman, and Barker (1998) found that most children viewed medication effects favorably, although children reported feeling worse than usual when treated with MPH (12.7%) and dextroamphetamine (18.8%). Although developmental issues (e.g., needs for autonomy at adolescence) partly account for children and adolescents wishing to discontinue medication, further investigation is needed to examine why some children and adolescents wish to discontinue use of stimulants prematurely.

Finally, in a survey of 50 middle and high school students treated with stimulants for the management of ADHD, adolescents endorsed the medication as somewhat helpful for their behavior and socialization with friends. They also reported that the medication was helpful in concentrating, but not very useful with academic achievement (Moline & Frankenberger, 2001).

Parental attitudes. To address parent perceptions and satisfaction about the use of stimulants for the treatment of ADHD in their children, Dos Reis et al. (2003) asked parents to complete a survey of their knowledge, attitudes, and satisfaction with the medication their children were receiving for ADHD. Few parents believed that stimulants could lead to drug abuse. However, over one-half of the parents were initially hesitant to use medication based on information they learned from the lay press. Moreover, nearly 40% of the parents believed that too many children receive medication for ADHD. Parents were more satisfied with behavioral and academic improvement as a function of the medication relative to improvement in their child's self-esteem. Parental attitudes toward stimulants were positively associated with satisfaction of stimulants as a treatment modality. Parents who were Caucasian endorsed more positive findings with stimulants than those of color. Two-thirds of the parents believed that sugar and diet affected hyperactivity. These results are corroborated further by Johnston et al. (2005) who found that although parents reported using primarily behavior management and stimulants in the treatment of ADHD, approximately one-half of the families also used diet and vitamin therapies, therapies that have not been empirically supported as a viable treatment modality for ADHD. Additional findings from this investigation also indicated that parents perceived

ADHD symptoms to be predominantly internal to the child and relatively enduring and pervasive.

Arcia, Fernandez, and Jaquez (2004) examined mothers' cognitions and attitudes toward the use of medication (primarily stimulants) for treatment of their young children's behavior problems. Mothers of Latina descent were compared to those mothers from nonethnic groups. Findings revealed that mothers from Latina descent overwhelmingly preferred treatment options other than medication primarily because they understood medication to be addictive, dulling of cognitive processes, and inappropriate for behavior problems relative to non-Latina mothers. These findings are important as they underscore the role of ethnicity in attitudes associated with medication administration.

One investigation examined the perceptions of mothers and children with ADHD regarding stimulants for the treatment of ADHD. Data revealed that mothers tended to view the use of stimulants as more beneficial than their children (McNeal, Roberts, & Barone, 2000). It is worth noting, however, that more than one-half of the children in the study reported that they did not view their disorder as an illness, which may have influenced the children's view of the effectiveness of stimulant treatment.

Teacher attitudes. Snider, Busch, and Arrowood (2003) surveyed regular and special education student teachers to assess their knowledge, opinions, and experiences related to the diagnosis of ADHD and its treatment with stimulants. Results revealed that teachers endorsed limited knowledge about ADHD and the use of stimulants. Teachers' opinions about the effect of stimulants on school-related behaviors were positive, although special education teachers were more positive than educators. Teachers were the school personnel who most frequently recommended an assessment for ADHD. These data were consistent with findings from previous investigations addressing the same issues (Frankenberger et al., 1990; Runnheim, Frankenberger, & Hazelkorn, 1996; Weber et al., 1992). The investigators concluded that teachers have a positive opinion about the effects of stimulants on school-related behavior; however, they endorsed limited knowledge about ADHD and its treatment with stimulants.

Finally, Frankenberger et al. (2001) examined school psychologists' knowledge, attitudes, and opinions regarding ADHD and treatment with stimulants. The majority of the school psychologists believed that stimulants could produce improvement in academic-related functioning but also reported that ADHD is overdiagnosed in schools.

Societal attitudes. The increasing use of stimulants to treat ADHD in both preschool and school-age children has raised concerns that our society may be choosing "quick-fix" remedies to treat ADHD. Some of these concerns originate from erroneous media reports that, in some cases, misrepresented the scientific literature (Kaminester, 1997). Therefore, it is important that health-care providers have informed conversations with children, parents, and teachers about the safety, efficacy, and limitations regarding treatment with stimulants. Moreover, these conversations should address realistic expectations regarding medication effects for children, parents, and teachers, as well as considering the attitudes of peers and significant others in the child's life.

Long-Term Outcome of Children Treated with Stimulants

As noted previously, the short-term safety and efficacy of stimulant treatment in school-age children treated for ADHD have been the most thoroughly documented therapy in all of child psychiatry (Wilens & Biederman, 1992). The studies have involved several thousand participants, and no studies have refuted the efficacy and safety of stimulants when used appropriately with school-age children. Unfortunately, there are few studies that have examined the long-term effects of stimulants. This has been primarily related to the ethical difficulties of conducting placebo-controlled trials in which children are assigned to placebo-control groups for extensive periods of time when therapies of demonstrated efficacy are available (Santosh & Taylor, 2000). In short, it is not reasonable to conduct studies where effective therapies are withheld for several weeks or months. One exception was the Multimodal Treatment Study of ADHD that was sponsored by the National Institute of Health (MTA Cooperative Group, 1999a). The MTA study indicated a persistence of medication effects over time as long as pharmacotherapy is continued (Brown et al., 2005).

Hechtman and Greenfield (2003) conducted a review of controlled studies of children with ADHD treated with stimulants relative to those who were not treated with stimulants, as well as long-term prospective follow-up studies of children with ADHD. The authors concluded that children with ADHD treated with stimulants for as long as 2 years continue to benefit from the treatment, with diminished symptoms, enhanced academic and social functioning, as well as reductions in symptoms associated with oppositional defiant disorder. No significant problems of tolerance or adverse effects were reported in any of the studies. Results from long-term, prospective follow-up studies into adulthood have shown that stimulant treatment in childhood has slight benefits regarding social skills and self-esteem. Follow-up studies that have examined the long-term effects of stimulants on deleterious physiological side effects have yielded valuable information, particularly as they pertain to growth suppression, cardiac effects, and potential for addiction.

Growth Suppression

Growth suppression and weight loss after long-term treatment with stimulant medication was a major concern and recurrent theme in earlier literature (see Brown et al., 1997). However, recent studies have demonstrated that height and weight suppression in children with ADHD treated with stimulants is not clinically significant. In fact, some experts have suggested that height and weight suppression is actually transitory and that there is actually a rebound phenomenon following cessation of stimulant drug therapy (see Bennett et al., 1999). Zachor and colleagues (2006) assessed the effects of long-term stimulant therapy on growth parameters in 89 children with ADHD. Data revealed that although significant weight loss occurred during the first few months of stimulant treatment, changes in weight over the course of 2 years of treatment did not reach clinical significance. Notably, no long-term impact of stimulant medication on height was observed. Various stimulant agents did not yield differences with regard to their effects on growth. In a similar investigation, Faraone et al. (2005) examined the long-term effects of extended-release mixed amphetamine salts ranging from 10 to 30 mg on the growth of children being treated for ADHD. Faraone et al. conclude that problems with growth are not likely to be a clinical concern for most children treated with extended-release amphetamine salts (e.g., Adderall). Thus, Hechtman and Greenfield (2003) conclude that the long-term impact of stimulant treatment during childhood is minimal including adult height and weight. Finally, another recent review of the literature of stimulant treatment and growth suppression concludes that the height suppression for children with ADHD managed with stimulant medication amounts to approximately 1 cm/year during the first 1–3 years of treatment (Poulton, 2005).

Cardiac System

Stimulants are sympthomimetic agents that result in increased heart rate. As a result, there has been concern about the potential effects of stimulants on the cardiac system. Studies that have examined the cardiac system following treatment with MPH in pediatric populations have found significant dose response elevations in some combination of systolic, diastolic, and mean blood pressure (Joyce et al., 1986; Volkow et al., 1996; Klein-Schwartz, 2002). In a recent double-blind, randomized, crossover trial, Samuels et al. (2005) studied the effects of stimulants on 24-h ambulatory blood pressure in children with ADHD. Results revealed that total diastolic blood pressure, waking diastolic blood pressure, and total heart rate were significantly higher during active medication. This might suggest a possible negative cardiovascular effect of stimulants in children with ADHD. Thus, potential cardiovascular risk should be balanced against the beneficial behavioral effects of stimulants. In a similar study, boys with ADHD receiving either long-term MPH or dextroamphetamine therapy were evaluated to determine the effect of these medications on blood pressure as measured by 24-h ambulatory blood pressure monitoring (Stowe et al., 2002). Findings indicated that blood pressure and heart rate were altered to some extent by receiving stimulant therapy. Unfortunately, there are few data to suggest the effects of long-term stimulant treatment on the cardiac system for pediatric populations.

Addiction

Parents, in particular, are frequently concerned that prolonged stimulant use in childhood may lead to substance abuse as teenagers or adults. Data from recent controlled studies provide evidence that contradicts this notion. Mannuzza, Klein, and Moulton (2003) conducted a randomized controlled clinical trial with ADHD treated children that examined whether stimulant treatment in childhood confers increased risk for substance use and abuse in later life. Findings from this randomized trial indicate that stimulant treatment in childhood does not lead to substance use or abuse in later life. Furthermore, available data suggest that children with ADHD who are treated with methylphenidate are actually at lower risk for a substance use disorder later in life (Huss & Lehmkuhl, 2002; Wilens, Faraone, Biederman, & Gunawardene, 2003). Finally, a meta-analysis that investigated whether stimulants were in fact addictive for pediatric populations provides data to suggest that there is insufficient evidence available to assess the addictive potential of stimulants (Shaw, Mitchell, & Hilton, 2000). Nonetheless, the practitioner who prescribes stimulants to children and adolescents must carefully monitor their patients for potential addiction that may include a history of addiction or substance abuse in the family. The astute practitioner should always be judicious in prescribing stimulant medication, particularly among adolescents or those youngsters who are especially impulsive.

Multimodal Therapies

The National Institute of Mental Health Collaborative Multisite Multimodal Treatment Study (MTA) of Children with Attention-Deficit/Hyperactivity Disorder (MTA Cooperative Group, 1999a) initiated a 14-month randomized clinical trial of ADHD treatment strategies. The multisite clinical trial was one of the largest studies conducted by the National Institute of Health. The investigation was conducted at six different sites and represented the first major NIMH collaborative clinical trial to focus on a childhood mental disorder. The trial included 579 participants who were children between the ages of 7 and 10 years and diagnosed with ADHD combined type. The participants were assigned randomly to one of four treatment groups: state-of-the-art medication management only, intensive behavioral intervention only, a combination of medical management and behavioral treatment, and routine community care (the control group) that most commonly received medication. Multiple outcome domains were assessed and included measures of ADHD symptoms, oppositional/aggressive symptoms, social skills, anxiety/depression, parent–child relationships, and academic performance (MTA Cooperative Group, 1999a,b). At the time of this writing, the children were followed longitudinally for approximately 2 years.

Statistical follow-up findings revealed that all four treatment groups showed sizable improvement over time in most areas that were assessed, although some treatments were superior to others in specific domains. Specifically, medication management produced superior results to behavioral treatment for the reduction of symptoms of inattention and hyperactivity as rated by parents and teachers. However, on all other outcome measures (oppositional behavior, peer relations, and academic achievement), medication management and behavioral treatment did not differ significantly. Medication management and combined treatment were superior to community care for reducing the core symptoms of ADHD. Combined treatment was superior to behavior modification and community care for reductions in oppositional/aggressive behaviors as rated by parents, improvement in social skills as rated by teachers, internalizing symptoms (anxiety/depression), parent–child relations, and reading achievement. Finally, there was no significant difference between the medication management and combined treatment groups for the core symptoms of ADHD, although the children in the combined treatment group were maintained on lower doses of medication than were the other treatment groups that received pharmacotherapy (MTA Cooperative Group, 1999a,b). Based on data from this large-scale clinical trial, the investigators concluded that for ADHD symptoms, crafted medication management (maintained through 14 months) was superior to behavior modification alone (faded by 14 months) and to routine community care including primarily medication.

Children in the combined treatment group showed significant advantages over those in the

community care group in every domain, whereas medication management proved superior to community care in the reduction of the core symptoms of ADHD. Nonetheless, combined treatment did not prove significantly superior to medication management for individual, specific outcome measures. However, combined treatment did result in modest significant advantages over medication management on global or composite outcome indices (Conners et al., 2001; Swanson et al., 2001). Of particular interest in the MTA study is that treatment outcome also was examined in the context of comorbidities with ADHD (Jensen et al., 2001b; March et al., 2000; Newcorn et al., 2001). Children with ADHD and a diagnosis of oppositional defiant disorder (ODD)/conduct disorder (CD) responded best to MTA medication treatments (with or without behavioral treatments), whereas children with multiple comorbid disorders (anxiety and ODD/CD) responded best to combined (medication and behavioral) treatments. Findings also revealed that for children with ADHD with coexisting anxiety disorders, behavioral intervention alone was as effective as both medication management alone and the combined treatment. It is worth noting that children with anxiety disorders who received medication management only did not have a poorer response to medication than did the other children without comorbidity of anxiety disorders.

In a subsequent analysis of the MTA study, Wells et al. (2000) examined the effects of the treatment on parent and family stress measures. Results revealed no differences among the four treatment groups on positive parenting or on family stress variables. However, parents in the behavior modification alone, medication management alone, and combined treatment groups reported significantly greater decreases in their use of negative or ineffective discipline when compared to the standard community care control group. It is worth noting that no significant differences between the three MTA treatment groups were observed on discipline practices. Teachers also were asked to rate the children's disruptive behavior at the end of treatment (Hinshaw et al., 2000). Findings revealed that for families that participated in the combined treatment group, children's disruptive behavior fell well within the normal range, and parents from this group reported the greatest reductions in negative and ineffective discipline practice. In

contrast, this effect was not observed for families who participated in the behavioral treatment group alone. Outcomes examined at the end of treatment as reported by peers indicated no evidence of superiority of any of the treatments, although there was limited evidence that favored treatments involving medication management (Hoza et al., 2005). It is worth noting that further analysis of the data indicated that children in each of the treatment groups remained significantly impaired in their peer relationships.

In a subsequent evaluation of the follow-up of these children, findings indicated that intensive medication treatment, either alone or in combination with behavior therapy, was significantly superior to behavior therapy alone and community care for core symptoms of ADHD and symptoms associated with oppositional defiant disorder at 24 months, although the magnitude of findings was not as great as at the initial 14-month follow-up assessment (MTA Cooperative Group, 2004a). Significant benefits of combined treatment over medication management alone and of behavior treatment alone over community care were not demonstrated. The groups did differ significantly in mean dose of stimulants (MPH equivalents 30.4, 37.5, 25.7, and 24.0 mg/day, respectively). Moreover, continuing medication use partly mediated the persisting superiority of combined treatment and medication management. Based on these data, the investigators concluded that the benefits of intensive medication management for ADHD extend 10 months beyond the intensive treatment phase only in specific symptom domains and also diminish over time. However, further exploratory analyses provide compelling data that suggest that changes in medication use mediated the 14- to 24-month change in ADHD symptom ratings (MTA Cooperative Group, 2004b). Specifically, consistent use of stimulants was associated with maintenance of effectiveness, whereas the subgroup of children where medication was discontinued showed the largest deterioration.

Finally, in a comprehensive review of the literature on the effectiveness of behavioral treatment in combination with stimulants, Brown et al. (2005) reviewed studies of behavior management alone, stimulant drug therapy, and psychotherapy, and concluded that stimulant treatment alone has shown a consistent pattern in improving the core symptoms of ADHD,

whereas behavioral interventions alone did not yield as large effect sizes as stimulants used alone. Moreover, the combination of stimulant treatment with behavioral intervention proved to be as beneficial as stimulant treatment alone.

Training Issues

Clinical neuropsychologists are well suited to participate in the assessment of children receiving stimulants given their extensive training in brain–behavior relationships. Specifically, their expertise in evaluation and diagnostic assessment procedures, particularly techniques that employ behavioral rating scales, observational techniques, and psychometric testing, proves valuable for assessing and monitoring stimulant drug response. Moreover, clinical, school, and neuropsychologists complete significant coursework and training in research methodology, enabling them to evaluate systematically the effects of stimulants on children's cognitive and behavioral functioning. Most important, the assessment procedure and standards that most psychologists adhere to may withstand the rigors of empirically validated assessment. Moreover, many neuropsychologists possess the specialized training in evaluating the link between neurobiologic data (fMRI, PET, EEG) and functional data (achievement tests), both of which are useful for examining the action mechanisms of stimulants.

Given that clinical psychologists often are intimately involved in the clinical evaluation, psychometric assessment, and treatment of children receiving stimulants, it is important to delineate the specific training needs—pharmacotherapy, psychoeducational services, or operant techniques in therapeutic intervention with children—that will lend specificity to the management of children. It is imperative that clinical neuropsychologists receive course work in neuroanatomy, neuropathology, pathophysiology, and the principles of basic psychopharmacology. Because the most significant experiential training occurs during internship and postdoctoral training, it is recommended that training programs provide seminars that address issues associated with pediatric psychopharmacology. Moreover, supervised experiences in working with children receiving stimulants, monitoring response to medication, and exposing trainees

to collaborative working relationships with other health-care providers will be essential.

Finally, because the stimulants represent the class of psychotropic agents most commonly prescribed for school-age children and adolescents (Jensen et al., 1999; Teitelbaum et al., 2001; Zito et al., 2003), coupled with the recent evidence to suggest a marked increase in the use of stimulants over the past two decades (Safer & Krager, 1988), psychologists employed in educational and school settings are likely to be working with more children on medication than in previous years. Therefore, it is also recommended that school psychologists receive specialized coursework and supervised experiences in assessing children for a trial of stimulants. School psychologists should also receive training in the monitoring of both behavioral and learning outcomes associated with stimulants as well as the potential toxicities of stimulants on learning and behavior (Brown, Dingle, & Landau, 1994). Thus, given the impact that stimulants have on children's school performance, it is critical that psychologists who are employed in school settings have thorough training in numerous areas associated with stimulants. These types of training and experiences are important considering the findings of a recent survey of school psychologists, which revealed that over one-half of the respondents were involved in monitoring the effects of stimulants on learning and classroom behavior for students with ADHD, and an even higher percentage of school psychologists reported that medication monitoring is an important role for school psychologists (Gureasko-Moore, DuPaul, & Power, 2005).

Concluding Comments

The child psychopathology literature offers considerable evidence to support the efficacy and safety of this class of psychotropics. The available evidence supports the use of stimulants for the management of the core symptoms of ADHD. Moreover, recent literature suggests that stimulants may be efficacious for symptoms associated with other psychiatric disorders of childhood (e.g., autism, conduct disorder, MR, oppositional defiant disorder), as well as symptoms and toxicities associated with other chronic diseases or their treatments (e.g., late effects of cancer, neurological disorders).

The advent of long-acting stimulant formulations has brought about improved adherence with stimulants, reductions in rebound effects that may occur more frequently with shorter-acting stimulants, and the additional advantage of single daily dosing that diminishes the stigma of many children and adolescents of needing to take a pill at school.

The beneficial effects of stimulants have been shown to persist over time as long as pharmacotherapy is continued. Comparisons of the safety and efficacy of stimulants such as MPH, amphetamines, and dextroamphetamine have not indicated that one agent is necessarily superior to the other. Moreover, short- and long-acting medications have also shown comparable safety and efficacy. Thus, if one stimulant does not prove effective, another stimulant may be beneficial. Approximately, 90% of children diagnosed with ADHD respond to one of the many available stimulants preparations.

It is worth noting that combining behavioral interventions with medication management offers additional benefits: enhanced teacher and parent acceptance, and lower stimulant doses needed to achieve the same therapeutic benefits as with stimulant drug treatment alone. Moreover, clinical experience provides support for the use of behavioral management as an adjunct to stimulants to improve functional outcomes.

There is no doubt that neuropsychologists have made significant contributions to the knowledge pertaining to the effectiveness and safety of stimulants. The research in this field is voluminous and, unlike that for other psychotropics, provides a model for evidence-based psychopharmacology treatment. It is anticipated that these empirical contributions will serve to enhance the quality of life for children, adolescents, and adults with attentional problems.

Note

1   The *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (APA, 1994), as well as the diagnostic criteria for ADHD, has undergone numerous revisions. Specifically, the *DSM* has been significantly updated four times—in 1968, 1980, 1987, and 1994. The majority of past research on ADHD was based on the nomenclature contained in the *DSM-III* (APA, 1980) and *DSM-III-R* (APA, 1987). However, recent studies on ADHD have employed the criteria set forth in the most recent editions of the manual, specifically, the *DSM-IV* (APA, 1994) and *DSM-IV-TR* (Text Revision) (APA, 2000). In these editions, there are several subtypes of ADHD: a predominantly inattentive subtype, a predominantly hyperactive-impulsive subtype, and a combined subtype. The subtyping of ADHD is the primary area that differentiates the most recent psychiatric nomenclature from previous nomenclature. Therefore, the majority of the literature reviewed here is based on studies that employed the *DSM-IV* and *DSM-IV-TR* criteria for sample selections.

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23

Nonstimulant Psychotropic Medication: Desired and Adverse Cognitive Events

MANUEL L. CEPEDA

This chapter reviews literature and presents guidelines for understanding the desired and adverse cognitive events associated with nonstimulant psychotropic medication. These events may influence cognition in the school setting, during counseling, and during psychoeducational testing. Studies involving children and adolescents are emphasized although some cognitive studies with adult subjects which have not been replicated with children are summarized. The more recent literature addressing improvements in cognitive function that can be demonstrated by neuropsychological testing comes almost exclusively from studies of adults with schizophrenia. Also target behaviors or symptoms that commonly respond to medication are briefly described. Guidelines are given for how soon to test when a medication has been recently started and how long to wait if testing must be free of possible drug influence.

Cognitive desired effects that are demonstrated with components of neuropsychological test batteries may not be apparent when testing with more routine or typical psychoeducational batteries. Some impairments demonstrated in the research laboratory cannot be corroborated during real-life activities such as operating a motor vehicle, sitting in a classroom, or on the job performance. Drug package inserts report adverse events that occur following administration of a single dose of medication to a healthy volunteer. The same adverse event may not occur during long-term administration of the drug to a patient. Most of the cognitive research does not directly translate into an understanding or appreciation of improvement at the clinical or educational level.

The first section looks at adverse events and the use of drug package inserts for information. Next is an overview of psychopharmacology with children followed by an overview of nonstimulant psychotropic drugs and the common mental disorders (psychopathology) and symptoms (independent of a disorder) treated with each class of medication. The chapter ends with a discussion of cognitive desired and adverse effects, along with guidelines for psychological testing while on newly prescribed medication or off recently discontinued medication.

Adverse Events

Adverse events are somatic, psychological, and behavioral responses to medication that are not pertinent to the desired therapeutic response. Adverse events are also known as side effects. Adverse events are not always undesirable. Sedation, a common initial side effect of some antidepressants, may be undesirable when medication is taken during the workday. The same side effect is beneficial when the depressed patient, with sleep onset disturbance as one of

MANUEL L. CEPEDA • Department of Psychiatry, College of Medicine, University of South Alabama, Mobile, Alabama 36617-2293.

the symptoms, takes the medication at bedtime. Some antidepressants may actually be prescribed to help with sleep. Sedation is an adverse event associated with some antipsychotic drugs. These same drugs might be prescribed for the sedation effect in a physically agitated patient without a psychotic disorder to help avoid injury to both patient and staff. When discussing the frequency of adverse effects, the following nomenclature is used. Adverse events considered "common" occur in more than 5% of patients using a given medication. Frequent adverse events occur in 1−5% of patients. Infrequent refers to the range from 0.001 to 1%. Rare events occur in fewer than 1 in 1000 patients using the drug.

Two different dropout rates (percentage of patients who discontinue medication) are reported in the medical literature. One is the overall dropout rate. The other is the adverse event dropout rate. The former is the number of patients who discontinue medication for any reason. The latter is the number discontinuing because of adverse events. Both rates are important. Some patients are quicker than others to discontinue after experiencing recognizable adverse events. Some physicians tolerate less risk and more quickly discontinue medication following an adverse event. The overall dropout rate is always higher than the adverse event dropout rate. Expense, lack of encouragement from the family to take medication, prescribing medication that is administered more than once a day, and the propensity to discontinue any treatment that is not of immediate benefit contribute to the higher overall dropout rate. Without careful education as to the specific target symptoms that will likely be helped by medication and a timetable for response, patients may discontinue medication prematurely. Sometimes family, friends, or therapists encourage a patient to ask the physician about using a different or newer medication because a symptom that is erroneously thought to be one that can be helped by medication does not improve. Encouragement to talk further with the prescribing physician and ask questions about the specific improvements that can be accomplished, the extent of improvement possible, and a timetable for improvement are critical to reducing the overall dropout rate.

Information from the medication package inserts is available from a pharmacist or online. This information is prepared by each drug manufacturer and contains data approved by the Food and Drug Administration (FDA) for use by drug manufacturers in labeling and advertising. The information usually reflects only the data from the investigational new drug clinical trials prior to initial approval for marketing the drug. Once approved, the manufacturer is not required to update the package insert to reflect new medical literature. When new indications and dosing practices appear in the medical literature, the drug manufacturer cannot use the information without updating the clinical trials and again requesting FDA approval. Physicians do use the updated medical literature as a basis for prescribing. It is important to understand that restraints placed by the FDA on what the drug manufacturer places in the package inserts are not synonymous with placing restraints on physicians' prescribing practices. Prescribing practices of physicians can differ significantly from the FDA-"approved" package inserts. The FDA has made clear to physicians that the current medical literature is to be used for those guidelines and for new uses of drugs not addressed in the package inserts (Department of Health and Human Services, 1982).

Medication package inserts always address the adverse effects profile. This includes profiles for both healthy volunteers versus placebo and mental disorder versus placebo adverse events. The adverse events reported for healthy volunteers are those that result from a single-dose administration of the drug. The data from patients with a mental disorder are from a drug trial that has extended over several weeks to several months. Details of the studies are not given in the medication package inserts supplied by manufacturers. Thus the information cannot be critically reviewed by the reader as could a scientific paper in a journal. A weakness is that sources of the adverse events warnings are rarely cited and often are not available even if requested directly from the manufacturer. During drug trials, over 50 common treatment-emergent somatic complaints are monitored. Items include skin rashes, flu-like complaints, respiratory complaints, palpitations, musculoskeletal aches, sexual dysfunction, neuropsychiatric problems, and weight change. Some of these complaints are reported by up to 20−25% of subjects using a placebo. Any clinical decision based upon the occurrence

of a suspected adverse event must be with a knowledge of the placebo rate for the same event. Blood chemistries to assess for possible hematologic or hepatic damage and electrocardiograms are a standard part of drug trials. Cognitive events demonstrable on psychoeducational or neuropsychological testing are not monitored as a part of the FDA-required adverse effects profile.

Psychopharmacology with Children

The use of psychotropic medications in the treatment of childhood psychopathology began in the late 1930 s with the stimulant medication Benzedrine. It was almost 15 years later, following the introduction of the antipsychotics chlorpromazine (Thorazine) and thioridazine (Mellaril), that additional drugs were administered for the treatment of childhood mental disorders. Most of the early target behaviors for treatment with drugs involved psychomotor excitement, restless behavior, anxiety, and hyperactivity. Many of the initial drug trials involved children with a diagnosis of delinquent behavior, brain damage, cerebral palsy, or mental retardation. Quickly, antianxiety (anxiolytic) medications such as hydroxyzine (Atarax) and, later, the tricyclic antidepressants such as imipramine (Tofranil) were added. These have been followed more recently by a newer generation of antidepressants, the selective serotonin reuptake inhibitors (SSRIs). Now lithium, an antimania drug, and several anticonvulsants also used to treat mania are being prescribed by child psychiatrists, child neurologists, and other physicians who treat the medication-responsive aspects of childhood psychopathology. The earlier antipsychotics have almost completely been replaced with the newer atypical antipsychotics such as risperidone. The field of childhood psychopharmacology has always been one of symptom treatment. Underlying disease processes have yet to be treated directly.

Overview of Nonstimulant Psychotropic Drugs

Six general categories of psychotropic medications are given to children: antipsychotic, antidepressant, antianxiety, antimania, antiseizure, and stimulant medications. The first five are discussed in this chapter. Stimulant medications are reviewed elsewhere in this book. The antiparkinsonian drugs used to attenuate some side effects associated with the antipsychotic drugs are also reviewed because they may have adverse cognitive effects.

Representative antipsychotic medications (also called neuroleptics) prescribed for children and adolescents include the atypical antipsychotics clozapine (Clozaril), risperidone (Risperidal), quetiapine (Seroquel), and olanzapine (Zyprexia). Older medications, seldom prescribed today, include chlorpromazine (Thorazine), thioridazine (Mellaril), haloperidol (Haldol), thiothixene (Navane), and fluphenazine (Prolixin). There is no clear difference in efficacy between the earlier classes of antipsychotics and the newer atypical antipsychotics, nor is any one drug clearly more efficacious than another. There is a difference in the adverse events profiles. Clozapine is the drug that requires the most intensive laboratory monitoring. Blood must be drawn weekly or biweekly for white blood cell counts for as long as the drug is administered because of the risk of agranulocytosis (failure of the body to produce white blood cells). If this does occur, life-threatening infections may quickly develop. There are at present emerging concerns about the atypical antipsychotics and endocrine and cardiovascular adverse events. Many physicians obtain every 6 months a lipid profile (HDL, LDL, triglycerides, cholesterol), a comprehensive metabolic profile with special attention paid to the liver (BUN, creatinine), a diabetes risk factor screen (A1C) and calculate the BMI (basal metabolic index) from height and weight to assess risk for cardiovascular events. At present the medical literature is not definitive about either the laboratory studies that are necessary or the frequency with which they should be obtained. As a consequence, clinical judgment and practice among physicians differ.

The antidepressant drugs have four major subclasses: tricyclics, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors (SSRIs), and medications in the "other" category. Most commonly, the selective serotonin uptake inhibitors and "other" category antidepressants are prescribed today. The SSRIs include fluvoxamine (Luvox), paroxetine (Paxil), fluoxetine (Prozac), and sertraline

(Zoloft). The "other" category includes venlafaxine (Effexor), mirtazapine (Remeron), nefazodone (Serzone), and buproprion (Wellbutrin). Representative tricyclic antidepressants include imipramine (Tofranil), amitriptyline (Elavil), and desipramine (Norpramine). They are seldom prescribed today. A knowledge of a drug's class does not always give an indication as to its mechanism (and consequently the side effects). Clomipramine is actually a selective serotonin reuptake inhibitor that belongs to the tricyclic antidepressant class! The monomine oxidase inhibitors include tranylcypromine (Parnate) and phenelzine (Nardil). As with the antipsychotics, there is no clearly demonstrable difference in clinical efficacy between individual antidepressants. There are differences in the adverse event profiles. The selective serotonin reuptake inhibitors have a far safer adverse event profile when taken in amounts that exceed normal therapeutic levels (i.e., drug overdose). Overdoses with tricyclic antidepressants are significantly more life threatening.

Most of the antianxiety drugs are of the benzodiazepine class. Commonly prescribed are chlordiazepoxide (Librium), diazepam (Valium), and alprazolam (Xanax). The benzodiazepines produce immediate relief of anxiety. Buspirone (Buspar) is an antianxiety agent from the azaspirodecanedione class. It is not related to the benzodiazepines and should not cause psychological or physical dependence as may the benzodiazepines. It is also less sedating. It may take several weeks of daily treatment for anxiety symptoms to respond to buspirone. Buspirone is also less efficacious overall than the benzodiazepines. The antihistamine hydroxyzine (Atarax or Vistaril) is used as an antianxiety agent. A drawback is that for many it loses efficacy during long-term use. It does not have the abuse or dependence profile of the benzodiazepines. It may be administered intramuscularly on an as-needed basis to children or adolescents hospitalized on a psychiatric inpatient unit for attenuation of rage behavior or as an adjunct to antipsychotic medication treatment of a psychotic disorder (here again, for agitation, not direct treatment of the psychotic process).

Lithium carbonate, used to treat mania, is a salt. It has a life-threatening adverse effects profile that closely parallels the level of drug in the blood. Initially, frequent monitoring of blood levels is necessary as medication is increased to therapeutic effect. Patients are warned to avoid table salt-free diets which might increase the serum levels of lithium. Patients are also warned not to get dehydrated when they exercise for the same reason. Adverse effects may appear quickly when serum blood levels exceed the upper therapeutic range. Patients prescribed lithium are screened for possible kidney problems (BUN, creatinine) and possible thyroid problems (TSH, T4, free T4) before starting lithium, whenever the dose is increased, and every 6−12 months thereafter.

Representative antiseizure drugs used to treat symptoms of mania and to treat rage behaviors include carbamazepine (Tegretol), clonazepam (Klonopine), valproic acid (Depakene), divalproex sodium (Depakote), topiramate (Topamax), and verapamil (Isoptin). Patients being treated with divalproex may be screened with a comprehensive metabolic profile with special attention paid to liver (AST, ALT, and bilirubin) and kidney every 6 months. Clonazepam has many properties characteristic of the benzodiazepine class of anxiolytics. This includes withdrawal symptoms similar to those seen with alcohol withdrawal and the risk of abuse and dependence. Others do not have the same abuse or dependence potential.

The antiparkinsonian agents include benztropine (Cogentin) and amantadine (Symmetrel). Although not psychotropic medications, they are important because they are often prescribed at the same time as the antipsychotic drugs to treat musculoskeletal adverse events. Benztropine can contribute to an anticholinergic-induced delirium and potentiates the same problem when used in conjunction with the more anticholinergic antipsychotic medications.

Antipsychotic Medications

The antipsychotic drugs are of well-established benefit in the treatment of schizophrenia, schizophreniform disorder, schizoaffective disorder, and delusional disorder. Attention-deficit hyperactivity disorder symptoms will respond to antipsychotic medications. They are also useful in the treatment of major depression with psychosis and the manic phase of a bipolar disorder. The psychotic symptoms responsive to medication include recent and rapid-onset delusions and hallucinations, incoherent or disorganized

speech, agitated behavior, and catatonic excitement or stupor. Additional target symptoms include the press of speech, flight of ideas, and motoric hyperactivity of mania. A significant response may be seen during the first few days of treatment. To prevent relapse, the antipsychotic drugs are continued even when the psychosis is in remission and for many mental disorders will be continued for a lifetime.

Patients with pervasive developmental disorders (e.g., autism) or significant mental retardation who have symptoms of agitation, physical aggression, or self-mutilatory behavior are also prescribed antipsychotic drugs. The medical literature does not support the efficacy of the antipsychotic drugs for these symptoms as clearly as it does for psychotic disorder symptoms. Significant attenuation of these behaviors over weeks to months is the goal. A total remission is not a practical goal and the core symptoms of the disorders are not treated. Medication may need to be continued for several years but seldom for a lifetime. Antipsychotic drugs are used to treat the multiple tic disorders (Tourette's disorder). They are prescribed for the occasional psychotic symptoms and frequent irritability seen early in the course of Huntington's disease. For these indications, no drugs treat the underlying disease or alter the ultimate course.

Agitation, anger, aggression, and rage that are not a part of a psychotic or dementing disorder may also be treated with antipsychotics. The indications for this use are not well established. Examples include the aggressive component of a conduct disorder, aggression as a part of an intermittent explosive disorder, and low frustration tolerance, rages, and hostility in conjunction with several of the Cluster B personality disorders (antisocial, borderline, and narcissistic disorders) or as part of the still evolving childhood onset bipolar disorder construct. Medical literature to support neuroleptic use for target symptoms not associated with a psychotic disorder is limited and many studies fail to support efficacy. Most efficiency studies report the use of multiple medications (both same class and different class) simultaneously, the need for frequent adjustments, and a much longer time from first use of medication to clinical response.

The common muscular adverse effects of the antipsychotic drugs involve central nervous system-mediated pathways. This is less a problem with the atypical antipsychotics than the earlier antipsychotics. An acute dystonic reaction with the sudden onset of muscle spasms may be seen. Although a dystonic reaction may look frightening to an observer, it actually causes little physical discomfort. Spasm of the masseter muscles may cause the jaw to pull over to one side and look as if it is dislocated. The head and neck may twist back and to one side because of sternocleido-mastoid muscle spasm. This is called torticollis. The child may complain that the tongue is being pulled into the back of the mouth or that there is a feeling of swallowing the tongue or not being able to swallow. Both eyes may roll up (oculogyric crisis) leaving only the bottom part of each pupil and iris showing. Rarely, the truncal muscles may be involved. The child may twist into an opisthotonos position with the head pulled backward in extension and back arched with arms drawn up and legs extended. The presence of acute dystonic reactions should be easily identified by an observer.

Akathisia is difficult to recognize if the symptoms are subjective only; fairly easy to identify if they can be seen. The complaints are of feelings of restlessness or the inability to sit still. If actually observable, both legs may appear as if they are "pacing" while the individual is sitting or standing. In children, the "fidgetiness" of the hyperactive child may be mistaken for akathisia, as may complaints of restlessness associated with anxiety.

A parkinsonian appearance may be seen. There may be muscular rigidity, a pill-rolling hand tremor, drooling, and mask-like faces. The reduced movement may be confused with catatonia or with the appearance of a retarded depression.

Dyskinesias should be easily recognized. These include facial tics and blinking (blepharospasm). Not all tics are due to a drug. Even if the child is using an antipsychotic drug, one child in ten not using any medication develops a tic disorder, usually transient, during childhood.

Tardive dyskinesia is a troubling adverse event. Symptoms include abnormal mouth movements that look like persistent chewing, lip-smacking, or repetitive tongue protrusions (fly catcher tongue). These are buccolingual-masticatory (BLM) movements. The movements may abate if antipsychotic medication is lowered or discontinued and may be temporarily hidden

or masked if medication is increased. The clinical picture is difficult to assess because withdrawal dyskinesias which will abate are indistinguishable in appearance from early tardive dyskinesia which may persist regardless of intervention. Those at greatest risk for tardive dyskinesia are elderly females. Although reported in children, it is not as common. Physicians may see patients on antipsychotic medications as often as every 2 months to screen for adverse events, especially if the patient has a prior history of tardive dyskinesia.

Weight gain in adults and children is associated with the antipsychotic medications (Silva, Malone, Anderson, Shay, & Campbell, 1993). The extent of weight gain differs for each medication. Hyperprolactinemia (elevated blood prolactin levels) may occur. This is associated with amenorrhea, secretion of breast milk, and loss of libido. Changes on the electrocardiogram (QTC interval prolongation) have been associated with fatal arrhythmias and for this reason some of the individual antipsychotic drugs are seldom prescribed for elderly patients, those of any age with specified pre-existing arrhythmias, or children with cardiac conduction anomalies. An increased risk of diabetes mellitus is associated with most of the atypical antipsychotic drugs (Wright & O'Flaherty, 2003). In children with autism, it is difficult to distinguish stereotypic behaviors (repetitive senseless movements or verbalizations) which can be characteristic of autism from the neuroleptic-mediated dyskinesias (Shay et al., 1993). Neuroleptics may induce tics in children with attention-deficit hyperactivity disorder (Guatrieri & Patterson, 1986).

Drug-induced dysphagia (difficulty swallowing) can occur with neuroleptic use. Choking on food and possible aspiration (food enters trachea and lungs) may lead to pneumonitis (inflammation of the lungs) or asphyxia (literally a "stopping of the pulse" resulting from lack of oxygen). This is a critical problem for patients with brain injuries who receive antipsychotics for control of psychomotor agitation. Some 25−30% of these patients already have dysphagia as a consequence of the brain injury (Sliwa & Lis, 1993).

Most of the antipsychotic medications cause sedation when first given or whenever high doses are prescribed. This is less of a problem with the atypical antipsychotics than it was with the earlier typical antipsychotics. This effect should abate over several days for the lower maintenance doses, or possibly weeks for the higher treatment doses. Usually the physician decreases the medication from the initial higher treatment dose to a lower maintenance level after a few weeks as a normal course of treatment of a psychotic disorder. This also helps alleviate the sedation or "drugged up" feeling. When antipsychotics are used to treat symptoms of anger or aggression independent of a psychotic disorder, the starting point is a lower dose with later increases to clinical effect.

It is the anticholinergic effect of the typical antipsychotic that may cause some initial confusion, memory problems, and disorganization when medication is first prescribed. This is a dose-related effect and varies widely by drug. In combination with a highly anticholinergic antiparkinsonian drug such as benztropine (Cogentin), delirium may occur. It may take a week or more for a serious anticholinergic delirium to clear once medication is stopped. Generally, those drugs with a greater risk for anticholinergic-mediated adverse effects have a lesser risk for causing dystonic reactions. Conversely, there is a greater risk for dystonic reactions from those drugs with a less pronounced anticholinergic profile. Because efficacies are so similar, most drug management decisions come down to balancing the tradeoffs inherent in the adverse events profiles.

If antipsychotic medication is discontinued, clinically significant pharmacologic effects persist for about 36 h. Almost all of the drug will be metabolized and cleared from the body within 3 or 4 days following cessation. At that point, there is no longer any noticeable clinical effect. With prolonged administration, metabolites may persist in the urine for several months to over a year. This latter finding is not of importance because there is no clinical effect.

Most research into the effects of the typical antipsychotic medications on cognition has studied children with mental retardation or with autism. Some 70% of this latter group has an IQ in the range for mental retardation. When patients are symptomatic with medication-responsive target behaviors, it is not possible to design studies that assess the effects of antipsychotic medications on cognition and learning alone. Several studies emphasize that as the symptoms of aggression, restlessness, and poor

concentration improve, tasks such as learning and school achievement improve (Anderson et al., 1984; Campbell et al., 1982; Helper, Wilcott, & Garfield, 1963; Sprague, Barnes, & Werry, 1970; Weise, O'Reilly, & Hesbacher, 1972; Werry, Weiss, Douglas, & Martin, 1966). When antipsychotic medications were given to children with a spectrum of nonpsychotic disorders (adjustment reaction, hyperactivity, conduct disorder, and personality disturbance), the results more often were inconclusive or actually suggested deterioration in test performance. For subjects with these diagnoses, it was concluded that any untoward effects on testing or learning were related to the sedation seen on initial administration. Higher doses also affected test scores. None of the studies with the earlier antipsychotics and autism or mental retardation conclude that medication directly improves learning ability. Most of the improvement follows the first month or two of medication treatment.

Early studies of the typical antipsychotics with adults yielded similar findings (Braff & Saccuzzo, 1982; Spiegel & Keith-Spiegel, 1967; Weiss, Robinson, & Dasberg, 1973). Those symptomatic with schizophrenia showed improved intelligence test scores following the administration of antipsychotics. Other aspects of cognitive function, including attention, improved with the use of medications (Eitan, Levin, Ben-Artzi, Levy, & Neumann, 1992; King, 1990; Strauss & Kleiser, 1990; Strauss, Kleiser, & Leuthcke, 1988). Again, the improvement came following a reduction in the severity of symptoms of the illness and was not attributed to a direct effect of the typical antipsychotic drug on learning. Any decrement in performance caused by medication was masked by the improved performance as other clinical symptoms abated. The earlier studies did not assess cognition with neuropsychological test components.

Schizophrenia is associated with a number of cognitive impairments identified via neuropsychological testing. There are studies showing that the newer antipsychotic drugs (atypicals) improve performance on selected neuropsychological tests. The studies involve adults with schizophrenia and the effect is independent of the antipsychotic effect on the clinical symptoms of schizophrenia (Rivas-Vazquez, Blias, Rey, & Rivas-Vazquez, 2000; Peuskens, Demily, & Thibaut, 2005). Analogous studies are not available for healthy adult volunteer subjects or for children and adolescents with or without schizophrenia.

Quetiapine is one of the atypical antipsychotic drugs that have been shown to improve cognitive function in schizophrenia. The improvements include improved attention (measured by the Digit Span Test), set shifting (from Trail Making Test, part B), and executive functioning (measured by the interference part of the Stroop Test) (Akdede, Alptekin, Kitis, Arkar, & Akvardar, 2005). These improvements are sustained over 12 months with continuing medication treatment (Good et al., 2002). For selected scales (e.g., Wisconsin Card Sorting Test), the newer drugs (atypicals) have been found to be superior to the earlier typical antipsychotics (Rossi et al., 2006). In a double-blind study, the atypical antipsychotic risperidone was superior to the typical antipsychotic haloperidol in its effects on verbal working memory (assessed by the Digit Span Distractibility Test) with and without distractions for patients with schizophrenia (Green et al., 1997). A within-subject double-blind study of patients with schizophrenia using a variety of atypical antipsychotics demonstrated cognitive improvements over placebo on a number of measures of executive function, attention, memory, and perception (Weickert et al., 2003). Similar improvements in cognitive performance are cited for schizophrenia and a number of the other atypical antipsychotics including risperidone, clozapine, olanzapine, and ziprasidone (Woodward, Purdon, Meltzer, & Zald, 2005; Harvey, 2003; Cuesta, Peralta, & Zarzuela, 2001). Reviews are available (Hawkins, Mohamed, & Woods, 1999; Sharma, 1999; Stip, Chouinard, & Boulay, 2005).

In nonpsychotic subjects, higher doses of antipsychotics are associated with impaired performance on psychomotor speed and attention tasks, independent of clinical diagnosis and level of intelligence (Sweeney, Keilp, Haas, Hill, & Weiden, 1991). The data suggest that for the drugs with a more prominent anticholinergic side effect profile, the impairment is more severe. The addition of selected antiparkinsonian medications intensifies the impairment (Cleghorn, Kaplan, Szechtman, Szechtman, & Brown, 1990; Eitan, Levin, Ben-Artzi, Levy, & Neumann, 1992).

The following are clinical guidelines for psychoeducational testing of children being prescribed antipsychotic medication. For children with nonpsychotic disorders receiving typical antipsychotics, adverse sedative effects of medication on test results may be seen for days to a week or two after the medication is started. At reasonable clinical doses, any adverse effect on testing should be negligible after the child has been on a stable dose of medication for a couple of weeks. A similar guideline should be used for the atypical antipsychotics even though sedation is not as prominent. A different guideline applies for patients with psychotic disorders. If testing is to be used for educational placement, it should be delayed for 4−8 weeks after medication is started or at least until the patient is free of psychotic symptoms and on a stable maintenance dose. Delay testing any time obvious sedation is present. A 2- to 4-day delay following cessation of drug should be sufficient if the testing must be done free of antipsychotic medication.

Antidepressants

The antidepressants are prescribed to treat major depressive disorder, dysthymia, the depressive phase of a bipolar disorder and panic disorder. The target symptoms most clearly responding to antidepressants for depressed patients include spontaneous crying spells, decreased appetite, weight loss, diurnal mood variation (less energy on arising than later in the day), and difficulty in falling asleep, middle of the night awakening, early morning awakening, and impairment of concentration. Less responsive to medications are sustained feelings of depression (mood) and anhedonia. Antidepressants do not alleviate ongoing depressed mood if it is unaccompanied by the specific melancholic symptoms associated with moderate to severe clinical depression.

Some attenuation of anxiety symptoms accompanying a depressive illness may be seen as quickly as 2 or 3 days after starting an antidepressant. It takes between 3 and 8 weeks for the core clinical symptoms of depression that are going to respond to medication to do so at a given dose. Because of the length of time necessary for response, antidepressants are not used to treat stress symptoms that might be expected to remit over a week or two without treatment.

In the early 1970 s, the tricyclic antidepressant imipramine (Tofranil) was used to treat hyperactive children. Most of the target clinical improvements included improved conduct in general, improved attention span, and reduced motor activity. Most studies concluded that the antidepressant was effective and the degree of improvement was the same as with stimulant medication (Quinn & Rapoport, 1975; Rapoport, Quinn, Bradbard, Riddle, & Brooks, 1974; Werry, Aman, & Diamond, 1979). This course of treatment did not retain popularity, however, and now the stimulant medications are used almost exclusively, although some antidepressants are still prescribed, e.g., atomoxetine (Strattera).

The selective serotonin reuptake inhibitor antidepressants such as clomipramine, fluoxetine, and sertraline are used to treat symptoms of obsessive−compulsive disorder. The compulsions or repetitive behaviors such as checking, touching, or hand washing respond better to medication than does obsessional thinking alone.

Panic disorders may be treated with antidepressant medications. This includes the older tricyclic antidepressants and the current SSRIs. Enuresis may be treated with the tricyclic antidepressant imipramine. Although imipramine is the prototype antidepressant for use with this problem, any tricyclic antidepressant should help equally as well. The most optimistic reports come in the treatment of secondary nocturnal enuresis. It is called secondary because the child has periods of days or weeks free of enuresis. Primary enuresis (no significant period free of symptoms) is less often responsive to medication and may be due to a medical problem such as a ganglionic megacolon. Half or more of those with secondary enuresis become asymptomatic with medication use. Antidepressant treatment of enuresis is superior to placebo treatment, but has not been demonstrated to be superior to desmopressin nasal spray or the many alternative treatments such as bell and pad, token economy, brief family or individual psychotherapy (Behrle, Elkin, & Laybourne, 1956; Kardash, Hillman, & Werry, 1968; Stenberg & Lackgren, 1994). Children with severe separation anxiety disorder are treated with SSRI antidepressants. Medication treatment for this disorder must be

in conjunction with psychotherapeutic and psychosocial/educational interventions.

Some antidepressants are more sedating than others. For these, reports of feeling sleepy peak between 2 and 3 h after administration and are gone by 7 h after the drug is ingested. The same problems have not been reported during long-term administration. The more sedating tricyclics do impair performance on serial addition and digit substitution tasks when the drug is first administered (DiMascio, Heninger, & Klerman, 1964; Ross, Smallberg, & Weingartner, 1984; Thompson, & Trimble, 1982). When drug treatment is initiated, the tricyclic antidepressants with greater anticholinergic potential can cause memory disturbances and even a delirium. The same effects are less evident or not evident during chronic administration (Thompson, 1991). This should not be as frequent a problem with the newer (SSRI) antidepressants. The delirium caused by tricyclics correlates with high blood levels of the drug (Meador-Woodruff, Akil, Wisner-Carlson, & Grunhaus, 1988). The incidence of delirium is also related to increasing age (Livingston, Zucker, Isenberg, & Wetzel, 1983).

The cognitive effects of tricyclic antidepressants during long-term administration have been studied in children being treated for enuresis, hyperactivity, childhood depression, and aggression. The results may vary by diagnostic category. Scores on such measures as the Wechsler Intelligence Scale for Children improved as melancholic symptoms of depression lifted. Improvements came following 2−3 months of drug therapy. Performance on a continuous performance test (a measure of sustained attention or vigilance) improved during administration of amitriptyline (Elavil). Several studies concluded that children using an antidepressant concentrated better. Studies of children with conduct disorder and enuresis that compared IQ scores before and after antidepressant treatment found no significant differences (Brumback & Staton, 1980; Kupietz & Balka, 1976; Rapoport, 1965; Staton, Wilson, & Brumback, 1981; Werry, Dowrick, Lampen, & Vamos, 1975).

The memory and attention changes during ongoing tricyclic antidepressant treatment of adults with depression have received more attention (Glass, Uhlenhuth, & Weinreb, 1978; Glass, Uhlenhuth, Hartel, Matuzas, & Fischman, 1981; Henry, Weingartner, & Murphy, 1973; Keeler,

Prange, & Reifler, 1966; Lamping, Spring, & Gelenberg, 1984; Legg & Stiff, 1976; Sternberg & Jarvik, 1976). Impairment in short-term memory is a clinical characteristic of depression and the greater the initial short-term memory impairment, the greater the clinical improvement with antidepressant medications. Imipramine facilitates psychomotor tasks such as tapping or reaction time. Clinical measures such as the Wechsler Adult Intelligence Scale are not sensitive enough to reflect adverse medication events while a patient is on a maintenance dose of tricyclic antidepressant. Although not as extensively studied, many of these findings are also true of the monoamine oxidase inhibitor class of antidepressants (Murphy, 1977).

Sexual dysfunction has been associated with the use of the tricyclic and monoamine oxidase inhibitor classes of antidepressants and the newer SSRIs. This includes inhibition of ejaculation in males and anorgasmia in females (Jani & Wise, 1988; Rosenbaum & Pollack, 1988; Segraves, 1988; Shen & Lindbergh, 1990). Although the literature addresses adult dysfunction and does not address the problem in adolescents, there is no reason why the adolescent would not be at risk. A decreased libido (sex drive), rather than inhibition of ejaculation and anorgasmia, is associated with clinical depression. Even with a careful sexual function screen prior to starting antidepressants, it is difficult to differentiate dysfunction related to antidepressants from the sexual dysfunction so often associated with depression (Petrie, 1980). It is equally difficult to attribute sexual function complaints in an individual patient to active ingredient if a significant percentage of those given placebo have similar complaints. Overdose of tricyclics has been associated with death resulting from cardiac arrhythmias. Sudden death reported in four children using a tricyclic antidepressant was not associated with postmortem blood levels above the therapeutic range (Riddle et al., 1991; Tingelstad, 1991). Sudden deaths in general are associated with cardiac arrhythmias as the mechanism of death and most of the deaths cited in the literature occurred in individuals with previously known heart conduction defects. At present, the conclusion is that if a tricyclic antidepressant is linked to sudden death (because of an adverse cardiovascular event) the occurrence is rare (Biederman et al., 1993). It is not certain that the risk associated with the

antidepressants is greater than the risk for sudden death in those free of medication. One study has concluded that depressed patients using antidepressant medication should be capable of driving (Hobi et al., 1982). The subjects were all adult patients using established clinical doses of antidepressant.

The following clinical guidelines apply for routine psychoeducational testing when patients use antidepressants. If the child is receiving any class of antidepressant to treat a depression with melancholic symptoms, testing should be delayed until clinical improvement is seen if the results are to be used for long-term educational placement. This means delay should be at least 3 weeks and perhaps as long as 6−8 weeks after the correct therapeutic dose is initiated. Testing earlier than this (while the patient is still symptomatic with melancholia) will reflect current function possibly influenced by symptoms of depression. For the child receiving tricyclic antidepressants for problems other than depression, the initial sedative and/or anticholinergic effect that may be seen in the first week or two of administration may influence the test results. It would be best to delay testing until the child has been on the same dose of medication for at least 2 weeks. For an SSRI antidepressant there is less concern and testing may be sooner but the cognitive research literature does not definitively address how much sooner. If the child must be tested free of antidepressant medication, a 3-day delay following discontinuation is suggested since clinical blood levels should be gone by then. There is insufficient research data to conclude that long-term administration of tricyclic antidepressants impairs performance on any routine psychoeducational batteries. Likewise, there is no body of literature concluding that antidepressants cause cognitive improvement independent of improvement in clinical depression. There is no analogous body of literature for the effects of SSRIs on neuropsychological testing.

Antimania Drugs

Lithium carbonate and a number of antiseizure medications are used for the treatment of the manic phase of bipolar disorders. Because clinical improvement of manic symptoms takes 7−10 days with lithium or with antiseizure drugs alone, an antipsychotic medication (which can reduce symptomatology over 3 or 4 days) is often prescribed at the same time an antimania drug is started and discontinued once the antimania drug reaches therapeutic effect.

Antiseizure medications which target mania may also be used to target symptoms of aggression, hostility, rage, and behavioral impulsivity and affective liability either as symptoms alone or under the rubric of childhood bipolar disorder (Kowatch et al., 2005). This diagnosis is not without dispute and in the opinion of some is an as yet to be validated diagnosis (McClellan, 2005). Reports of medication efficacy for such use are mixed, as are reports on the treatment of episodic dyscontrol, aggression, and repetitive self-injuries (Israel & Beaudry, 1988).

One study (Judd, Hubbard, Janowsky, Huey, & Takahashi, 1977) reported that in normal volunteers, therapeutic levels of lithium did impair performance on the Digit Symbol subtest of the WAIS and the Trail Making A Test. Another study concluded that lithium caused a decrement in WAIS IQ scores (Aminoff, Marshall, Smith, & Wyke, 1974) in patients being treated for Huntington's chorea, a neurological disorder associated with dementia. Similar studies are not available for the antiseizure medications. Other lithium studies have specifically addressed memory tasks (Bonnel, Etevenon, Benyacoub, & Slowen, 1981; Christodoulous, Kokkevi, Lykouras, Stefanis, & Papadimitriou, 1981; Huey et al., 1981; Kusumo & Vaughan, 1977; Marusarz, Wolpert, & Koh, 1981; Squire, Judd, Janowsky, & Huey, 1980). All of the studies used either specialized scales or selected parts of more common tests. Patients with a comorbid dementia and the elderly are at more risk for memory dysfunction when lithium is used. Some studies suggest that those with more severe psychiatric illness show more impairment. There is some evidence that lithium does not affect the more global measures on the WAIS or the Wechsler Memory Scale in nondemented patients. In contrast with the other drugs covered, studies with lithium did not show a clear improvement in cognitive function paralleling clinical improvement. Again, analogous studies are not available for the antiseizure drugs. There is insufficient literature from which to develop guidelines for psychoeducational or

neuropsychological testing other than to say that the patient should be sufficiently free of clinical symptoms to participate in the testing.

Antianxiety Drugs

Antianxiety medications see widespread use for the symptomatic relief of anxiety in adults. They are less often prescribed for similar target symptoms in children and adolescents. Physicians do prescribe anxiolytics for brief symptomatic treatment of overwhelming stress in children as a part of crisis stabilization. Anxiolytics are also used to attenuate alcohol and street drug withdrawal symptoms (tremor, insomnia, psychomotor agitation, anxiety). They are used to treat pavor nocturnes (night terrors) and somnambulism (sleepwalking). The anxiolytic alprazolam (Xanax) is used to treat panic disorder.

Anxiety can be a prominent symptom during an acute psychosis. Hospitalized adolescents with these problems may also receive anxiolytics until they respond to antipsychotics. Then the anxiolytic will be discontinued. Depressed patients may receive anxiolytics until sleep improves with concomitant antidepressant treatment.

There is a paucity of literature on the cognitive and behavioral adverse effects of anxiolytics in children. One study that did specifically evaluate benzodiazepine class anxiolytic drug effects on the cognitive function of children concluded that at therapeutic doses there is no adverse effect on cognition (Ferguson & Simeon, 1984). Most studies with adult subjects conclude that, at common therapeutic doses, little if any difference between placebo and drug groups can be demonstrated (Healey, Pickens, Meisch, & McKenna, 1983; Pishkin, Fishkin, Shurley, Lawrence, & Lovallo, 1978; Zimmermann-Tansella, 1984). A decrease in vigilance may occur with single-dose administration (Gotestam & Anderson, 1978). Experienced drivers receiving diazepam for relief of anxiety had more difficulty with normal perception and anticipation of events. This may be more of a problem during less interesting, low attention level driving on highways than in dense city traffic where a high attention level is constantly required (deGier, 't Hart, Nelemans, & Bergman, 1981).

For the benzodiazepine class of anxiolytics, several reviews are available that summarize the effects (Cole, 1986; DiMascio, Giller, & Shader, 1968; Ghoneim & Mewaldt, 1990; Kornetsky, Williams, & Bird, 1990; Lister, 1985; Wittenborn, 1988). While using benzodiazepines, more problems occur with the acquisition of new information than the retrieval of previously learned material. If sedation is present, the impairment is more pronounced. The impairment is more pronounced for tasks that require more effort (e.g., learning new material) than for automatic processes requiring minimal attention. At nonsedating doses, short-term or working memory remains intact. No similar literature is available for buspirone.

The addiction potential of the benzodiazepines is of concern during long-term administration. Possibly one patient in five using benzodiazepines over an extended period of time increases the dose surreptitiously. This suggests the development of tolerance and/or abuse. Even low doses are associated with withdrawal symptoms after about 4 months of use. Clinical evidence of dependence may appear by 4−6 weeks of daily use (Miller & Gold, 1990; Zisook & DeVaul, 1977).

Paradoxical rage reactions (aggressive dyscontrol) have been reported during benzodiazepine use. There is no clear conclusion that aggressive dyscontrol is a specific side effect of the antianxiety medications (Dietch & Jennings, 1988; Gardos, 1980).

Both the ability to sustain attention during a repetitive task under time pressure and visual−spatial ability may be impaired in those using benzodiazepines in normal therapeutic doses for 1 year or longer (Golombok, Moodley, & Ladner, 1988). Buspirone, a non-benzodiazepine class antianxiety agent, does not affect memory as adversely (Lucki, Rickels, Giesecke, & Geller, 1987). It is easier to show memory effects in the elderly. Less or no impairment is seen in young adults (Block, DeVoe, Stanley, Stanley, & Pomara, 1985). Analogous studies are not available for children and adolescents. Although the greatest effect may be on the acquisition of new material (episodic memory), tolerance to these problems does develop (Koelega, 1989).

As with the antimanic drugs, there is insufficient research data regarding the use of anxiolytic drugs in children to comment on the

cognitive effects in relationship to routine psychoeducational testing. If the child is tested while using an anxiolytic, testing should be delayed until a clinically efficacious dose is reached and clinical anxiety is no longer of such an extent as to interfere. Avoid testing the day an anxiolytic drug is started, the day of a dose increase, and possibly the next day also. The clinical effect for single-dose administration of most anxiolytics is about 4−6 h. The half-life for most is longer and drugs may be detected through routine blood and urine assays for 1−2 days following administration of a single dose. If the child must be free of anxiolytic medication effect at the time of testing, a delay of 1 day following the last dose should be sufficient.

Antiseizure Drugs

See the section (this chapter) covering the antimania drugs for a discussion of the antiseizure drugs. There is insufficient literature from which to base an opinion about the effects of these drugs on common psychoeducational testing batteries.

Antiparkinsonian Agents

Antiparkinsonian agents are used to treat acute dystonic reactions, parkinsonian symptoms, and akathesia associated with neuroleptic use. They are usually prescribed after a patient develops an adverse event rather than prophylactically. Most patients only need coverage for a few weeks, although for some patients daily use for months is necessary.

Brain-damaged patients of any age and the elderly are more sensitive to the anticholinergic effects of antiparkinsonian agents on memory (Fayen, Goldman, Moulthrop, & Luchins, 1988). This problem is not seen with amantadine (Symmetrel). It does not have the same anticholinergic profile and may be used in place of benztropine (Cogentin). Nondemented patients are far less sensitive to anticholinergic effects on cognitive performance (Thienhaus, Allen, Bennett, Chopra, & Zemlan, 1990). Some patients come to appreciate the stimulant-euphoric effect associated with high doses of antiparkinsonian medication and become skilled at self-inducing a mild anticholinergic delirium

by using extra medication. This can develop into drug abuse (Dugas, 1977).

Because of the concern that these drugs may contribute to impaired cognitive function in a patient with dementia, the prescribing physician can be asked about the medical advisability of discontinuing the antiparkinsonian drug prior to testing. The discontinuation may need to be for at least a week and perhaps two if an anticholinergic delirium is suspected or present.

Summary

Childhood psychopharmacology began in the late 1930 s. Today it includes the use of antipsychotic, antidepressant, anxiolytic, antiseizure, and antimania drugs.

Recommendations concerning the advisability of psychoeducational testing while the patient is using psychotropic medication vary by class of drug, whether a mental disorder or a symptom alone is being treated, dose, and time since starting the medication. Depending on the variables, testing may be possible as early as the day after starting medication or may need to be delayed as long as 6−8 weeks after medication has begun, giving time for the symptoms of a mental disorder to remit.

For selected mental disorders (e.g., schizophrenia) there is improvement in cognitive function that can be attributed to the use of antipsychotic drugs and not just to clinical improvement alone. For most other disorders, the improvements in cognition are attributed to an improvement in clinical status and not to the effect of a drug per se.

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IV

Special Topics in Clinical Child Neuropsychology

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Child Clinical Neuropsychology of Drug Abuse

ARTHUR MACNEILL HORTON, JR.
AND ARTHUR MACNEILL HORTON, III

Introduction

The use of substances to modify moods, behaviors and perceptions, drug abuse has been a problem since the beginning of recorded history. Human beings for centuries have used alcohol and natural substances such as peyote from the cactus and leaves from the opium plant for their psychoactive properties. After the industrial revolution, chemical technology has produced new psychoactive substances with abuse potential such as heroin, cocaine, LSD, PCP, designer drugs and Ecstasy. Indeed, the likelihood is that new psychoactive drugs will be developed in the future and they will present additional potential for abuse.

Addiction to drugs of abuse is an important issue for a number of reasons. One reason is that prohibition of drugs of abuse has not been very successful as a social policy. Tobacco use was discouraged in England in the early 1600s but smoking still increased and growing tobacco was a major source of income for the British colonies in the Americas. England also made chocolate illegal in the 1700s with little success. Later, England, going the other way, in order to overcome a balance of payments problem over tea purchases with China fought two wars with China in the 1700s and 1800s to be allowed to export opium into China and gain control of the island of Hong Kong as a site to store imported opium. The United States prohibited alcohol use in the 1920s but prohibition was a complete failure as a social policy and the sale of alcohol was legalized by a constitutional amendment in 1933. The United States has also prohibited drug use of a number of substances but the effort has not been a complete success and significant illegal drug use has continued (SAMHSA, 2006).

Survey data indicate that in 2005 (the most recent available findings) 19.7 million Americans or 8.1% of the US population aged 12 or older used illicit drugs during the month prior to the survey interview (SAMHSA, 2006). Of illicit drug users, marijuana is the most commonly used illicit drug, with 14.6 past month users or 6.0% in 2005 (SAMHSA, 2006). For other commonly used illicit drugs in 2005, 2.4 million persons (1.0%) were current cocaine abusers, 1.1 million or 0.4% used hallucinogens (including 502,000 or 0.2% users of Ecstasy) (SAMHSA, 2006). For prescription psychotherapeutic drugs non-medical use there were 6.4 million (2.6%) users aged 12 and older, of these users 4.7 used pain relievers, 1.8 million used tranquilizers, 1.1 million used stimulants (including 512,00 using methamphetamine) and 272,000

ARTHUR MACNEILL HORTON, JR. • Psych Associates, Towson, Maryland. **ARTHUR MACNEILL HORTON, III** • Eastern Virginia Medical School, Norfolk, VA.

used sedatives (SAMHSA, 2006). For youths aged 12–17 in 2005, 9.9% were current illicit drug users (SAMHSA, 2006). The rate of illicit drug use among youths aged 12–17 in 2005 was similar to the rate of illicit drug use in 2004 (10.6%) but significantly lower than the rate of illicit drug use in 2002 (11.2%) (SAMHSA, 2006).

Alcohol use was higher. In 2005, it was estimated that 126 million Americans, aged 12 or older, were recent alcohol drinkers (51.8%) or more than half of the US population in that age range (SAMHSA, 2006). Of those current alcohol users age 12 or older, 55 million (22.7%) were monthly binge drinkers and 16 million (6.6%) were heavy drinkers (SAMHSA, 2006). For youths aged 12–20, 10.8 million reported monthly drinking (28.2%) in 2005 (SAMHSA, 2006). Generally speaking there were few increases in illicit drug and alcohol use from 2004 to 2005 (SAMHSA, 2006).

Numbers, however, fail to capture the damage to society caused by drugs of abuse. Drug abuse has been estimated as costing the United States more than 275 billion dollars a year (Harwood et al., 1998). Drug abuse costs are from multiple sources. Health costs increase due to the pathological consequences of alcohol and illicit drug use. In addition, there are costs from the results of domestic violence, traffic accidents and crime (Hubbard et al., 1989). In addition, there are significant traumatic stress effects on the spouses and children of drug addicts and alcoholics that produce initial and later delayed psychological damage.

While there are multiple negative effects of illicit drug use and excessive alcohol use, the social question is not as simple as to suggest simple prohibition of any psychoactive substance as a creditable social policy. It must be noted that under some circumstances, the use of certain substances to modify moods and behaviors may be regarded appropriate. Social norms may be seen as strongly influencing decisions as to whether the use of a psychoactive substance is pathological. For example, the fact that chocolate was made illegal in England for a period of time, years ago, suggests that social factors rather than non-social issues are involved. In the United States the government allows Native Americans tribes in the southwestern United States to use peyote in religious rites. Also, many adults use caffeine in the form of coffee, tea or cola drinks. In addition, on a state-by-state basis, limited use of marijuana for certain medical diseases are allowed by state legal authorities for selected individuals in the United States but on the federal level any use of marijuana is discouraged. In the State of Nevada, a measure to make the use of marijuana legal and a state monopoly was narrowly defeated in recent years after substantial federal pressure was applied.

The above examples argue that it is important to realize that society's views regarding the use of addictive substances are dependent on social factors and may change over time. The first use of many psychoactive substances abused today, it should be noted, was for alleviation of pain during surgery. The father of psychoanalysis, Sigmund Freud, for example, advocated the use of cocaine as a pain medication. Freud changed his mind regarding the use of cocaine after the addiction potential became clear. Substances such as chocolate, tobacco and alcohol that were earlier prohibited by society are legal and accepted today. Alternately, many substances that are illegal now were legal some years ago. The problem of psychoactive drug abuse is of great importance and all persons need to understand the multiple aspect of this important problem as society must make wise decisions as to which psychoactive substances should be prohibited. Perhaps the most important scientific factor that should be considered is the physical effects of psychoactive substance on the human brain. Psychoactive substances by definition are drugs that affect the human brain. The possible negative effects of drugs of abuse on the human brain should be considered in making social decisions regarding prohibition of psychoactive drugs. The effects on the human brain are, of course, not the only factor to consider in formulating America's drug abuse policy but it is an area regarding which clinical child neuropsychologists have unique scientific expertise that can be used to inform national and state policy makers.

The use of psychoactive drugs that may be abused by children is an issue of great important concern. Because children are in a developmental period and their brains are still maturing the effects of drugs of abuse may be more impairing than when adults whose brains are mature abuse similar drugs. Also, drug abuse by children of school age may preclude education processes. The use of drugs of abuse by school age children may interfere with learning and memory

processes that underlie their mental abilities to profit from educational instruction. The aim of this chapter is to review what is currently known about psychoactive drugs of abuse, the negative neuropsychological effects of exposure to psychoactive drugs and approaches to the neuropsychological assessment of children and youth that have been exposed to drugs of abuse, with special attention to the role of child clinical neuropsychologists.

Overview

Research has documented that there are neuropsychological effects from psychoactive drugs of abuse (Horton, 1996). Because of the extent of drug abuse, as earlier reported, there are important implications for the assessment and treatment of drug abusers (Spencer & Boren, 1990). Tarter and Edwards (1987) were among the first researchers to address the issue of impaired functional adaptive capacity of individuals with substance abuse problems. Tarter and Edwards (1987) averred that the use of neuropsychological assessment to measure an individual's organic integrity would provide a basis for estimating an individual's potential for recovery and future adaptive ability. For children who are of school age, the degree and pattern of neuropsychological impairment can provide important information to guide educational instructional decisions.

Studies to assess the neuropsychological treatment implications in populations of drug abusers are few because agreement that there are residual neuropsychological effects of abused drugs in adults and children is a recent advance (Spencer & Boren, 1990). It should be noted that a distinction should be made between residual and transient neuropsychological deficits caused by psychoactive drugs of abuse (Spencer & Boren, 1990). As is well known, selected drug-related states such as intoxication and withdrawal and delirium are considered to be relatively transient. For example a person could drink too much alcohol and for a time be incapable of operating a motor vehicle for a period of time but after some hours would regain the ability to drive safely. While the effects on learning and memory and executive functioning from intoxication from alcohol are serious, it is expected that with most individuals these effects

are state dependent rather than enduring after withdrawal from alcohol and in some cases other abused substance or substances. The residual neuropsychological effects of psychoactive drugs to be examined in this chapter would be expected to be enduring organic syndromes of greater time duration.

Regarding the other substance abuse syndromes, other than alcohol, the major substance abuse syndromes associated with organic deficits recognized by (APA, 2000) include post-hallucinogen perception disorder, PCP organic mental disorder not otherwise specified and amnesic disorder caused by sedative hypnotic drugs.

Brain Structures and Processes Underlying Addictive Behaviors

Because the brain is the organ which subsumes human behavior, a basis understanding of the brain structures and processes underlying addictive behavior is essential to understand substance use and abuse. The notion is that understanding brain–behavior relationships will aid in gaining insight into behavior that often appears painful and chaotic. Addiction processes based in the brain result from changes to the reward pathway upon exposure to psychoactive drugs such as cocaine, heroin, and marijuana, among others (Figure 1).

Reward pathways promote positive conditioning whereby behaviors that precipitate the experience of pleasure are increased. The brain associates the behavior to the feeling of pleasure, and the behavior increases in frequency in expectation of eliciting the same pleasurable experience again. An exposition of neurophysiology, admittedly very brief and over simplified, is presented and is followed by examples of drug– brain interaction to provide for a simplistic understanding of the brain processes underlying abuse of psychoactive substances (Figure 2).

The brain is composed of 100 billion cells, known as neurons, and functions intracellular communication. Messages among and between cells are transmitted through chemical and electrical means. The parts of a given individual neuron allow classification relevant to the transmission of information (Figure 3).
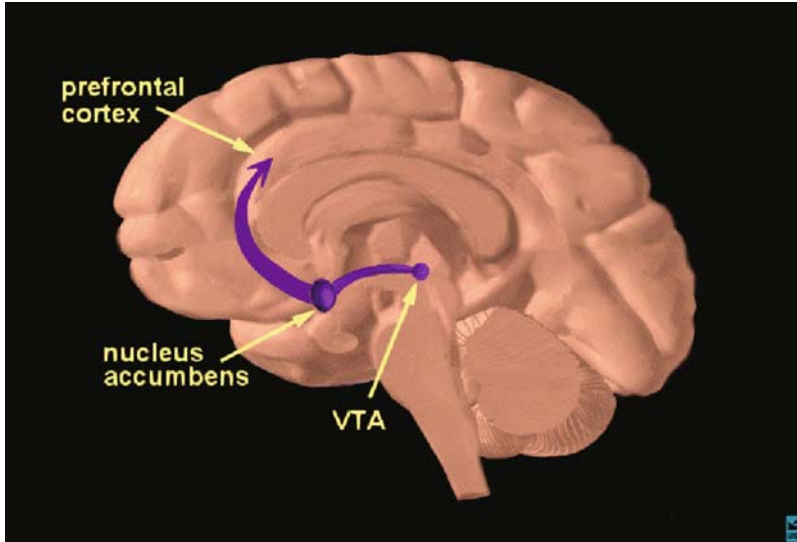
FIGURE 1. The reward pathway consisting of three brain structures the VTA, nucleus accumbens and prefrontal cortex, and the connections between the parts (http://www.nida.nih.gov/pubs/teaching/Teaching3.html).
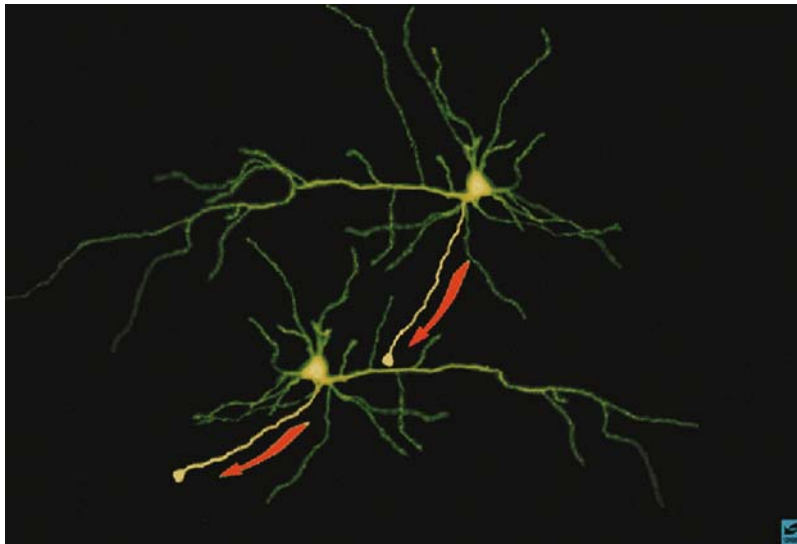
FIGURE 2. Two neurons able to communicate. The arrows designate the route of transferred information (http://www.nida.nih.gov/pubs/teaching/Teaching2.html).

Information from other neurons comes through the dendrites and soma. Initiation of chemical processes in the neuron are elicited in response to inter-neuron transmissions. Each neuron's membrane controls the internal chemical environment of the cell. Cell membranes maintain an electrical potential. The electrical potential is the difference of electrical charge between the inside of the neuron and the outside. The difference results from concentrations of positively and negatively charged ions on each side of the cell membrane. Such differences seek
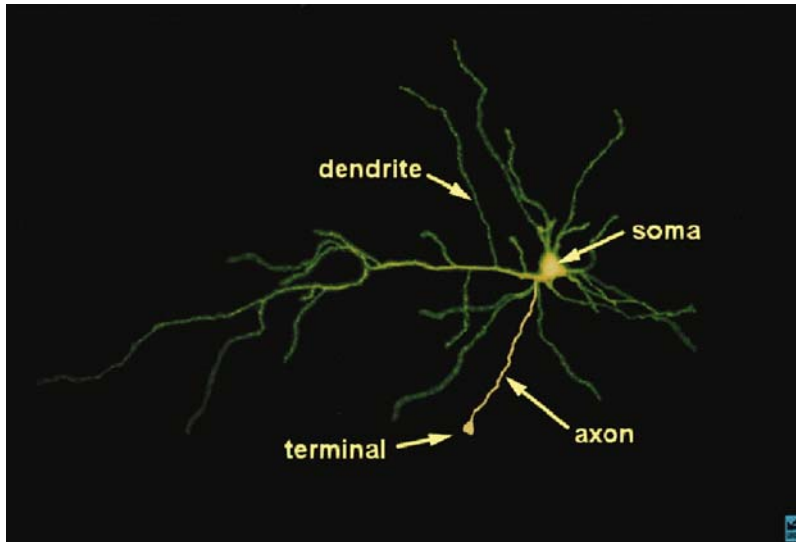
FIGURE 3. An overview of a neuron with its major parts labeled (http://www.nida.nih.gov/pubs/teaching/Teaching2.html).

equilibrium (balance) where the concentrations of ions and thus electrical charge do not differ. Membranes preclude this tendency impeding the flow of ions between the two areas. Ions are allowed to pass through the membrane through channels in the membrane specific for that ion and/or charge. These channels may be activated through a number of mechanisms.

At baseline a neuron is said to be at resting potential prior to receiving signals from other neurons. The dendrites and soma of cells contain receptors which bind selectively with the chemical signals sent between neurons (neurotransmitters). Certain neurotransmitters cause bindings in the electrical potential through the opening and closing of ion channels nearby. When bombarded with signals from surrounding neurons that excite, an action potential is produced. With an action potential, an electrical current travels from the dendrites and/or soma to the axon of the neuron as ion channels sensitive to electrical charge are opened. The cascading effect of ions flowing across the plasma membrane pushes the local electrical potential past its resting equilibrium. The current generated moves to the end of the axon at the terminal. Packages of stored neurotransmitters cause the release of the contained neurotransmitters into the external cellular.

The membrane at the terminal is known as the presynaptic membrane which in combination with the postsynaptic membrane of another neuron forms the synapse. The area in between the two neurons that the neurotransmitters travel is known as the synaptic cleft. When the synaptic cleft is crossed, the neurotransmitters attach to receptors on the postsynaptic membrane. The response of the neuron to the attachment of a receptor will vary with the type of neurotransmitter and the type of receptor. Ion channels will allow for the entering or exit of ions. Neurotransmitters leave the receptor after attaching and then are taken from the synaptic cleft by uptake pumps on the terminal of the presynaptic membrane. The process of inter-neuron communication is the method by which information moves through the brain. Reward pathways related to the development of addiction have been associated with the neurotransmitter dopamine, among other neurotransmitters, because of its prevalence in the reward pathway. Also, neuromodulators (endorphins) bind to both pre-synaptic and postsynaptic receptors to modify neuronal responses synaptic activity (Figure 4).

The human brain has multiple structural subdivisions. The different brain structures subsume specific neuropsychological functions and interact with one another to yield more complex and abstract behaviors. Examples of brain structures related to function are the hippocampus and memory, parietal lobes and tactual perception,
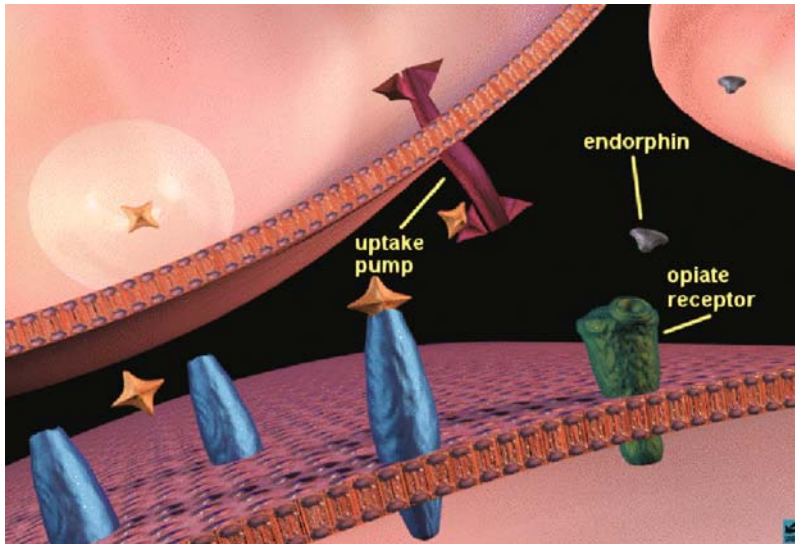
FIGURE 4. A synapse with the presynaptic neuron on the top releases a neurotransmitter and on the bottom the postsynaptic neuron contains two types of receptors (http://www.nida.nih.gov/pubs/teaching/Teaching4.html).

temporal lobes and auditory perception, visual cortex and sight and hypothalamus and homeostasis. Routes of communication between structures rely on intra-neuronal interaction, and the interconnections send and integrate information between and among brain regions. A particular example is the brain reward pathway which is associated with the development of addictions. The brain reward pathway progresses from the ventral tegmental area (VTA) to the nucleus accumbens to the prefrontal cortex. The brain reward pathway is activated when positive reinforcement (a reward) occurs paired in time with a certain behavior (www.nida.nih.gov/pubs/Teaching/). The behavior in close temporal sequence becomes associated to the reward. Living organisms perform the behavior so long as a positive reinforcer (reward) accompanies the behavior. Positive reinforcers may vary in reinforcement potency depending on temporal factors. For example, if a person has not eaten for several hours then a preferred food may be a positive reinforcer but after a heavy meal more food may not be seen as a positive reinforcer (reward), but after several hours things would change. It is well established from experimental results that stimulation of the nucleus accumbens or VTA with cocaine activates the brain reward pathway. Activation of the brain reward pathway did not occur with cocaine administered to other parts of the brain even if in close proximity to parts of the brain reward pathway.

Psychoactive substance can establish relationships between feelings of pleasure and drug-taking behavior by activating the brain reward pathway. This activation of the brain reward pathway causes drug-taking behavior to be selected over behaviors such as eating or hygiene or parenting. Changes in brain function that are good examples of drug–brain interaction are cocaine, heroin and marijuana. Other psychoactive drugs affect the brain in similar ways to these three examples. For example, the frequently abused drug cocaine when smoked, snorted or injected yields high concentrations in the VTA and nucleus accumbens where dopamine is heavily used in transmissions between neurons. The high concentration of the abused drug cocaine in these areas binds to dopamine's uptake pump precluding it from removing dopamine from the synapse. Thereby increasing brain reward pathway stimulation and causing feelings of pleasure (Figure 5).

Synaptic dopamine levels and dopamine receptors activity both increase. Dopamine receptors bind to a G-protein. The G-protein with the inclusion of an enzyme forms a dopamine receptor–G-protein/adenylate cyclase complex. The enzyme is turned on and produces cAMP
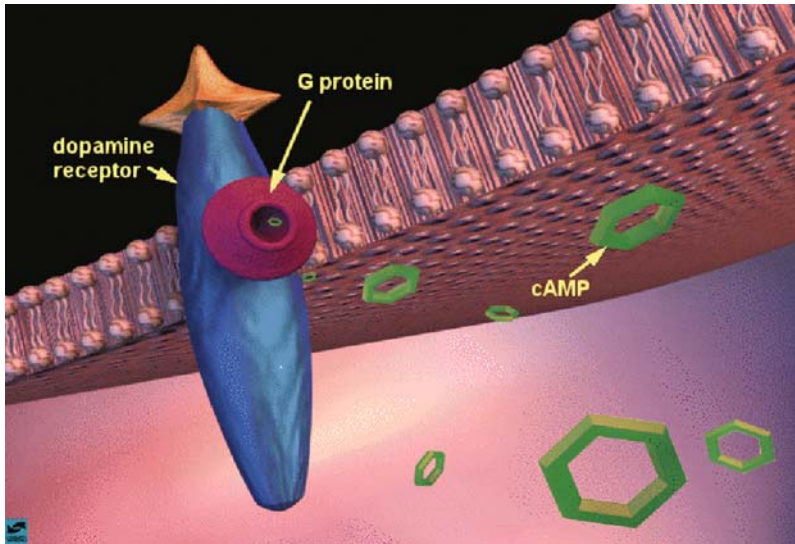
FIGURE 5. The normal effects of the neurotransmitter, dopamine bound to a dopamine receptor. Here, an enzyme is activated to produce a certain molecular compound (http://www.nida.nih.gov/pubs/teaching/Teaching2.html).
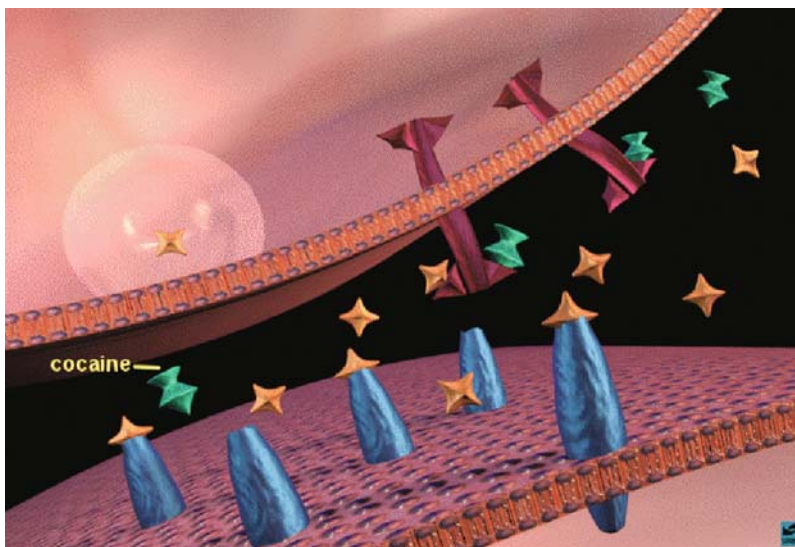
FIGURE 6. Cocaine in the synapse blocks the uptake pump increasing dopamine activity (http://www.nida.nih.gov/pubs/teaching/Teaching4.html).

(cyclic adenosine monophosphate) molecules which control the neurons ability to generate action potentials (Figure 6).

Cocaine increases the amount of cAMP in the postsynaptic neuron with the net effects of increased activation of the brain reward pathway (Figure 7). Because of the temporal association of cocaine use with increased activation of the brain reward system, use of cocaine is associated with feelings of pleasure. The activation of
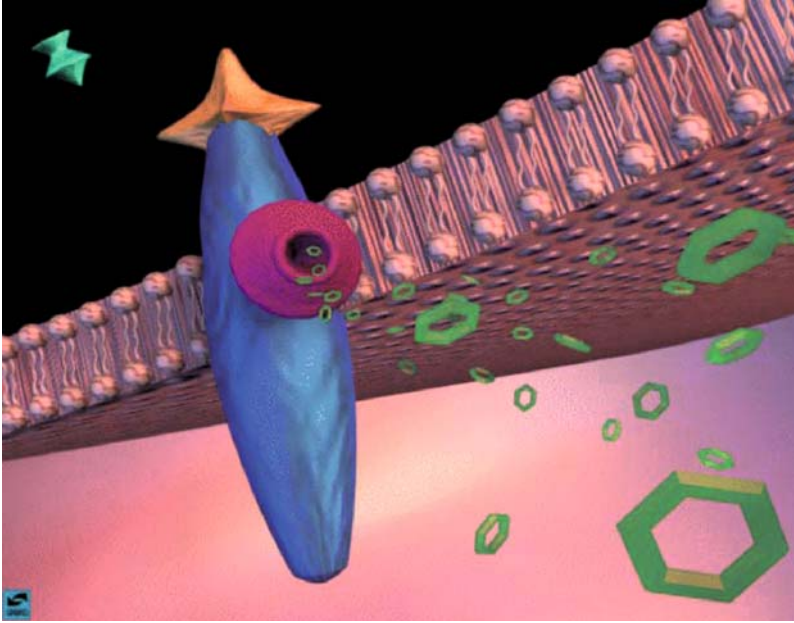
FIGURE 7. The effects of increased dopamine in the presence of cocaine. Contrast to Figure 5 to see difference in activity and production of cAMP (http://www.nida.nih.gov/pubs/teaching/Teaching4.html).

the brain reward pathway is responsible for the addictiveness of cocaine. At the same time, however, cocaine invades other brain areas. For example, use of cocaine impairs the brain's ability to utilize glucose (energy fuel of the brain) for metabolic activity. Ineffective use of glucose can cause impairment of brain functions not related to the brain reward system.

Opiates and other psychoactive drugs can activate cells in the VTA and nucleus accumbens of the reward pathway and increase dopamine release. The cellular mechanisms by which opiates activate the brain reward system, however, differ from those of cocaine. Opiates bind to opiate receptors other than the presynaptic neuron or the postsynaptic neuron. Opiates bind rather to an additional neighboring neuron. Opiate binding to the neuron influences the neuron to send signals to the dopamine terminals to increase the amount of dopamine released. Higher levels of synaptic dopamine released produces greater production of cAMP in the postsynaptic neuron and the brain reward pathway is activated. Again, the association of the use of opiates and other psychoactive drugs with feelings of pleasure produces addiction to the drug (Figures 8 and 9).

Marijuana, in terms of drug–reward pathway interaction, requires additional explanation relative to the well-explained cocaine and opiates reward pathway systems. Marijuana is represented by its active ingredient cannabinoids or THC (delta-9-tetrahydrocannabinol). It is established that regions of the reward pathway such as the VTA and nucleus accumbens contain high concentrations of THC receptors. It is postulated that THC activation of the reward system follows a process similar to that of the opiate with a neighboring neuron yielding more production of cAMP in the postsynaptic neuron (Figure 10).

The human reward pathway is activated by impulses sent from the nucleus accumbens to the prefrontal cortex. While the short term or transitory effects of THC are well studied, the residual effect of marijuana use on the reward pathway will require additional study. As with other psychoactive drugs, THC can be found in brain areas other than the brain reward system pathway. For example, it has been established that presence of THC in the hippocampus reduces memory function, and in the cerebellum the presence of THC can cause transient lack of coordination and loss of balance.
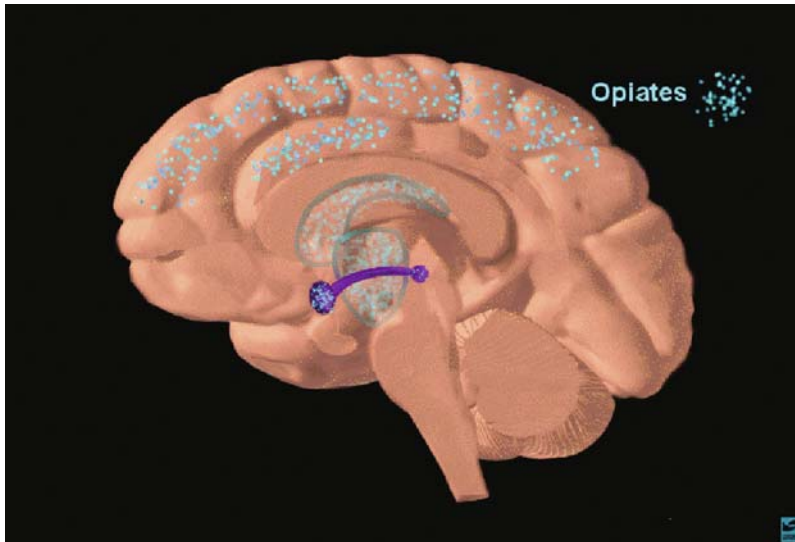
FIGURE 8. A side view of the brain showing where opiates are found and active in the brain (http://www.nida.nih.gov/pubs/teaching/Teaching4.html).
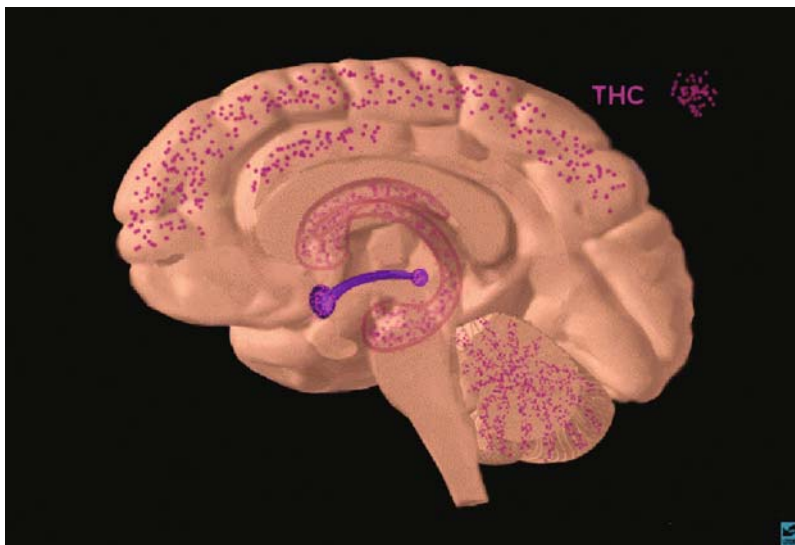
FIGURE 9. Areas where THC is found and active in the brain (http://www.nida.nih.gov/pubs/teaching/Teaching5.html).

Psychoactive Substance Abuse Research Issues

In order to understand the residual effects of different psychoactive substances of abuse some discussion of possible residual effects of drug using behaviors would be necessary. Following sections will present cursory reviews of the neuropsychological test research data currently available regarding the residual effects of various psychoactive abused substances. There are, however, many very serious methodological
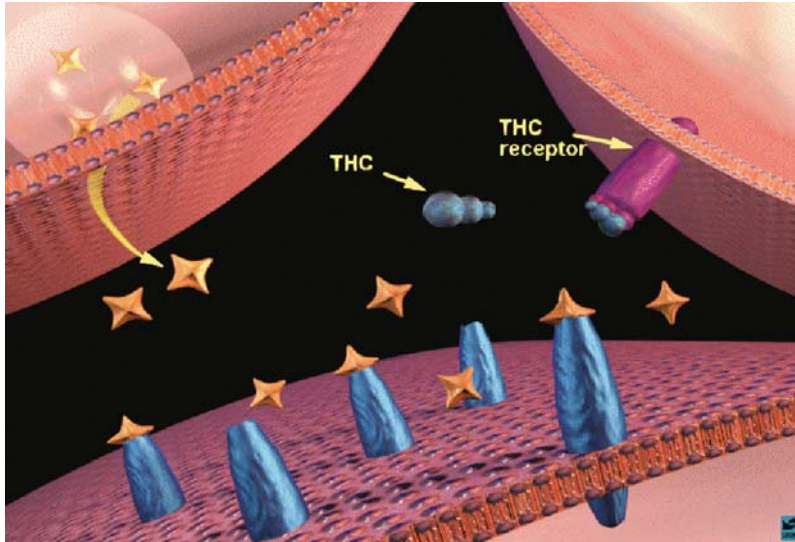
FIGURE 10. High level of dopamine resulting from THC binding to its receptor on a neighboring neuron (http://www.nida. nih.gov/pubs/teaching/Teaching5.html).

difficulties involved with measuring residual drug abuse effects in human beings. Prior reviews by Reed and Grant (1990) and Horton (1996) addressed many of these issues. As is well known, some neuropsychological tests are correlated with demographic variables such as age, gender, ethnicity and education. The issue of correcting for age, gender and education methodological confounds is very complex. While age, gender, ethnicity and education norms for a number of neuropsychological tests have been developed to address this problem area (Heaton, Miller, Taylor, & Grant, 2004), there are multiple methodological limitations to the new demographic norms and the problems of correcting demographic variables that are too numerous to be detailed (Fastenau & Adams, 1996; Fastenau, 1998; Horton, 1999, Reitan, 1967; Reitan & Wolfson, 1995, 2005).

Also there is the vexing issue of use of multiple substances of abuse. What substances drug abusers have abused is difficult to control in research investigations. Most drug abusers are known as "garbage can" abusers. In brief, they have used a wide variety of psychoactive substances with the most critical variable being availability. Research studies characterize drug abusers as having a preference for one substance, but in reality, their daily consumption of addictive substances is primarily a product of drug availability. In short, the psychoactive substance available is abused. In estimating residual neuropsychological effects of a particular drug of abuse such as cocaine, heroin or marijuana it is very difficult to disengage the effects of a single drug if the research subjects have used all three drugs in combination with alcohol.

Similarly determining the amount of drugs taken by research subjects is very problematic. Most frequently research studies ask patients to estimate post hoc the amount or amounts of a drug or drugs they had previously abused. The research subjects' self-report is solicited days, weeks, months and years after the episode or episodes of substance abuse. Substance abusing patients may be expected in some cases to have impaired memory abilities. Also recall of what drugs were abused can be confounded with the type and pattern of learning and memory deficits.

The issue of assessing residual drugs effects based on the mode of consumption is also problematic. Psychoactive drugs such as cocaine or heroin may be ingested through a number of modalities. For example, drugs can be taken through needle injection, orally or through the nose. Each method of consumption can produce different effects with respect to the action of the

drug and possibly any residual neuropsychological impairment.

In addition, pre-existing and co-existing medical risk factors can also cause residual neuropsychological deficits that could be mistaken for residual neuropsychological deficits due to exposure to drugs of abuse. Tarter and Edwards (1987) were among the first researchers to identify many of these factors. They noted that premorbid and co-existing risk factors could also influence a person's reactions to various drugs. For example, pre-existing factors such as learning disabilities and attention-deficit hyperactivity disorder could both present as residual neuropsychological deficits and possibly interact with similar conditions to produce greater levels of neuropsychological impairment. With respect to co-morbid conditions or factors, a variety of serious psychiatric conditions could co-occur with substance abuse and these mental disorders are very difficult conditions to diagnose in an addict population. Also, it has been averred that poor nutrition (Tarter & Edwards, 1987) can impair neurocognitive functioning. In addition, drugs of abuse can produce medical problems in various organ systems other than the human brain and thus have secondary effects on a person's mental ability. Multiple psychological, psychiatric, medical and nutritional factors can produce residual neuropsychological effects that would need to be distinguished from residual neuropsychological deficits of drugs of abuse in human beings Benedict and Horton (1992).

An additional research issue is that of the criteria to accept that a neurotoxic substance may cause residual neuropsychological deficits in human beings. In many cases, researchers are willing to conclude that a drug may cause residual neuropsychological deficits simply based on a level of performance model. That is to say that for many researchers the sole criterion, for concluding that a drug of abuse causes residual neuropsychological deficits, is low scores on various neuropsychological and intelligence tests (Parson & Far, 1981). The problem with such a conceptualization is that multiple factors may cause low scores on neuropsychological and intelligence tests. When multiple factors are involved selecting a single factor as the only cause is very poor logic. The particular problem with drug abuse research is that because of the health problems associated with drugs of abuse it is not possible to use true random research designs. Rather, only quasi-experimental research designs using non-equivalent control groups can be utilized. Therefore, all drug abuse research with human beings has limited control of potentially confounding variables. The point for concluding that a specific drug of abuse may cause residual neuropsychological deficits is that low neuropsychological and intelligence test scores may be due to another factor other than exposure to a specific drug. In neuropsychological testing, it is well established that there are four methodological methods of inference (Reitan & Wolfson, 1993), such as level of performance, patterns of impairment, specific deficits and left–right comparisons. The usual criterion used to conclude there are residual neuropsychological deficits following exposure to drugs of abuse is level of performance or, in other words, low scores on neuropsychological and intelligence tests. A better model would require that the other methodologies of inference of neuropsychological testing (Horton & Wedding, 1984; Parson & Farr, 1981; Reitan & Wolfson, 1993) such as patterns of impairment, specific deficits and left–right comparisons be satisfied before it can be concluded that a specific drug of abuse would cause residual neuropsychological deficits.

Marijuana/Cannabis

Residual neuropsychological deficits in marijuana abusers are subtle as initial research studies (Mendelson & Mayer, 1972; Grant, Rockford, Flemming, & Stunkard, 1973; Carlin and Trupin, 1977) failed to find significant neuropsychological deficits in marijuana users. The initial studies contained few measures of short-term memory functioning and that could be the reason for the negative results. Later studies which included better measures of short-term memory, however, suggested that memory functions may be impaired after consistent marijuana use (Page, Fletcher, & True, 1988; Schwartz, Gruenewald, Klitzner, & Fedio, 1989). Additional research (Pope & Yurgelun-Todd, 1996) suggested there were residual neuropsychological effects on memory and executive functioning at least for a period of 6 weeks. Bolla, Eldreth, Matochik and Cadet (2005) noted short-term (25 days abstinence) decision-making deficits and decreased

activation in the left medial orbital frontal cortex and increased activation in the cerebellum.

Grant, Gonzalez, Carey, Natarajan and Wolfson (2003) conducted an excellent quantitative synthesis of empirical research (meta-analysis) pertaining to the residual neuropsychological effects of cannabis in adult human subjects. After screening 1,014 studies for methodological flaws, they found 15 studies that were methodologically adequate and which provided data on 704 cannabis users and 484 non-users. Grant et al. (2003) calculated effects sizes for eight neuropsychological ability domains (motor ability, executive functioning, learning and memory, etc.). Essentially an effects size is a statistical method for comparing disparate research studies. In the simplest case the means of control and experimental groups are compared for differences using either the standard deviation of the control group or a pooled standard deviation composed of the standard deviations of both the experimental and control groups. In brief, if the experimental and control groups differ less than a quarter standard deviation the effect is small, half a standard deviation a moderate effect and a strong effect for a full standard deviation difference. The Grant et al., (2003) research group found small but significant effects sizes only for learning and forgetting domains. Grant et al. (2003) postulated that where cannabis compounds are found to have therapeutic value, the use of marijuana for therapeutic purposes might have an acceptable margin of safety in medical settings as the effects size of residual neuropsychological deficits was small and limited to a single neuropsychological domain.

The quantitative meta-analysis described above was limited to adult human subjects only. There is no comparable meta-analysis for children unfortunately. It has been argued that children and adolescents who are in the process of development and undergoing neuropsychological developmental changes, however, may be more vulnerable than adults to the residual neuropsychological deficits effects of cannabis. For example, Fried and Smith (2001) have published research that concluded that executive dysfunction was found in children of mothers who abused small amounts of cannabis in a Canadian sample. Similarly, Goldschmidt, Day and Richardson (2000) published research that concluded there were residual neuropsychological deficits in a United States sample of children of mothers who used cannabis.

Hallucinogens/LSD

Research studies of hallucinogens/LSD have not identified marked residual neuropsychological deficits. Early studies by McGlothlin, Arnold and Freeman (1969) and Acord and Baker (1973) presented initial research findings that suggested possible visual abstraction and concept formation deficits. These neuropsychological deficits were extremely mild and may have been due to the pre-existing or co-morbid risk factors identified by Tarter and Edwards (1987). In the period of time since the early studies no further replications had been conducted. Additional well-controlled research that confirmed earlier findings would be necessary before reaching a conclusion regarding residual neuropsychological deficits.

Ecstasy

The drug "Ecstasy" (3, 4-methylenedioxy-methamphetamine or "MDMA") has been considered a stimulant but it also has hallucinogenic properties which have been more recently appreciated. Ecstasy is different from other hallucinogens and research studies have demonstrated that Ecstasy can impair memory in abstinent users (Bolla, McCann, & Ricaurte, 1998; Zakzanis & Young, 2001). More recent research has demonstrated learning and memory deficits can persist up to a year post-abstain (Parrott, 2001; Reneman, Booj, Majoie, van den Brink, & den Heeten, 2001). In addition, use of Ecstasy was associated with task-switching and the degree of neuropsychological deficit was related to the extent of drug usage (Dafters, 2006).

Opiates

Research studies on opiates and residual neuropsychological deficits are contradictory. An early study with heroin users in a Veterans Administration Medical Center by Fields and Fullerton (1975) found no evidence for residual neuropsychological deficits. Rounsaville, Novelly, Kleber, and Jones (1982) at Yale

University published research that suggested heroin addicts who also were polydrug users had neuropsychological deficits and addicts with the most impairment had childhood histories of hyperactivity and a poorer academic record. The next year, however, the same research group (Rounsaville, Jones, Novelly, and Kleber, 1982) who earlier found neuropsychological impairment conducted a follow-up study (using the same heroin addict subjects as in 1981 study) also found their heroin addict users performed better than demographically similar controls on neuropsychological tests. One possibility is the first study failed to adequately control for demographic and premorbid factors. Another possibility could be that heroin addicts, like professional boxers, are a physiologically superior group and even with a degree of neuropsychological impairment they are more able than normal individuals. There has been little subsequent research on residual neuropsychological impairment in heroin addicts.

Sedatives

In an early study, Judd and Grant (1975) reported residual neuropsychological deficits among sedative abusers but their patients had also been abusers of stimulants, alcohol and opiates. Bergman, Borg, and Holm (1980) found residual neuropsychological deficits in subjects that were treated only for illicit sedative abuse and better controlled for polydrug abuse. Allen and Landis (1998) note the fact that elderly individuals are at greater risk for adverse reactions such as confusion and delirium and neuropsychological impairment. The evidence for organic deficits is so well accepted that (APA, 2000) contains a category for sedative–hypnotic, amnestic impairment.

Phencyclidine (PCP)

PCP or "angel dust" has been reported to provoke violent uncontrollable psychotic outbursts in the absence of an external threat. Research studies have not found strong evidence for residual neuropsychological deficits in PCP users. In one of the few studies on PCP, Carlin, Grant, Adams, and Reed (1979) found very subtle evidence for neuropsychological deficits

and the study used a small sample size and has not been replicated. Indeed, a PCP organic mental disorder category that existed in DSM–III-R was dropped from (APA, 2000). Few conclusions can be confidently drawn regarding the potential effects of PCP use on neuropsychological functioning.

Cocaine

In an early study, O'Malley and Gawin (1990) found a mild degree of neuropsychological impairment in chronic cocaine users but the level of deficits found was mild. More recent studies (Bolla, Funderberk, & Cadet, 2000; Simon et al., 2002; Strickland et al., 1993; Van Gorp et al., 1999) clearly document residual neuropsychological deficits with respect to cocaine abusers. Jovanovski, Erb, and Zakzanis (2005) note that neuropsychological abilities with respect to attention, executive functioning, working memory and declarative memory were the most frequently observed pattern of residual neuropsychological deficits.

There have also been neuroimaging findings that support the notion of residual neuropsychological deficits. For example, Strickland et al. (1993) correlated the results of neuropsychological with single photon emission computerized tomography (SPECT) findings. In addition, Volkow et al. (1992) found decreased blood flow in the frontal lobes of cocaine users. Neurocognitive deficits in cocaine users were suggested to be due to strokes and seizures (Volkow, Mullani, Gould, Adler, & Krajewski, 1988).

Stimulants

Animal research has suggested the possibility of residual neuropsychological deficits in humans due to stimulants but prior studies failed to demonstrate deficits (Reed & Grant, 1990). Recent human studies (Kalechstein, Newton, & Green, 2003; Nordahl, Salo, & Leamon, 2003) have indicated neuropsychological deficits in attention executive functions and memory are related to methamphetamine use. Verbal memory impairment in methamphetamine addicts has been noted to be due to poor verbal encoding and retrieval strategies (Woods et al. (2005).

In addition, Thompson et al. (2004) found structural abnormalities in the brains of human subjects who have used methamphetamine.

Inhalants/Solvents

There is strong evidence for residual neuropsychological deficits after exposure to inhalants/solvents. One of the first studies was a case report by Bigler (1979) which found a generalized pattern of neuropsychological deficits. A subsequent study by Korman, Matthews and Lovett (1981) found clear neuropsychological impairment by inhalant abusers. Korman et al. (1981) found that inhalant abusers were significantly more impaired than other drug abusers with clear neuropsychological effects found on both global measures (such as intelligence and achievement measures) and more specific tests (such as perception of speech sound, sensory perception and set shifting ability). The nature of the neuropsychological deficits found by Korman et al. (1981) suggested that inhalant abuse produces neuropsychological deficits that are severe and widespread. Similarly, Tsushina and Towne (1977) found glue sniffers were neuropsychologically impaired. Moreover, Berry, Heaton, and Kirley (1977) found a group of chronic inhalant abusers impaired on neuropsychological tests. Exposure to organic solvents has also been shown to cause long-term neuropsychological impairment on measures of speed of processing, memory and verbal fluency (Wood and Liossi (2005). Another study (Rosenberg, Grigsby, Dreisbach, Busenbark, & Grigsby, 2002) found that solvent abusers performed worse than other drug abusers on neuropsychological tests of working memory and executive cognitive functions. Interestingly, Rosenberg et al., 2002) also found a dose– response relationship between solvent abuse and MRI findings. Consistent and strong research findings make it possible to conclude that inhalants/solvents cause residual neuropsychological impairment.

Polydrug Abuse

Polydrug abusers are more the norm than an exception in drug abuse research. An early national study by Grant, Mohns, Miller, and Reitan (1976) demonstrated neuropsychological impairment in 50% of a sample of polydrug users. In addition, Judd and Grant (1975) provided evidence for impairment of neuropsychological functioning. There is concern, however, that polydrug users who demonstrate neuropsychological deficits suffer from possible confounds with respect to risk factors that are medical and psychiatric in nature. Some of the poly drug users studied also abused alcohol and the effects seen are more due to alcohol consumption than specific drug effects but others have suggested greater impairment when cocaine and alcohol are combined (Bolla et al., 2000). Additional research is needed to address this issue.

Summary

As noted by Spencer and Boren (1990) there are residual neuropsychological deficits from repeated drug abuse. Nonetheless, the magnitude of effects is subtle. Future research should investigate subcortical effects of the action of drug abuse on the brain rather than use instruments that were developed to focus on cortical functioning. As the most common pattern of deficits found are on measures of attention, memory and executive functioning, very subtle assessments of memory, attention and executive functioning are needed.

In terms of general conclusions regarding residual neuropsychological deficits, it is clear that

1) These neuropsychological deficits are very subtle.
2) They do not impair gross language, motor functioning or sensory– perceptual functioning.
3) They involve higher levels neurocognitive abilities such as attention, short-term memory and executive functions such as visual abstract problem solving and complex concept formation.

It may very well be that some drug abusers can perform relatively well at low level positions or relatively non-demanding social situations, yet they will show pronounced problems with mentally demanding employment tasks or in complex social situations.

This chapter has briefly discussed brain structures and processes underlying addictive

behaviors. Difficulties involved in assessing the residual neuropsychological effects of various psycho–active substances have been alluded to and a very selective review of neuropsychological test results with drug addicts has been presented. The current research with respect to the neuropsychological effects of abused drugs is composed of a small number of flawed studies so there is ample room for additional research.

A crucial research issue is that of the criteria to accept that exposure to a drug may cause residual neuropsychological deficits in human beings. In the past, researchers were willing to conclude that a drug may cause residual neuropsychological deficits simply based on a level of performance model. Many researchers would accept that a drug of abuse causes residual neuropsychological deficits if there are low scores on various neuropsychological and intelligence tests. The conceptualization is flawed because multiple factors may cause low scores on neuropsychological and intelligence tests. When multiple factors are involved selecting a single factor as the only cause is very poor logic. The major problem with drug abuse research with human beings is that because of the health problems associated with drugs of abuse it is not possible to use true random research designs. Rather, only quasi-experimental research designs using non-equivalent control groups can be utilized. Therefore, all drug abuse research with human beings has limited control of potentially confounding variables. The point for concluding that a specific drug of abuse may cause residual neuropsychological deficits is that low neuropsychological and intelligence test scores may be due to another factor that exposure to a specific drug. In neuropsychological testing, it is well established that there are four methodological methods of inference (Reitan & Wolfson, 1993), such as level of performance, patterns of impairment, specific deficits and left–right comparisons. The usual criterion used to conclude there are residual neuropsychological deficits following exposure to drugs of abuse is level of performance or, in other words, low scores on neuropsychological and intelligence tests. A better model would require that the other methodologies of inference of neuropsychological testing (Reitan & Wolfson, 1993) such as patterns of impairment, specific deficits and left–right comparisons be satisfied before it can be

concluded that a specific drug of abuse would cause residual neuropsychological deficits.

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25

Neuropsychological Aspects of Attention-Deficit Hyperactivity Disorder

SAM GOLDSTEIN AND KORDELL KENNEMER

The childhood cognitive and behavioral problems categorized as disorders of attention, impulsivity, and hyperactivity have over the past 50 years presented a clinical challenge for neuropsychologists. The symptom constellation referred to as *attention-deficit disorder* or *attention-deficit hyperactivity disorder* (ADHD) (APA, 2000) has become one of the most widely researched areas in childhood and adolescence with an increasing interest throughout the adult life span. Problems arising from this constellation of symptoms have constituted the most chronic childhood behavior disorder (Wender, 1975) and the largest single source of referrals to mental health centers (Barkley, 1990; Gadow, Sprafkin, & Nolan, 2001). In clinic-referred settings males outnumber females 6 to 1. In epidemiological studies of community-based settings the ratio is 3:1 (Barkley, 1990). The incidence of diagnosis continues to increase with a 70% increase in the diagnosis of children and nearly a 100% increase in the diagnosis of adults between 2000 and 2003 (CDC, 2005). It is now estimated that between 4 and 8% of the population has received a diagnosis of ADHD (CDC, 2005; Cuffe, Moore, & McKeown, 2005). Females are the fastest growing group (Medco, 2005). Broad-based definitions of ADHD find epidemiology of nearly 16% in adults while more narrow definitions report an incidence of 3–4% (Faraone & Biederman, 2005). Additionally, incidence has been reported to be higher in populations of individuals with other impairments (Altfas, 2002).

Even as neuropsychologists utilize the current diagnostic criteria involving symptoms of inattention, hyperactivity, and impulsivity, increasing data have been generated to suggest that for the majority of affected children impulsivity and impaired executive functions represent core deficits (for review see Goldstein & Schwebach, 2005; Barkley, 2006). Children with ADHD typically experience difficulty in all aspects and situations of their lives. Their behavior is often uneven, unpredictable, and inconsistent. Neuropsychologists evaluating ADHD today must be concerned not only with the core symptoms of this disorder and their impact on childhood, but with the significant secondary impact these problems have upon children's current and future lives as well as the lives of their family members. An increasing body of research is demonstrating increased vulnerability adults with ADHD face for psychiatric, emotional, cognitive, academic, vocational, substance, and antisocial problems (Barkley, Fischer, Smallish, & Fletcher, 2004; Barkley & Gordon, 2002; Murphy, Barkley, & Bush, 2002).

In part, the controversy and at times confusion concerning various aspects of ADHD may be the result of a tradition to view this disorder as a unitary phenomenon with a single

SAM GOLDSTEIN • Department of School Psychology, George Mason University, Fairfax, Virginia 22030. KORDELL KENNEMER • Oregon State Hospital, Portland, Oregon 97232.

cause. Voeller (1991) suggests that rather than viewing ADHD as a single behavioral abnormality with associated comorbidities it may be better to conceptualize ADHD as a "cluster of different behavioral deficits, each with a specific neuro-substrait of varying severity occurring in variable constellations and sharing a common response to psychostimulants" (S4). There is no doubt, however, that the cluster of symptomatic problems that comprise the diagnosis of ADHD represents a distinct disorder from others of childhood and adulthood (Biederman et al., 1996; Accardo, Blondis, & Whitman, 1990). A significant percentage of affected youth continue to demonstrate the condition into adulthood, often under-reporting their symptoms and impairment relative to observers (Barkley et al., 2004). The consensus among researchers and clinicians is that the core symptoms of ADHD effect a significant minority of our population. For affected individuals, however, ADHD represents a poor fit between societal expectations and these individuals' abilities to meet those expectations. This phenomenon is distinct from other disorders of child and adulthood and can be reliably evaluated and effectively treated.

Toward a Working Definition of ADHD

From a neuropsychological perspective the concept of attention as an executive function has gained increasing popularity. Sustained mental effort, self-regulation, planning, execution, and maintenance are considered measures of executive functioning (Daigneault, Braun, & Whitaker, 1992). Mirskey, Anthony, Duncan, Ahearn, and Kellam (1991) developed a neuropsychological model of attention defining four basic concepts involving the ability to focus, execute, sustain or code, and shift. Eight traditional assessment measures of attention were used in a factor analytic study to arrive at this model.

Increasingly, there is a consensus that ADHD represents a problem of faulty performance rather than faulty input. It is not so much that this population of individuals does not know what to do but they do not do what they know consistently. It is a problem of inconsistency rather than inability (Goldstein & Goldstein, 1998). Even in their adaptive skills, this pattern of difference between possessing a skill and using it efficiently has been well defined for individuals with ADHD.

As DSM-V is not expected to be published in 2012, it is important for neuropsychologists to possess a working understanding of the DSM-IV-TR diagnostic criteria for ADHD, a practical understanding of the manner in which the symptoms impact the individual's functioning, and a diagnostic strategy. The traditional disease model is not relevant to the definition of ADHD (Ellis, 1985). ADHD is more like obesity or intelligence. Individuals differ not in having or not having the traits but in the degree of manifestation. ADHD symptoms are multi-dimensional rather than unitary (Guevremont, DuPaul, & Barkley, 1993). However, there continues to be discussion as to which dimensions represent the most distinguishing deficits of the disorder. The frequency and severity of symptoms fluctuate across settings, activities, and caregivers (Tarver-Behring, Barkley, & Karlsson, 1985; Zentall, 1984). Neuropsychological profiles have also been demonstrated to differ between subtypes (Chabildas, Pennington, & Willicutt, 2001). However, these differences have not lent themselves to a differential diagnosis. There is a general consensus, however, that symptoms of ADHD fall into two broad factors defined by those related to the behavioral manifestation of faulty attention and those related to hyperactivity and impulsivity (Faraone, Biederman & Friedman, 2000; Crystal, Ostrander, Chen, & August, 2001). Symptoms of hyperactivity and impulsivity appear to co-occur at such a high frequency that it is difficult on a factor analytic basis to separate them. However, research has demonstrated subtype differences in neuropsychological profiles and patterns of comorbidity (Eiraldi, Power, & Nezu, 1997). It is also important for neuropsychologists to recognize that at times the lines blur between the symptoms and consequences or impairments of ADHD. Thus, a diagnostic strategy for ADHD should include identifying symptoms as well as a list of skills and life impairments hypothesized to be directly impacted by symptoms (Gordon et al., 2006). Having the symptoms but not having a negative impact would, in fact, preclude the diagnosis of ADHD according to current DSM-IV-TR criteria.

The DSM-IV diagnostic criteria published in 1994 made an effort to move forward and correct the mistaken course that ADHD represents a unipolar disorder. The field studies for

the ADHD diagnosis were more comprehensive and better structured than previous efforts. The DSM-IV-TR (APA, 2000) criteria appear in Table 1. They are identical to the DSM-IV criteria. Since DSM-III, each succeeding diagnostic protocol has focused increasingly on the issue of impairment. Impairment has and will continue to be a critical lynchpin in making the diagnosis of ADHD but is not well explained by symptom severity (Gordon et al., 2006). Further, the

TABLE 1. DSM-IV-TR Criteria for Attention-Deficit/Hyperactivity Disorder

The guidelines for a diagnosis of ADHD outlined in the *Diagnostic and Statistical Manual of Mental Disorders* (4th Edition – Text Revision, 2001) are as follows:

A. Either(1) or (2):

(1) Six or more of the following symptoms of **inattention** have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Inattention

   a. often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities

   b. often has difficulty sustaining attention in tasks or play activities

   c. often does not seem to listen when spoken to directly

   d. often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)

   e. often has difficulties organizing tasks and activities

   f. often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)

   g. often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)

   h. is often easily distracted by extraneous stimuli

   i. is often forgetful in daily activities

(2) six (or more) of the following symptoms of **hyperactivity-impulsivity** have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

   a. often fidgets with hands or feet or squirms in seat

   b. often leaves seat in classroom or in other situations in which remaining seated is expected

   c. often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)

   d. often has difficulty playing or engaging in leisure activities quietly

   e. is often "on the go" or often acts as if "driven by a motor"

   f. often talks excessively

Impulsivity

   g. often blurts out answers before questions have been completed

   h. often has difficulty awaiting turn

   i. often interrupts or intrudes on others (e.g., butts into conversations or games)

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years

C. Some impairment from the symptoms is present in two or more settings (e.g., at school [or work] and at home)

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning

E. The symptoms do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder (e.g., Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).

Types

Attention-Deficit/Hyperactivity Disorder, Combined Types: if both Criteria A1 and A2 are met for the past 6 months

Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type: if Criterion A1 is met but Criterion A2 is not met for the past 6 months

Attention-Deficit/Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type: if Criterion A2 is met but Criterion A1 is not met for the past 6 months

TABLE 1. (continued)

Coding note: For individuals (especially adolescents and adults) who currently have symptoms that no longer meet full criteria, "In Partial Remission" should be specified.

Attention-Deficit/Hyperactivity Disorder Not Otherwise Specified

This category is for disorders with prominent symptoms of inattention or hyperactivity-impulsivity that do not meet criteria for Attention-Deficit/Hyperactivity Disorder.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed. – text revision). Washington, DC: Author.

measurement of neuropsychological processes may also be considered as part of the DSM-V criteria for DHD (Goldstein & Naglieri, 2006).

Of the 276 children diagnosed with ADHD in the DSM-IV field studies 55% had the Combined Type, 27% the Inattentive Type, and 18% the Hyperactive-Inattentive Type (Lahey et al., 1994). Less than half of the ADHD Hyperactive Type (44%) received that diagnosis when DSM-III criteria for ADD with Hyperactivity were used. These two diagnoses, therefore, only partially overlapped. The hyperactive-impulsive group had fewer symptoms of inattention in comparison to children with the Combined Type. They also had fewer symptoms of hyperactive-impulsive problems suggesting that this represents a less severe variant of the disorder. The hyperactive-impulsive group contained 20% females, the combined group 12%, and the inattentive group 27%. This latter number represents neuropsychologists' perceptions that females more often demonstrate the Inattentive Type of ADHD (Biederman et al., 2002). This over-representation has not been well explained by any theoretical model (Silverthorn, Frick, Kuper, & Ott, 1996) nor has it been understood why preliminary research suggests that females with ADHD may be less likely to demonstrate executive function deficits than males (Seidman et al., 1997). The hyperactive-impulsive population was also younger in the field studies. Additionally, they had fewer disruptive symptoms of oppositional defiance or conduct disorder than the Combined Type of ADHD.

A number of researchers have demonstrated the validity of the current DSM-IV diagnostic conceptualization for ADHD utilizing a variety of clinical and laboratory measures. Such research has included a full battery of neuropsychological tests (Brand, Das-Smaal, & De Jonge, 1996; Halperin et al., 1993; Harrier & DeOrnellas, 2005): reversal and memory tasks (O'Neill & Douglas, 1996); executive function tasks (Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2005; Hart & Harter, 2001; Clark, Prior, & Kinsella, 2000); and neurological evaluation (Luk, Leung, & Yuen, 1991). The general consistency of symptom, comorbid, and related findings among large, well-controlled clinic and epidemiologic studies suggest that the conceptualization of ADHD in DSM-IV has become increasingly more refined. Nonetheless, these criteria continue to focus excessively on inattention as the primary problem for the disorder, limiting the scope and focus on the impact of impulsivity as the core deficit. This perpetuates a number of major misconceptions, including that the Inattentive Type of ADHD represents a subtype of the combined disorder (Anastopoulos, Barkley, & Shelton, 1994). Increasing research suggests that it does not. More likely, the Inattentive Type represents a distinct disorder, primarily reflecting difficulty attending to repetitive, effortful tasks and problems with organization. Carlson and Mann (2002) described children with the Inattentive Type ADHD as distinct from the Combined Type as possessing hypoactivity, lethargy and a lack of ability to stay focused. The problems this group experiences may very well be the result of faulty skills as opposed to inconsistent or inadequate use of skills. There is also emerging data raising questions about the lack of stability of DSM-IV ADHD subtypes over time as children mature (Lahey, Pelham, Loney, Lee, & Willcutt, 2005).

The Genetics and Etiology of ADHD

ADHD is among the most common disorders of childhood. It is estimated that it affects between 5 and 8% of the population throughout life. Estimates vary with the American Psychiatric Association suggesting an incidence of 4–6%

(APA, 2000). Statistics vary depending upon populations studied, thresholds, and definitional criteria (Sherman, Iacono, & McGue, 1997). The genetic contribution has been postulated by a number of authors (Hechtman, 1993; Rutter et al., 1990; Swanson et al., 2000). The underlying mechanism genetically has recently been suggested to be associated with a single dopamine transporter gene (Cook et al., 1995) as well as with a variation in the DRD4 (LaHoste et al., 1996) and DRD5 (Lowe et al., 2004) receptor genes as well as in the DAT1 transporter (Winsberg & Comings, 1999). Further, it has been suggested that the trait locus for reading disability on chromosome 6 identified by Cardon et al. (1994) may also be a locus for ADHD (Warren et al., 1995).

Eaves et al. (1993) note two complementary approaches to the genetic analysis of ADHD. The first, a dimensional approach, involves the study of a normal range of activity and assumes that ADHD is at one end of the continuum or trait. The second, a categorical approach, is based upon studying children of families who meet diagnostic criteria and assumes that ADHD is a discrete disorder (Faraone et al., 1992). It is important for neuropsychologists to recognize that dimensional approaches have been found to better predict life outcome (Fergusson & Horwood, 1995).

Among trait approaches Willerman (1973) found the heritability of scores on an activity questionnaire to be 0.77 for a sample of 54 monozygotic and 39 dizygotic twin pairs. However, Goodman and Stevenson (1989) reported a heritability estimate of greater than 1 in a sample of 285 twin pairs. This finding appeared to be due to an extremely low dizygotic correlation. Corresponding dizygotic correlations for father and teacher reports were much higher, resulting in heritability estimates from 0.48 to 0.68. A subsequent twin study by Thapar, Hervas, and McGuffin (1995) using the same three activity items confirmed the low dizygotic correlation in maternal ratings and suggested the role of reciprocal sibling interactions in which twins interact with each other to be different or mothers exaggerate differences between their dizygotic twins. The low dizygotic correlation may, however, be unique to these specific questions about activity level. Edelbrock, Rende, Plomin, and Thompson (1995) reported correlations predominantly from mothers' of 0.86 for monozygotic

twins and 0.29 for dizygotic twins, giving a heritability estimate of 0.66. Zahn-Waxler, Schmitz, Fulker, Robinson, and Emde (1996) obtained a very similar estimate (0.72). However, somewhat lower heritability values were obtained from fathers' and teachers' ratings and the correlations between raters was low.

From a categorical or diagnostic approach Goodman and Stevenson (1989) demonstrated a proband-wise concordance rate of 51% in 39 monozygotic twin pairs and 30% in 54 dizygotic twin pairs, yielding a heritability estimate of 0.64. De Fries and Fulker (1985, 1988) utilizing a statistical method developed by Gillis, Gilger, Pennington, and De Fries (1992) estimated the heritability of ADHD as 0.91 ± 0.36 for twins participating in a research project.

The issue of phenotypic definition as indicated by the variation in estimates of siblings' risk as 53, 25, or 17%, depending upon whether the behavior is defined as hyperactivity, attention-deficit disorder, or ADHD, speaks to the complexity of relating phenotype to genotype (Biederman, Faraone, Keenan, Knee, & Tsuang, 1990; Biederman et al., 1992; Safer, 1973; Faraone et al., 1992). Levy, Hay, McStephen, Wood, and Waldman (1997), based upon a cohort of 1938 families with twins and siblings aged 4–12 years recruited from the Australian National Health and Medical Research Council Twin Registry, reported that ADHD is best viewed as the extreme of behavior that varies genetically throughout the entire population rather than as disorder with discreet determinants. In this study, as with others, heritability estimates for monozygotic versus dizygotic twins were significantly higher. As Levy et al. note, ADHD has an exceptionally high heritability compared with other behavioral disorders. These authors reported that 82% of monozygotic twins and 38% of dizygotic twins met an 8-symptom ADHD cut-off for proband concordances.

Studies linking polymorphisms in the dopaminergic system to ADHD (Comings, Wu, & Chiu, 1996) and the DRD4 receptor polymorphisms to dimensional aspects of impulsivity (Benjamin et al., 1996; Ebstein et al., 1996) suggest that polymorphisms identified to date do not account for all of the relevant, heritable variation. The findings of Sherman et al. (1997) suggest that future molecular-genetic studies of ADHD may yield more information defining ADHD as a disorder composed of two quantitatively, continuously distributed dimensions –

inattention and hyperactivity/impulsivity – rather than a homogeneous categorical disorder.

Etiology of ADHD must also be considered from a related disorders or teratogen basis. Fragile X, Turner's syndrome, Tourette's, neurofibromatosis, sickle cell anemia, fetal ketonuria, Noonan's syndrome and Williams syndrome are all chromosomal and genetic abnormalities in which attentional problems and ADHD have been reported (Hagerman, 1991; Mautner, Kluwe, Thakker, & Laerk, 2002). Bastain et al. (2002) suggest that expensive laboratory tests for genetic disorders are not indicated unless a genetic disorder is suspect due to family history, clinical signs, or low IQ. Toxins resulting in disorders such as fetal alcohol syndrome, cocaine exposure in utero, lead and vapor abuse, perinatal complications, medical problems such as hypothyroidism, encephalitis, even radiation therapy secondary to leukemia have all been reported as responsible for creating inattentive and impulsive problems (for review see Barkley, 2006; Goldstein & Goldstein, 1998). ADHD and depressive symptoms are commonly identified after pediatric traumatic brain injury but may pre-date the trauma (Bloom et al., 2001).

The neurobiology of ADHD implicates impairment in brain structure, particularly differences in the size of certain structures, interacting with metabolic differences (Zametkin & Rapoport, 1987). Efficient brain metabolism in prefrontal and cingulate regions as well as the right thalamus caudate, hippocampus, and cerebellum have been reported in adults with ADHD (Zametkin, Nordahl, & Gross, 1990). Regional abnormalities of glucose metabolism demonstrated by PET studies generally demonstrate a fundamental biologic difference between ADHD and normal subjects. Castellanos et al. (1996) suggest that connections between the right prefrontal cortex, caudate, and cerebellum reflect the brain's "braking system," a system that operates inefficiently in individuals with ADHD. Semrud-Clikeman et al. (2000) found reversed caudate asymmetry on MRI scans of ten males diagnosed with ADHD. They noted the right prefrontal cortex, cerebellum, and basal ganglia appear to be associated with behavioral measures of inattention and inhibition. Children with ADHD have been found unable to activate the caudate nucleus suggesting core abnormality in this function for ADHD (Vaidya et al., 2005). These authors conclude that children with ADHD experience reduced engagement of a frontal-striatal-temporal-parietal network when engaging in inhibitory tasks.

Developmental Course and Comorbidity

Although the core problems children with ADHD experience are homogeneous reflecting difficulty with impulse control, attention, and hyperactivity, each child's presentation is unique in terms of the manifestation of these problems and associated comorbid factors (Goldstein & Goldstein, 1998). As an increasing body of scientific data is generated concerning the developmental course and adult outcome of children with ADHD, it appears that the comorbid problems they develop rather than the diagnosis of ADHD best predicts their life outcome. ADHD in isolation appears to best predict school struggles, difficulty meeting expectations without the home setting, and possible mild substance abuse as an adult. However, it does not predict the significant negative emotional, behavioral, and personality outcomes that have been reported.

Infants who have been noted to demonstrate difficult temperament do not handle changes in routines well. They exhibit a low frustration threshold and a high intensity of response (Carey, 1970; Chess & Thomas, 1986; Thomas & Chess, 1977). In follow-up studies of such infants, as many as 70% develop school problems (Terestman, 1980). These infants appear at greater risk than others of receiving a diagnosis of ADHD. It is also important to note that these difficult infants exert a significant negative impact on the developing relationship with caregivers – a relationship that is critical in predicting a child's life outcome (Katz, 1997).

Although early symptoms of ADHD may be viewed as transient problems of young children, research data suggest that ignoring these signs results in the loss of valuable treatment time. At least 60–70% of children later diagnosed with ADHD could have been identified by their symptoms during the preschool years (Cohen, Sullivan, Minde, Novak, & Helwig, 1981). Young children manifesting symptoms of ADHD are more likely to present with speech and language problems than are children not suffering from those symptoms (Baker &

Cantwell, 1987) and to develop a wide range of behavioral problems (Cantwell, Baker, & Mattison, 1981; Cohen, Davine, & Meloche-Kelly, 1989; DuPaul, McGoey, Eckert, & Van Brakle, 2001). Current research cogently suggests that the comorbidity of speech and language disorders with ADHD merits routine screening of children suspected of ADHD and language disorders, especially during their younger years. Children with concurrent ADHD and language disorders appear to have a much poorer prognosis than those with ADHD alone (Baker & Cantwell, 1992).

Within school settings children with ADHD appear to be victims of their temperament and of their learning history which often involves beginning but not completing tasks. The negatively reinforcing model utilized by most educators in this circumstance tends to focus on misbehavior rather than on termination of the behavior. This may further disrupt the classroom by having a disinhibitory effect on other students. Although 25 years ago it was suggested that children with ADHD were intellectually less competent than their peers, it appears more likely that weak performance on intellectual tasks results from the impact of impulsivity and inattention on test-taking behavior rather than an innate lack of intelligence (Barkley, 1995). Kaplan, Crawford, Dewey, and Fisher (2000) identified a normal IQ distribution in children diagnosed with ADHD. Children with ADHD often underperform but may not underachieve during the elementary years. However, by high school it has been reported that at least 80% of these children fall behind in a basic academic subject requiring repetition and attention for competence such as basic math knowledge, spelling, or written language (for review see Barkley, 2006; Goldstein & Goldstein, 1998). Depending upon diagnostic criteria, approximately 20–30% of children with ADHD also suffer from a concomitant, often language-based, learning disability (for review see Willcutt & Pennington, 2000). Although it has been hypothesized that ADHD may prevent a child from achieving his/her academic potential (Stott, 1981), the presence of a learning disability may make a child appear more inattentive than others (McGee & Share, 1988; Aaron, Joshi, Palmer, Smith, & Kirby, 2002).

Sociometric and play study suggests that children with ADHD are not chosen as often by their peers to be best friends or partners in activities (Pelham & Milich, 1984; Bagwell, Molina, Pelham, & Hoza, 2001). They appear to be cognizant of their difficulties, an awareness that likely precipitates lower self-esteem for children with ADHD (Glow & Glow, 1980). Moreover, they appear to experience either high incidence–low impact problems which result in poor social acceptance or low incidence–high impact problems which result in social rejection (Pelham & Milich, 1984). In addition, these children have difficulty adapting their behavior to different situational demands (Whalen, Henker, Collins, McAuliffe, & Vaux, 1979). It has been suggested that the impulsive behavioral patterns of children with ADHD are most responsible for their social difficulty, making those with comorbid hyperactive-impulsive problems of greater severity at even greater risk of developing social difficulties (Pelham & Bender, 1982; Hodgens, Cole, & Boldizar, 2000). ADHD has been found to be a risk factor heading to a wide variety of ineffective social-coping strategies as youth transition into adolescence (Young, Chadwick, Heptinstall, Taylor, & Sonuga-Barke, 2005). It should also be noted that children who are good responders demonstrating symptom and impairment reduction with medication appear to exhibit fewer chronic social impairments (Gallagher et al., 2004).

Some primary symptoms of ADHD may diminish in intensity by adolescence (Weiss & Hechtman, 1979). However, most adolescents with ADHD continue to experience significant problems (Milich & Loney, 1979; for review see Goldstein & Ellison, 2002; Barkley, 2006). At least 80% of adolescents with ADHD continue to manifest symptoms consistent with ADHD. Sixty percent develop at least one additional disruptive disorder (Barkley, Fischer, Edelbrock, & Smallish, 1990). Between 20 and 60% of adolescents with ADHD are involved in antisocial behavior, with a normal occurrence of 3–4% (Satterfield, Hoppe, & Schell, 1982). At least 50–70% of these adolescents develop oppositional defiant disorder, often during younger years, with a significant number progressing to conduct disorder (Barkley, Fischer, Edelbrock, & Smallish, 1991). However, the high prevalence of antisocial problems in adolescents with ADHD likely reflects the comorbidity of ADHD with other disruptive disorders, principally conduct disorder (Barkley, McMurray, Edelbrock, & Robbins,

1989). As Barkley (1997) succinctly points out, the preponderance of the available data suggests that while ADHD is clearly a risk factor for the development of adolescent antisocial problems, life experience, principally factors within families most powerfully contribute to the onset and maintenance of delinquency, conduct disorder, and subsequent young adult antisocial problems (Dalsgaard, Mortenson, Frydenberg, & Thomsen, 2002).

Neuropsychological Impairments in ADHD

The ecological validity of laboratory tests to identify, define, and determine the presence and severity of symptoms of ADHD has been increasingly questioned (Barkley, 1991a; Barkley & Grodzinsky, 1994). As ADHD is a disorder defined by behavior in the real world, it is not surprising that laboratory measures frequently fall short in defining and identifying symptoms of the disorder in comparison to naturalistic observation, history, and organized report in the form of questionnaires. Nonetheless, it has been increasingly recognized that neuropsychologists take comfort supplementing their clinical impressions with laboratory-generated, objective scores (DuPaul, Guevremont, & Barkley, 1991). It is increasingly accepted, however, that these scores do not make the diagnosis of ADHD but may be helpful in the process of differential diagnosis (e.g., when is impulsivity a function of ADHD versus other disorders) as well as facilitating the process of differentiating severity or related prognosis in a group of individuals with ADHD (Gordon, 1995; Hall, Halperin, Schwartz, & Newcorn, 1997).

The development of a norm-referenced, psychometric assessment battery specifically designed for ADHD has been an elusive goal for researchers and clinicians. Thus, it is not surprising when one reviews the extensive literature, attempting to hypothetically and objectively define specific neuropsychological impairments occurring consistently in children with ADHD, that no tried and true battery nor pattern of impairment comes to light. As Levine (1992) has noted, ADHD symptoms appear to reflect "elusive entities and . . . mistaken identities." The comorbidity issue and the lack of specificity that many tests hold in discriminating ADHD from other disorders further complicate

this endeavor. Compromised scores may be due to a variety of causes, leading some researchers to suggest a profile of test scores be utilized in defining and explaining neuropsychological impairments in children with ADHD (Aylward, Verhulst, & Bell, 1993; Naglieri, 2000). Neuropsychologists should be aware that clinic or laboratory tests alone or in combination have been found to result in classification decisions that frequently disagree with the diagnosis of ADHD when it is based upon parent interview, history, and behavior-rating scales (DuPaul, Anastopoulos, Shelton, Guevremont, & Metevia, 1992; Doyle, Biederman, & Seidman, 2000). Further, Szatmari, Offord, Siegel, Finlayson, Tuff, (1990) report that neuropsychological tests appear to distinguish children with ADHD from those with pure anxiety or affective disorders. However, they may not as efficiently distinguish ADHD from other disruptive disorders. These authors concluded that neuropsychological tests were more strongly associated with externalizing than internalizing diagnoses. They appear to correlate with psychiatric symptoms at school but not at home. Further, traditional neuropsychological instruments used to infer attention and impulse problems often do not correlate with each other (Naglieri, Goldstein, Delauder, & Schwebach, 2005). Thus, it is not surprising that Barkley (1991b) suggests that when results of the standardized behavior ratings, observations, and history conflict with laboratory measures, the latter should be disregarded in favor of the former as these are considered more ecologically valid sources of data.

Cherkes-Julkowski, Stolzenberg, and Siegal (1991) suggest that perhaps the drop-off in performance for children with ADHD is a function of an inability to control focus of attention. These authors suggest that when prompts are provided during testing, children with ADHD perform significantly better. In a study evaluating children with ADHD with and without medication compared to learning-disabled children and a group of normal controls, the greatest gains for prompts were observed in the unmedicated group with ADHD. However, neuropsychologists should be cautioned that prompts, especially on measures designed to evaluate response inhibition, may actually test the ability of the child to follow directions rather than to inhibit. Neuropsychologists should also keep in mind that there are data to suggest that level of

reinforcement during test performance may also have an impact on scores. Devers, Bradley-Johnson, and Johnson (1994) found improvement in Verbal IQ scores of 12 points accrued when token reinforcers followed immediately for correct responses. The impact of praise on test performance has not been systematically evaluated. Finally, Draeger, Prior, and Sanson (1986) reported a deterioration in the performance of children with ADHD on a Continuous Performance Test, more so than controls, when the examiner left the room. These authors suggest that even examiner's presence acts to mitigate test performance. It may well be that some children who perform poorly on test measures under these circumstances have an application rather than an ability deficit.

Evaluation

Due to the pervasive, multi-setting nature of problems related to ADHD and the high comorbidity with other childhood disorders, assessment for ADHD must be accompanied by a thorough emotional, developmental, and behavioral evaluation. It should be noted, however, that the diagnosis of ADHD should be firmly based on the accepted standard, in this case the DSM-IV-TR diagnostic criteria. Neuropsychologists should be aware that efforts to include additional data to prove/disprove the diagnosis run the risk of introducing increasing variance (Naglieri, Goldstein & Schwebach, 2004). The comprehensive evaluation should collect data concerning the child's behavior at home, with friends, and at school, academic and intellectual functioning, medical status, and emotional developmental. It is suggested that neuropsychologists consider the following multi-step process to accompany the evaluation of ADHD. This processing includes the following:

1. A complete history must be obtained. This is not a cursory process. Sufficient time (approximately 1½–2 h) should be set aside to obtain a narrative of the child's development, behavior, extended family history, family relations, and current functioning. Within the context of the interview efforts should be made to trace a developmental course that appears to fit ADHD as well as to identify core symptoms and those related to other childhood disorders. Obtaining thorough knowledge of the diagnostic criteria for common and uncommon (e.g., high-functioning autism) childhood internalizing and externalizing disorders should be a paramount concern for the neuropsychologist to facilitate the identification of high- as well as low-incidence disorders.

2. Data obtained from the history should be supplemented by the completion of a number of standardized, factor-analyzed questionnaires concerning children's problems. At least two adults who interact with the child on a regular basis, ideally a parent and a teacher, should be requested to complete questionnaires. For general child assessment, the most valuable questionnaire is the Child Behavior Checklist (Achenbach & Edelbrock, 1991). This well-developed questionnaire organizes childhood behavior on a disruptive/non-disruptive continuum. Recent research supports that the Attention Problems Scale correlates well with the current two-factor DSM-IV ADHD diagnosis (Achenbach, 1996). The Conners' parent Teacher Rating Scales – Revised (Conners, 2008); the Comprehensive Teacher's Rating Scale (Ullman, Sleator, & Sprague, 1988); Childhood Attention Problems Scale (Edelbrock, 1990); Academic Performance and ADHD Rating Scales (DuPaul, 1990) are also helpful. However, these questionnaires alone do not provide sufficient information for diagnosis. They simply provide an organized report of behavior. They describe what the observer sees but not why it is being seen.

3. Based upon the history and questionnaires the neuropsychologist should be able to generate a consistent set of data and a series of hypotheses to explain the child's behavior across a variety of settings.

4. Requests should be made to review school records including report cards and results of group achievement testing. If weak performance or learning disabilities are suspected or if the child is already

receiving special education services, the neuropsychologist should review all assessment data as well as the child's Individualized Education Plan. Then it is proper to decide which tests and what amount of time should be used to arrive at the most accurate evaluation of the child. Neuropsychologists should be cautioned, as just reviewed, there are no specific laboratory tests to evaluate ADHD that have demonstrated sufficient positive and negative predictive power to be relied on. The primary purpose of face-to-face assessment with a child should involve addressing issues related to the child's emotional status, self-esteem, cognitive development, and learning disabilities. Observation of the child's behavior during assessment may also yield clues regarding his/her interpersonal style and temperament.

5. Although a number of paper and pencil tasks have been used over the years in research settings to identify symptoms of ADHD, most have not lent themselves easily to clinical use. In research studies some of these tests such as the Matching Familiar Figures Test (Kagan, 1964) appear to have strong positive and negative predictive power for identifying impulsive children. However, in clinical practice such instruments have not proven reliable for confirming the diagnosis of ADHD. Computerized instruments designed to measure sustained attention and the ability to inhibit impulsive responding (Conners, 1995; Greenberg, 1991; Gordon, 1993) have become increasingly popular among neuropsychologists. However, it is important to remember that although these instruments may demonstrate strong positive predictive power (e.g., if the child fails the task it strongly confirms the presence of symptoms related to ADHD), they possess poor negative predictive power (e.g., if the child passes the task conclusions cannot be drawn one way or the other concerning the diagnosis) (McGee, Clark, & Symons, 2000). Nonetheless, many neuropsychologists rely on such instruments to provide additional data as part of the diagnostic process rather than a specific data point to confirm or disconfirm the diagnosis of ADHD (Riccio, Reynolds, & Lowe, 2001). The interested reader is referred to Conners (1994b) or Homack and Reynolds (2005) for a thorough review of the literature concerning computerized assessment of ADHD. A number of studies have suggested that measurement of specific intellectual processes may differentiate youth with various subtypes of ADHD (Paolito, 1999; Naglieri, 1999). However, data generated by instruments such as the Cognitive Assessment System (Naglieri & Das, 1997) are not necessary in making the diagnosis of ADHD but can provide useful information concerning differences in cognitive processes among diagnosed youth.

Treatment

Treatment of ADHD must be multi-disciplinary, multi-modal, and maintained over a long period (for review see Goldstein & Goldstein, 1998; Teeter, 1998; Goldstein & Ellison, 2002). By far, the most effective short-term interventions for ADHD reflect the combined use of medical, behavioral, and environmental techniques. Medication has demonstrated the ability to reduce the manipulative power of the child's behavior in eliciting certain responses from teachers, peers, and family members.

An extensive literature attests to the benefits of medicine, specifically stimulants in reducing key symptoms of ADHD and thus improving daily functioning (Klein, 1987; for review see Barkley, 2006; Goldstein & Goldstein, 1998). Stimulants and other drugs principally impacting dopamine and norepinephrine (Volkow et al., 2001) have consistently have been reported to improve academic achievement and productivity as well as accuracy of class work (Douglas, Barr, O'Neill, & Britton, 1986); attention span, reading comprehension, complex problem-solving, and to enhance inhibitory processes (Balthazor, Wagner, & Pelham, 1991; Pelham, 1987). Related problems, including peer interactions, peer status, and even relationships with family members, have been reportedly improved with these drugs as well (Whalen & Henker, 1991).

Behavior management increases the salience of behaving in a way consistent with environmental expectations. The manipulation of the environment (e.g., making tasks more interesting and payoffs more valuable) reduces the risk of problems within the natural setting. Zentall (1995) suggests that students with ADHD possess an active learning style with a demonstrated need to move, talk, respond, question, choose, debate, and even provoke. Thus, in classroom settings children with ADHD do not fare well in sedentary situations. Managing interventions have included positive and negative contingent teacher attention, token economies, peer-mediated and group contingencies, time-out, home–school contingencies, reductive techniques based on reinforcement, and cognitive behavioral strategies (Abramowitz & O'Leary, 1991). Environmental and task modifications are also critical for classroom success for the child with ADHD. However, additional research is needed, especially in the area of school-based intervention for adolescents with ADHD.

Though popular, the use of cognitive strategies (e.g., teaching a child to stop, look, and listen) and other non-traditional treatments (e.g., dietary manipulation, EEG biofeedback, etc.) to reduce symptoms of ADHD have not stood the test of scientific research and thus should not be advocated as first-line treatments of choice for children with ADHD. Abserson, Shure & Goldstein (2007), however, suggests that the patient application of cognitive training over a long period of time, applied in the real-world setting, can improve the self-regulatory skills of children with ADHD. The interested reader is referred to Braswell (1998) for a review of these issues.

Regardless of the treatment modality employed, the basic underlying premise in managing problems of ADHD involves increasing the child's capacity to inhibit before acting. This is consistent with the theoretical construct that the core problem for ADHD reflects an inability to permit sufficient time to think or respond consistently to consequences.

Summary

Neuropsychologists, given their theoretical background, training, and assessment skills, are in a unique position to evaluate and treat children with ADHD. At this time, neuropsychologists must be prepared to rely extensively upon history, report, and observation and less so upon structured laboratory testing when attempting to understand the behavior and problems of children with ADHD. This chapter provided an overview of the current literature concerning the definition, evaluation, and treatment of ADHD in children.

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Neurobehavioral and Neurodevelopmental Sequelae Associated with Pediatric HIV Infection

ANTOLIN M. LLORENTE, CHRISTINE LOPRESTI, AND PAUL SATZ

Neurodevelopmental and neurobehavioral manifestations in infancy and childhood, resulting from Human Immunodeficiency Virus-Type 1 (HIV-1) infection, continue to warrant special and distinct consideration in this handbook. As noted in our chapter in the previous edition of this volume (Llorente, LoPresti, & Satz, 1997), this merit partly stems from the unique impact of this disease process on the rapidly maturing Central Nervous System (CNS) of the child (Belman, 2002; Epstein et al., 1985, 1986; Falloon, Eddy, Wiener, & Pizzo, 1989; Lyman et al., 1990; Pizzo & Wilfert, 1994, 1998) in conjunction with the scientific purview of developmental neuropsychology and neuroscience, the study of brain–behavior relationships (Lezak, Howison, & Loring, 2005). However, aside from these developmental and scientific reasons, duly attention also stems from several other factors including clinical, epidemiological, and humanistic factors requiring dedicated space in this volume and the expenditure of significant amounts of societal economic and intellectual resources. In this regard, HIV has reached pandemic proportions in selected areas around the globe, the virus has been unequivocally implicated in Acquired Immunodeficiency Syndrome (AIDS), and more specifically related to this volume, HIV infection has been shown to be associated with significant cognitive and behavioral effects during the developmental period (Boivin et al., 1995; Brouwers, Belman, & Epstein, 1994, 1999; Brouwers, Moss, Wolters, & Schmitt 1994,; Chase et al., 2000; Drotar et al., 1997; Hittleman et al., 1991; Llorente et al., 1997, 2000, 2001, 2003, 2006; Llorente, Turcich, & Lawrence, 2004; Mellins et al., 2003; Pizzo & Wilfert, 1994), findings which have become increasingly documented in the literature since the last edition. Finally, the impact of HIV-1 infection on the developing brain has been the focus of significant attention by the neuroscientific community and has become one of the main health-related concerns of our generation in the United States and abroad. Although not applicable to countries where treatments are readily available such as United States, it remains true today, as noted in 1997 (Llorente et al., 1997), mortality resulting from pediatric HIV infection and AIDS continues to experience a sharp and dramatic increase in selected parts of the world, despite decreases in other areas around the globe (WHO, 2005). This continued rise in the number of infected cases and deaths, whether the result of enhanced surveillance techniques,

ANTOLIN M. LLORENTE • Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD 21209. **CHRISTINE LOPRESTI, AND PAUL SATZ** • Department of Psychiatry and Biobehavioral Sciences, University of California School of Medicine, Neuropsychiatric Institute and Hospital, Los Angeles, CA 90024.

continued increases in the rate of disease transmission, greater reporting accuracy, or lack of available treatments has led to enormous social and economic consequences worldwide (WHO, 2005), as was the case a decade ago. Thus, neuropsychology and neuroscience has been called upon, as part of a multidisciplinary approach, to scientifically investigate the effects of this viral infection on higher brain functions and to participate in the assessment and rehabilitation of patients with this disease. Therefore, a chapter in this volume dedicated to the neurodevelopmental and neurobehavioral sequelae of pediatric HIV infection is not only sufficiently justified and pertinent but it continues to remain timely.

This chapter provides an overview of the neurodevelopmental and neurobehavioral effects associated with HIV-1 infection, an evolving infectious disease, in infancy and childhood as understood in 2005. A review of basic concepts is initially presented to introduce the reader to the pediatric HIV and AIDS terminology and diagnostic nomenclature. Subsequently, updated American and global epidemiological data depicting the continued spread and staggering impact of this epidemic are examined. The chapter then briefly traces the virological and immunological effects of the virus. Next, neuropathological and other biological concomitants associated with an HIV-positive status and immunocompromised states are briefly reviewed. The bulk of the remainder of the chapter is devoted to the neurodevelopmental and neurobehavioral sequelae associated with HIV infection. Finally, treatment and neurodevelopmental issues, as well as potential avenues for future research, are presented.

However, before proceeding, it is critical to understand that an attempt has been made in this chapter to be inclusive, describing information and findings from studies conducted not just in the United States and European countries where treatments are readily available, but from studies conducted in other areas of the world less fortunate in terms of economic resources. Therefore, the reader should note that when information is presented, for example addressing rates of vertical transmission, that significant differences exists in rates of reduction in HIV-1 transmission in nations and areas around the world where treatments are readily available compared to impoverished areas around the globe where rates of vertical transmission have not been reduced. Therefore,

although some of the information presented in this chapter may appear to be obsolete to some readers, they are quite applicable and up to date to readers outside the United States and other nations with substantial resources. Such a comment is applicable to other topics within this chapter (e.g., epidemiology, neuropathology, etc; see Shankar, Mahadevan, Satishchandra, Kumar, Yasha, 2005).

Basic Concepts, Terminology, and Diagnostic Nomenclature

Infants passively acquire maternal antibodies in-utero through placental transmission, including the anti-HIV IgG antibody, which persist at least throughout the first year of life (Koup & Wilson, 1994). Virtually all infants born to HIV-positive mothers will test positive for the virus at birth but may in actuality not be infected. Therefore, the use of existing diagnostic assays for the presence of HIV antibodies, indirectly suggesting the presence of the HIV retrovirus, routinely employed with adults since mid-1985 (e.g., Western blotting; cf., Sarngadharan, Popovic, Bruch, Shupbach, & Gallo, 1984), is inadequate for diagnosing newborns to HIV-positive mothers (Hanson & Shearer, 1994). For this reason, pediatric diagnosis using antibody assays solely, without clinical presentations of the disease, is generally not made until infants reach the age of 15–18 months. At this age, it is believed that the child's own immune system is being assayed (Prober & Gershon, 1991; see below for diagnostic criteria).

Currently, the most sensitive procedures for detecting HIV infection in babies born to HIV seropositive mothers are the polymerase chain reaction (PCR) and virus culture (Burgard, Mayaux & Blanche, 1992; Krivine, Firtion, Cao, Francoual, Henrion, & Lebon, 1992). Use of these assays is accurate in nearly 100% of infected newborns 3–6 months post-delivery, and 30–50% of infants tested at birth. The standard p24-antigen assay is less sensitive than PCR and virus cultures, especially when HIV-antibody levels are very high. However, modifications (cf., Hanson & Shearer, 1994) of this assay have increased its sensitivity in diagnosing infected infants born to HIV-positive mothers.

Two important concepts in the pediatric HIV literature are those of vertical versus

horizontal viral transmission. HIV infection can be transmitted from a seropositive mother to her child during the perinatal, delivery, and postnatal periods. Transmission has been found to occur in utero through the placental barrier (cf., Sprecher, Soumenkoff, Puissant, & Degueldre, 1986), during intrapartum as a result of contact with blood or other body products (Friedland & Klein, 1987), and after birth through breast feeding (de Martino, 1994; Rogers, 1989). Regardless of the actual course of retroviral transfer, HIV-positive mother-to-child viral passage is considered a form of vertical (perinatal) transmission. In contrast, viral transmission through blood or blood-related products associated with the treatment of medical disorders (e.g., von Willerbrand's disease), drug use, or other insult is considered horizontal transmission by definition. Although advances in viral detection have decreased the rates of horizontal transmission via infected blood products, a resurgence in horizontal transmission has occurred, associated with needle sharing by children and adolescents who use controlled substances or who come in contact with infected partners or individuals in sex-oriented businesses in the United States and abroad (cf., Booth et al., 2004). As noted in 1997, and although modulated by advents in treatments, the distinction between vertical versus horizontal transmission is not only important from a pedagogical and scientific viewpoint as noted in the previous edition of this chapter, it also has significant clinical importance since the disease process tends to express itself in different fashions in children afflicted through these two distinct routes of transmission (Brouwers, Moss et al., 1994; Smith et al., 2000). According to Brouwers, Moss et al. (1994), vertical versus horizontal transmission also has significant gender- and age-related consequences. With regard to gender, males, relative to females, have a greater likelihood of becoming infected via horizontal transmission since they are more prone to suffer from medical conditions necessitating treatment with blood products (males relative to females have a higher prevalence of diseases requiring the use of blood products; e.g., hemophilia A, an X-linked recessive form requiring coagulation Factor VIII). In terms of age-related differences as it applies to mode of transmission, horizontally transmitted HIV in the United States is most likely to have occurred in boys whose chronological age in 1995 was approximately 10 years. This uncanny state of affairs is the result of the advent of available and reliable procedures to detect the presence of HIV antibodies in the blood supply. Therefore, since safe blood supplies have been available since early 1985, long-term survivors who acquired HIV as a result of a contaminated blood supply are at least in their 30s. In other words, in the United States and other nations around the world with appropriate blood screening, children born since 1985 have primarily acquired HIV through perinatal transmission since sources associated with horizontal transmission as a result of unsafe blood products have been virtually eliminated, except for children and adolescents exposed to horizontal transmission as noted above.

In addition, the rate and course of disease progression to encephalopathy, as well as the onset of symptoms subsequent to infection (incubation), have been found to differ as a function of transmission mode (Brouwers, Belman et al., 1994). With regard to the onset of symptomatic disease, in maternally infected children, investigators have discovered two distinguishable subgroups (Auger et al., 1988; DePaula et al., 1991). According to Auger et al. (1988), in a study conducted in New York examining the incubation period for pediatric AIDS, one group exhibited early symptomatic disease expression in infancy marked by an approximate median age of onset of 4.1 months associated with brief survival periods, whereas a second group of children had a median incubation period of 6.1 years with lengthier periods of survival. In contrast, the time lapsed between infection and onset of symptomatology in children infected through blood transfusions is greater (Rogers et al., 1987), relative to vertically infected children. With regard to these varying periods of incubation, Oxtoby (1994) reported that the median age at which AIDS is diagnosed in perinatally infected children was 12 months while the distribution of age at AIDS diagnosis is negatively skewed, with the majority of children under the age of 2 and a small number who are diagnosed as late as age 13. In summary, from a prognostic viewpoint, age of onset of symptomatic disease plays a major role in predicting length of survival.

Several other factors including viral and host characteristics have been implicated in outcome. Although viral load and strain have been

hypothesized to play a major role in incubation periods, the variability in onset of symptoms and course of illness remains poorly understood. Nevertheless, research examining risk factors in maternal–fetal infection has revealed interesting results. For example, Bryson et al. (1993) presented the first data examining *timing* of vertical transmission (in utero vs. intrapartum) to help explain the developmental course of the disease. In this prospective study of 74 mother–infant pairs, 22 (28%) seropositive mothers transmitted the virus to their newborns. The median time to onset of AIDS-defining symptoms was significantly earlier in the group infected in utero (6 weeks) compared with the group infected in the intrapartum period (86 weeks). Brouwers, Moss et al. (1994) have also described in detail the abundance of environmental factors affecting the expression of HIV infection. Finally, host factors may play an important role. For example, genetic factors such as specific mutations (cf., Kostrikis et al., 1999) may account for differences in outcomes and neurodevelopmental profiles (cf., Llorente et al., 2006), and in adults, Satz (1993) has put forward the concept of threshold theory to explain some of the individual differences observed in the expression of the disease after infection.

As the reader may have already surmised, the population of children infected with pediatric HIV is quite heterogeneous (Brouwers, Moss et al., 1994; Llorente et al., 1997). This heterogeneity is partly the result of differences in transmission mode, coupled with the rapid developmental changes occurring in the CNS of children, age of onset of symptomatic disease, and viral load and strain(s) among other factors. In addition, environmental, host-related factors, and treatment (cf., Shankar, Mahadevam, Satishchandra, Kumar, & Yasha, 2005) are also responsible for a great deal of the individual and group differences observed in the pediatric HIV population worldwide. This heterogeneity is also exhibited in the profiles of patients who undergo neurodevelopmental and neurobehavioral evaluation.

Just as procedures and methods used to identify infected adults are ineffective with infants born to HIV-positive mothers, adult diagnostic criteria also are inappropriate for children. The Centers for Disease Control and Prevention (CDC) initially published a pediatric classification scheme in 1987 to better describe the spectrum of HIV disease and updated the classification system in 1994 (Centers for Disease Control and Prevention, 1994). Diagnosis of HIV in children is based on infection, immunologic, and clinical status. The three infection diagnostic groups are "HIV infected, perinatally exposed (E), and seroreverter (SR)." Children are diagnosed as HIV infected under the following conditions: A child is younger than 18 months and is born to an HIV-positive mother and (a) has had positive laboratory results on two HIV detection tests, or (b) has an AIDS-defining illness based on the 1987 CDC surveillance case definition. A child 18 months or older is diagnosed as infected if either born to an HIV-positive mother or infected through any route of transmission and has repeatedly tested HIV-positive by antibody tests (e.g., Western blot). A perinatally exposed child is one who is (a) under 18 months of age and is HIV seropositive by antibody tests, or (b) is born to an HIV-positive mother but has unknown antibody status. A seroreverter is a child born to an HIV-positive mother but who is antibody negative, has no laboratory evidence of viral infection, and has not had an AIDS-defining illness. Children who are infected or perinatally exposed based on the criteria described above are further classified according to their immunologic and clinical status. Immunologic categories are based on both age and level of immunosuppression based on CD4+ counts and percent of total lymphocyte and range categorically from "no evidence of suppression to severe suppression." Clinical categories are based on the presence and severity of symptomatology ranging from asymptomatic to severe signs and symptoms (Centers for Disease Control and Prevention, 1994).

American and Global Pediatric HIV Epidemiology

Since the first case of pediatric HIV was reported to the CDC, the population of HIV-1 infected children dramatically grew in the United States, yet declines have occurred in the incidence of pediatric cases since the mid-1990s as a result of the introduction of maternal prophylactic antiretroviral treatments and their subsequent reduction in the rate of mother-to-child transmission (Cooper et al., 2002; Connor, Sperling, Gelber, 1994). This decline is evidenced in the current incidence and prevalence rates of

pediatric cases in the United States In 1992, 945 new cases were reported with subsequent declines to 645 new cases in 1995 and 48 new cases in 2004 (CDC, 2005). An estimate as of December 2004 indicates a cumulative prevalence of 9,943 children under the age of 13 with HIV/AIDS accounting for approximately 1% of the total number of reported AIDS cases in the United States. Although by 1993, infected children had been documented in all regions (e.g., rural vs. metropolitan) (Oxtoby, 1990) within the 50 states (Centers for Disease Control and Prevention, 1993), and there has been an increase in the spread of HIV infection to rural areas in the United States (Steinberg & Fleming, 2000), the majority of pediatric patients continue to come from metropolitan areas in California, Florida, Illinois, New Jersey, New York, Pennsylvania, and Texas (Centers for Disease Control and Prevention, 2004). The total number of children with AIDS from New York as of December 2004 accounts for approximately one quarter (25%) of all cases reported in the United States (CDC, 2004). Nevertheless, in view of the fact that approximately 24–27% of individuals with HIV-1 infection are unaware of their infection and go undiagnosed, including children under the age of 15 years, the figures above are probably conservative estimates (CDC, 2004).

As of December 2004, 92% of children with AIDS were perinatally infected. Fifty one percent of their mothers acquired HIV through IV drug use or sex with an injecting drug user (CDC, 2004). The prevalence of perinatally infected cases continues to reflect the number of infected women and the relative decreases in other methods of transmission including infection from blood and blood products (Andiman & Modlin, 1991; Lindegren et al., 1999), and the fact that the introduction of AZT to reduce mother-to-infant transmission was successful (Connor et al. (1994). For this reason, and despite the introduction of AZT to reduce mother-to-infant transmission, perinatal transmission accounts for virtually all pediatric HIV/AIDS cases in the United States.

Because most children are exposed to HIV through perinatal transmission, as of December 2004, the distribution of children in the United States with AIDS continues to reflect that of their mothers demographically. Therefore, of the pediatric population of cases reported with AIDS, 59% are African-American, 22% Hispanic, 17% Caucasian, <1% Asian/Pacific Islander, and <1% American Indian/Alaskan Native (CDC, 2004). It is evident from these data that the epidemic has had a greater impact on selective minority groups, especially African-Americans and Hispanics, relative to other racial groups. In addition, despite the fact that recent declines have been noted in the incidence and prevalence of children from ethnic minority backgrounds with the introduction of AZT in the United States to reduce perinatal transmission, similar declines have not been noted in African-American populations.

Although epidemiological data from the United States continue to be informative as they were a decade ago, these figures continue to serve as poor indicators of the magnitude of this pandemic when examined from a broader perspective such as the global prevalence of HIV/AIDS, and this is a difference that is critical to note as indicated earlier. As of December 2005, the prevalence of HIV in children 15 years of age or younger had been *conservatively* estimated at 2.3 (2.1–2.8) million cases around the world (WHO, 2005). Sub-Saharan Africa continues to lead in the number of infected children with a population estimate of 2.1 (1.8–2.5) million or 91% of the total population of infected children which actually represents an increase in prevalence since 1995. South and Southeast Asia, Latin America, North Africa and the Middle East, the Caribbean, and North America were the next geographic areas of greatest prevalence with conservative estimates of 130,000, 50,000, 37,000, 17,000, and 9,000 children, respectively. Eastern Europe and Central Asia, Western and Central Europe, East Asia, and Oceania had the next highest estimated number of cases at 7,800, 5,300, 5,000, and 3,300 children, respectively (WHO, 2005).

Basic Virology and Immunology of HIV Infection in Children

Although a detailed examination of the virology and immunology of pediatric HIV infection continues to be beyond the scope of this chapter, a brief introduction to these topics will be presented in order to familiarize the reader with a rudimentary understanding of these biological processes (cf., Connor & Ho, 1994; Feigin & Cherry, 1992; Hanson & Shearer, 1992;

Overall, 1981). It is important that the reader understands these basic concepts since they are interwoven with the CNS and neurocognitive effects of HIV infection to be covered in later sections, particularly specific viral, immunologic, and genetic factors and their potential impact on neurodevelopmental and neurobehavioral outcomes (see Llorente et al., 2006).

Virology

The Human Immunodeficiency Virus (e.g., HIV-1 and HIV-2) is an RNA virus belonging to the lentivirus family of retroviruses (Connor & Ho, 1994). HIV is a linear, nonsegmented, single-stranded, 7–12 kb long retrovirus of positive polarity. It is referred to as a retrovirus due to the fashion in which it carries its genetic code. In contrast to other RNA viruses (e.g., proviruses), HIV reproduces itself through reverse transcription (its genetic code [virion RNA] is inserted into the DNA genome [into linear double-stranded DNA] of the host cell). Unlike "simple" retroviruses, HIV-1 contains additional regulatory proteins increasing its complexity and mechanisms of action. Regardless of the actual mechanism of transcription, retroviruses are capable of producing, among other pathologies, profound immunosuppressed states and cancers. Specifically, HIV-1 causes immunosuppression of the T-cell lymphotropic system in children increasing the probability of occurrence of opportunistic infections associated with this state (e.g., pneumocystis carinii, lymphomas, etc.). Although relatively recent advances have been made enhancing our understanding of the virus and its mechanisms of action, including the importance of mutations in some chemokine receptor proteins, polymorphisms in genes associated with chemokine receptors and ligands, particularly those that impact monocytes-macrophages that may play a role in the child's susceptibility to neuropathology, the actual pathogenetic process of HIV in the CNS is not fully understood. However, it is clear from the scientific evidence that successful treatment outcomes in youth infected with HIV-1 are highly associated with low viral replication (RNA load) in the host.

Immunology

The immune system protects against pathogens following antigenic challenge through several mechanisms, including humoral, cell-mediated, and polymorphonuclear responses (Macdonald, 1984; Mills, Regelmann, & Quie, 1981). Humoral immunity occurs primarily secondary to the development of humoral circulating antibodies. This type of response assists in the reduction or elimination of foreign microorganisms from the body. In contrast, cell-mediated or cellular immunity is predominantly moderated by a set of cells labeled T-cells (lymphocytes) which are responsible for protection against infectious agents.

In the uterus, the fetus depends on the immune system of the mother for protection against pathogens, a process known as maternal immunity (Mills et al., 1981). In fact, the mother passively donates her immunity to her fetus through the placenta in the form of immunoglobulin G (IgG). Similarly, the neonate and newborn also depend on this donated immunity. According to Koup and Wilson (1994), adult immunoglobulin levels are not found in normal children at adult concentrations until 5–6 years of age (IgM) or adolescence (IgA) by which time the child's own immune response system operates in a fashion similar to that of an adult. Although it is known that B- and T-lymphocyte differentiation can commence as early as 10 weeks during the gestational period, vertical infection can occur earlier. In addition, most immune system mechanisms known to protect infected adults, and responsible for their longer survival periods, have been shown to be impaired in normal newborns. This secondary state of immunodeficiency is also partly responsible for the inception and rapid development of HIV infection in the newborn. In this regard, Wilfert, Wilson, Luzuriaga, and Epstein (1994) reported that mother-to-child transmission is most likely the result of a single virus strain which evolves into related but different strains over time These investigators also reported that increased maternal virus burden appears to enhance the probability of vertical infection. Obviously, all these factors combined are responsible for the inability of the fetus and newborn to protect themselves against pathogens, making them highly susceptible to HIV infection and its sequelae (e.g., opportunistic infections).

Regardless of etiology, infection with HIV (HIV-1 or HIV-2) leading to the disease progression, including AIDS, is the result of disruption in T-cell-mediated coordination responses responsible for protection or safeguard, specifically T4-cells (CD4+), secondary to the progressive disintegration of the T4 cell supply. This progressive breakdown and arrest of coordinated responses are the result of a yet inexplicable process due to the HIV pathogens (Hanson & Shearer, 1992). As the number of CD4+ cells decreases below certain critical threshold levels (relative to adults, children's CD4+ concentrations have been shown to be clinically significant at higher levels), the probability substantially increases that the infected child will become immunocompromised and develop AIDS, cancer, an opportunistic disease(s), or a combination of these diseases linked to the immunodeficient condition. Although the rate of disease progression depends on complex interactions between environmental factors, the host, and the virus, one of the chief goals of treatment is to reduce viral load, as noted above, while maintaining the integrity of the immune system as intact as possible.

In addition to the pathogenesis of pediatric HIV proper, the immune system itself is partly responsible for the catastrophic effect of HIV infection on the CNS secondary to HIV-induced encephalopathy. This state of increased susceptibility is probably secondary to the incomplete myelination of the young CNS.

Neurological, Neuroimaging, and Neuropathological Findings in Pediatric HIV-1

In children, evidence that HIV infection was actually associated with neurological complications was initially published in the early 1980s (cf., Belman et al., 1984, 1985), approximately 1½ years after the first cases of pediatric AIDS were reported to the CDC in the United States. Nevertheless, there appears to be ample evidence in 2005 from several avenues of research (neurological, neuroimaging, neuropathological, etc.) to suggest that the Human Immunodeficiency Virus targets and invades the CNS shortly after initial systemic infection (Davis et al., 1992; Lyman et al., 1990), and penetrates the young and maturing CNS (Koenig et al., 1986; Lyman et al., 1990; Resnick, Berger, Shapshak, & Tourtellote, 1988; Sharer et al., 1990), and is capable of causing dramatic neuropathology and neurological impairments (Belman, 2002; Belman et al., 1988; Brouwers, Belman et al., 1994; Brouwers et al., 1999; Masliah et al., 1992). These findings now are reviewed briefly.

Neurological Findings

Although neurological symptomatology experienced by children as a result of HIV infection varies substantially from child to child, with some children exhibiting mild alterations in motor or other skills, more severe expressions of the disease are manifested through childhood encephalopathy capable of causing substantial deviations from normal development and death. Although the introduction of antiretroviral therapies, particularly highly active antiretroviral treatment (HAART), prevent or delay the onset of the most severe types of encephalopathy (Belman, 2002), Belman (1990) and her colleagues (Belman et al., 1988) described two forms of HIV-1 encephalopathy, namely progressive and static HIV-related encephalopathy capable of affecting children.

Progressive encephalopathy is further subcategorized into two different types (subacute and plateau) to describe the distinct rates of disease progression observed in infants and children. Subacute progressive encephalopathy, most commonly seen in infants and young children (Belman et al., 1988; Belman 2002), is the most crippling neurological expression of HIV infection. Although advances in treatment have led to the complete prevention or delay of its onset (Belman, 2002), it is marked by a gradual but progressive decline across most domains of neurological functioning, particularly in overall cognition, expressive functions including motor and language skills, and adaptive functioning in preschool age children, or loss of already attained developmental milestones in infants and younger children with no further development in some instances leading to death (Belman, 2002; Epstein et al., 1985). Subacute encephalopathy is capable of causing serious CNS debilitation including profound cerebral atrophy and microcephaly (acquired as a result of lack of continued CNS development; Epstein et al., 1985, 1986). Neurologically, it is not

uncommon to see a child with a chronological age of 4 years functioning at an age level of 6–8 months during HIV-1-related subacute encephalopathy. A plateau course is often observed in infants and young children in which they fail to acquire new developmental milestones or acquire them very slowly. Unlike youngsters experiencing progressive subacute encephalopathy, they typically do not display losses from previously acquired levels of functioning (cf., Belman et al., 1989; Brouwers, Belman et al., 1994). Before the availability of modern therapies, Belman (1990) reported that these children suffered from motor deficits as well as declines in overall neurodevelopmental functioning, a finding still observed in children who do not have access to therapies or who have experienced poor treatment adherence.

Static, relative to progressive encephalopathy, is less debilitating. The gradual decline or lack of gains in development observed during progressive encephalopathy is not seen in children with static encephalopathy. Instead, static encephalopathy is demarcated by continued acquisition of skills at rates below expected levels of normal development but commensurate with their initial level of functioning. Furthermore, the delays observed during static encephalopathy longitudinally remain relatively stable from initial levels of functioning (Belman et al., 1985; Brouwers, Moss et al., 1994; Brouwers et al., 1999; Epstein, 1986).

Although the American Academy of Neurology amalgamated the various categorizations of HIV-related encephalopathy, as identified by Belman (1990) and discussed above, under one category termed HIV-associated encephalopathy of childhood (American Academy of Neurology AIDS Task Force, 1991), Brouwers, Belman et al. (1994) argue that the singular categorization scheme fails to account for the different neurological presentations associated with the various types of encephalopathy. In fact, these investigators contend that Belman et al.'s (1988) categorization better characterizes the various course of progression observed during the three types of encephalopathy, and some studies assessing the impact of HIV-1 have developed their own definitions of encephalopathy to address some of these concerns (cf., Cooper et al., 1998).

In addition to the encephalopathic processes described above, a host of other neurological diseases associated with an immunodeficient state secondary to HIV infection has also been observed in children (Belman, 1990; Belman, 2002). Although the actual frequency of occurrence of these disorders is not high, and there has been a decrease in their incidence subsequent to modern prophylactic therapeutic interventions (Belman, 2002), co-infections (e.g., cytomegalovirus, CMV), opportunistic diseases, and other CNS complications (e.g., neoplasms) have been reported. According to Belman (1990), the majority of these children concurrently develop encephalopathy as a result of HIV-1 infection. For example, neoplasms have been documented in the literature, the most common type being primary CNS lymphoma (Belman, 1990; Epstein, Sharer, & Goudsmit, 1988). These have been observed in children between 6 months and 10 years of age but occur primarily after the first birthday (Epstein, Sharer, & Goudsmit, 1988). Their most prominent location is in the basal ganglia and areas surrounding the third ventricle (Belman, 1990). Secondary CNS lymphomas have also been noted (Dickson et al., 1989) as well as cerebrovascular complications, including infarctions (Belman, 1990; Frank, Lim & Kahn, 1989), strokes (Park et al., 1988), myopathies, and Guillain–Barré syndrome-like conditions, to name a few (Raphael, Price, Lischner, Griffin, Grover, & Bangasra, 1991). Although there is a great deal of consensus regarding the infrequency of CNS opportunistic infections and additional disorders linked to HIV infection in children (Epstein et al., 1988), particularly since the advent of modern therapies when available, they have nonetheless been reported in the neurological literature (Belman et al., 1988; Dickson et al., 1989). Of these, bacterial meningitis, candida meningitis, and CMV have been some of the most commonly reported. In contrast, HIV-related CNS toxoplasmosis, commonly observed in adults (McArthur, 1994), continues to be more rare in children as was noted in the past (Belman, 1990), and the data continue to suggest that a small number of children, particularly those receiving effective treatments, are affected (cf., Nicholas, 1994). Finally, it should be pointed out that encephalopathy is still capable of emerging, even in nations with readily available resources, if poor treatment adherence occurs, with significant cognitive effects (cf., Mellins, Brackis-Cott, Dolezal, & Abrams, 2004).

With regard to more specific definitions of encephalopathy, particularly related to research protocols (e.g., WITS), the diagnosis of encephalopathy requires at least one of the following to be present for at least 2 months in the absence of a concurrent illness other than HIV-1 infection: (1) failure to attain or loss of developmental milestones, or loss of intellectual ability, verified by standard developmental scale or neuropsychologic tests; (2) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements, or brain atrophy demonstrated by serial computerized tomography or magnetic resonance imaging; and (3) acquired symmetric motor deficit manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbances (Cooper et al., 1998).

Findings from Neuroimaging Studies

Several investigations have reported abnormalities in the brains of HIV-infected children using various neuoradiological procedures (c.f., Tardleu, 1991). For example, Belman et al. (1985) found varying degrees of abnormality using Computed Tomography (CT) in an 18-month old with AIDS, marked by cortical atrophy with dilation of the ventricular system and calcification of the basal ganglia and frontal white matter. These abnormalities were again observed longitudinally at 18 and 21 months. Other CT studies conducted by Belman et al. (1988) found cortical atrophy and white matter abnormalities (basal ganglia [bilaterally] and frontal calcification) in children with AIDS or "ARC." In addition, 16 of 17 participants who were longitudinally evaluated in the study showed progressive levels of atrophy. These results have been substantiated by DeCarli, Civitello, Brouwers, and Pizzo (1993) who found bilateral symmetrical calcification of the basal ganglia and frontal white matter calcification in 100 children with symptomatic HIV infection. Figure 1 shows a CT scan of a child with these types of calcifications.

In a study assessing the clinical significance of CT scan abnormalities as they relate to neurodevelopmental delays subsequent to symptomatic HIV-1 infection, Brouwers et al. (1995) revealed a positive and significant relationship between these two independent procedures. In that investigation, increasing cognitive delays (Full Scale Intellectual Quotient) were significantly associated with increasing degrees of calcification (CT Scan Severity Rating).

Studies using Magnetic Resonance Imaging (MRI) have also detected CNS abnormalities associated with pediatric HIV infection. Belman et al. (1986) found decreased and increased signal intensities on T_1- and T_2-weighted images, respectively, in a 10-year old as a result of white matter atrophy in the basal ganglia (bilaterally) and cerebral atrophy. Similar findings using T_2-weighted imaging were found by other investigators (cf., Epstein et al., 1986).
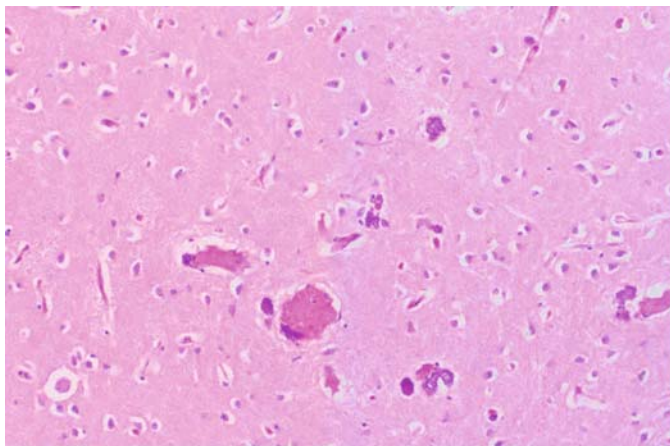
FIGURE 1. Photomicrograph showing calcifications (calcium deposits) in the basal ganglia of a symptomatic HIV-1-positive 2-year-old child. Courtesy of Celine Hanson, M.D., Department of Pediatrics, Baylor College of Medicine.

A study examining cerebral metabolism through Positron Emission Tomography (PET) supported the findings obtained with the structural neuroradiological methods described above. Pizzo et al. (1988), while conducting a study assessing the effects of AZT pharmacotherapy, found diffuse cortical, focal right frontal, and right superior temporal hypometabolism prior to treatment in an 11-year-old male with HIV-1 infection.

Keller et al. (2006, 2004) most recently examined cerebral metabolites as a measure of brain health by proton MR spectroscopy (H MRS) in a small group of HIV-infected children, all but one of whom were receiving HAART, and uninfected controls. Brain metabolites examined in five regions (left frontal matter, right frontal matter, right basal ganglia, right hippocampus, and midfrontal gray matter) were "N-acetylaspartate (NAA), a marker of neuron density and integrity; soluble choline compounds (CHO), an assessment of cell membrane turnover, gliosis, and myelination; myoinositol (mI), a glial cell marker; and total creatine (CR), molecules involved in energy metabolism." Findings among the HIV-positive children in the initial study were an absence of the expected age-associated increase in NAA in the hippocampus and white matter; a correlation between the glial marker (mI) and age and $\log_{10}$ viral load in the frontal white matter; and an elevation of CHO in the frontal gray matter in relation to higher viral load. When comparing the HIV-infected children and controls as a group, the only metabolic difference observed was a 12% decrease in CHO in the left frontal white matter of the HIV-positive group. In their longitudinal follow-up of the HIV-positive children, Keller and her associates found that metabolite concentrations and metabolite/CR ratios were stable over three time points during a 10-month period, and there was no significant change in subjects' clinical or cognitive status. The authors pointed out the need to examine additional brain regions in a larger sample size to assess the usefulness of cerebral metabolic measurements as an early predictor of active CNS infection in children with HIV.

Because structural and functional neuroimaging investigations have provided converging data suggesting that pediatric HIV-1 infection is capable of causing significant CNS effects that are easily detected using these procedures, in addition to emphasizing the continued documentation of neuropathological states, recent neuroimaging also has focused on documenting positive treatment effects or probable negative side effects of such treatments. For example, Tepper et al. (1998) reported recovery documented through repeat MRI of a child subsequent to treatment with HAART which included an HIV-specific protease inhibitor, and other studies have noted similar treatment outcomes with other therapy combinations (cf., Angelini et al., 2000; Safriel, Haller, Lefton, & Obedian, 2000 for comprehensive reviews). Most recently, a study with 49 HIV-1 uninfected children with a mean age of 26 months exposed to AZT perinatally investigating the incidence of cerebral MRI findings in children with mitochondrial dysfunction reported that the images noted in children with AZT-induced mitochondrial dysfunction were similar to those noted in congenital mitochondrial illnesses (Tardieu et al., 2005). In addition, these investigators noted that similar findings were observed in asymptomatic or symptomatyic children "without evidence of systemic mitochondrial dysfunction" (Tardieu et al., 2005).

Neuropathological Features

Substantial evidence suggests that neuropathology in the CNS of children is caused by AIDS secondary to pediatric HIV infection (cf., Ho et al., 1985; Resnick et al., 1988). Evidence to support this hypothesis comes from research revealing measurable degrees of neuropathology in microscopic and gross specimens of the brain and spinal cord in these children responsible for the encephalopathic states and debilitating neurological and neurodevelopmental profiles sometimes observed in children with HIV-1 disease.

Several investigators reported abnormalities in the brains of children afflicted with HIV (HTLV-III) as early as 1985 (e.g., Sharer, Cho, & Epstein, 1985). In this study, 11 children underwent autopsy. The results of these autopsies revealed diminished gross brain weight for their age, inflammatory cell infiltrates, multinucleated cells and multinucleated giant cells, cerebrovascular calcification, vascular and perivascular calcification, and white matter changes. In addition, inflammatory and vascular lesions were most pronounced in the basal ganglia and

FIGURE 2. Axial (horizontal) CT imaging showing significant bilateral calcifications (note significant translucency in these areas) in the basal ganglia and frontal regions. CT scan courtesy of Celine Hanson, M.D., Department of Pediatrics, Baylor College of Medicine.

pons (Sharer et al., 1985). Figure 2 shows bilateral calcifications in the basal ganglia of a child with HIV-1 infection similar to those reported by Sharer et al. (1985).

Similar findings have been observed by other investigators (Belman et al., 1988; Epstein et al., 1988; Pang et al., 1990). The results of the investigation by Epstein et al. (1988) revealed diminished brain weight for age under gross examination in the children who had died of AIDS-related infection and progressive encephalopathy. That study also noted the presence of inflammatory cell infiltrates, multinucleated giant cells, white matter changes, and vascular calcification under microscopic examination as reported earlier by Sharer et al. (1985). More important, several studies have identified viral particles or HIV-related antigen in the multinucleated cells and other cells (Lyman et al., 1990; see also Epstein et al., 1985). This finding would argue in favor of hypotheses postulating the presence of neuropathology as a direct result of HIV-related pathogens.

Within the spinal cord, corticospinal tract degeneration (Dickson et al., 1989), a disorder marked by remarkable myelin pallor, has been one of the most common histopathological finding in children infected with HIV-1. In this study, corticospinal tract (CST) degeneration was evidenced in more than two thirds of the children with AIDS who had undergone autopsy. Furthermore, nearly half the cases reported suffered from axonal loss and loss in myelination in the corticospinal tract (CST). Disproportionate pallor of myelin, relative to axonal loss, in the CST was observed in the other half of the cases. Those children who suffered from losses both in myelin and axons usually displayed the greatest amount of cerebral pathology (Belman, 1990). Finally, Sharer et al. (1990) found inflammatory cell infiltrates and multinucleated cells in 9 and 6 of the cases evaluated, respectively, as part of a study with 18 children who died as a result of HIV-1 infection and had undergone autopsy (only 16 spinal cords were evaluated). Sharer and his colleagues (1990) also identified degenerative changes marked by myelin pallor in the CST in nearly half the cases, consistent with previous studies (e.g., Dickson et al., 1989).

It is important to note the neuropathological expression noted above, predominantly from patients in the United States, and similar findings from European investigations, may not be identical to those of patients from other countries where children remain naïve to

medications, different HIV subtype predominate, and where the natural course and evolution of HIV/AIDS may be different, in conjunction with the presence of different environmental pathogens, and contextual factors (e.g., nutrition, interventions), leading to different neuropathological profiles (cf., Shankar, Mahadevan, Satishchandra, Kumar, & Yasha 2005). Nevertheless, based on the evidence presented above, it appears that the neuropathological effects of HIV infection on the developing CNS are so devastating that they can be detected under gross examination in some instances.

Electrophysiological Findings

Given the abnormalities observed in the CNS using other diagnostic procedures (e.g., imaging, postmortem examinations, etc.), it should not be surprising to find negative findings in the gross electrical activity of the brain while conducting electroencephalographic studies with HIV-positive children. In fact, correlative EEGs have revealed abnormal findings. For example, in the study conducted by Belman et al. (1985) with six children who suffered from AIDS, five out of six displayed EEG abnormalities consistent with the imaging results. Three of the five showed mild diffuse slowing while the other two displayed moderate diffuse slowing. Four of the six also displayed abnormalities in brain stem auditory evoked potential (BAEP) marked by an abnormal rate function (1 child) and prolongation of the I–V interwave latency (three children). Other studies have found similar abnormalities (Bradley, Daroff, & Fenichel, 2004; Ultmann et al., 1985).

Findings from Other CNS Biological Correlates

Other abnormalities have also been identified in several CNS biological markers as a result of HIV-1 infection in children (Epstein et al., 1987; Ho et al., 1985). Although from a clinical standpoint, CSF markers may be less informative because the CSF may show abnormalities unless an opportunistic infection is suspected; from a research standpoint, Brouwers et al. (1993) found a high correlation between cerebrospinal fluid (CSF) levels of quinolinic acid (QUIN) and degree of encephalopathy in 40

children with HIV infection relative to 16 controls. In addition, this study revealed decreasing levels in mental abilities (Bailey Scales [MDI], McCarthy Scales [GCI], and WISC-R [FSIQ]) to be associated with increasing levels of QUIN. Similarly, in a study assessing levels of serum tumor necrosis factor alpha (TNF_α), Mintz (1989) found elevated levels of this marker related to progressive encephalopathy in children with AIDS. Tardieu, Blanche, Duliege, Rouzioux, and Griscelli (1989), using antigen capture assays specific to HIV-1-p24, also found detectable levels of this marker in the CSF of children. In the same year, also reported abnormalities in the CSF of children infected with HIV. Finally, the importance of CSF studies could not be underscored more than in studies examining CSF markers to investigate the ability of antiretroviral therapies to penetrate and enter the CNS, and a large number of these investigations appeared in the literature with the advents of new treatments (cf., Wynn, Brundage, & Fletcher, 2002). This is particularly important because neurodevelopmental factors may not be impacted by treatments that are less efficacious crossing the brain–blood barrier.

In summary, other CNS biological markers, including CSF abnormalities (Ho et al., 1985), have been found in children with HIV infection, especially those with advanced encephalopathy. More important, these findings suggest that the CNS proper is indeed invaded during "primary HIV-1 infection" (Belman, 1990, 2002), and the virus has been noted to be neurotropic directly implicating this infection on CNS disease.

Neurodevelopmental and Neurobehavioral Sequelae Associated Pediatric HIV-1 Infection

Neurodevelopmental and neurobehavioral sequelae associated with HIV infection have been frequently reported in the literature (Boivin et al., 1995; Chase et al., 2000; Brouwers, Belman et al., 1994, Brouwers, Moss et al., 1994; Brouwers et al., 1999; Cohen et al., 1991; Diamond et al., 1987; Fowler, 1994; Llorente et al., 1997, 2001, 2003, 2004, 2006; Mellins et al., 2003, Ultmann et al., 1985). Therefore, the remainder of this chapter reviews these correlates of HIV infection. An attempt is made to integrate

neurological, neuropathological, and other findings presented thus far with the neurodevelopmental and neurobehavioral literature, thereby describing the brain–behavior relationships associated with this disease and its associated immunocompromised states. In order to present these findings in a coherent and orderly fashion, neurodevelopmental and neurobehavioral sequelae associated with pediatric HIV-1 infection are presented by domains.

Emerging Neurodevelopment and Intellectual Functioning

Several studies have reported delays in levels of emerging neurodevelopment and overall intellectual abilities correlated with HIV-1 infection in some children. In infants, although initial investigations comprised small samples or small series of descriptive cases (Belman et al., 1985; Diamond, 1989; Epstein et al., 1986; Ultmann et al., 1985), those studies originally noted the presence of neurodevelopmental deficits, and those findings have now been corroborated by larger and better controlled investigations with populations worldwide (Aylward et al., 1992; Chase et al., 2000; Drotar et al., 1997; Englund et al., 1996; McGrath 2006).

Several recent investigations with appropriate investigational controls support earlier findings suggesting that, as a group, infants with HIV-1 infection, relative to seronegative infants, exhibit early and marked developmental delays or deficits independent of other potential risk factors for such delays including environmental variables (cf., Blanchette et al., 2001; Chase et al., 2000; Drotar et al., 1997; McGrath et al., 2006). This outcome is particularly expected if children are not treated, poorly treated, or even treated but with poor response or inadequate treatment adherence. In a prospective, comprehensive study conducted by Chase and her colleagues (2000) as part of the WITS with a large cohort ($n = 595$) of HIV-1 infected ($n = 114$) and uninfected ($n = 481$) infants, the results revealed that HIV-1 infection was associated with increased cognitive (Mental Developmental Index, MDI) and motor (Psychomotor Developmental Index, PDI) developmental delays as the children underwent serial surveillance over the course of 36 months with the Bayley Scales of Infant Development (BSID, Bayley, 1969).

Differences in neurodevelopmental indices were apparent as early as 4 months of age during follow-up between the HIV-1 infected infants, compared with the uninfected infants. Most important, because such a finding underscores the importance of investigational controls, although HIV-1 infection was significantly associated with increased risks for all developmental cognitive and motor delays, including "time to confirmed drop of one and two standard deviations" on the BSID's MDI and PDI indices, neither prenatal exposure to illicit drugs nor other selected environmental factors (e.g., primary language other than English) was associated with abnormal neurodevelopment. Other investigations have confirmed these results. In addition, it should be noted that some of these studies indicated the presence of significant neurodevelopmental delays in the absence of more severe stages of disease progression (e.g., encephalopathy), and some infants with HIV-1 infection can exhibit significant neurodevleopmental deficits in less severe symptomatic stages.

With regard to older children and intellectual abilities, similar findings have been reported in the literature (Boivin et al., 1995; Havens et al., 1993; Levenson, Mellins, Zawadzki, Kairam, & Stein, 1992), and a substantial lowering in overall intellectual functioning within the Borderline and Mild Mental Retardation ranges has been reported in the literature by several researchers, particularly during symptomatic stages of the disease. Havens et al. (1993) reported significantly lower scores in overall intellect on a measure of intellectual ability in 5–12 year-old HIV-1 infected children compared to seronegative children. In a published report, consistent with previous findings of overall intellectual compromise, Boivin et al. (1995) showed that a group of Zairian asymptomatic HIV-positive children obtained lower K-ABC Mental Processing Composite (MPC) scores (MPC $= 75.1 \pm 10.9$) relative to HIV-negative controls born to uninfected mothers (MPC $= 109 \pm 21.2$) and a control group of HIV-negative children born to HIV-positive mothers (MPC $= 89.6 \pm 9.6$). In contrast, although Cohen et al. (1991) found differences between a group of horizontally infected HIV-positive (only 1/3 of the participants were symptomatic) versus HIV-negative children in school achievement, motor speed, visual scanning, and cognitive flexibility, no differences were observed in overall intelligence for as long as 8½ years after infection. Several factors

including illness severity, poor controls, mode of disease transmission, treatment variables, and inappropriate standardization samples most likely accounts for the differences in findings between studies.

Although it would appear that in some instances symptomatic HIV infection is capable of causing substantial impairment in the overall neurodevelopment and cognitive abilities in children, a great deal of variability is observed when these children undergo neurodevelopmental evaluation (cf., Cohen et al., 1991 vs. Boivin et al., 1995). Although from an empirical standpoint, originally it was not known what specific variables were responsible for the variability in research findings (e.g., environmental factors, host characteristics, treatment, viral factors, etc.), yet these factors were known to either moderate or modulate disease expression, a more clear picture is emerging regarding the effects of these factors on the neurodevelopmental manifestations of pediatric HIV-1 infection. As noted earlier in this chapter, timing of infection with HIV can impact disease expression (severe disease onset, etc.). In addition, because several factors had been implicated in HIV-1 disease onset, progression, and severity, including infant and maternal host characteristics, initial speculations centered around the impact of timing and other variables on neurodevelopment found support in the scientific literature, where it had been demonstrated that infants who had been infected "early" in life had exhibited poorer immunologic, virologic, and clinical outcomes, relative to children who had been infected later in life ("late") (cf., Bryson et al., 1993; McGrath et al., in-press). Such initial speculations led to similar conjectures related to the relationship between "timing of HIV-1 infection" and neurodevelopmental outcome, spearheading research examining this issue, particularly in light of the fact that a direct impact of timing of infection on neurodevelopment had not been properly investigated empirically and prospectively in infancy almost 20 years after the first case of pediatric AIDS had been reported to the CDC. To address this issue, investigators (Smith et al., 2000) set out to test whether timing of infection played a role in neurodevelopmental outcome. In this investigation, neurodevelopmental evaluations were performed with 114 HIV-1 positive infants, a large proportion of which had been identified with early positive cultures ("early") versus a large proportion of which had been identified with late positive cultures ("late"). Longitudinal regression analyses evaluating three surveillance points were used to assess the neurodevelopmental functioning of children with early versus late positive cultures. The results, consistent with findings from basic and other clinical sciences, suggest that infants who probably had been infected in utero ("early" infection) exhibited significantly lower neurodevelopmental scores than infants who had been infected during the intrapartum period or later ("late" infection) as the children were longitudinally tracked over the course of 30 months after birth. The results revealed the negative impact of early infection, and early infection was associated with declines over time in both mental and motor scores on a developmental measure, and by 24 months of age, infants infected "early" scored significantly lower
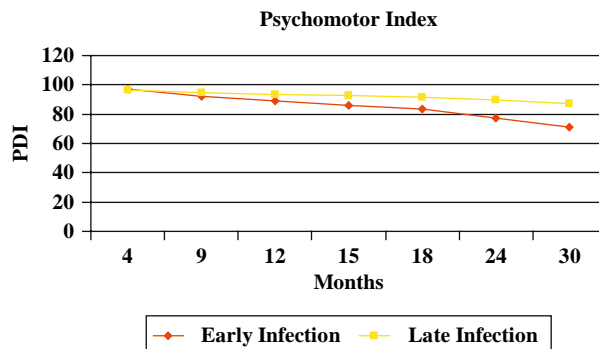
FIGURE 3. Predicted motor index standard scores (BSID, Psychomotor Developmental Index [PDI]) shown on the ordinate and time since birth shown in months on the abscissa. The lines represent PDI outcome as a function of timing of infection ("early" vs. "late"). Reprinted from Smith et al. (2000). Copyright Lippincott, Williams & Wilkins. Reprinted by permission.

than infants infected "late." Figure 3 shows differences in curves slopes on the Bayley Scales of Infant Development (BSID) Psychomotor Developmental Index associated with "early" versus "late" infection. These findings led these investigators to conclude that "early HIV-1 infection increased a child's risk for poor neurodevelopmental functioning within the first 30 months of life," underscoring the importance of timing of HIV-1 infection and neurodevelopment, information with significant surveillance and treatment implications.

Aside from being able to document CNS effects associated with HIV-1 infection, and its impact on the rapidly developing brain of infants and young children, neurodevelopmental indices have been shown to be able to serve as *independent* markers of morbidity and mortality in children with HIV-1 infection. This is best depicted by an investigation conducted by Llorente et al. (2003) in which 157 perinatally infected HIV-positive infants underwent longitudinal assessment during the course of 36 months of follow-up to determine whether early neurodevelopmental markers, based on a baseline assessment conducted at 4 months (baseline), were able to predict mortality. In

that investigation a neurodevelopmental measure (BSID) was administered to 127 children who had survived at least 4 months and to 30 children who had perished by the end of the study. Survival analyses were used to estimate the time to death of 4-month scores (baseline), and Cox proportional hazards progression was used to estimate relative hazard of death for developmental scores and potential confounders, including clinical category, CD4+ percentage, demographic factors, gestational age, head circumference, plasma viral load, and treatment. The analyses revealed greater mortality (decreased survival) risk rates in infants with the lowest developmental scores (Quartile 1; BSID, PDI scores < 83). Unadjusted univariate analyses revealed increased mortality associated with baseline CD4+ 29%, gestational age < 37 weeks, smaller head circumference, advanced HIV and higher plasma viral load, and data modeling corrected for these variables. Figure 4 shows psychomotor index scores as a function of follow-up (a similar finding was obtained for emerging cognition, MDI). Most important, the results revealed that neurodevelopmental scores *independently* predicted mortality after
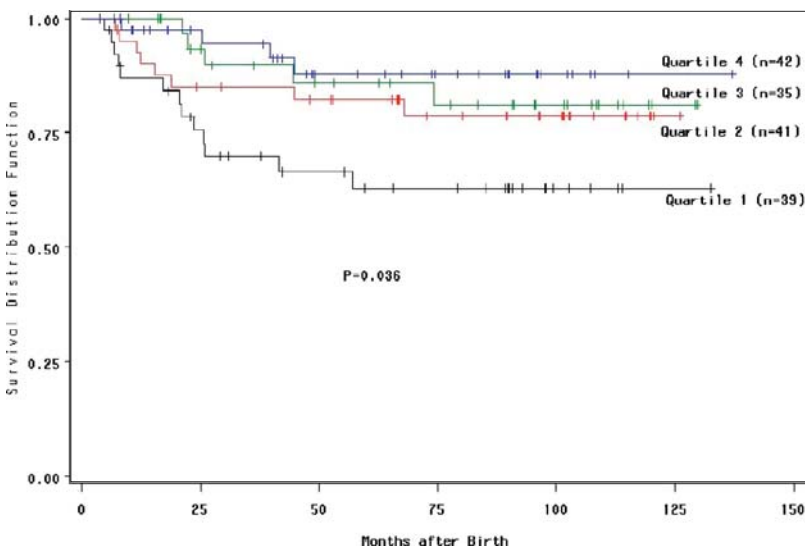
FIGURE 4. Kaplan–Meier curves showing cumulative incidence of survival according to quartiles (Q) of motor scores (BSID, Psychomotor Developmental Index [PDI]). The ordinate shows the survival distribution function, whereas the abscissa depicts months since birth. Children who obtained scores in the lowest quartile (<83) exhibited the lowest survival rate (increased mortality). Similar findings were observed in the cognitive index (BSID, MDI). Reprinted from Llorente et al. (2003). Copyright Cambridge University Press. Reprinted by permission.

adjusting for the aforementioned confounds including viral load and CD4+ count.

As noted earlier, host factors may play a significant role in the neurodevelopmental expression of HIV-1 in pediatric populations. In this regard, genetic factors may account for a large proportion of specific neurodevelopmental outcomes, and mutations in some chemokine receptor proteins have been reported to be associated with decreased risk of perinatal HIV-1 transmission and slower disease progression among HIV-1 infected infants (Buseyne et al., 1998; Ioannidis et al. 2003; Kostrikis et al., 1999; Misrahi et al., 1998), and it may impact neurodevelopment. Polymorphisms in genes associated with chemokine receptors and ligands, particularly those that impact monocytes-macrophages, also may play a significant role in the child's susceptibility to neuropathology, leading to specific neurodevelopmental profiles. These polymorphisms hypothetically could affect the ability of HIV-1 to infect CNS monocytes-macrophages, the chief cells in the brain that have been documented to be infected with HIV-1, or they may influence the production of potentially damaging cytokines by these cells, thereby influencing CNS manifestations during infancy and childhood. A polymorphism also might influence the ability of infected or activated monocytes and lymphocytes to penetrate brain parenchyma that might decrease the secondary activation of glial cells, an important mechanism in the pathophysiology of the disease. A chemokine receptor meriting scrutiny is chemokine receptor 5 (CCR5) because CCR5 has been shown to be present on the cell surface of monocytes-macrophages and has been identified as a *necessary* co-receptor for cell entry of macrophage-tropic HIV-1 isolates (Dragic et al., 1996). CCR5 and other receptors (e.g., CXCR4) also have been found in the brains of children with acquired immune deficiency syndrome (Vallat et al., 1998). Unfortunately, these factors have received little attention in the neurodevelopmental literature.

In an attempt to investigate the impact of specific host genetic factors on neurodevelopmental outcome, Llorente et al. (2006) investigated the effects of chemokine receptor polymorphisms on neurodevelopment and the onset of encephalopathy in infants and young children with perinatal HIV-1 infection. In their study, infected infants and children ($n = 121$) between the ages of 4 and 72 months who underwent longitudinal neurodevelopmental assessment over the course of 72 months were categorized into dichotomous groups (heterozygous or homozygous mutant vs. homozygous wild type) for each CCR5 allele while using the CCR2 I64 allele as an internal control. Longitudinal outcome instruments included neurodevelopmental measures with neurocognitive and motor scales for infants and young children age ≤ 30 months (BSID) and more advanced neuropsychological measures of cognitive and motor development for children aged 30–72 months (MSCA, McCarhty Scales of Children's Abilities, McCarthy, 1972). Modeling of neurodevelopemental and neuropsychological data was accomplished using a basic linear spline with the mean value at each visit for the relevant test index, with determination of the slope between 4–12 months, 12–30 months, and 31–72 months of age. A mixed model analysis of variance was used to compare differences between slopes ($\Delta\beta$) and intercepts ($\Delta\alpha$) according to the presence or absence of the specified CCR2 or CCR5 polymorphism. In addition, to investigate the impact of these polymorphisms on more severe neurodevelopmental outcomes as noted earlier in this chapter (e.g., encephalopathy), survival analyses were used to model and compare the onset of encephalopathy by chemokine receptor allelic grouping. Finally, clinical and demographic characteristics that were found to be statistically significant were controlled for in an attempt to reduce the effects of these potential confounds on outcomes variables. After adjusting for potential confounds, statistically significant differences emerged in several of the CCR5 polymorphisms. Unfortunately, although the protective effects emerged associated with specific polymorphic expressions, such effects appeared to be discrete and transient, yet children with mutant CCR5 genotypes exhibited better neurodevelopmental outcomes than children with the wild type alleles. As expected, mutations in CCR2 I64 had no effect on any outcome. In this study, chemokine polymorphisms also did not appear to impact the onset of encephalopathy. Figures 5 and 6 show the results of this investigation from selected polymorphisms and outcome variables. On the basis of these findings, but subsequent to investigational weaknesses (note that children with homozygous and heterozygous mutations were
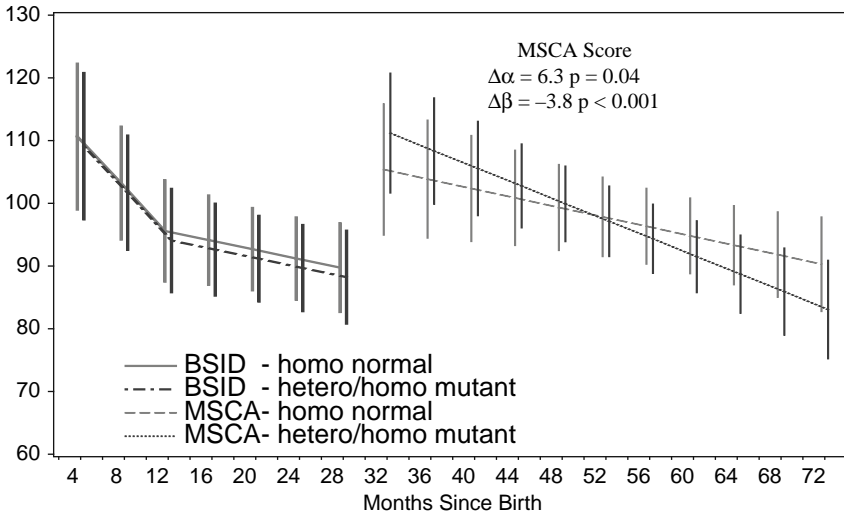
FIGURE 5. Estimated mean Motor (BSID, PDI) and Perceptual (MSCA, P) Index for infants and children by group (homozygous or heterozygous mutant vs. homozygous wild type) for CCR5-39402 genotype. The ordinate shows BSID or MSCA standard scores, whereas the abscissa shows chronological age (months since birth). Reprinted from Llorente et al. (2006). Copyright Lawrence Erlbaum Associates, Inc. Reprinted by permission.
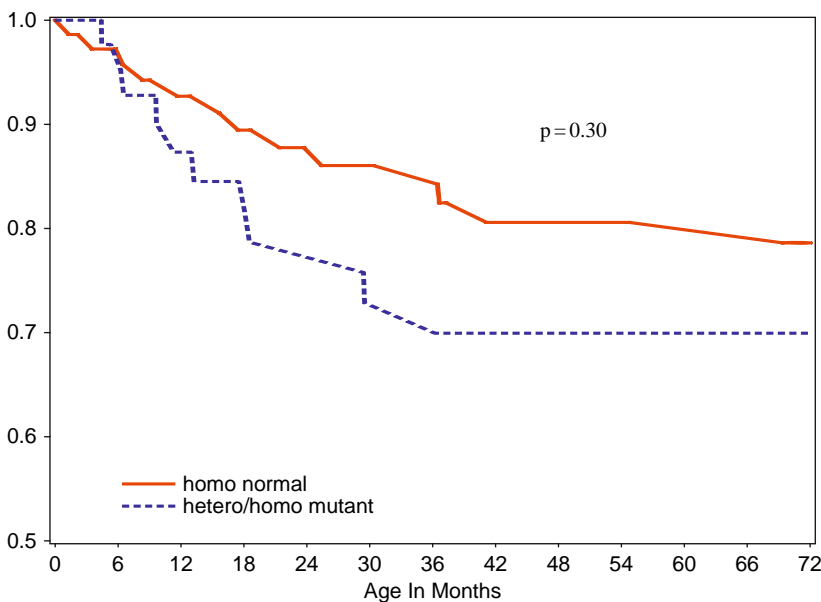
FIGURE 6. Kaplan–Meier curves showing (ordinate axis) cumulative incidence of time until encephalopathy (age in months shown in the abscissa) according to group (homozygous or heterozygous mutant vs. homozygous wild type) for CCR5-39402 genotype. *P*-value is for the log-rank test. Reprinted from Llorente et al. (2006). Copyright Lawrence Erlbaum Associates, Inc. Reprinted by permission.

amalgamated), these investigators tentatively concluded that although possibly a temporary effect, HIV-1 infected children with selected mutant chemokine receptor polymorphism may exhibit better neurodevelopmental outcome than children with the wild type allele.

Whereas early studies investigating the effects of HIV infection in children were poorly controlled and cross-sectional in nature, more rigorous longitudinal studies examining the spectrum of neurodevelopmental and cognitive deficits across a larger span during childhood have revealed a clearer picture suggesting that substantial and dramatic impairments are sometimes observed in this domain. The degree of impact on overall cognitive functioning as a result of infection, particularly during more advanced disease stages, is consistent with the type of neuropathological insult commonly seen in this disease. Specifically, the reader may recall the presence of neuropathological findings including cerebral atrophy, acquired microcephaly, and encephalopathy in these children (cf., Belman, 2002; Epstein et al., 1988). These CNS abnormalities, in and of themselves, are capable of accounting for the profound dampening in overall development and intellectual functioning observed in some of these children.

Attention and Concentration

Difficulties in vigilance and attention are among the most frequent problems associated with any type of brain damage (Lezak, 1978), probably as a result of the fragile nature of these cognitive processes. In HIV infection, this domain of functioning is sometimes compromised even in seemingly asymptomatic patients. One study (Brouwers Belman & Epstein, 1999) examined the effects of viral involvement on attentional processes by looking at the WISC-R Freedom from Distractibility factor (Kaufman, 1975). The results from this investigation revealed that seropositive children experienced "relative weaknesses" on this marker. In another study using cluster analytic procedures, Brouwers et al. (1992) discovered that one subgroup of symptomatic seropositive children could be identified by a cluster comprised of items loading heavily on attention deficits. Similarly, in the study reported by Boivin et al. (1995), a review of the results reveals that HIV-positive children relative to HIV-negative controls born to seronegative mothers obtained lower levels of performance on tasks believed to be partly dependent on attentional skills (e.g., K-ABC Hand Movements, Number Recall

and Spatial Memory subtests). Although tentative, these data suggest that the virus may be capable of causing attention difficulties. However, Brouwers, Moss et al. (1994) appropriately caution that these deficits could very well be the result of other intervening variables not related to the infection per se, such as the high base rates of attention difficulties in children for this age group in the general population, acting as potential confounds. A similar cautionary posture is to be taken if findings from more recent investigations (cf., Mellins et al., 2003) are supported by future research, indicating that demographic and environmental factors may account for a portion of the neurodevelopmental and neurobehavioral difficulties observed in HIV-1 infected children. Factors such as poverty, number of changes in caretakers, and other psychosocial factors may be able to mimic neurodevelopmental declines, or at the very least contribute to such declines.

Although a number of studies conducting behavioral assessment also has revealed that these children may indeed suffer from attentional deficits (e.g., Hittleman et al., 1991), the preschoolers studied in those investigations were quite young (15 months old) and prone to suffer from the same high base rates of diminished attention as postulated by Brouwers, Moss et al. (1994; Brouwers et al., 1999). Children in this developmental stage also display a great deal of variability in attention from day to day. Finally, although mild alterations in attention or vigilance may be observed in these children, such alterations may not rise to the level of a disorder or a diagnosable condition. As previously noted (Llorente et al., 1997), further studies with good controls will have to be conducted with children infected with the HIV virus to determine in an evidenced-based fashion, whether the attention deficits observed during neuropsychological and behavioral assessments are the result of the disease process or other unrelated etiologies.

Despite the aforementioned caveats, given the fragile nature of these processes, there is a likelihood that these mechanisms are indeed influenced by this virus, particularly during more involved expressions of the infection. During more advanced and debilitating stages of the disease, white matter involvement has been identified as a neuropathological hallmark of pediatric HIV (Sharer et al., 1986). In particular, as it relates to

this domain, neuropathological and electrophysiological findings have indicated the presence of calcification in the pontine nuclei (Sharer et al., 1986) and brain stem auditory evoke potential abnormalities (Belman et al., 1985), respectively. Therefore, it is possible that the HIV compromises attention mechanisms, responsible for the deficits observed in this domain while undergoing neuropsychological evaluation, by encroaching and infringing upon the ascending pathways of the reticular activating system or pathways that lead to executive regulatory systems.

Memory

Although complications in attention are sometimes accompanied by memory difficulties, in some cases as an immediate consequence of deficits in the former domain, at first glance it appears that HIV infection may also cause direct and independent memory deficits (Belman et al., 1988; Diamond, 1989; Havens et al., 1993; Levenson et al., 1992). Boivin et al. (1995) found impairments on tasks which were *presumably* capable of assessing emerging memory skills in young children. In their study with HIV-positive asymptomatic youngsters, these investigators demonstrated difficulties in verbal and visual processing tasks believed to assess memory functions in children 2 years of age or older. Specifically, HIV-positive participants, relative to HIV-negative controls born to noninfected mothers and HIV-negative children of infected mothers, obtained significantly lower levels of performance on the K-ABC Immediate Recall and Spatial Memory subtests (these measures attempt to assess among other functions immediate verbal and visual recall, respectively). Significant differences were also observed on yet another K-ABC subtest of visual immediate recall (Hand Movements). Similarly, data from 5- to 12-year olds reported by Havens et al. (1993) were supported by Boivin et al. (1995). Havens et al. (1993) using a measure of intellect with an attention index, similar to the study by Boivin et al. (1995), revealed the presence of lower scores in the HIV-positive cohort compared to the HIV-negative cohort on a short-term memory index (STM).

However, given the insufficient number of well-controlled studies with large samples of children examining this domain with psychometrically sound procedures during early childhood, in conjunction with the potential confounds as a result of the high base rates of attention difficulties in this population, the present results are suggestive at best. The primitive nature of these functions at this developmental stage coupled with our limited ability to validly assess them in young children also render the present findings hypothetical at this time.

Expressive Language Functions and Auditory Processing

Complications and impairments in language, specifically expressive language and auditory processing difficulties associated with HIV infection, often have been often reported in the literature (Belman, et al., 1985; 2002; Brouwers, Belman, & Epstein, et al., 1991; Brouwers et al., 1999; Coplan et al., 1998; Ultmann et al., 1985, 1987; Wolters, Brouwers, Moss, & Pizzo, 1994). Although a great deal of variability is observed, and some children, particularly HIV-positive asymptomatic youngsters undergoing successful treatment, may not show any difficulties, language-related impairments are usually present during symptomatic states (e.g., CDC Class C). In addition, these deficits seem to be affected by the mode of viral transmission in conjunction with the degree of disease progression. In addition, although the introduction of antiretroviral therapy has reduced the number of children who progress and experience encephalopathy, when treatment becomes inefficacious, or treatment adherence is poor, or not available, some infants and children will progress and experience encephalopathy. An infected infant who suffers from subacute progressive encephalopathy will display delays acquiring and developing language while progressively losing previously attained milestones, whereas an older child who becomes infected with HIV via drug use, or via transfusion prior to modern techniques to detect the virus, may develop regression or slurred speech as well as regression in other language skills from previous level of functioning. A complete loss of speech may also be observed in older children in the late stages of disease involvement, but particularly in encephalopathic states. These differences in performance underscore the heterogeneity in patients noted earlier.

Although both receptive and expressive language skills have been found to be affected by

the virus (Epstein, 1986; Wolters et al., 1994, 1995), the majority of insults occur in the expressive domain with relatively spared or less affected receptive skills (Brouwers, Moss et al., 1994; Brouwers et al. 1999). Data-based evidence for this observation comes from research by Wolters and her associates (Wolters et al., 1994) who demonstrated, as part of a study of adaptive functioning using the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cichetti, 1984), that expressive language skills underwent greater insult relative to receptive skills in both encephalopathic and non-encephalopathic groups of children. Another study with the participants from her study in 1994 by Wolters et al. (1995) again discovered the presence of declines in both expressive and receptive language skills, with greater impact noted in expressive skills. However, it should be noted that the 1994 studies used caretaker's verbal report to assess difficulties in receptive and expressive functions in these children rather than cognitive tests designed for this purpose. Nevertheless, a study using direct evidence through inferences from the direct performances of children also support a hypothesis suggesting that HIV-1 is capable of producing independent language impediments. Coplan et al. (1998), a year after the first edition of this chapter was produced, published a report in which HIV-1 infected infants and children obtained significantly lower scores on a formal, objective, and standardized language test designed to measure emerging language skills. In that investigation, Coplan and colleagues (1998) noted that the infected children obtained a composite language score in the low average, whereas the uninfected children obtained a composite language score in the average range.

In light of the scarce number of longitudinal and well-controlled investigations with large number of participants assessing this domain, several issues deserve mention. First, it should be clear that more advanced stages of the disease are indeed associated with serious deficits in language with greater impact on expressive language skills. Second, some of these language complications are probably caused by oral-motor difficulties as a result of basal ganglia insult as previously noted (Llorente et al., 1997), yet other aspects of these insults appear to be direct impact on neurological substrates supporting language abilities. Third, while

some insults may be the result of direct effects, others may be the result of test or assessment artifact (it may be easier to detect deficits in emerging expressive language skills than in complex receptive language skills) or the effects of other factors such as neurodevelopment interacting with demographic or environmental factors such as acculturation (cf., Llorente et al., 2004). Finally, it is important to flush several issues reported in the literature impacting these skills, including the differential effects on expressive language skills compared to receptive language skills. This is critical because such an effect may be the result of developmental factors interacting with the virus, as a result of the fact that expressive skills, in general, are under rapid maturation at this developmental stage making them more vulnerable to insult (Ewing-Cobbs, Fletcher, Levin, & Landry, 1985), and this phenomenological finding requires further scrutiny.

Motor Functioning and Processing Speed

Given the striking and profound involvement in the basal ganglia complex and associated circuits in children suffering from HIV infection and HIV-1 encephalopathy (see Figure 1), specifically calcification, vasculopathy, and inflammatory CNS diseases (Belman, 2002; Belman et al., 1988), it is not surprising to observe motor deficits in these children during neurodevelopmental evaluation, particularly when the correlative responsibilities for motor functions of such neurological substrates and circuits are taken into consideration. As a result, gross and fine motor delays are very prominent in symptomatic seropositive infants and children.

Motor skills are often the most frequent aspect of functioning vulnerable to the disease process (Brouwers et al., 1999; Fowler, 1994; Hittleman et al., 1990, 1991; Ultmann et al., 1985, 1987). Specifically, many symptomatic infants display muscle tone abnormalities and very slowed rate of gross-fine motor skills acquisition and in some instances declines in motor skills. Even seemingly unaffected HIV-positive asymptomatic infants, less than 2 years of age, have recently been observed to suffer from motor delays using a standardized developmental screening measure (Boivin et al., 1995). Symptomatic preschoolers and school-age children may also display abnormalities in this domain as expected, initially marked by

disturbances in gait and balance (Brouwers, Moss et al., 1994; Brouwers et al., 1999). However, Fowler (1994) reported that unlike infants and toddlers, some older children and adolescents tend not to suffer from mild neurologic impairments, including motor dysfunction (e.g., fine motor tremor) until the later stages of symptomatic disease process.

The authors of this chapter have observed these deficits in gross and fine motor tasks (e.g., fine motor deficits on the Grooved Pegboard Test; Kløve, 1963) in these children, during the middle-late stages of symptomatic disease, similar to those observed in adults (Selnes & Miller, 1994). In more severe cases, the ability to ambulate is lost due to pronounced involvement in the lower extremities, most likely associated with neuropathological processes affecting the basal ganglia nuclei and circuits as reported earlier. Brouwers, Moss et al. (1994) report that more serious deficits in this domain may be observed, including spastic quadriparesis and pyramidal tract signs, with greater levels of CNS involvement such as progressive encephalopathy (cf., Belman, 2002; Belman et al., 1988).

Difficulties also have been observed in speed of information processing, in a group of HIV-1-positive children. Using a rapid color naming task administered to 5- to 7-year-old children, a cohort within the research sample exhibited lowered speed of information processing (Llorente et al., 2004), and these findings also are consistent with well-controlled studies from the adult literature (cf., Llorente et al., 1998). Finally, these motor and speed of processing deficits remain after controlling for potential confounds.

In summary, pronounced delays in motor performance are frequently evidenced in symptomatic seropositive infants and older children, including motor tone abnormalities and other motor delays, with more arrest in development associated with more progressive and debilitating disease courses (e.g., subacute progressive encephalopathy). Even in seemingly unaffected HIV-positive asymptomatic infants, subtle or mild delays in this domain are sometimes evident. Although less common, due to the low frequency of occurrence of these diseases in children with the advent of prophylactic treatments, opportunistic processes also can sometimes cause abrupt motor complications, vastly different from the gradual and progressive course of motor difficulties described above, as a result of an immunocompromised state. These complications include, for example, abrupt motor deficits subsequent to neoplasms, strokes or other causes (Park et al., 1990). It is also critical to note that the motor delays can occur independent of cognitive effects that may surface, and in some instances such early motor delays and deficits can be predictive of future morbidity and mortality (cf., Llorente et al., 2003).

Academic Achievement

Given the degree of impairment evident in cognitive abilities and adaptive functioning that is sometimes present in selected groups of HIV-infected children, infringing upon various neuropsychological domains, it is only rational to expect them to suffer from learning difficulties. Although there is a lack of investigations examining this domain systematically, difficulties in academic achievement associated with HIV infection have been reported in the literature (e.g., Cohen et al., 1991). Cohen et al. (1991) found mathematics and reading achievement scores below the range of expectation in a group of children infected neonatally through transfusion relative to a group of uninfected controls. It is important to note that Cohen and colleagues (1991) retrospectively (parent questionnaire) examined the rates of absenteeism in this cohort of children. Their results revealed that lack of school attendance could not account for the academic achievement discrepancies observed between their groups of control and HIV-positive children. However, given the scarce number of investigations assessing this domain, further research would need to elucidate how these potential confounds affect academic achievement apart from the direct effects of the infection on the CNS.

Adaptive and Neurobehavioral Considerations

Other areas of functioning, such as alterations in the adaptive and behavioral repertoire of children resulting from pediatric HIV infection, are capable of producing further impact on the overall profile of children. Brouwers, Moss et al. (1994; Brouwers et al., 1999) distinguished between direct and indirect effects. HIV-direct impacts are those immediately associated with the disease process such as the behavioral and

emotional disturbances encountered with encephalopathic states. Indirect effects are consequences of HIV indirectly related to the disease. These effects are usually the result of demographic characteristics, environmental factors, treatments and their side effects, coupled with host variables (e.g., coping strategies, genetic factors, psychological resources, etc.), and the disease process (e.g., undergoing multiple medical procedures and hospitalizations as part of radiation treatment for an opportunistic disease), synergistically operating to create specific neurobehavioral profiles. These adaptive and behavioral factors may play a major role in the way that HIV-related symptoms exhibit themselves from patient to patient and must be taken into consideration when evaluating, performing research, or providing rehabilitative services to pediatric patients.

However, it is critical to attend to indirect effects. In this regard, care must be exercised when attributing behavioral problems sometimes observed in children with HIV-1 infection to the direct effects of the disease as these problems may not be attributable to HIV-1 disease, and this issue requires significant investigation. This investigative course of action was necessary because many descriptive studies and clinical reports had indicted that HIV-positive children were at increased risk for behavioral difficulties. Unfortunately, inadequate control groups, small sample sizes, as well as the inability to control for potential confounders that place HIV-positive children at increased risk for negative neurobehavioral outcomes plagued the literature requiring that this issue be clarified. Therefore, Mellins and her colleagues (2003), as part of the WITS, examined the "unique and combined influences" of HIV-1, "prenatal drug exposure, and environmental factors" on children's behavior. In this investigation, caregivers of 307 children born to HIV-positive mothers (96 HIV infected; 211 seroreverters) completed a parental behavioral rating scale (Conners' Parent Rating Scale, CPRS; Conners 1989) starting at 3 years of age. In addition, data were also collected related to potential confounders including birth complications, gender, prenatal drug exposure, race/ethnicity, as well as caregiver relationship to child. Multivariate analytic methods were employed comparing the neurobehavioral profiles on the CPRS of HIV-infected children with perinatally exposed but uninfected controls (children) from similar demographic backgrounds. These analyses failed to find a significant relationship between prenatal drug exposure and poor neurobehavioral outcomes (CPRS, Conduct Scale) or between HIV status and poor neurobehavioral outcomes. Based on these findings, these investigators concluded that although a high prevalence of neurobehavioral difficulties are present among HIV-infected children, neither HIV infection nor prenatal drug exposure is directly responsible for these difficulties. Therefore, it would appear as if "other biological and environmental factors" (secondary factors) are probable "contributors toward" these poor neurobehavioral outcomes, as noted during the last decade (Brouwers et al., 1991). In fact, demographic characteristics were found to be most strongly correlated with increased neurobehavioral symptoms, and this issue has been supported by other research suggesting the importance of specific demographic factors (cf., Llorente et al., 2001). As noted in the previous edition of this chapter (Llorente et al., 1997), it is also possible that the fact that these children are affected by a chronic medical illness (i.e., HIV-1) is partly responsible for the academic, adaptive ,and neurobehavioral difficulties observed as well, as would be the case for other children with other chronic and debilitating medical illnesses (Routh, 1988).

A large number of children infected with the HIV-1 come for assessment, research protocols, and/or treatment from low SES backgrounds. For example, in the United States, a large proportion of perinatally infected children have mothers who acquired the virus via sexual contact with men who are IV drug users or are IV drug users themselves. For this reason, some families with infected children often struggle with basic necessities such as housing and nutrition, and many HIV-positive women receive services for themselves and their children from several community and state agencies. LoPresti, Llorente, Guzzard, and Brumm (1998) evaluated a community-based sample of 26 women (Caucasian, African-American, and Latinas) who were referred by social service agency staff for neuropsychological (NP) evaluation due to concerns of cognitive deterioration affecting daily living skills including child care, women whose premorbid features would generally exclude them from neuropsychological research studies. Only six demonstrated a sufficient

degree of neuropsychological impairment to warrant a diagnosis of an HIV-associated disorder, despite multiple risk factors including significant immunosuppression, alcohol and drug use, mood disturbance, and limited education, and half reported a mild to moderate level of depressive and anxious symptomatology related to their own and their child's medical condition and life stressors. Yet women's problems with daily living skills which would have been attributed to substance use, unfamiliarity with bureaucratic systems, and limited coping strategies in the absence of an HIV diagnosis were being routinely interpreted by staff as HIV-related cognitive decline. Conversely, signs of frontal system disorder often observed with increasing immunosuppression, such as disinhibition and difficulty shifting set, were misperceived as personality features. Clearly, these findings highlight the complexity of environmental and other factors, and psychobiosocial variables must be carefully considered when interacting with these children and their families (cf., Guarino et al., 2002). A large segment of the pediatric population infected with HIV-1 additionally belong to ethnic minorities for which there is sometimes little normative data or for which inferences made on the data available would be invalid for the population under investigation or the patient undergoing intervention. For these reasons, caution must be exercised when interpreting neurobehavioral findings as abnormal, in light of these potential confounds. In the same vein, since children with HIV infection tend to display augmented behavioral disturbances (Ultmann et al., 1985), similar to children who suffer from other types of medical illnesses (Routh, 1988; Tarter, Edwards, & van Thiel, 1988), careful interpretation of behavioral observations and assessment results should follow suit in order to avoid misinterpreting normal findings as aberrant or behavioral disturbances as normative. From a clinical standpoint, the combined experiences of the authors also require that other important factors be addressed related to neurobehavioral problems sometimes observed in these infants and children. Unlike families with children who suffer from other chronic illnesses, particularly those that are not acquired through perinatal transmission or where mortality is not an issue, families with children who have been infected perinatally commonly suffer from guilt associated with the

fact that they transmitted the disease to their offspring(s). Mothers of perinatally infected children also have to provide care for their own illness, while caring for their children, and in instances where death or unavailability of the mother is present, caregivers other than the mother have to care for the infant or child. Finally, acute medical crises as a result of opportunistic diseases associated with an immunosuppressed state, as would be expected, increase stress in caregivers and the child. Similarly, legal issues including custodial rights (legal, medical, etc.), academic and school problems and their legal ramifications, sometimes are at issue as well, and these and similar factors create further stress in the immediate environment and family circle and should be seriously considered during any type of contact and intervention with these patients or research participants (cf., Zeichner & Read, 2005).

Neurodevelopment and Pharmacological Treatments

Although the previous edition of this chapter (Llorente et al., 1997) did not have a section dedicated to treatment and its impact on neurodevelopment, and it is beyond the scope of this chapter to comprehensively review the topic, given the number of new therapies available to treat pediatric HIV-1 infection, in conjunction with the number of studies that have been published in the last decade addressing treatments and their cognitive outcome, a section related to neurodevelopment and pharmacotherapy is warranted. Early pediatric studies concentrated on documenting the neurodevelopmental efficacy of nucleoside reverse transcriptase inhibitors (NRTIs), therapies that operate by reducing viral replication through their effect on the enzyme reverse transcriptase, of which zidovudine (AZT, ZDV) is considered the prototype. Although early investigations showed promise as a result of neurodevelopmental and neurobehavioral improvements associated with AZT administration (Brouwers, Moss, & Wolters et al., 1990; Pizzo et al., 1988, 1989), particularly when administered through continuous infusion (cf., Pizzo et al., 1988), and later studies confirmed earlier findings (Brady et al., 1996; McKinney et al., 1991; Wolters et al., 1994), it eventually became clear, that over time, HIV-1

overwhelmed its host and that AZT alone could not maintain the integrity of the immune system or reduce viral load (replication) in some infants and children as a result of rapidly acquired resistance, unable to maintain them free of declines in neurodevelopment. These findings fortunately led to the development of new treatments. Some of those studies even showed that the reported gains may have had differential effects in infants relative to older children, with the greatest effects occurring in the youngest children, or that specific psychometric factors could account for the differential effects observed (cf., McKinney et al., 1991). The protective effects of AZT in some instances were temporary, at least as they related to neurodevelopmental factors, as had been shown by Llorente et al. (2001) for mildly symptomatic adults where the neurocognitive gains associated with AZT administration present at 26 weeks, noted by earlier adult studies (cf., Schmitt, Bigley, Mc Kinnis, Logue, Evans, Drucker, 1988), disappeared over the course of the subsequent 26 weeks. Yet, at this point, it is important to note, as indicated by Llorente et al. (2001), that AZT monotherapy continues to be a viable treatment when used as a prophylactic, in the reduction of mother–child transmission, in patients who are not able to tolerate more complex antiretroviral treatment combinations (e.g., HAART) or where the availability of complex treatments is limited or not available as a result of economic or other constraints around the world such as in some underdeveloped countries, and AZT remains the treatment of choice for many a pediatric patients.

The transitory nature of therapeutic success as a result of the acquired resistance to AZT monotherapy partially led to the development of new NRTIs to be used in combination with AZT, or alone in instances of intolerance to AZT, that also showed initial promise (Butler et al., 1991; Pizzo et al., 1990; Wolters et al., 1990, 1991). Butler et al. (1991) reported on the effects of dideoxynosine (ddI) while Pizzo et al. (1990) reported on the effects of dideoxycitidine (ddC). While Butler et al. (1991) did not report significant overall improvements in intellect, similar to the investigation by Pizzo et al. (1990) using ddC alone, the combination of AZT/ddC revealed improvements in intellect in the study by Pizzo et al. (1990). Further investigations showed that resistance to combination

therapy with NRTIs could also occur and new treatments had to be devised. Therefore, a new line of therapies emerged using a distinct mechanism of action, namely protease inhibitors (PIs). These new therapies showed potent activity against HIV-1 viral replication by precluding maturation of the virus through inhibition of the native protease enzyme, precluding the infection of new cells. Recent consensus reports have noted that treatments that include a combination of protease inhibitors taken with reverse transcriptase inhibitors (highly active antiretroviral therapy, HAART) tend to be most successful in treating symptoms associated with HIV-1 infection, including neurodevelopmental and neurobehavioral effects (cf., Cooper et al., 2002).

Unfortunately, a limited number of investigations have suggested that these treatments may not be free of significant side effects in infants and children, in some instances with possible pernicious collateral consequences, including mitochondrial damage (cf., Blanche et al., 1999; Brinkman, Ter-Hofstede, Burger, Smeitink, & Koopmans, 1998; Loubery-Unique, Gauthier, vaugelle-Gardier, & Tibayrence, 2001), and as noted earlier in this chapter, a number of studies have begun to investigate this issue (Tardieu et al., 2005), particularly as it relates to neurodevelopment (Carneiro et al., 2001; Culnane, Fowler, & Lee, 1999; Lange, Stellato, & Brinkman, 1999). For example, although Culnane et al. (1999) failed to find any differences in neurodevelopmental status over the course of 4 years among uninfected infants born to HIV-1 positive mothers who received zidovudine compared to uninfected infants born to HIV-1 positive mothers who received a placebo, other studies have reported neurodevelopmental problems in infants whose mothers received prenatal AZT treatment (cf., Carneiro et al., 2001). Clearly a great deal of empirical work remains to be conducted in this area to ascertain the safety of antiretroviral treatments, and the impact of any collateral side effects on pediatric cognition.

Over time, several factors have become clear related to the relationship between treatment and neurodevelopmental factors that require mentioning in this chapter. First, select treatment combinations have been shown to be very successful for some children. In fact, in the study reported by Llorente et al. (2003) addressing the ability of neurodevelopmental markers to predict mortality in infants, where such

markers were shown to serve as independent predictors of poor neurodevelopmental outcome, treatment was one of the few variables that was shown to modulate negative outcomes, including morbidity and mortality. Similarly, the introduction of HAART has changed the incidence of opportunistic diseases and other negative disease expressions, particularly severe neurodevelopmental effects related to encephalopathic states associated with pediatric HIV-1 infection in the United States and abroad. Second, the chief aim of treatment should be to maintain the immune system as intact as possible while keeping viral replication and load to minimal levels (Chantry et al., 2003). Third, the effects of these treatments on neurodevelopmental factors partly depend on the therapies' ability to penetrate the brain–blood barrier (BBB; cf., Pizzo et al., 1990; Wynn, Brundage, & Fletchner 2002). In this regard, it has become evident that not all antiretroviral therapies are able to cross the BBB with the same degree of efficacy, and this factor can have significant effect on neurodevelopmental outcomes. For example, ddC has been shown to be less capable of penetrating the BBB than ddI, and the differential effects reported above in the study by Pizzo et al. (1990), where ddC in combination with AZT had greater positive effects than ddC monotherapy, were partially attributed to the inability of ddC to efficaciously penetrate the BBB (cf., Toledo-Tamula, Wolters, Walsek, Zeichner, & Civitello, 2003). Finally, relatively recent reports have noted the presence of declines in neurodevelopment despite the presence of stable immunological and virologic function and the administration of antiretroviral treatment (Toledo-Tamula, Wolters, Walsek, Zeichner, & Civitello, 2003). All these findings have significant surveillance and treatment implications when addressing treatment and neurodevelopmental factors.

Diagnostic, Surveillance, and Rehabilitative Issues

As was the case a decade ago, the contributions of neurodevelopmental and neurobehavioral methods to the scientific understanding of this disease, and the applications of these findings to the diagnostic, surveillance, and rehabilitative process, remain potentially unlimited. The numerous opportunities for significant contributions on these fronts stem from the number of HIV-1-related, prominent deficits observed in some infants and children across neurodevelopmental and neurobehavioral spectrums, in addition to emerging data suggesting that declines in cognitive functioning can and do occur despite the presence of stable immunologic functioning (Toledo-Tamula, Wolters, Walsek, Zeichner, & Civitello 2003) and other markers without the inclusion of cognitive markers for surveillance and rehabilitative interventions.

This assistance is particularly valuable during the early stages of HIV disease involvement, where a child may not display readily observable symptomatology (unremarkable brain scans are often seen in some of these children), except for mild or very subtle impairments in higher brain functions or behavioral alterations. The potential for diagnostic support also results from specific medical complications. Certain CNS opportunistic diseases, present in some immunocompromised patients, initially manifest themselves behaviorally. Similarly, a number of "apparently" asymptomatic HIV-positive children appear not to have any complications from the infection. However, when these seemingly unaffected children undergo detailed neurodevelopmental and neurobehavioral examination, their profiles reveal subtle deficits in selected domains of cognitive functioning (Brouwers, Belman et al., 1994; Brouwers, Moss et al., 1994; see Martin et al., 2006). Therefore, this discipline continues to significantly contribute to the diagnostic process in several ways. For example, longitudinal assessment and surveillance of children at risk can provide information associated with changes in symptomatic status early on in the disease process while furnishing the treatment team data-based information regarding cognitive status changes and possible diagnostic information. In fact, for some children, particularly living abroad, aside from medical assays, neurodevelopmental and neurobehavioral assessment may be the only diagnostic procedure available.

Although neurodevelopmental and neurobehavioral methodologies have significantly contributed in the past, treatment outcome paradigms continue to be another area where the discipline should continue to play a role of considerable significance. For example, opportunistic diseases (e.g., neoplasms) as a result of

immunosuppression sometimes require the use of treatments involving radiation or chemotherapy. Radiotherapy has been shown to be positively correlated with detrimental neuropsychological effects as a result of the impact of this treatment on cerebral white matter (Filley, 1994) and/or other substrates. Thus, these procedures must be monitored in order to assess their efficacy and impact on higher order brain functions, especially in HIV infection where white matter compromise is present prior to the administration of radiotherapy making these structures of the brain more susceptible to further insult. Similarly, drug treatment outcome research is another source of continued involvement (cf., Pizzo, Brouwers, & Poplack, 1989; Pizzo et al., 1990; Wolters et al., 1990, 1991). In fact, treatment outcome research abound in the literature assessing the efficacy of zidovudine, ddI, ddC, d4T, and other antiretroviral treatments (e.g., Butler et al., 1991; DeCarli et al., 1991; Pizzo et al., 1988). Finally, the discipline can assist investigate the side effects of such treatments, particularly potentially damaging effects of nerve cells (cf., Carneiro et al., 2001).

In conclusion, neurodevelopmental and neurobehavioral methodologies can potentially play a pivotal role in diagnostic and rehabilitative processes, through its ability to assess cognitive functions subsequent to therapeutic interventions, and in the diagnostic process, especially during early stages of disease involvement or documentation of acute declines that initially show expression through neurobehavior. It has been shown that indices from neurodevelopmental evaluations can serve as independent predictors of mortality (Llorente et al., 2003), and in this sense, it is evident that these methodology can be employed in surveillance protocols. The examples presented above are but a few of the areas of extant and prospective contributions.

Summary and Putative Directions for Future Research

This chapter provided a succinct overview of the effects of pediatric HIV infection on the developing CNS. The sequelae associated with this infectious disease implicate various facets of functioning as detected by multiple procedures including neurodevelopmental, neurobehavioral, neurological, neuroimaging, and neuropathological procedures and methods, which easily account for the dramatic impact observed in some HIV-infected children.

Research findings to date tend to suggest that several neurodevelopmental domains may be afflicted by HIV-1 infection and possible, subsequent immunosuppressive states during infancy and childhood, particularly in more advanced stages of disease progression (e.g., encephalopathy) or more severe expressions of the disease (e.g., CDC Class C). Specifically, difficulties in emerging overall neurodevelopment, attention, language, learning and memory, motor skills, speed of processing and behavioral/adaptive functioning are readily observed in some children, particularly more subtle impact in successfully treated children.

Aside from reducing the CNS sequelae of HIV-1 infection in children, delaying or completely eliminating the onset of severe disease expression, the advent of pharmacological treatments, particularly HAART, also has increased the homogeneity of neurodevelopmental profiles, and for children in the United States and other regions of the world with available resources, the disease primarily has become a chronic treatable disease, as infants and children are maintained medically stable. Although treatment has increased the homogeneity of their profiles, it is important to keep in mind that a great deal of heterogeneity remains in pediatric HIV-infected populations. This is particularly true for populations of children outside the United States, or other developed nations, where treatment is not readily available, where large numbers of children remain naïve to treatment (cf., Shankar, Mahadevan, Satishchandra, Kumar, & Yasha, 2005), are unresponsive to AZT treatment, or are infected with the virus yet unaware of their infection status. However, it is also true for specific populations of children, even in the United States or other countries where treatments are readily available, but where poor treatment compliance has occurred (cf., Mellins et al., 2004). This fact alone should remind investigators and clinicians that despite significant advents in pharmacological treatment during the last decade, environmental and other factors continue to play a major in the expression of pediatric HIV disease in children in the United States and abroad, and that pharmacological treatments alone is in many cases

not sufficient. As noted earlier in this chapter, HIV-1 infection is an evolving disease as a result of changing trends in epidemiology, partly the result of advances in treatments or other interventions, including large-scale, population-based behavioral modifications. In that sense, selected aspects of this chapter, based on research conducted prior to the current state of disease evolution, may not be applicable to specific populations of infants and children with HIV infection. In addition, although advances in treatment and behavioral interventions may impact select populations in some areas around the globe, they have little if any impact in other areas due to the unavailability of advanced treatments such as HAART or failure to implement large-scale behavioral interventions in such areas.

As noted by Llorente et al. (1997), it is hoped that the reader takes away a balanced view of the impact of this disease process on neurodevelopmental and neurobehavioral functioning. On the one hand, severe disease involvement, particularly encephalopathy, is capable of causing serious impairments in neurodevelopmental functioning across most domains, and cognitive decline subsequent to HIV-1 infection may be predictive of morbidity and mortality (Llorente et al., 2003). Opportunistic diseases as a result of an immunosuppressed state consequent to HIV infection also are capable of producing similar devastating neurodevelopmental profiles, particularly in untreated children or children who exhibit poor response to treatments. In contrast, there are a number of children who seem to be mildly affected by HIV-1. However, detailed neurodevelopmental evaluations of these youngsters reveal a different picture. In some instances, these evaluations reveal minor and subtle deficits across selective domains, motor and information processing skills being some of the most susceptible abilities to the disease process. Another group emerges from the population of HIV-infected children. These children remain asymptomatic for years without any type of neurodevelopmental difficulties or complications. The absence of difficulties is present in some of these youngsters despite the fact that they occasionally suffer from varying degrees of immunosuppression. This remains an area of importance in terms of future research associated with host factors. A number of children with HIV-1 infection do not exhibit

cognitive delays or disease progression, and in some cases specific genetic polymorphisms have been associated with a lack of HIV-1 transmission (cf., Kostrikis et al., 1999), in some instances evidenced in long-term survivors who remain stable with HAART, but in some instances, children who are infected without knowledge of their infected status without treatment. Such an outcome may be associated with specific genetic factors, particularly specific genetic expression(s) that protect such individuals. From a cognitive standpoint, Llorente et al. (2006) provided a hint related to such factors. Unfortunately in that study, individuals with a heterozygous or homozygous expression had to be amalgamated for methodological reasons, and well-controlled, longitudinal studies addressing the unique protective factors or lack thereof of homozygous genetic mutations on cognition in perinatally infected children remain to be conducted.

Despite the fact that a number of studies have begun to elucidate in greater detail the impact of this infectious disease on the developing brain, it remains clear through a review of the literature that pediatric HIV-1 is an evolving disease as noted above. Therefore, as further advances in treatments emerge, in conjunction with the evolving nature of HIV-1, future investigations will be required to document the impact of new treatments and their potential side effects. In this regard, research addressing pharmacological treatment side effects deserves careful scrutiny. It appears that some treatments may have significant side effects as noted earlier, including possible mitochondrial dysfunction and its impact on development (Carneiro et al., 2001), yet the neurodevelopmental collateral effects associated with such dysfunction remain poorly understood and deserve future research efforts. As was the case a decade ago, it remains advantageous to ascertain if the deficits observed in several neurodevelopmental and neurobehavioral domains are the direct result of HIV-1 infection or "secondary" etiologies. Although the study noted by Mellins et al. (2003) indicated that environmental and/or demographic factors ("secondary") may account for a portion of the neurobehavioral difficulties observed in pediatric HIV-1 infection, and several other studies support that assertion, these investigations have used caretakers' rating scales not diagnostic instruments, or have been poorly

defined or controlled, or conducted before the advent and introduction of modern pharmacological treatments. Therefore, future investigations should attempt to determine whether the difficulties observed in any of the neurodevelopmental or neurobehavioral domains in HIV-infected children are subsequent to "primary" or "secondary" effects, particularly in the case of syndromal conditions, or domains where it is difficult to tease apart specific effects such as memory versus attention, etc. In other words, a programmatic program of research should be employed to investigate the origins of these conditions while controlling as much as possible for potential confounds. Future research also should investigate the effects of HIV-1 infection on emerging executive skills in children (cf., Martin et al., 2006).

It is patently evident that a great deal of work continues to lie ahead. Although the emergence of new investigations has increased our understanding of the effects of HIV-1 infection on the developing brain, and new longitudinal investigations have provided a better elucidation of the impact of the virus during infancy and early childhood, a great deal of research will be required in the future examining the natural history of the virus and its impact on cognition, particularly as the disease becomes a treatable chronic condition. The emerging nature of specific neurocognitive abilities during adolescence and the impact of the disease process on such functions in older children and adolescents require attention. Although research thus far has appeared addressing the impact of HIV-1 infection in infants and children, particularly longitudinal studies examining the natural history of pediatric HIV-1 infection such as the WITS (Sheon et al., 1996) and the European Collaborative Study (1991), the impact of HIV-1 infection on cognition during adolescence, particularly in older youth transitioning into adulthood, remains a wide open avenue for future research using well-controlled investigations. In addition, this is a critical issue because specific emerging neurocognitive skills begin to develop at greater pace and complexity during this period, including higher order executive skills, with particular ecological relevance for academic, adaptive, coping, emotional, leisure, and vocational factors leading to specific neurocognitive profiles with important relevance for quality of life.

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27

Neuropsychological Sequelae of Chronic Medical Disorders in Children and Youth

RICHARD A. BERG AND JOHN C. LINTON

Introduction

When this chapter was originally conceived and written several years ago, neuropsychologists had been largely concerned with the evaluation of neurologic conditions that result in impairment in intellectual functioning. At that point, the majority of both clinical work and published research has been done with adults. By comparison, clinical child neuropsychology was in its infancy. These statements were true when this chapter was first written in 1989, redone 5 years later, and sadly remain largely true today, another 10 years later. While there have been a few major contributions to the field (e.g., Baron (2004) and more clinicians are focusing their efforts on children, the amount of research pales in comparison to that in the adult literature.

Clinicians and researchers who work with children tend to focus their energies on the brain itself and tend to view most problems of concern as occurring within the brain or some other portion of the central nervous system (CNS). As our knowledge base grows, child neuropsychologists continue to remain involved in the evaluation of children suffering from diseases that affect any

part of the body. The majority of this work, however, is clinically based whereas the research literature is still heavily based in brain-related injury research.

Although the brain and other parts of the body are separate in terms of anatomy, they function as an integrated whole. Thus, when other organ systems are affected by a disease process, the brain in general, and cognitive functioning in particular, also may become impaired. This impairment may result from damage to brain tissue from the disease itself, or alternatively, brain dysfunction may occur as a secondary effect of a disease process elsewhere in the body. For example, the failure of other organ systems to provide nutrients to the brain may result in diminished cognitive functioning. The notion of multiple interactive systems is primary to the discussion of the diseases and conditions presented in this chapter. As nothing in the human body functions in total independence, there can be no single causal mechanism. Easily acknowledged on one level, this concept is both pervasive and essential to the understanding of brain–body relationships.

In the assessment of a child with medical problems, however, it is important that clinicians consider multiple causes for any noted neuropsychological disturbance. Additionally, psychiatric and social problems may impact on a child's behavior and overall functioning. The determination of the presence and severity of any brain effects thus requires knowledge of the possible contribution of a variety of factors

RICHARD A. BERG • Private Practice, Wilmington Health Associates, Wilmington, North Carolina 28401. **JOHN C. LINTON** • Department of Behavioral Medicine and Psychiatry, West Virginia University, Health Sciences Center, Charleston, West Virginia 25326.

including the disease itself, those organ systems directly and indirectly affected, the specific phase of the illness, any current medical treatment, premorbid personality, the coping capacity of the child, and the child's estimated functional level prior to the illness. It may be that these additional levels of complexity with a multitude of potentially confounding variables available which works to hinder more research in the area.

In many disease conditions, the cognitive sequelae have only been assumed to clinically report mental or behavioral changes of some children with the disease. There has been comparatively little research on the neuropsychological effects of individuals suffering from a great many nonneurologic diseases. Even when CNS effects are reported as possible or frequent, there is little understanding of the type of cognitive deficits likely to occur with differing disease processes, and even less is known about recovery patterns or residual effects.

In this chapter, we will discuss the functioning of some the major organ systems in the body and the ways in which its malfunction may potentially impact on brain functioning. Additionally, we will attempt to pull together the comparatively little research that has been done on disease processes specific to an organ system and the neuropsychological effects that have been reported. In a number of cases, specific neuropsychological data are not available: In those instances, clinical symptomatology that implicated possible neuropsychologic dysfunction will be offered.

The Brain and CNS

The basics of brain structure and function are reviewed in other sections of this book. We are concerned with the function of the brain as it relates to other body processes. The brain has large energy requirements. Although it comprises only about 2% of total body weight, it receives as much as 15% of cardiac output and accounts for 20% of the body's oxygen consumption (Freedman, Kaplan, & Sadock, 1976). As a result of this high demand for energy, brain cells tend to be extremely sensitive to alterations in their energy supply, which is mainly oxygen and glucose. Even minimal to mild energy deficits can impair the function

and integrity of brain cells (Ariel & Strider, 1983). Consequently, circumstances that can significantly alter the nutrient supplies to the CNS clearly can alter brain function.

In the normally functioning brain, energy is obtained through a process of oxidation of glucose to carbon dioxide and water. Energy resulting from this process is then expended in the transportation of various compounds across cell membranes and for the synthesis of other cell constituents. Because oxygen and glucose are transported to brain cells by blood, an adequate cerebral blood flow is essential for brain metabolism. Additionally, adequate availability of nutrients is dependent on proper functioning of the digestive system.

When portions of the brain are damaged, other organs systems can be disrupted depending on which area(s) of the brain is involved. If, for example, damage occurs to areas of the cortex, generally an individual's cognitive and sensorimotor skills are affected. Damage to the subcortex may disrupt the automatic functioning of other systems, however, such as heart rate, blood pressure regulation, breathing, hormonal balance, water regulation, or immune response. Such disruption can lead to further damage to the brain.

If portions of the peripheral nervous system are damaged, only the area subserved by those nerves typically demonstrates impairment. However, if a major organ system is involved, it may begin to function improperly, creating other imbalances in other systems that may, in turn, impact on brain functioning. Thus, it appears that all parts of the body in some way contribute to maintaining brain functioning and vice versa, as a disturbance in one system is highly likely to lead to a disruption elsewhere.

Infections of the CNS

The effects of encephalitis on the developing brain have been of interest since the outbreak of epidemic encephalitis following World War I, which resulted in high mortality among children and a high frequency of subsequent psychiatric morbidity (Graham, 1983). Ebaugh (1923), Kennedy (1924), and Strecker (1929) all reported studies of children who had been followed for a number of years after the initial acute illness. The acute phase of encephalitis was

characterized by sleepiness, fever, and other signs of localized CNS involvement and was followed by a gradual onset of a number of significant personality changes. Ebaugh (1923) reported a wide range of behavioral and emotional sequelae that involved insomnia with nocturnal agitation, affective disorders of the depressive type, hysterical reaction, and unwarranted fearfulness as well as mental retardation.

Since the 1920s, reports of epidemic encephalitis and subsequent behavioral sequelae have been sporadic, and Graham (1983) notes that encephalitis is now generally considered a rare cause of childhood cognitive disturbance. Levy (1959) described 100 children with hyperkinetic and antisocial behavior disorders to whom he ascribed the cause as encephalitis. However, since that study, doubt has been raised as to the actual etiology of the disorders manifested by these children. Sabatino and Cramblett (1968) reported that 14 children who had contracted documented cases of California encephalitis between the ages of 5 and 14 demonstrated auditory perceptual deficits as well as unspecified deficits in visual perception. A variety of emotional disorders were also reported including nervousness, hyperactivity, restlessness, and disruptive behavior together with learning problems.

Hern & Hynd (1992) report a case of a 12-year-old male who had three large right frontal lobe abscesses at 18 months of age. Recurrent seizures followed surgery and were controlled with medication. Neuropsychologic examination revealed decreased verbal and performance IQ levels as well as poor math achievement, decreased constructional praxis, impaired prosody, and poor social skills. Facial recognition also was poor. Hern discusses this case in terms of a right hemisphere syndrome. Few such cases are reported in the literature, and it is hard to know if an actual right hemisphere pattern exists or if this is an anomalous finding. As additional cases of focal right hemisphere damage are identified, patterns should emerge to help better delineate right hemisphere functioning in children.

Symptomatic congenital cytomegalovirus (CMV) is frequently associated with CNS involvement, including sensorineural hearing loss, microcephaly, chorioretinitis, neuromuscular disorders, and seizures. Infants born with congenital CMV clearly have increased risk for mental impairment. The reported incidence has ranged from 36 to 90% (Weber, Dolske, Pass, & Boll, 1993). Some children are reported as symptomatic at birth with severe developmental difficulties, whereas others have variably mild to moderate deficits. The intellectual status of 73 of 135 children with congenital CMV infection was assessed. A bimodal distribution was found in which 29 children were classified as mentally retarded with the remainder in the borderline or higher ranges (Weber et al., 1993). These data suggest that the infectious process, although not uniformly associated with impaired mental functioning, places the children at higher risk for such problems than the noninfected population.

Childhood meningitis is a relatively common infection, occurring in children under age 2, and acting on the immature brain, possibly disrupting cerebral development. A prospective study of 80 children with bacterial meningitis documented acute and long-term recovery patterns (Anderson et al., 1992). Children were evaluated at three times: at discharge, 12 months postdischarge, and 6 years postmeningitis. On the initial evaluation, motor and behavioral deficits were noted in 20% of the children. At 1 year, language and behavior problems were identified. A complicated recovery process and convulsions were related to lowered intellectual ability. At 6 years postinfection, children were found to be of average intelligence with specific deficits in expressive language, memory, and reading (Anderson et al., 1992).

Ellsworth, Bawden, and Bortolussi (1993) compared the cognitive, academic, and behavioral profiles of 34 children who had had *Haemophilus influenzae* type b meningitis with their nearest age siblings. Significantly poorer performance was noted on tests requiring processing of symbolic information, but the effects were of comparatively small magnitude. No differences on global measures of intelligence, academic achievement, or behavior were found. These authors suggested, therefore, that neuropsychological morbidity for most children with this type of meningitis is minimal, which contrasts with the work of Anderson et al. (1992). The reason for these differences is not clear but is typical of research of the neuropsychological effects of a disease process in children.

In a small study, Whitsett, Kneppers, Coppes, and Egeler (1999) looked at the impact of the presence of Langerhans cell histiocytosis

(LCH). Manifestations of LCH in children may range from only a rash to bony lesions accompanied by pain to major organ disease. With CNS involvement, there may be symptoms of hypothalamic and pituitary dysfunction or more global neurological and neuropsychological sequelae (Whitsett et al., 1999). Neuropsychologic assessment of two patients with CNS-positive LCH indicated the presence of significant deficits in a number of functional areas. Full-scale IQ declines were noted as were deficits in memory, attention and concentration, and perceptual organizational capabilities.

Generally, the morbid consequences of CNS infections are oftentimes overlooked in the face of higher mortality rates. A systematic review of the occurrence and pattern of persisting neurological impairment following common CNS infections was conducted by Carter, Neville, and Newton (2003). The results of their review of 46 studies indicated that postinfectious neurologic impairment does persist most commonly in cognition and motor functions. The deficits found included subtle problems which are typically difficult to detect on gross neurologic examination but which may still be deleterious to social and educational functioning.

Periventricular Brain Injury (PVBI)

Within the last several decades, significant advances in technology have made possible major improvement and advances in obstetric and neonatal care.

Despite such improvements, low birthweight (LBW) infants continue to be at an increased risk for problems with a variety of cognitive functions which can impact on intellectual functioning and acquisition of academic skills (Aylward, 2002; Daniel, Lim, & Clark, 2003). It has been reported that as many as 40% of LBW children repeat a grade by grade 8 or require special learning assistance lends credence to the argument that LBW status has a significant negative impact on academic and cognitive functioning (Calame et al., 1986; Hall, McLeod, Counsell, Thomson, & Mutch, 1995).

The incidence of PVBI increases with decreasing birthweight (Volpe, 1995), with children being born at extremely low birthweight (ELBW; < 1,000 gm) being at particularly high risk. The two most common forms of PVBI,

germinal matrix/ intraventricular hemorrhage (GM/IVH) and hypoxic/ischemic injury (H/I), often destroy glial precursor cells, and this is thought to interfere with early neurodevelopmental processes such as myelination and cortical organization (Evrard, Gressens, & Volpe, 1992; Maalouf et al., 1999; Van de Bor, Guit, Schreuder, Wondengrem, & Vielroye, 1989). Recent findings suggest that the resultant brain abnormalities persist into adolescence, with individuals who were born very preterm showing significantly smaller brain volume and enlarged lateral ventricular volumes than full-term controls (Nosarti et al., 2002).

A recent study was designed to investigate the long-term consequences of both the presence and the severity of periventricular brain injury (PVBI) on intellectual, academic, and cognitive outcome in extremely low-birthweight (ELBW: < 1,000 g) children (mean age = 11 years) and to determine the nature of the underlying difficulties associated with academic problems in these children (Downie, Frisk and Jakobson, 2005). The results of this research indicated that ELBW children without PVBI performed as well as full-term children on intelligence, academic, and cognitive ability tests. In contrast, ELBW children with mild and severe PVBI achieved significantly lower scores than either ELBW children without PVBI or children who were born at term. Downie et al. (2005) concluded that the presence and severity of PVBI, and not ELBW status alone, is associated with performance on tests of intelligence, and academic and cognitive functioning, and that some of the same factors known to be associated with learning disabilities in full-term children contribute to learning disabilities in ELBW children.

Although it has been assumed in the past that the young brain is more plastic and therefore more likely to recover from brain injury than the adult brain (Lenneberg, 1967), recent theories suggest that the extent and nature of recovery depends on the particular stage of brain development at the time of injury, the age at which a follow-up assessment is made (Kolb, 1995), and the specific neural structures that are damaged (Stiles, 1995). In the study by Downie and colleagues, the "No PVBI" group performed in a manner that was indistinguishable from full-term controls on every measure. The severe PVBI group demonstrated a high risk of academic difficulties, with 40–60% of children

with severe PVBI performing in the abnormal range on tests of reading and spelling at a mean age of 11 years. This suggests that the effects of early brain injury may be compounded as cognitive development continues without adequate neural support (Downie et al., 2005).

Human Immunodeficiency Virus (HIV)

A new and emerging area of study is that of HIV infection in children. It is not yet clear if, when, and how the CNS of infants and children becomes infected with HIV. CNS infection also may vary with subsets of patients and by itself does not necessarily mean that there will be clinical symptoms of the HIV infection (Tardieu, Blanche, Duliege, Rouzioux, & Griscelli, 1989).

In children with encephalopathy, neurologic changes associated with HIV infection include impaired cranial growth resulting in acquired microcephaly, cerebral atrophy, enlargement of the ventricles, and calcification in the basal ganglia (Brouwers, Moss, Wolters, & Schmitt, 1994). Clinically, extrapyramidal and cerebellar signs, delays or regression in motor or language development, and deterioration in cognitive abilities have been described, particularly in children younger than 5 (Belman et al., 1985; Epstein et al., 1985, 1986; Falloon, Eddy, Wiener, & Pizzo, 1989).

Two main domains of cognitive functioning appear to be most susceptible to the effects of CNS HIV infection in children: attention and expressive behavior. Attention difficulties have been widely recognized in adult and pediatric patients with HIV disease (Brouwers, Wolters, Moss, & Pizzo, 1993; Brouwers et al., 1994). In children, attention deficits may be documented as a relative weakness on the "freedom from distractibility" subscales of IQ tests and on behavioral assessments (Moss et al., 1996). In adults, attention deficits are one of the clear hallmarks of AIDS dementia complex (Price et al., 1988). When working with children, however, it is not clear whether attention problems are directly attributable to HIV as other etiologies are possible. Additionally, the base rate of attention disorders for this age group tends to be comparatively high in the general population. In one study, the WISC-R subtests of children with symptomatic HIV disease were analyzed, and 21% of these children had performance patterns consistent with attention deficits. In another

group of children with other chronic diseases (e.g., ALL), a similar group of comparable size (25%) was identified with a similar pattern (Brouwers et al., 1994). Thus, whether attention deficits can be directly associated with HIV infection or are associated with chronic illness in general remains to be further investigated.

Expressive behavior across several modalities appears to be differentially affected in a number of pediatric HIV patients (Brouwers et al., 1994). Speech and language abilities frequently become impaired in children with symptomatic HIV disease (McCardle, Nannis, Smith, & Fischer, 1991). Language may become slurred, speech may be labored, and children who were speaking in full sentences have been found to regress to using single words. Expressive language disruption appears to be more common than receptive language difficulties.

In children and infants with HIV infection (symptomatic), motor skills are frequently one of the first, and often the most severely, affected area of functioning (Hittleman et al., 1991). Infants tend to exhibit a delay in overall motor development and abnormalities in muscle tone. Preschool or older school-age children are more likely to develop impairments in lower extremity motor skills such as disturbances in gait and balance, and in some cases, they may lose the ability to walk.

HIV-infected children also may exhibit impaired social skills and affect (Moss et al., 1996; Ultmann et al., 1987). Some children become withdrawn and apathetic, and they have difficulty expressing their feelings and emotions both verbally and nonverbally. In extreme cases, some children display autistic-like characteristics (Moss, Wolters, Eddy, Weiner, & Pizzo, 1989). HIV-positive children demonstrated subtle impairments in verbal concept formation, attention, mental flexibility, and/or working memory, in the absence of any global or obvious cognitive decline (Smith et al., 1993).

It is important to note that a number of HIV-positive children are unimpaired on neuropsychological measures as well as on neurologic examinations. However, subtle effects of HIV on the CNS have been observed in a number of older children who may have had opportunistic or chronic bacterial infections (Pizzo et al., 1988). Brouwers et al. (1990) noted that some children demonstrated significant improvement with AZT therapy. It is likely

that the incidence of HIV infection in children will continue to rise, and new treatments will likely lead to longer term survival for these children.

When this chapter was last revised, it was our thinking that the neuropsychologic problems secondary to HIV disease and treatment would likely provide fertile ground for research for many years to come. Unfortunately, this seems to have not been the case. While an occasional report has appeared in the literature, there have yet to be any major, large-scale studies reported. Such research may be ongoing, and the results of which will hopefully be available in the near future.

Chronic Granulomatous Disease

Chronic granulomatous disease is an inherited immunodeficiency in which phagocytes fail to generate superoxide and its metabolites, resulting in severe recurrent infections and frequent hospitalizations. Chronic illness and frequent hospitalizations can affect growth and development as well as social and educational opportunities.

Since no data had been reported on cognitive functioning in patients with this illness, Pao et al. (2004) examined cognitive functioning in a group of patients with chronic granulomatous disease. A retrospective chart review of 26 patients seen and followed at the National Institutes of Health who had received cognitive evaluations was performed. These individuals had been referred for evaluation by parents or staff. As such it was a selected population, not necessarily representative of all children with the disease. Demographic information including medical, psychiatric, and developmental histories was gathered. Six patients (23%) were found to have an IQ of 70 or below, indicative of cognitive deficits, and all of those individuals had defects in membrane-linked cytochrome processing. The prevalence of cognitive deficits in this selected population of chronic granulomatous disease patients was high. The authors felt that determination of the true distribution of cognitive functioning in the general chronic granulomatous disease population is important, since cognitive deficits have implications for educational planning and potential therapies such as transplantation and gene therapy in children.

Brain Tumors

After malignancies of the blood-forming tissues such as leukemia, brain tumors are the most common type of malignancy in children (Graham, 1983). It has been calculated that there are approximately 600 new cases in the United States annually (Till, 1975). About 60% of childhood brain tumors occur in the subtemporal part of the brain, and of these, most are either medulloblastomas or cerebellar astrocytomas. The remainder consist of subtentorial tumors or tumors of the brain stem. About 3% of these tumors are metastatic, in marked contrast to that found in adults. Surprisingly, it has been unusual for children with brain tumors to present with symptoms of intellectual decline or behavioral change (Graham, 1983). Headache and vomiting are the most common symptoms present, and although there may be some accompanying irritability, this typically has not led to any diagnostic confusion.

Over the past several years, a good deal of longitudinal research has revealed that brain tumors in children do lead to cognitive changes. Cerebellar lesions have been associated with significantly impaired performance on the Wechsler subtests of mathematical reasoning and digit span, whereas diencephalic and cerebellar lesions are associated with deficits in verbal learning and sentence span. Additionally, attentional problems have been found with cortical and cerebellar lesions (Fennell et al., 1993). Carpentieri and Mulhern (1993) studied children who had survived temporal lobe tumors and treatment for at least 1 year. They found evidence of auditory–verbal memory dysfunction in children with left and right temporal lobe tumor. In addition, poor reading and spelling performance was found to be correlated with impaired memory functioning.

Age at diagnosis and treatment has been an area of recent investigation. Very young children who were treated aggressively with surgical intervention and chemotherapy but did not receive radiation prior to age 3 years were studied. Thirty-nine percent of the children remained stable cognitively or exhibited increases in test scores, suggesting that avoiding radiation therapy before age 3 can be associated with acceptable survival and relatively good cognitive/adaptive functioning (Seidel et al., 1994).

Gliomas in the pontine area in children generally present with what have been described as personality changes (Arseni & Goldenberg, 1959; Cairns, 1950; Lassman & Arjona, 1967). Characteristically, the symptom pattern seen includes a period of withdrawal, apathy, and lethargy followed by aggression, hyperactivity, temper tantrums, and physical violence. These tumors usually occur between the ages of 3 and 13. The course of the tumor may last for several years and the outcome is generally fatal despite a variety of treatments and radiation therapy. Other types of brain stem tumor are likely to present with gait disturbance and symptoms such as squint indicating cranial nerve involvement, but behavioral changes involving lethargy, irritability, inability to concentrate, enuresis, and sleep disturbance also have been known to occur (Panitch & Berg, 1970).

The prognosis for brain malignancies in children is at best poor, despite the use of the best available treatments such as surgery and irradiation. Although research has increased dramatically over the past 5–10 years on the effects of brain malignancies in children, the clearest information available is still that concerning the most common brain tumor in children, namely, medulloblastomas. The 5-year survival rate is roughly between 40 and 75%, and 50% after 10 years (Bloom, Wallace, & Henk, 1969; Hope-Stone, 1970). In one study, 18 of 22 survivors were reported to be without serious deficit (Bloom et al., 1969). Two of the children followed were found to have partial disability, and two others demonstrated significant intellectual decline. It is important to note that the two children who demonstrated intellectual deterioration were those who were diagnosed at the youngest ages (11 and 15 months). These findings are similar to those noted above in the study of children with temporal lobe tumors (Seidel et al., 1994) as well as to findings reported in studies of children with leukemia comparing early and later diagnosed children. Children diagnosed at an earlier age appeared to be at greater risk for the development of cognitive dysfunction (Eiser, 1979; Meadows et al., 1981). (Further discussion concerning leukemia and its effects can be found later in this chapter.)

Craniopharyngiomas in childhood are histologically benign tumors which have their origins in the remnants of Rathke's pouch in the hypothalamic–pituitary region of the brain.

Typically, treatment for these tumors includes total resection or limited resection followed by radiation therapy. Twenty five children who had had primary surgical treatment of craniophyaryngioma were followed. Endocrine deficiency, visual dysfunction, neurological and neuropsychologic complications were found in as many as 24 of 25 children studied. Additionally, significant school problems were reported for 10 of 20 individuals. Quality of life ratings was lower for these children than for healthy controls (Poretti, Grotzer, Ribi, Schonie, & Boltshauser, 2004).

Children who had received treatment for craniopharyngioma via microsurgery demonstrated normal intelligence; however, 45% of these individuals were found to have moderate to severe impairment in the delayed recall of verbal and nonverbal information (Kerr, Smith, DaSilva, Hoffman, & Humphries, 1991).

Although the number of investigations of a child's neuropsychological status following a brain malignancy continues to increase, additional efforts are still needed.

Neuromuscular Diseases

There are numerous neuromuscular diseases that afflict children. It is beyond the scope of this chapter to detail the effects of each on the cognitive status of children. One disease entity, Duchenne muscular dystrophy (DMD), will be offered as a possible model for the effects that such diseases can have on the developing brain. It is important to note that the sequelae of such diseases tend to have variable identifiable effects depending on a wide variety of factors including age at diagnosis, age at testing, and so on.

DMD is a hereditary disease causing progressive muscular weakness and degeneration of skeletal muscle tissue. Its course generally includes confinement to a wheelchair by age 11 and death in the late teens. It affects males almost exclusively. Many studies on intellectual functioning in DMD patients have reported diminished or retarded intellectual development, supporting the position of Duchenne in 1872 (Dubowitz, 1979). The group IQ scores generally average about 85, one standard deviation below the mean of the general population (Dubowitz, 1977; Karagan, 1979). Although there is some support for the notion of intellectual impairment in DMD patients, there is no common consensus

in the research literature. Some have reported a decline in intellectual performance (e.g., Black, 1973; Florek & Karolak, 1977), whereas others have found no significant differences in longitudinal studies (e.g., Cohen, Molnar, & Taft, 1968; Worden & Vignos, 1962).

A study attempting to clarify the picture by studying 14 younger and 11 older children with DMD was reported by Sollee, Latham, Kindlon, and Bresnan (1985). It found that younger children with DMD performed more poorly on tasks requiring some language and attentional–organizational skills, but not on visual–motor tasks. The older group generally had higher IQ levels in the average range, and the younger group had low-average IQ scores. The authors noted that individuals with DMD did not appear to demonstrate fixed, global cognitive deficits. Rather deficits appeared to vary at different ages with no specific pattern evident.

More recently, Hinton, DeVivo, Nereo, Goldstein, and Stern (2001) demonstrated that verbal working memory skills seem to be more selectively impaired in DMD and that this deficit likely contributes to limited academic achievement often noted in this population of children. In the study, verbal, visuospatial, attention/memory, abstract thinking, and academic achievement skill were tested. Results indicated that boys with DMD performed similarly to their siblings on a majority of measures, indicating intact verbal, visuospatial, long-term memory and abstract skills. However, the DMD group did significantly more poorly than siblings on specific measures of story recall, digit span, auditory comprehension as well as in all areas of academic achievement.

Other CNS Disorders

Neurofibromatosis (NF) is an autosomal dominant genetic disorder affecting 1 in 3,000 persons. It is characterized by numerous physical stigmata and by intellectual and cognitive impairment that may range from mild to severe. A study (Moore, Needle, Ater, Brewer, & Copeland, 1993) of 76 children with NF, brain tumor, or both was conducted to determine patterns of cognitive function characteristic of the conditions. In this study, no patient had been treated except by surgical resection of tumor. The groups were comparable in intellectual

functioning, language, memory, fine motor, and attentional functioning; all test performance scores were in the average range except for memory, which was impaired across all individuals. Children with NF did, however, demonstrate significant impairment in academic achievement, visual–spatial abilities, and ability to maintain attention and concentration. In general, children with NF appear to be at significantly greater risk for learning deficits, visual–spatial processing deficits, and attention deficits than their counterparts with undifferentiated brain tumor.

The relationship of early childhood hydrocephalus and cognitive development is poorly understood. Most children who develop hydrocephalus early are not mentally deficient, although children with hydrocephalus typically demonstrate reductions in their overall level of cognitive development (Fletcher et al., 1992). An investigation of 90 children of age 5–7 years with hydrocephalus caused by aqueductal stenosis or prematurity–intraventricular hemorrhage or associated with spina bifida was conducted. Comparison groups of normal controls, children with spina bifida and no corrective shunt, and premature children with no hydrocephalus were evaluated as well. As a group, children with hydrocephalus demonstrated poorer nonverbal than verbal skills. No memory deficits were noted. Fletcher et al. (1992) note that this is likely a function of effects on white matter development. Additionally, MRI studies of these children found considerable pathology in the commissural tracts.

Cognitive and academic problems have been identified as the most common neurologic complication of neurofibromatosis type 1 in childhood (North, Hyman, & Barton, 2002). There is a slight increase in the frequency of mental impairment (IQ < 70) but the mean full-scale IQ for such children is within 1 standard deviation of the population mean. The frequency and severity of specific cognitive deficits in children with neurofibromatosis type 1 was studied (Hyman, Shores, & North, 2005). It was found that 81% of children with neurofibromatosis had moderate to severe impairment in one or more areas of cognitive functioning. While slightly over half of the children studied ($N = 81$) performed poorly on tasks of reading, spelling, and mathematics, specific learning deficits were present in 20% of the children. Over 60%

of the children had problems with attention, and 38% of the children studied met the criteria for attention-deficit-hyperactivity disorder. The authors posited a neuropsychological profile for individuals with the disease which includes deficits in perceptual skills (visuospatial and visuoperceptual), executive functioning (planning and abstract concept formation), and attention (sustained and "switching"). While expressive and receptive language were impaired in this population, these skills were better preserved than nonverbal abilities.

Additional research should help to address these issues.

Leukodystrophy

There are a number of different types of leukodystrophy. Degeneration of the white matter of the brain (leukodystrophy) leads to a dementia-like state in children. Shapiro (1991) attempted to identify a neuropsychological performance pattern in children with white matter disease. Decreases in visual perception, visual–spatial functioning, visual–motor skills, motor skills, and attention were noted. A study of 39 children with leukodystrophy revealed a developmental course of slowing of development in one or more areas of cognitive functioning, gradual spreading of deterioration to other cognitive domains with plateauing of development, followed by a loss of achieved developmental milestones (Shapiro, Lockman, & Krivat, 1993). Treatment (via bone marrow transplantation) was found to be more successful when done before plateauing of development occurs.

Blood and Circulatory System

The primary function of the blood system is that of a carrier and delivery service transporting oxygen from the lungs to tissues and returning carbon dioxide, conveying metabolites to tissues, and returning waste products for disposal. It has other important functions such as maintaining the water content of the tissues, harboring the body's defense cells, carrying hormones that regulate a variety of bodily functions, and helping to maintain and regulate body temperature. A disruption in either the blood or circulatory system can directly impact brain functioning.

Anemia

Anemia, or an abnormal decrease in red blood cells, can produce variable CNS effects. Erythrocytes (red blood cells) contain hemoglobin, which carries oxygen, and any unusual decrease in the number of these cells can lead to an overall lowering of brain functioning as a result of cerebral hypoxia (deficiency in oxygen supply). Convulsions, diffuse organic brain syndrome, focal vascular lesions, cerebral hemorrhage, and blindness have been reported in severe cases (Aita, 1964).

Research conducted with children having sickle-cell disease found that the overall intellectual capabilities of these children were lower than those of an age- and sex-matched group of black children (Berg & Wilimas, 1983). In this pilot project, the WISC-R and the children's revision of the Luria–Nebraska Neuropsychological Battery were administered to a group of 30 black children with the disease who had not undergone hypertransfusion of packed red cells and to a similar group of black children without the disease who had been selected on the basis of age and sex. In all cases, children with the disease performed significantly more poorly on all IQ measures. No significant differences were reported on the Luria–Nebraska tests, although the results appeared to follow the same direction as those found on the WISC-R.

A study assessing 58 children with sickle-cell disease with no documented history of cerebrovascular accident (CVA) found that subtle neuropsychological deficits were present in those children of lower socioeconomic backgrounds (Goonan et al., 1992). In children who had sustained a CVA, those who had had a left hemisphere stroke demonstrated a significant global decline on intelligence testing as well as on specific tests of language, visual–spatial construction ability, memory, and academic achievement (Cohen et al., 1993). Those who had sustained a right-sided CVA demonstrated marked declines in performance IQ scores, visual–spatial construction, visual memory, and arithmetic achievement suggesting a somewhat more focal pattern of impairment (Cohen et al., 1993). In contrast, a recent investigation by Goonan, Goonan, Brown, Buchanan, and

Eckman (1994) reported no generalized deficits in the absence of specific laboratory findings (hemoglobin levels, days of hospitalization, and emergency room visits). These findings suggest a lack of disease-related neurocognitive impairment for children with sickle-cell syndrome.

A meta-analysis of studies of cognition in SCD to determine the size of any statistical difference between children with SCD and controls was conducted (Schatz et al., 2002). Methodological factors were evaluated according to the size and frequency of group differences. Small but reliable decrements in cognitive functioning on IQ measures (4.3-point difference overall) were noted. The most methodologically rigorous studies showed a highly similar pattern. Sampling issues associated with the effect size for IQ were identified by the investigation. Measures of specific abilities appear more sensitive than IQ scores to cognitive decrements in sickle-cell disease. Sickle-cell disease is associated with cognitive effects even in the absence of cerebral infarction. Scahtz et al. postulate that the causes of this cognitive decrement may include direct effects of sickle-cell disease on brain function or indirect effects of chronic illness.

Polycythemia Vera

Just as an abnormal decrease in red blood cells can lead to abnormal cognitive functioning, the converse also is true. Abnormal increases in red blood cell production in the bone marrow (polycythemia vera) can cause erythrocytes to clump together, creating a situation that slows blood flow and impedes circulation. Although there is an adequate oxygen supply in this condition, there is difficulty in breathing, and the individual may become cyanotic. Brain functioning may become lowered as a result of insufficient circulation or blockage of a cerebral vessel. Aita (1964) discussed a number of commonly reported neurologic symptoms in diseases that result in excess erythrocytes. These include headaches, dizziness, vision and hearing difficulties, and parasthesias. Children who tend to hemorrhage easily may show more focal deficits such as aphasia and hemiparesis, or they may exhibit a progressive dementia-like condition as more and more cerebral tissue is destroyed by repeated hemorrhaging (Aita, 1964; Ariel & Strider, 1983).

Excessive Increases or Decreases in Platelets

A severe reduction in the number of platelets or defects in coagulation factors in the blood may result in spontaneous bleeding. This can be a primary disease (e.g., thrombocytopenia purpura) or it can develop secondarily to another disease process such as leukemia (discussed below), toxic chemical exposure, irradiation, infection, or massive blood transfusion. If such bleeding occurs within the brain, it may be at single or multiple sites, small or large in size, and may resemble a focal stroke (Aita, 1964). The cognitive sequelae of such an incident can be tremendously varied depending on the location and size of the hemorrhage and can range from comparatively minor to pervasive with the patient existing in a vegetative state (Walton, 1977). In the more minor circumstances of such bleeding, temporary general confusion, paresis, and convulsions can be seen (Heron, Hutchinson, Boyd, & Aber, 1974).

Matoth, Zaizov, and Frankel (1971) reported that 20 children with chronic thrombocytopenia had been found to have learning and behavioral problems when compared with patients with other medical disorders. This study, which used the WISC, Bender Visual–Motor Gestalt, and Human Figure Drawing tests, revealed no statistical differences between the two groups on any test. However, it was noted that over two-thirds of the group of children with thrombocytopenia exhibited "soft" neurological signs of minimal brain dysfunction. Over half of this group also demonstrated mild, diffuse EEG abnormalities. To date, there has been no long-term follow-up of such groups to determine if noted behavioral or cognitive abnormalities persist into adulthood.

An excessive increase in the number of platelets can result in the formation of a thrombus and subsequent blockage of a blood vessel. Tissues supplied by the blocked vessel will then receive an insufficient supply of blood, and an ischemic condition wherein the tissue starves may result. If the tissue dies or is damaged, an infarction is the result. Thrombus formation anywhere in the body can be serious because of the high tendency for the thrombus to pass through the heart and be carried to the lungs or brain. When cerebral vessels become blocked and an infarction occurs, deficits in cognitive functioning can occur (Walton, 1977). If the

blocked vessel supplied a small portion of the brain, the cognitive sequelae will generally resemble those seen with a fairly discrete cerebral lesion. Where the blocked vessel supplied a larger region of the brain, pervasive deficits can result.

Leukemia

Leukemia is a disease in which there is uncontrolled multiplication of certain white blood cells resulting in their accumulation in large numbers (LODAT, 1981). An abnormal growth and division of lymphoblasts (one type of white blood cell) in the bone marrow results in acute lymphocytic leukemia (ALL). ALL is the most prevalent form of malignancy in children and the one that has been the most heavily researched with respect to the effects of the disease and its treatment. This is because the therapy for the disease has become so effective that long-term disease-free survival can be expected in at least 50% of patients (Bowman, 1981; Mauer, 1980). Survival of these children has permitted an increasing emphasis on the late sequelae of ALL and its treatment. Treatments for other childhood malignancies have not been quite so effective. Thus, research into the cognitive sequelae has been restricted. The research investigating the long-term effects of ALL and its treatment, however, may be used as a temporary model for the effects of other malignant disease processes.

A complicating factor in the study of neuropsychological functioning of children with ALL lies in the standard treatment regimen for the disease. Common treatment involves the intrathecal and intravenous administration of a neurotoxic medication, methotrexate. Coupled with this is the administration of at least 1,800–2,400 rad of cranial irradiation, which is done prophylactically in an attempt to destroy those leukemic cells that may have migrated to the brain. Some reports over the past several years suggest that cranial irradiation may not be necessary in the treatment of what is referred to as "standard risk" leukemia and that such prophylactic measures need only be employed with "high-risk" patients whose disease is diagnosed at a more advanced stage and is more likely to have invaded the CNS (Copeland, Pfefferbaum, Fletcher, Jaffee, & Culbert, 1982). It is clear that it is very difficult, if not impossible, to assess the effects of the disease alone in such instances.

Despite all of the research that has been conducted since about 1975, our understanding of the effects of the disease process and its treatment is inconsistent. Eiser and Lansdown (1977) and Goff, Anderson, and Cooper (1980) found that leukemic children who had received irradiation demonstrated significant deficits. This was particularly true for those individuals diagnosed and treated prior to age 5. Deficits included declines in intellectual abilities as well as a pattern of distractibility and memory deficits. In contrast, other investigators found that the disease and its treatment resulted in no documented dysfunction (Ivnik, Colligan, Obetz, & Smithson, 1981; Obetz et al., 1979). A longitudinal study in which a group of leukemic children were followed for a period of at least 3 years found no specific pattern of deficits or IQ declines (Berg et al., 1983). However, almost half of the children did have performance patterns consistent with mild, specific learning dysfunction when performance patterns were analyzed individually rather than as a group.

More recently, Stehbens et al. (1991) in a review of 20 years of published research report that the majority of studies suggest that CNS prophylaxis, including both cranial irradiation and intrathecal methotrexate, results in a variety of learning problems in many children who were younger than 5 when first treated. A study of the neurocognitive status of 46 children with ALL treated with systemic chemotherapy and prophylactic CNS chemotherapy found that those children receiving a 3-year course of chemotherapy were more impaired on tasks involving right hemisphere simultaneous processing than controls or ALL children whose diagnosis was recent and treatment was just begun (Brown et al., 1992).

Raymond-Speden, Tripp, Lawrence, and Holdaway (2000) assessed the effects of treatment for ALL on children's cognitive functioning. Long-term survivors of ALL who had been treated with cranial irradiation and CNS chemotherapy or CNS chemotherapy only were compared with healthy children and children with chronic asthma. Measured included intellectual, neuropsychological, and academic functioning. The study demonstrated that it is CNS chemotherapy, either with or without cranial irradiation, that was associated with

can result in dehydration, progressive obtundation, and ketoacidosis, a buildup of acids in the blood resulting from the breakdown of fats and proteins to meet metabolic needs. This acidosis can lead to diabetic coma and death (Miller & Sperling, 1986).

Once diagnosis is made, treatment of IDDM involves management of the disease by control of diet, exercise, and daily injections of exogenous insulin. The goal of such treatment is the maintenance of proper blood glucose levels. In the normal individual, such levels are maintained at between 60 and 120 mg/100 ml of blood plasma; however, in the diabetic the glucose level may be chronically elevated and may fluctuate widely. Management of diabetes becomes an attempt to maintain blood glucose levels as close to normal as possible, but this is not always easily accomplished. Both chronically high blood glucose levels (hyperglycemia) and the too-low blood glucose levels that may result from too much insulin or too little food (hypoglycemia) have implications for behavioral and cognitive functioning.

Because the neurons of the brain require glucose for metabolism, the possible effects of abnormal glucose metabolism on the central nervous system have prompted a great deal of study. Animal research has suggested that chronic hyperglycemia may be related to structural changes in the brain. Such changes may include thickening of the blood vessels and capillaries that supply the cortex, thus reducing the supply of oxygen and other nutrients to the brain (Mukai, Kuno, & Seki, 1980).

The effects of hypoglycemia on the central nervous system have also been studied. Severe, acute hypoglycemia may result in symptoms ranging from confusion and lethargy to convulsions, coma, and even death (Malouf & Brust, 1985). Of course, the concern is that repeated episodes of hypoglycemia may be related to more permanent changes in central nervous system functioning.

The study of the effects of diabetes on cognitive and behavioral functioning has taken place largely within the context of a developmental perspective. As noted earlier, the peak incidence of IDDM occurs around the time of puberty. A particular concern has been the effect of the disease on the developing nervous system of the child. It has been hypothesized that the immature brain may be more vulnerable to the effects of metabolic disturbances than the mature, fully developed brain (Rovet, Ehrlich, & Hoppe, 1988). As such, children who develop diabetes early in life may be at particular risk for impaired cognitive functioning. In fact, a number of studies have demonstrated that children with early onset of diabetes show impaired performance on a variety of neuropsychological measures (Rovet et al., 1988; Ryan, Vega, & Drash, 1985). These studies will be reviewed in some detail, as they highlight the potential effects of this disease on cognitive functioning.

Ryan and associates (1985) compared the performance of three groups of diabetic children and adolescents: those with early onset of the disease (before age 5), those with later onset, and a group of nondiabetic subjects. Subjects ranged in age from 6 to 16, with equal numbers of males and females. The groups were compared on a comprehensive battery of neuropsychological measures, including measures of intelligence, memory, attention, visual-motor coordination, and academic achievement. The results indicated that children with early onset of diabetes performed more poorly than the other two groups on measures of visuospatial ability, motor speed, and eye-hand coordination. No significant differences were found between the later-onset and nondiabetic groups.

can lead to ketoacidosis, diabetic coma, and death. This previously fatal disorder was converted to a manageable chronic disease after 1922 with the availability of exogenous insulin (Johnson & Rosenbloom, 1982). For the youngster with IDDM, management of near-normal metabolism involves constant monitoring of bodily systems and daily insulin injections. Insulin needs vary with nutrition, exercise, physical health, and emotional state. As mentioned, insufficient insulin can lead to dangerous hyperglycemia. Conversely, too much insulin or too little food, or an imbalance of food, exercise, and insulin can result in a marked decrease in blood sugar (hypoglycemia). Hypoglycemia can progress from an insulin reaction, with mental confusion and anxiety, to hypoglycemic seizures, to insulin coma (Miller & Sperling, 1986). This metabolic seesaw may have important implications not only for the psychological adjustment but also for the brain of the diabetic youngster.

Investigation of neuropsychological functioning in IDDM is currently being carried out by several research teams in the United States and Canada. Excellent reviews of this area include those by Ryan and Morrow (1987a) and Ryan (1995). Discussing the history of research in this area, they point out that early on, diabetes per se was thought to be benign with respect to impact on brain functioning, the only connection thought to be secondary to involvement of renal or cardiovascular disease in older patients who had the disease for many years. A series of studies from the 1930s through the 1960s challenged this notion by comparing the intelligence of diabetic children with general norms, yielding results that were equivocal. Although the findings were inconclusive, two important methodological innovations were introduced in these series. These were the use of nondiabetic sibling controls to control for effect of family influences and socioeconomic status, and the attempt to experimentally relate specific diabetic characteristics such as age of onset and duration of illness to outcome (Ack, Miller, & Weil, 1961). One important global finding from such work was that age of onset seemed to be an important variable, with those diagnosed as diabetic before the age of 5 having average IQs 10 points lower than their siblings. A trend was also seen suggesting an inverse relationship between number of hypoglycemic seizures experienced and measured intelligence. Thus, although no

clear evidence of specific neurobehavioral dysfunction in diabetic children emerged, researchers were made aware that there may be some neurobehavioral differences between diabetic and normal children, and that the age of onset and the number of hypoglycemic seizures noted in the history may be related to the extent of this difference (Ryan & Morrow, 1987a).

Because global measures of intelligence were used in that series of studies, differences between diabetics and controls could not be assigned to specific structural or operational changes in the brain. However, a series of EEG studies did find a significantly higher number of clinically abnormal EEGs in a group of diabetic children compared with age-matched normal controls, further finding that the variable most related to this EEG difference was the number of severe hypoglycemic episodes (Eeg-Olofsson & Peterson, 1966), or the number of severe episodes of both hypoglycemia and hyperglycemia (Haumont, Dorchy, & Pelc, 1979).

Ryan and Morrow (1987b) posited that this IQ and EEG evidence seemed to demonstrate that diabetic children and adolescents showed a greater tendency than their nondiabetic age mates to have mild, diffuse brain dysfunction, and that multiple episodes of severe hypoglycemia were in some fashion responsible for the development of this "diabetic encephalopathy." They noted with some surprise that although these findings firmly established a basis for further investigation of this diabetes-related organic syndrome, such research essentially dried up for no apparent reason during the 1970s, in favor of studies of the psychosocial aspects of diabetes (see Cerreto & Travis, 1984).

Given these early findings, and the fact that a medical colleague found a high incidence of school difficulty in diabetic patients, Ryan and his associates at the Children's Hospital in Pittsburgh began a series of neurobehavioral studies to re-assess the degree to which diabetic youngsters are at risk to develop cognitive deficits secondary to CNS defects. The goal of their series of studies was to describe particular neuropsychological difficulties found in this population and to relate these problems if possible to specific variables associated with each case. Based on previous findings and some preliminary work, they focused on the examination of age at onset, duration of disease, and degree of metabolic control as they related to cognitive

functioning, which was measured by neuropsychological testing.

To test the notion that both age at which diabetes mellitus is diagnosed and duration of the disease are potent variables, Ryan, Vega, and Drash (1985b) administered a comprehensive neuropsychological battery to 125 randomly selected diabetic adolescents, all of whom had been diabetic for at least 3 years, but ranged in age of onset from 2 months to 14 years. They divided the subjects into an "early onset" group (diagnosed before age 5, $n = 46$), a "later onset" group (diagnosed after age 5, $n = 79$), and a sibling control group ($n = 83$).

A factor analysis of the cognitive measures used in their testing battery generated five clusters of tests, namely, general intelligence, visuospatial processes, learning and memory, attention and school achievement, and mental and motor speed. Statistical analyses found significant differences between early and late-onset subjects on all five clusters. Further, cutting scores of two standard deviations below the control mean were assigned to each of the 20 tests that discriminated early from late-onset subjects, with at least three such low scores necessary to be seen as "impaired." On the basis of these rules, 24% of the early onset were seen as impaired, whereas only 6% of both the late onset and controls met impairment criteria.

Further analysis of these data suggested that age at onset and disease duration differentially affected the testing results. Age at onset appeared to predict results of tests measuring "fluid intelligence," described by the authors as adaptive abilities used to process relatively unfamiliar information in novel ways, such as scanning and identification of visual stimuli. Duration of illness seemed more able to predict performance on tests tapping "crystallized intelligence," defined as the use of well-practiced skills depending largely on stored knowledge, such as reading and spelling skills, and sequencing ability. Regarding the differential effects of duration and age at onset, there is some evidence indicating that the relationship between duration and crystallized intelligence can be accounted for by the fact that school attendance is a factor in both. Ryan, Longstreet, and Morrow (1985a) found that diabetics missed significantly more school than matched controls over time, and further that cognitive and achievement test findings in this group were best predicted by measures of school attendance. Therefore, perhaps like most chronically ill youngsters, diabetics miss a significant amount of school (Gortmaker & Sappenfield, 1984), and this attendance problem may reduce their ability to master classroom-related learning, or crystallized intelligence. Thus, longer duration of diabetes would lead to greater attendance problems, and more difficulty in school. However, Fowler, Johnson, and Atkinson (1985) found diabetic children miss less school than children from most other chronic disease categories, so this issue remains unclear.

Ryan et al. (1985b) and Ryan and Morrow (1987a), on the other hand, suggested the findings regarding age of onset and performance on tasks assessing fluid intelligence may reflect structural or functional disturbances in the brain. This mild brain damage may develop from multiple episodes of severe hypoglycemia and resultant hypoglycemic seizures early in life. There is some evidence (Ternand, Go, Gerich, & Haymond, 1982) that younger diabetics are more sensitive to the effects of insulin, and therefore have more reactive hypoglycemic seizures. This is consistent with the finding of Ryan et al. (1985b) that early onset diabetics had more of a history of hypoglycemic seizures.

In general, the work of Ryan and colleagues suggests that cognitive deficits in diabetics can be seen as early as age 10. Rovet and her colleagues in Toronto have undertaken the study of even younger diabetic patients, in an effort to further examine neurobehavioral findings in this group. Rovet, Ehrlich, and Hoppe (1988) administered an extensive series of neuropsychological tests to a diabetic sample including children as young as 6. They divided the sample into 27 early onset (pre-age 4), 24 later onset (post-age 4), and 30 sibling controls.

In contrast to Ryan's studies, they found no differences among the three groups on intelligence or achievement, actually finding that diabetics out-performed controls on tasks measuring verbal ability. However, they found some interesting results related to gender. Early onset girls performed less well on spatial tasks and had a lower performance IQ than later-onset or control girls, but this finding did not hold for boys. These early onset girls also had more academic problems, including failed grade and special education placement, than the other groups.

A multiple regression analysis for each sex separately found that for both genders taken together, the best predictor of verbal performance was socioeconomic status; for girls only, the best predictor of spatial performance was age at onset; and again for both genders, the best predictor of spatial performance was seizures before the age of 5.

Other interesting results regarding gender and age at onset include those of Ryan and Morrow (1987b), who found that early onset diabetic adolescent girls had significantly poorer self-esteem, as measured by the Piers–Harris subscales of Physical Appearance and Anxiety, than did early onset boys, later-onset boys and girls, and controls. However, the extent to which this represents a result of greater cognitive deficit, bodily changes differentially experienced by girls over time, or a unique coping reaction in the face of chronic illness is undetermined. Ryan and Morrow (1987b) summarized this literature by stating that both their and Rovet's teams have found age of onset of diabetes to be an important risk factor for the development of significant neurological deficits in both children and adolescents. They speculated that this strong association between diabetes early in life and brain dysfunction may be accounted for by two different phenomena, namely, that the brain of a young child is very sensitive to the deleterious effects of any sort of metabolic insult, and that this sensitivity may be greater in females; or that the young child has a heightened responsivity to insulin, and thus has more hypoglycemic seizures, with resultant increase in damage to the brain.

These findings seem to be consistent with increasing evidence that the time from birth to 5 years may constitute a "critical period" for the development of serious brain dysfunction from a variety of causes with a number of outcomes. Rovet, Ehrlich, and Czuchta (1990) proposed possible critical periods of sensitivity of different functional or structural substrates in the brain to the effects of diabetes, with spatial abilities vulnerable to diabetes presenting earlier, and verbal abilities more vulnerable to diabetes presenting later. The proposed mechanism suggested is that cerebral structures seem to myelinate at different times and rates, and that chronic hyperglycemia could disrupt this myelinization.

However, in an important development, Rovet and her colleagues have found that the effects of early onset diabetes on the brain may not be as clear as previously assumed. As noted, most studies in this area are retrospective, to determine if diabetic children or specific subgroups of such children are at risk for later neurocognitive impairment. Since methodological problems exist with this approach, Rovet et al. (1990) began a prospective study, following a cohort of 63 newly diagnosed diabetic children through their first 3 years of illness. In this first report, they found that relative to nondiabetic siblings, there was no evidence of any neurocognitive impairment in diabetic subjects either at the outset of the disease, or on retesting 1 year after the onset of the disease. In their second report (Rovet, Ehrlich, Czuchta, & Akler, 1993), they found that after 3 years, this lack of impairment among diabetic children was still seen; in fact, it was the normal siblings who were having school problems, perhaps because of the stress of being a sibling of a chronically ill child who received a great deal of family attention. In addition, there was no measured negative impact of mild or severe hypoglycemia. Their findings were clearly inconsistent with previous results, and they offered several explanations for this. Perhaps the instruments chosen were not sufficiently sensitive to measure deficits, any learning deficits are cumulative and need to be followed for greater than 3 years to be seen, or new treatment methods used with diabetic youngsters in recent years have had a positive effect on their neuropsychological outcome. They also suggest that perhaps diabetic children who are learning disabled have different CNS insulin requirements than those who are not due to dietary and activity variants, and this may lead to too much insulin and more episodes of hypoglycemia, thereby questioning the direction of causation.

Northam, Bowden, Anderson, and Court (1992) also report results inconsistent with those found earlier. Using retrospective accounts of disease history, they found no relationship between neuropsychological functioning and variables such as age of onset, chronic poor control, or major metabolic crises in 100 diabetic adolescents. They criticized the sampling of earlier studies that either used volunteers or had a small percentage of potential participants agree to be studied. They suggested families who volunteered to participate in such studies might already have concerns about the

patient's cognitive status, thereby skewing findings in the direction of cognitive dysfunction in diabetic subjects. Their study used a larger sample size and had a high rate of participation, and they recommended a prospective study like that in progress by Rovet's team. Finally, Jyothi, Susheela, Kodali, Balakrishnan, and Seshaiah (1993) found no relationship between age at onset and duration and neuropsychological performance in a group of diabetic children in rural India.

It is worthy of note that even though early onset has been viewed as an important variable, diabetes appears to affect performance even in those who are diagnosed later in life (Franceschi et al., 1984). Ryan, Vega, Longstreet, and Drash (1984) tested 40 diabetic adolescents (aged 12–19) who were classified as late onset (diagnosed at 5–12) and a group of 40 matched nondiabetic controls using a neuropsychological battery and critical flicker fusion. They found that all subjects performed within normal limits, but that the diabetic sample had verbal IQs lower than controls (which may be related to the duration effects and school attendance noted above), but also did less well on psychomotor tasks, performing more slowly than controls.

However, similar findings regarding psychomotor performance were presented by Ryan and Williams (1993) who tested subjects with childhood-onset IDDM an average of 26 years after diagnosis. They found that diabetic subjects performed as well as nondiabetic controls on measures of learning and memory, but performed poorly on measures of psychomotor efficiency, with degree of chronic hyperglycemia best predicting psychomotor slowing. They suggested that specific neural systems in the brain may be differentially sensitive to the toxic effects of hyperglycemia at different stages of life. It has also been hypothesized that diabetics may develop a characteristic personality style that may account for some of this psychomotor task performance difference, which will be addressed briefly later.

Another variable to receive research attention is that of degree of metabolic control. As mentioned earlier, poor metabolic control implies a tendency for hyperglycemia that is implicated in the risk for disorders of the vasculature, both large and small vessels, and hypoglycemia, which has been shown to have clearly deleterious effects on the brain. Work by Holmes and her team at Iowa suggests that a recent history of poor metabolic control may increase the risk of mild neuropsychological disturbances in young adults. Holmes (1986) compared two matched groups of diabetic men in their early 20 s, one classified as in "good" and the other in "poor" control as measured by tested hemoglobin AIC levels. This test measures the relative degree of metabolic control, or avoidance of blood glucose extremes, over the preceding 3 months. Holmes found that the poor-control group had lower scores on the Information and Vocabulary subtests of the WAIS, and also performed worse on reaction time tasks. Ryan and Morrow (1987a) suggested caution in interpreting this finding, as metabolic control was only measured for the 3 months before testing. They speculated that perhaps if these subjects were out of control as children, they may have attended poorly, and now retrieve poorly as adults.

In a typical day, the blood glucose level of a diabetic child may vary widely, being dependent on food, insulin dose, and exercise (Miller & Sperling, 1986). Cerebral metabolism depends on the ability of serum glucose to circulate freely in the brain. Because little glucose is stored in the brain, when its supply has been compromised, there is a lag time before fatty acids are utilized as a backup source (Holmes, Koepke, Thompson, Gyves, & Weydert, 1984). Temporary change in cerebral functioning might therefore be possible at the time of testing, perhaps affecting psychomotor tasks if0 not global intelligence. In a series of studies (Holmes, Hayford, Gonzalez, & Weydert, 1983; Holmes et al., 1984; Holmes, Koepke, & Thompson, 1986), Holmes and her colleagues inspected the acute neuropsychological consequences of deviant blood glucose levels. By use of an automatic insulin/glucose infusion system, they were able to stabilize young individuals with diabetes for extended periods at one of three blood glucose levels: hypoglycemia (55–60 mg/dl), euglycemia (110 mg/dl), or hyperglycemia (300 mg/dl). All subjects were tested in all three conditions, using a balanced design in which neither experimenter nor subject knew in which level the subject was. They found that relative to euglycemia, subjects tended to perform more slowly in the hypoglycemic state on a variety of tasks involving simple mental calculation and word production, as well as responding in choice

reaction time situations. A tendency was noted for subjects to perform in a similar fashion in the hyperglycemic state.

Ryan and Morrow (1987a) summarized such research by stating that the hypoglycemic state reduces efficiency and increases response time on brief tasks. They further speculated about the possibly more dramatic effects that this state might produce on more lengthy tasks under conditions of greater fatigue, a situation that may have occurred during previously described measurements of cognitive functioning in diabetics by use of neuropsychological testing. Ryan et al. (1990) also found that transient episodes of experimentally induced hypoglycemia were associated with reduced mental efficiency in both diabetic children and adolescents, and further noted that total recovery of cognitive function is not always achieved with the restoration of euglycemia, although there is a good deal of individual variation from subject to subject. Therefore, the school-age child with diabetes may not function optimally not only immediately after a hypoglycemic episode but for some time after it is corrected.

Reich et al. (1990) and Puczynski, Puczynski, Reich, Kaspar, and Emanuele (1990) found similar results with naturally occurring episodes of hypoglycemia, and stressed that the delay in recovery puts especially the young child at an unrecognized disadvantage in school and social situations because even after overt physical symptoms have subsided, the child suffers from cognitive deficits for a longer period and may return to the classroom prematurely. Gold, Deary, and Frier (1993) point out that small children have difficulty recognizing and relating the symptoms of hypoglycemia, and Bischoff, Warzak, Maguire, and Corley (1992) suggest interventions to assist such children in the classroom.

Finally, there has been some question as to the relative contribution of nonorganic variables to performance on measures of neurobehavioral functioning. A number of studies have commented on behavior and personality styles among diabetics. Some have stressed problems in the family (*Lancet* Editorial, 1980; Winter, 1982) and school (Weitzman, 1984), whereas others have focused on IDDM as a risk factor in certain clinical syndromes, such as eating disorders appearing in adolescent females (Daneman, Johnson, & Garfinkel, 1985). Other authors have tried to conceptualize the effects of diabetes as the child and adolescent attempts to cope with normal developmental tasks at different cognitive stages (Cerreto & Travis, 1984; Johnson & Rosenbloom, 1982). Some of the self-esteem problems found in early onset diabetic females may be of interest here, although Northam et al. (1992) found no gender differences in the measured emotional adjustment of diabetic adolescents. Research in this area of diabetic personality functioning has been fraught with methodological problems, and at least one study (Skenazy & Bigler, 1985) found that diabetics are no more poorly adjusted than other chronic disease groups, and further that degree of psychological adjustment was not predictive of performance on a battery of neuropsychological tests. Ryan and Morrow (1987b) commented that they have observed a "cautiousness" in their young diabetic patients, perhaps reflecting the youngsters' daily need for constant attention to detail. However, they admit that this is more a matter of clinical observation than evidence.

The impact of severe hypoglycemia on memory functioning was studied (Hershey, Craft, Bhargava, & White, 1997). A relatively homogeneous sample of childhood-onset diabetes patients was evaluated as there is a deleterious effect of hypoglycemia on medial temporal lobe structures. Patients who had experienced severe hypoglycemia demonstrated impaired declarative memory while nondeclarative memory was relatively spared.

Rankins, Wellard, Cameron, McDonnell, and Northam (2005) studied the impact of diabetes on three children who were evaluated within 48 h of the first hypoglycemic seizure and then again at 6 months. The most consistent finding was that at baseline all three children demonstrated significant decrements in attention and concentration while at follow up, all children demonstrated significant improvement in selective attention. However, there was a considerable amount of variability across subjects on other neuropsychological measures. Neurometabolite profiles also showed variability suggesting that hypoglycemia differentially affected neuronal integrity for each case.

Results of research on the impact of diabetes in cognitive functioning are still contradictory to a degree even several years after this chapter was originally written. McCarthy, Lindgren, Mengeling, Tsalikian, and Engvall

(2002) hypothesized that children with type 1 diabetes would demonstrate deficits in academic performance when compared with classmates and siblings, and that academic performance in children with diabetes (type 1) would decline slightly but significantly over tie whereas the performance of the comparison groups would not. Two hundred and forty four children with type 1 diabetes, 110 sibling controls, and 209 anonymous matched classmates were studied. Surprisingly, the children with type 1 diabetes did not show lower performance on standardized academic achievement tests. In fact, children with diabetes performed better than siblings on math and better than their matched classmates on reading measures. The authors concluded that while subtle cognitive deficits often are associated with diabetes, these deficits may not significantly limit functional academic abilities over time.

In summary, in recent years a good deal of progress has occurred in understanding the neuropsychological correlates of insulin-dependent juvenile-onset diabetes in children and adults. Specific neurobehavioral impairments have been identified, as have several diabetes-related variables that appear to be important risk factors for the development of such impairments. Ryan and Morrow (1987a) reiterated that age at onset of IDDM is a most potent variable, with those diagnosed before the age of 5 to be much more likely to show evidence of cognitive impairment than those with onset later than age 5. They suggested that diabetic encephalopathy yields deficits in a wide selection of cognitive domains, with performance disrupted on measures of attention, learning, memory, problem-solving, visuospatial, and visuomotor efficiency.

Some early onset diabetics have lower IQs than their siblings or nondiabetic peers, but not all early onset diabetics have diminished intellectual functioning, and in fact most do not. Evidence from both electrophysiological and neuropsychological measures suggests that those who have had multiple episodes of serious hypoglycemia early in life are likely to be impaired on a wide range of tasks. These findings imply clearly that because young children are quite insulin sensitive, keeping an excessively tight metabolic control (rigidly preventing hyperglycemia) may increase the risk of starting serious and perhaps debilitating hypoglycemic episodes in these patients.

Yet with all of this evidence, several recent studies and prospective work by Rovet suggest that for a variety of reasons, this impairment related to early onset diabetes may not be a given. Such prospective studies may hold the key to the next level of knowledge in this area. Most diabetic children and adults are late onset, and show relatively subtle impairments. When detected, they tend to appear on difficult information-processing tasks requiring the subject to complete novel assignments as rapidly as possible. The slowness noted may be involuntary (reflective of a transient hypoglycemic state) or voluntary (resulting from learned caution in the face of decision-making situations). It is also possible that information-processing mechanisms in this population may be disrupted by complex biochemical disturbance, resulting from a long history of poor metabolic control. And finally, performance may be impaired as a result of increased absences from school, with related academic problems. All of these hypotheses continue to be grist for the research mill, for at this time there is no strong evidence that extensive structural damage to the brain is directly causative of the subtle deficits sometimes found in patients with late-onset IDDM.

Kidney Disease

The kidneys act as a filtering mechanism in the body and aid in the elimination of a variety of waste products which build up in the blood. When the kidneys malfunction, problems arise throughout the body. The memory and executive functioning of children and adolescents with chronic kidney disease were studied (Gipson et al., 2006). Twenty children were examined in this study. Of the 20, 12 were receiving dialysis while the other 8 were managed with "conservative" therpy. A comprehensive neuropsychological evaluation was administered to all participants. Intellectual functioning was found to be within the low average to average range which was significantly lower than that of a healthy control group. Multivariate analyses controlling for age demonstrated group differences in all memory measures, as well as in initiation and sustaining executive functions domain. In all instances, children with kidney disease performed more poorly than the control group. Unfortunately, little other research in this area is

currently available but it is clear that this is an important area for future research.

Cardiovascular System

The primary functions of the cardiovascular system are to pump blood through the body, to pick up and deliver fluids, gases, chemicals, and nutritive substances, and to increase or decrease blood flow in response to activity levels of the body. The cardiovascular system is composed of the heart, large arteries and veins, smaller arterioles and venules, and the capillaries. The manner of blood flow and its regulation are crucial factors to be considered in discussing cardiovascular functioning and the effects of dysfunction.

Blood traveling through vessels exerts different pressures and moves at different speeds according to the size of the vessel. The cardiovascular system acts to maintain a relatively constant and limited range of pressures and blood flow velocities within the vessels. Any increase in friction, such as occurs with blockages, narrowing, or roughness along the vessel walls, increases the work load of the system and can lead to failure.

CNS Effects

Disease or malfunction anywhere in the cardiovascular system tends to initiate a vicious cycle of adjustments that cause the heart to work harder to compensate for these changes, resulting in further damage. A compromised heart eventually leads to a compromised brain. Although the brain will still receive a greater share of the materials needed by the body, prolonged cardiac function will ultimately lower the amount available to brain cells. Insufficient oxygen and nutrients are likely to produce results of diffuse neuropsychological dysfunction in children with cardiovascular disease or irregularities (Cravioto & Arrieta, 1983). The child is likely to have deficits in a wide variety of functions, although these may be mild unless damage to the heart (or reduction of blood flow) has been severe. Many of the cognitive deficits in individuals with cardiac problems may not even be noticed because of the concern over other more attention-demanding physical symptoms. Mild deficits that are noticeable are often temporary and tend to be viewed with less concern (Ariel & Strider, 1983).

When circulation to the heart itself is blocked and tissue is damaged ("heart attack"), there is often an extreme drop in blood pressure. This may produce symptoms of dizziness or massive changes in mental functioning such as delirium or dementia. The lack of oxygen to brain tissue may produce focal deficits such as aphasia, sensorimotor disturbances, or visual difficulties (Rowland, 1984). Such effects can be either temporary or permanent. A cerebral hemorrhage may occur because of the increased pressure and destruction of blood vessels, producing either diffuse or focal effects that tend to be more permanent (Rowland, 1984). As these deficits are generally more disruptive to a child's ability to function, they are more likely to lead to a concern to the child, parent(s), and/or physician, and are often the symptoms that lead to requests for evaluation. If such diseases progress slowly, then compensation usually occurs and the child may appear to have normal cognitive functioning. This is particularly true for children as the developing brain tends to be somewhat more amenable to recovery of function than is the more mature adult brain. It must be cautioned, however, that there is a growing body of literature suggesting that the developing brain may not be as "plastic" as once was thought (Golden, 1981).

Another outcome of cardiac disease may be the development of bacterial endocarditis, an infection of the cardiac tissue wherein bacteria collect in damaged valves or in the pericardial sacs. In addition to creating inflammation and edema, bacteria may spread to other parts of the body by means of blood circulation. If the brain is entered, the result is usually a septic embolism (a blockage creating infection in that area), widespread meningitis, or development of a focal brain abscess (Rowland, 1984). Neuropsychological effects can be quite variable, ranging from focal deficits that resemble an adult stroke to a diffuse encephalopathy (widespread inflammation). The variations possible make it a quite difficult condition to accurately diagnose. In such instances, it has been suggested that the evaluation be conducted on a follow-up basis to determine if additional damage has occurred or to assess the extent and severity of residual impairment (Ariel & Strider, 1983; Golden, 1981).

The development of hemorrhages in the brain from hypertensive destruction of vessels also produces variable effects. Although hypertension in children is comparatively rare, it occurs with enough frequency to merit some discussion. Hemorrhages typically result in focal deficits, but these can be singular or multiple. Mild or severe disruption of cognitive functional systems can result depending on where bleeding occurs (Walton, 1977). Acute hypertensive encephalopathy may produce massive edema and pressure effects leading to severe diffuse deficits, convulsions, decerebrate rigidity, coma, or death from cerebral hemorrhage.

Hypotension, or low blood pressure, generally has only mild or unnoticeable effects on brain functioning (Ariel & Strider, 1983); however, it can produce diffuse impairment of moderate to severe degrees as well. Children may complain of amnesia, excessive fatigue, fainting, convulsions, or loss of specific cognitive abilities, all of which indicate that ischemia to brain tissue has likely occurred (Gold, 1984). As such sequelae are variable and often fluctuating, the diagnosis of brain dysfunction or permanent injury is a difficult one to make. Cardiovascular difficulties can also modify blood constituents, producing brain ischemia because of the alteration in blood flow or inability of erythrocytes to carry oxygen. Many such problems may first be labeled as "psychiatric" or emotional disorders because the child exhibits depressive symptoms or confusion as the first signs (Taylor, 1979).

Surgery for cardiovascular problems also carries a certain risk. Circulation of blood to the brain may become impaired while the patient is connected to a heart–lung machine. Thrombosis, embolism, anoxia, or toxic/allergic reactions to anesthesia or injected medications may occur. Infections can develop that spread to the brain, or the heart may simply fail to regain normal rhythm after surgery. All of these may lead to cognitive deficits of varying degree and location (Ariel & Strider, 1983).

Brobeck (1979) reported that EEG tracings revealed more abnormalities after than before cardiac surgery. He further noted that if the patient's EEG does not return to normal within 3–4 weeks after surgery, the likelihood of cerebral damage having occurred is quite high. Studies using neuropsychological tests have found that signs of cerebral dysfunction prior to surgery place the child at even higher risk for the development of later cerebrovascular problems as well as at a higher risk for death during surgery (Kilpatrick, Miller, Allan, & Lee, 1975).

In the research literature on adults, there have been a number of investigations conducted on patients who have undergone surgery for occlusions or narrowing of the internal carotid arteries. Such patients are often so diagnosed because they experience transient ischemic attacks with such symptoms as dizziness, memory loss or deterioration, mild speech problems, visual changes, or mild sensorimotor deficits. If untreated, a cerebral stroke is likely (Thompson, Patman, & Talkington, 1978).

Little such work has been conducted with children, and therefore, inference must be drawn from the adult research literature. Those studies that have been done with adults to determine if surgical intervention improves or changes cognitive status have reported mixed findings. Several studies have reported significant improvement (e.g., Bornstein, Benoit, & Trites, 1981; Goldstein, Kleinknecht, & Gallo, 1970; Owens et al., 1975), whereas a similar number of investigations have found either no improvement or deterioration in functions (e.g., Drake, Baker, Blumenkrantz, & Dahlgren, 1968; Murphy & Maccubbin, 1966). One study concluded that any reported performance increase was likely to be a function of test—retest practice effects and not true improvement in functioning (Matarazzo, Matarazzo, Gallo, & Weins, 1979).

Children with similar cardiovascular dysfunction, therefore, may suffer from much the same forms of dysfunction; however, there remains the caveat that one is dealing with a developing brain. As the brain appears to develop functional capacity during development, early damage may impede this development. Damage incurred at later ages may result in a loss of established functional capabilities. However, it is generally felt that the prognosis for recovery of cognitive functioning or reacquisition of lost functions depends primarily on an interactive effect of a number of variables including type, location, and extent of damage, to name a few (Rourke, Bakker, Fisk, & Strang, 1983).

Finally, in cases of cardiovascular system abnormality or malfunction that has led to cognitive impairment, personality changes such as depression, irritability, anxiety, and so on may

occur with some frequency (Lishman, 1978). These changes often are noticed before actual intellectual deficits appear and may be attributed to the child's inability to adjust to the illness. In some cases, the changes may be the sequelae of damage to the brain and this possibility needs to be fully explored.

Cardiac Arrest

The impact of a sudden cardiac arrest on the neurodevelopmental and adaptive functioning of young children with congenital heart disease was examined. Sixteen children with heart disease who had sustained an in-hospital cardiac arrest were compared with a "medically similar" group of children who had not experienced an arrest. Children who had sustained a cardiac arrest displayed more impairment in general cognitive, motor, and adaptive behavior functioning as well as greater disease severity (Bloom, Wright, Morris, Campbell, & Krawiecki, 1977). The authors noted that the occurrence of a cardiac arrest along did not contribute to the prediction of outcome measures. Rather there was a significant interaction between cardiac arrest and cumulative medical risk found. Not surprisingly, children who had incurred a cardiac arrest and who had more severe disease demonstrated increased deficits.

Congenital Heart Disease Surgery

There are increasing survival rates in children who have congenital heart disease. This has lead to an increased interest in the neurodevelopmental sequelae of such lesions. One neuropsychological study examined 243 5-year-old children (age at surgery ranges from 1 to 1791 days; median age = 61 days) who had had surgical repair of cardiac lesions (Forbess et al., 2002). Results of the study indicated that children with congenital heart disease, on the whole, appear to be performing within the average range intellectually. Generally, the results of this study suggest that children who had more significant disease initially, or who had to undergo more extensive repair procedures, did more poorly on neuropsychological tests.

Lymphatic and Connective Tissue Systems

The lymphatic system, often referred to as the immune system, is similar to the blood and cardiovascular system in its structure, but differs greatly in function. Its primary purposes are to defend the body against invasion by injurious agents, to gather and destroy worn-out cells, and to produce antibodies. It also stores extra red blood cells and produces hormones that help to regulate the development of new red blood cells. The lymphatic system is composed of the spleen, lymph vessels and nodes, and defensive cells (Rowland, 1984).

Spleen

The spleen is the main storage center for new red blood cells and the destruction center for old ones. It also makes some types of white cells (the lymphocytes). In emergency situations, large numbers of red cells are dumped into the bloodstream to ensure adequate oxygen supply.

Lymph Vessels

The lymphatic system has its own vessel system that drains fluid from the tissue space. These vessels form into larger ducts that eventually merge into the blood. Along the vessels are lymph nodes that act to help prevent large particles or foreign bodies from entering the bloodstream. Lymph cells in the nodes are generally effective in eliminating most foreign bodies with the exception of viruses. Lymph ducts and nodes are found almost everywhere in the body except in the CNS. The lymph capillary system is laid out in such a manner so that virtually all materials that enter the body through the skin or the mucosa must first pass through the lymphatic system. As the lymph system is in essence a dumping/disposal system, any disruption of it can impact on water and electrolyte balance within the body, which in turn can increase pressure on the capillary system, shut down blood flow, and eventually result in death.

Disorders of the Connective Tissue System

Connective tissue refers to fibrous tissue that provides support for holding cells together and forms a protective covering around the body

and internal organs. Connective tissue cells are found everywhere in the body, but large amounts of them are found in bones and joint tissues. The connective tissue system is composed of ligaments, tendons, cartilage, skin, blood vessels, internal membrane linings, and sheath coverings of organs and muscles. It also constitutes a large portion of organs such as the eyes, lungs, heart, kidneys, and liver (American Rheumatism Association Committee, 1973).

Disorders of the connective tissue can be inherited or acquired. The genetic maladies are comparatively rare and are beyond the scope of this chapter. Acquired conditions generally include rheumatoid arthritis, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, dermatomyositis, Sjogren's syndrome, amyloidosis, various forms of vasculitis, and rheumatic fever. Although different in terms of severity and the age group affected, these diseases all display features associated with inflammation and destruction or alteration of connective tissue. Common symptoms include fatigue, fever, muscular weakness, joint swelling and pain, skin lesions, gastrointestinal erosions with hemorrhages, peripheral vascular dysfunctions, neuropathies, and blood cell disorders such as anemia and thrombocytopenia. The course of the illness may vary greatly from individual to individual, with periods of both remission and exacerbation, a chronic mild illness, severe and rapidly progressing deterioration, or fluctuations between mild and severe episodes. Some children with these diseases may become severely disabled from crippling joint deformities or loss of function in a major organ system, such as the kidneys. Initial symptoms can mimic many other diseases because they are so variable and thus difficult to diagnose in many instances (Gilroy & Meyer, 1975).

CNS Effects

Comprehensive research on the neuropsychological effects of diseases of lymph and connective tissue systems in children remains minimal, at best. The medical literature indicates that the effects on the brain and CNS tend to be variable and generally predictable (Gilroy & Meyer, 1975; Rutter, 1983; Walton, 1977). The small vessel inflammation and destruction that can occur in many of these diseases can produce focal ischemic lesions in many organs, causing

them to malfunction and reduce their support to the brain. Vessels in the brain may also be affected, although pathological studies have been inconsistent in confirming this with most disease types with the exception of giant cell arteritis, a condition rarely found in children (American Rheumatism Association Committee, 1973). Hypertension is a frequent outcome of these diseases, the effects of which were described above. Compression or ischemia may result in peripheral neuropathy, with sensory or motor losses in digits or limbs (Graham, 1983). Diffuse or focal cerebral infections may occur as a result of the suppression of immune systems from drugs taken during treatment.

Although evidence of the disease process in the brain itself has not yet been confirmed, studies have indicated the presence of immune complexes associated with connective tissue and lymphatic system disease processes in the choroid plexus of the brain (Atkins, Kondon, Quismoro, & Friou, 1972; Bresnihan et al., 1979; Winfield, Lobo, & Singer, 1978). Psychoses, depression, and mental confusions have frequently been reported as sequelae of these conditions. Reactions to corticosteroids, antihypertensives, antidiuretics, anti-inflammatory agents, and other medication used for treatment have been found to produce changes in emotional or mental state, although it is difficult to separate this from the effects of the disease itself.

CNS effects have been most often reported with systemic lupus erythematosus (Ariel & Strider, 1983). The reported sequelae include emotional disorders, convulsions, choreiform movements, and cerebrovascular accidents with focal neurologic deficits. These usually occur in children with highly active and severe disease. In the early stages of lupus, the CNS effects may be mild and transient, or may so resemble a psychiatric disorder that the patient is treated as such (Bennett, Bong, & Spargo, 1978; Hughes, 1979).

CNS Effects of Liver Dysfunction

A relatively recent area of study is that of the effects of liver disease or dysfunction. Children who have received liver transplants appear to be at significant risk for the development of neuropsychologic deficits (Stewart et al., 1990). Significantly lower performance IQ scores, academic achievement, and age-adjusted z-scores in

learning, abstraction, visual–spatial functioning, and motor functions were found. Alertness, sensory–perceptual, and perceptual–motor skills appear not to be affected. The children in this study demonstrated greater cognitive dysfunction than adults with end-stage liver disease.

Respiratory System

The respiratory system is composed of the upper airway, including the nose, pharynx, larynx, and epiglottis; the lower airway, including the trachea, the primary or main bronchi, the segmental bronchi, and bronchioles; and the lungs, located within the thoracic cavity on either side of the heart. The exchange of gases provided by this system is vital to the brain. The cardiovascular system's function is to supply oxygen to body tissues via circulating blood. The blood also removes carbon dioxide produced by metabolism, and transports this waste product to the lungs. Here the carbon dioxide is replaced by oxygen, and the newly oxygenated blood is recirculated to the tissues, including the brain.

A network of airways provides the pathway for the transport and exchange of oxygen and carbon dioxide. Under normal circumstances, by inhalation the upper airway provides air for the lower airway, where it is conducted through smaller and smaller pathway branches in each lung field. The final branches of bronchioles (terminal respiratory bronchioles) end in clusters of alveoli, or air-filled sacs. Thus, the working area of the lung is a network of air tubes and blood vessels, through which blood ultimately reaches the alveoli, which are the primary structures for the exchange of carbon dioxide and oxygen (Luckman & Sorenson, 1980). Given that the need for oxygen by the brain is so great, a significant disruption in the functioning of the respiratory system may have negative cerebral consequences.

Bronchial Asthma

Asthma is the most common chronic disease of childhood, estimated to occur in 5% of adults and children in the United States, over 10 million people, of whom over 2 million are under the age of 16. The onset of asthma is usually within the first 5 years, although it can occur at any age. A more favorable prognosis appears to be related to an early onset, unless significant asthma attacks begin before the age of 2 (King, 1980). Asthma accounts for nearly one-fourth of all days absent from school by children, and it ranks third among all chronic illnesses as a cause of physician visits (Sadler, 1982). It also contributes greatly to acute visits to emergency rooms, days in the hospital, and problems related to psychosocial adjustment (Rubin et al., 1986).

Although the symptoms of asthma have been recognized for centuries, there is currently no commonly agreed on definition of the syndrome, nor any consensus with regard to whether asthma is primarily a medical or psychological disorder (Creer, 1982). A great deal has been written about the onset of asthma from several psychological perspectives, notably psychoanalytic and behavioral (Sadler, 1982), and a variety of psychological interventions have been presented to deal with this condition (King, 1980). Basically, asthma is a bronchial disorder characterized by airway obstruction that is intermittent, variable, and reversible. The lung pathology may occur in the central or larger airways, and the peripheral or smaller airways. Obstruction of these bronchial airways may be related to smooth muscle constriction, swelling of tissue, swelling of the mucosa, and dried mucus plugs (Chai, 1975; King, 1980). The one common denominator is a peculiar hyperreactivity of the airways, whether to physical, chemical, pharmacologic, or immunologic stimuli (Sadler, 1982).

The clinical symptoms present as spasms of difficult breathing, coughing, and wheezing, with the attacks lasting from several minutes to several hours, although in a condition known as "status asthmaticus" obstruction may last for days or weeks. Attacks can vary along a continuum of severity from very mild to very severe, the latter increasing the risk of brain damage or even death (Bierman, Pierson, Shapiro, & Simons, 1975). Although the notion that cerebral anoxia secondary to bronchial asthma attacks may lead to neurobehavioral deficits seems to be defensible and stimulating, very little solid research has been conducted in this area.

Dunleavy and Baade (1980) stated that there have been a number of studies reporting on the adaptive behaviors of asthmatic children, particularly as applied to the classroom situation. Most are speculative, whereby observed maladaptive behaviors and learning problems

are assumed to be related to organic damage, which is further assumed to be a result of transient hypoxia accompanying their severe asthmatic attacks.

In an effort to make use of assessment instruments better designed to detect brain–behavior relationships, Dunleavy and Baade (1980) evaluated a sample of asthmatic children using the Halstead Neuropsychological Test Battery for Children. Their goal was to identify patterns of neurobehavioral deficit characteristic of severely asthmatic children 9–14 years of age. Nineteen severely asthmatic subjects and 19 matched nonasthmatic controls who had no history of organic damage were administered the Halstead Battery. Significantly, poorer test performance was noted for the asthmatic group, with eight Halstead Battery tests showing most difference between the groups. Three of these tests, Trail Making, Tactual Performance, and WISC Mazes, were more sensitive than the others in discriminating asthmatic from nonasthmatic subjects. The authors concluded that the primary deficits of impaired asthmatic children are in visualizing and remembering spatial configurations, in incidental memory, and in planning and executing visual and tactile motor tasks.

Using both a classification battery, developed from four of the eight Halstead Battery tests that showed greatest discrimination between groups, and blind clinical analysis, Dunleavy and Baade (1980) identified 7 of the 19 asthmatics (37%) as impaired, whereas only 1 of the controls was so labeled. They further compared the test score means of the seven neuropsychologically impaired asthmatic children with the Halstead Battery test score means of the 9- to 14-year-old brain-damaged (cerebral tumor, traumatic injury, inflammatory disease) group studied by Boll (1974). The asthmatic sample performed better than did the Boll sample, in line with the clinical assessment of very mild to mild brain damage for the asthmatic children in their study. The authors also mentioned that five of their asthmatic subjects reported they had experienced periods of unconsciousness and had "turned blue" during their attacks. Of these five, four were classified by their Halstead scores as impaired. This finding was thought to add credence to the notion that loss of consciousness and cyanosis, which occurs during some severe asthmatic attacks, can

contribute to later occurrence of organic dysfunction.

Suess and Chai (1981) suggested that the conclusions of Dunleavy and Baade were premature because the possibility of similar performance deficits as a function of antiasthma medications was not taken into account. In essence, the treatment and not the disease may account for the obtained neurobehavioral deficits. Dunleavy (1981) responded that in their sample, they found no relationship between drug use, as obtained from detailed medical history, and neuropsychological test performance. Further, he reported that of the 7 children classified as impaired, only 3 were receiving antiasthma medication, and of the 12 asthmatic children who showed no evidence of performance deficit, 7 were receiving such medication.

However, Chai (personal communication, March 21, 1986) and his research team at the National Jewish Hospital in Denver completed a 3-year study of the effects of antiasthma drugs such as steroids on information retention in asthmatic children. Their preliminary analyses suggested the use of such medications has no noticeable effect on retention in reading and writing, but quite significant effects on the automatic memory required for retention of math skills. Other investigators (Bender, Lerner, & Poland, 1991; Bender & Milgrom, 1992; Schlieper, Alcock, Beaudry, Feldman, & Leikin, 1991) suggest antiasthma medications tend only to exacerbate already existing tendencies toward behavioral or attentional difficulties in asthmatic children.

In summary, limited research has demonstrated that some severely asthmatic children exhibit very mild to mild brain-damage-like behaviors, that certain such behaviors are more likely to be seen than others, and that these deficits can be predicted to a degree by previous episodes of loss of consciousness and cyanosis. Other research has suggested that such findings are consistent not only with the assumption of underlying change in cerebral structure or function but also as an iatrogenic effect of antiasthma drugs over time.

Cystic Fibrosis

Cystic fibrosis (CF) is the most commonly seen lethal genetic syndrome of infants, children, and young adults. It is most prevalent in

Caucasian youngsters, with one case of CF in every 1,500–2,000 live births; it is much less common in black and Asian populations. Inheritance appears to be by an autosomal recessive gene, suggesting a specific biochemical defect, but no single, unifying hypothesis exists at this time to account for the pathogenesis of CF (Matthews & Drotar, 1984).

CF is a very complex condition affecting a wide variety of bodily functions. It causes abnormalities in the exocrine gland network, pancreas, liver, gastrointestinal tract, reproductive system, and especially in the respiratory system. Chronic obstructive pulmonary problems seem to account for the majority of morbidity and mortality in the CF patient. In the past, children with CF simply died young. But the introduction of the sweat test in 1954 permitted early diagnosis, and coupled with newer treatment regimens, children with this disease are now surviving fairly well into late adolescence, young adulthood, and in some cases into early midlife (Taussig & Landau, 1986). A tremendous adjustment to the disease is required because it requires lifetime care, a great deal of medicine, a strict diet, a mechanical apparatus to assist breathing, daily postural drainage and breathing exercises, and living in constant danger of respiratory infections.

Individuals with CF are prone to such infections, and their breathing is often altered as a result of increased airway resistance. Some of the issues discussed above with asthmatics regarding decreased cerebral oxygenation and its effect on cortical integrity may be germane here, although symptoms seem to be less severe. CF is not seen as a disease that directly affects the brain. In fact, Breslau (1985) and Breslau and Marshall (1985), in studies of psychiatric disorders in children with physical disabilities, used CF subjects as non-brain-involved chronic disease controls. They found that healthy and CF subjects, previously diagnosed as troubled, improved in their mentation and psychological adjustment over a 5-year period, whereas brain-damaged subjects showed no such improvement. Stewart et al. (1991) used CF patients as controls for growth retardation and chronic disease to assess the neuropsychological outcomes of pediatric liver transplantation, finding the CF patients similar to normals. However, Matthews and Drotar (1984) suggested that CF children express some of their difficulties in adjusting to this multisystem disease by the development of learning problems in school. As is seen with other chronic diseases, these learning problems may in fact be symptomatic of psychological difficulties, absenteeism, and decreased sensory stimulation; however, they may also be related to mild neurobehavioral deficits. Currently, no research specifically addresses this issue in children with CF.

Sleep Apnea (Snoring)

While not a chronic medical disorder per se, obstructive sleep apnea syndrome (OSAS) has been associated with reduced neurocognitive performance in children (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000; Kennedy et al., 2004). Recently, there have been attempts to evaluate the relationship between hypoxemia, respiratory arousals, and neurocognitive performance. Thirteen snoring children who had been referred for evaluation regarding the need for adenotonsillectomy underwent detailed neuropsychological and polysomnographic examination. Even though the snoring children had an obstructive respiratory disturbance index within the normal range, several domains of cognitive functioning were reduced. Decreases were noted in verbal IQ, full-scale IQ, selective attention scores, and memory index scores. A direct relationship was noted between the number of mild oxygen desaturations, obstructive hypopneas, and respiratory arousals and severity of deficits with memory being impacted the most. The authors suggest that future studies would be useful in determining if these deficits reverse post-surgically (Kennedy et al., 2004).

Central Nervous System Infection

The morbid consequences of CNS infections are typically overlooked in the face of high mortality rates. Neurological impairment not only can affect a child's development and future prospects but also place an economic and social burden on the community in which the child lives. Carter, Nevill, and Newton (2003) conducted systematic review to investigate the occurrence and pattern of persisting neurologic impairment following common CNS infections. Forty-six eligible studies were found using a comprehensive search of electronic

databases (MEDLINE, EMBASE, and Psy-chINFO). The analysis of the studies showed that postinfection neurological impairment persists, most commonly in cognitive and motor functions. Deficits noted were varied and included more subtle problems which can be difficult to detect on gross neurologic examination but "may still be deleterious to the child's social and educational functioning." Thus, the need for more comprehensive neuropsychological evaluation procedures will likely continue for the foreseeable future.

Childhood-Onset Schizophrenia

While not traditionally thought of as a chronic medical disorder of childhood, recent anatomical brain magnetic resonance imaging studies show a striking postpsychotic progressive loss of cortical gray matter in patients with childhood-onset schizophrenia (Rapoport et al., 1997, 1999). A recent study demonstrated that cortical gray matter volume losses occurred in the frontal, temporal, and parietal regions of the brain of 23 adolescents diagnosed with childhood-onset schizophrenia (Gogtay et al., 2004). The authors suggest that an ongoing neurodevelopmental process and/or brain response specific to the illness may account for the volume changes and attendant apparent cognitive decline. Interestingly, the authors cite unpublished data that a larger sample ($N = 50$) with childhood-onset schizophrenia showed no cognitive decline despite "pronounced" gray matter loss. It is speculated that the gray matter loss represents in part a plastic response of the brain to dysfunctional synaptic processing. Further studies are planned to investigate.

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Coping and Adjustment of Children with Neurological Disorder

TIMOTHY B. WHELAN AND MARIE L. WALKER

Introduction

The opportunity to test the limits of one's clinical acumen is clearly apparent in the field of clinical child neuropsychology. The explosion of related theory and research, the complexity of case material, and the growing demand for applied expertise continue to challenge us daily. Indeed, the study of developmental brain– behavior relationships can be so intrinsically fascinating, so alluring, that many of us cannot imagine being satisfied in another domain of study. Yet there may be a subtle trap in all of this, the trap of becoming so enthralled with exploring brain–behavior relationships in isolation that we lose sight of the total experience of the child.

It is the premise of this chapter that children and adolescents who have sustained an insult to the brain not only face the likelihood of altered brain function and its attendant problems, but must also contend with the effects of neurological disorder in a social context. In other words, like children with chronic illnesses, they may face severe developmental challenges during diagnosis, hospitalization, medical intervention, rehabilitation, schooling, family development, and socialization. As a consequence, there is the risk throughout the course of the disorder for the creation of secondary deforming effects on

psychosocial adjustment in addition to the primary cognitive, sensory, and motor changes commonly associated with these disorders. As with the victims of other diseases, accidents, or faced with major personal and developmental crises, the presence of neurological impairment may force children and their families to question their fundamental assumptions and expectations about themselves and their world, and to react to or "cope" with multilevel effects of the disorder. It is therefore apparent that the helping professional concerned with the psychological well-being of children must remain cognizant of the nonbiological systems with which children interface.

This chapter is concerned with multiple systems affecting the coping and adjustment of children with neurological disorder. Investigation of this topic often leads to psychological literature that is conceptually relevant but somewhat apart from traditional neurodiagnostically oriented neuropsychology. For instance, social psychologists investigating coping mechanisms have primarily been concerned with adults, and the pediatric psychology literature regarding coping with neurological disorder is not highly developed. However, despite variation in specific targets of study, "good practice" in the area of clinical child neuropsychology requires a continual integration of theoretical and applied information from the domains of clinical child, developmental, educational, social, and family psychology. A related point was made by Boll (1985) who described a "threshold" movement

TIMOTHY B. WHELAN • Department of Psychiatry, Baystate Medical Center, Springfield, Massachusetts 01199. MARIE L. WALKER • Austin, Texas.

within the field of neuropsychology toward a more psychological emphasis:

> In addition to the utilization of behaviors for exquisite neuroanatomical appreciation which represents a continuing and legitimate investigational area, neuropsychologists provide, with increasing sophistication, psychological descriptions designed primarily to help in understanding the whole person, rather than being confined only to the person's neuroanatomy. (p. 474)

As detailed below, mechanisms of coping and adjustment in neurologically impaired children are, perhaps, best viewed globally from developmental and systems-theoretic models of child psychology. After a discussion of this conceptual framework, general considerations regarding the constructs of coping and adjustment are presented. Further topics related to the coping and adjustment of neurologically impaired children are then selectively reviewed and provide a flavor of the complexity of related theory and practice.

General Systems and Developmental Models

A conceptual framework for studying the processes of coping and adjustment in children with neurological impairment can be derived from general systems theory, a general science of "wholeness" examining sets of elements standing in interrelationship (von Bertalanffy, 1968). The systems-theoretic model posits that the human organism exists in a hierarchy of systems ranging from the biological realm, through cognitive, intrapsychic, and behavioral levels of analysis, to the family and social spheres. This is an information flow-through model in which developments at one level theoretically have ramifications throughout the systems hierarchy. Whereas von Bertalanffy has perhaps been most eloquent in expressing the systems approach, these central tenets are not unfamiliar to scientists in general and they have appeared in the writings of seminal thinkers in the history of neuropsychology. For instance, more than 50 years ago Kurt Goldstein (1939, 1940) concluded that any particular symptom displayed by a patient could not be easily understood as being uniquely the product of a specific lesion or disease, but instead had to be considered as a manifestation of the total organism that behaved as a unified whole.

General systems theory has also been cited in support of a fundamental reorientation in medical education and practice (Engle, 1977, 1980). Such a shift in thought leads to reconceptualization of disease as a biopsychosocial product and to the study of disease and medical care as interrelated processes. The reliance on such an approach is now particularly evident in the literature on families with illness (Gochman, 1985; Kerns & Curley, 1985; Kerns & Turk, 1985; Leventhal, Leventhal, & Van Nguyen, 1985) and in the field of clinical health psychology (Millon, Green, & Meagher, 1982). Moreover, this conceptual framework may become increasingly central in the era of medical care cost containment.

This application of a general systems approach to understanding the functioning of adults with neurological impairment seems reasonable and logical: Disorders of biological functioning are likely to affect an individual's psychosocial status. The consideration of nonbiological systems in the lives of neurologically impaired children, however, is virtually mandatory. Children do not exist in isolation from others as adults can choose to do. Rather they are enmeshed in nonself systems to a far greater extent, influencing and being influenced by family, peers, health professionals, and schools. One cannot even approximate a clear clinical description, however elegant, of a child without reference to relationships between that child and those with whom they are bound.

An additional dimension of complexity must be added to the clinical child neuropsychologist's systems-theoretic model: the process of development and change. Although the notion that the individual is an active, developing organism is a fundamental concept among child development and life-span psychologists, neuropsychological literature has historically neglected this aspect of our functioning (Parsons & Prigatano, 1978; Smith, 1979). Walter Riese (1977) captured the problem aptly:

> Overpowered by the ever-increasing intricacies of anatomical arrangements, . . . yielding in this self-inflicted intellectual emergency to the always threatening danger of oversimplification, the modern student of brain lesions forgot that every functional disturbance has its natural or evolutionary history. Whether affected by neurosis, psychosis or brain injury, man must write the history of his new condition which implies the

history of his whole life. Nobody, healthy or not, can escape the law of time and change. (p. 77)

The need for consideration of developmental issues in child health psychology has been well described by Maddux, Roberts, Sledden, and Wright (1986) and Garrison and McQuiston (1989). Schmidt, Peterson, and Bullinger (2003) emphasized that the study of coping in children and adolescents differs from that in adults because of the inherent connections between coping and development. Reviews of the literature regarding the psychosocial adjustment of children with chronic physical conditions may be found in Drotar (2006), Frtiz and McQuaid (2000), Kliewer (1977), Miceli, Rowland, and Whitman (1999), Tarnowski and Brown (2000), Thompson and Gustafson (1996), and Wallander, Thompson, and Alriksson-Schmidt (2003). Whelan (1999) also reviewed some of the critical variables in integrative developmental neuropsychology.

Bernstein and Waber (1990) have articulated these points with particular clarity in their model of developmental neuropsychological assessment—an approach, not a technique—in which the goal is "not to diagnose deficits in a child, but rather to construct a *Child-World System* that characterizes the reciprocal relationship of the developing children and the world in which that child functions" (p. 312). This approach is derived from the systemic tradition of Luria and Vygotsky as well as the Wernerian approach most elaborated in neuropsychology by Kaplan. More specifically, the model considers manifestations both neurological and psychologic of the structure (three neuroanatomic axes, cognitive structures), development (neurological and psychological developmental timetables), alternative mechanisms (alternative pathways, alternative strategies), and context (role of experience, environmental interactions). Consistent with this approach, attributions of difficulty are shifted from the child to the system.

This, then, is the model: The child is conceptualized on multiple levels standing in interrelationship, with the hierarchy of systems set in temporal motion. It would of course be extravagant to assert that neuropsychologists can excellently or adequately conceptualize all of our clients in this fashion, but the goal of doing so seems worthy.

Coping and Adjustment

In most theoretical models, coping is a process that is initiated when an individual perceives or experiences stressful stimuli, such as a change in the pace of life or a subjective perception of an event as negative or undesirable and beyond the competence of the coping person (Chan, 1977). For example, hospitalization, sensorimotor disability, or loss of cognitive integrity associated with neurological disorder could obviously all be considered untimely, unexpected, and undesirable life changes. Coping presumably leads to adaptation or adjustment to stressful events and perceptions, and successful coping implies successful adjustment. Generally, people cope with daily stressors by responding with habitual and automatic patterns of cognition and behavior (Folkman & Lazarus, 1980). Such coping strategies may involve the cognitive functions of perception, memory, speech, judgment and reality testing, motor activity, emotional expression, and psychological defenses (Mattsson, 1972). When these customary automatic responses become unavailable, individual attempts at coping will require that old resources be used in new ways. This may be particularly true for children whose increasing cognitive and behavioral abilities continually alter the effectiveness of their previous automatic responses. Coping, then, can be conceptualized as purposeful behavioral and/or intrapsychic activity at either conscious or unconscious level that serves to ameliorate the experience of stress while facilitating adjustment to stressful stimuli.

In relation to coping, the process of adjustment allows a return to effective (though not necessarily prior) automatic patterns of behavior, and implies that an individual is functioning effectively. More specifically, for the child with neurological impairment, adjustment includes acceptance and age-appropriate understanding of the disease or handicap, medical compliance, absence of severe psychopathology, age-appropriate interpersonal functioning with family, peers, and in school, and "normal" or age-appropriate personality functioning (Drotar, 1981).

Cautions

Although full treatment of the constructs of coping and adjustment is beyond the scope of

this chapter, several considerations are in order. First, we have implied that coping is a process and adjustment is an outcome of this process, and this may indeed be the case. However, such a scheme may also be an unfair simplification of the relationship between coping and adjustment. It may also be true, for example, that levels of adjustment influence attempts at coping. For instance, high self-esteem may be an outcome of a child's successful attempts at coping. Similarly, it may be that children who already experience high self-esteem will be better able to cope with stressful events.

Second, coping is a uniquely individual process and its exposition depends on experiential insight and/or observer inferences; it is not a construct that can be measured directly. Currently, psychosocial science relies on personality and adjustment measures, such as levels of self-esteem, depression, anxiety, and locus of control, among others, to infer both the presence and the effectiveness of the coping process. Scales to assess stress and coping specifically in children have been developed (Roder, Boekaerts, and Kroonenberg, 2002). Cognitive and behavioral components may also be evaluated (Curry & Russ, 1985). Nevertheless, though the process of coping and adjustment are well understood intuitively, they remain scientifically and empirically vague.

Interested readers are referred to a series of studies reported by Tobin, Holroyd, Reynolds, and Wigal (1989) which develop a hierarchical model with three levels of the structure of coping. Eight identified primary factors (problem-solving, cognitive restructuring, emotional expression, social support, problem avoidance, wishful thinking, self-criticism, and social withdrawal) were organized into two types of problem-focused and two types of emotion-focused coping activities, and at the tertiary level there appeared two basic approaches to stressful situations, namely, engagement and disengagement. This structure was examined by means of hierarchical factor analysis of the Coping Strategies Inventory administered to young adults, and its developmental nature has yet to be established. For a more child-specific theory, see Ryan-Wenger (1992).

Third, it should be noted that coping and adjustment are processes that occur continually; they are not discrete and isolated events. People experience multiple levels of stress simultaneously, from the trials of getting to school or work on time, to fears of being perceived as different or odd, and feelings of unworthiness. Even positive changes in life events, such as promotions, may be experienced as stressful, and the perceived intensity of a stressor at a given time will influence an individual's attempt at coping. Further, what may constitute successful coping behavior at one time may change with age and other intervening variables. Again, this is especially true for children where constant development in their abilities may render previously effective patterns of coping obsolete. When neurologically based disorganization of cognitive and affective functions are superimposed on normal developmental patterns of organization, the complexity of these processes can be magnified.

Finally, coping and adjustment are processes that reflect an interaction between individual and environment (Rutter, 1981, 1986). It has long been recognized that people perceive stressful stimuli differently and that individuals will make unique attempts to cope with stress, whether by flight, fight, or inaction, based in part on personality determinants, history with coping experiences, and environmental constraints, including peer and societal expectations (Chan, 1977). The significance of this interaction, especially for children, is reflected in increasing research on the influence of the family in children's abilities to cope with their handicaps.

Societal Influence on Coping and Adjustment

A paradoxical dilemma exists when one considers the relationship of coping and neurological disorders. Traditional definitions of coping, including those presented here, suggest that stressors such as neurological deficits are external to the individual and must be adjusted to as unwanted alien agents. This idea originates from the societal doctrine of normalcy, where certain parameters of behavior are acceptable and occurrences outside of these bounds are regarded as deviant. Deviance is then considered unacceptable, obviating the need for a return (adjustment) to normalcy.

This viewpoint can be both unfortunate and not entirely necessary. Children born with a neurological deficit, for example, have always interpreted their worlds through a unique lens, and

their "deficits" are a part of their identity as surely as being physically whole is a part of most of ours. Often, however, individuals with visible physical differences are considered deviant and treated accordingly. The process of accepting one's handicap is thus made more difficult when one is continually regarded by peers and society as "different."

The problem we are suggesting, then, is that handicap is defined normatively and from an "outsider's" perspective (Shontz, 1982). "Insiders," or people who have either always experienced a particular state, such as neurological disorder, or who have come to accept their differences and/or limitations, do not necessarily view their handicap as something to overcome (Massie, 1985). Once an individual has learned to cope with a handicap, the deficit itself no longer remains the focus of attention. Handicapped individuals, like ourselves, must answer the question, how does one achieve satisfaction and happiness in life, given the uniqueness of every individual? Although this question is made no less easy by the presence of a handicapping condition, the burden might be eased if it were not necessary to feel that one had to meet the normative standards of today's society.

Making Meaning of Neurological Disorder

Words, Words, Words—*Hamlet*, Act II, Scene ii

Whether in the role of consultant or therapist, child neuropsychologists are often called on to provide information to their clients regarding the nature of the neurological disorders. The process of clear and appropriate explanation may be problematic enough with adults. We are reminded of the elderly gentleman with cerebrovascular disease who had carefully listened to his physician's explanation of regional cerebral blood flow measurement, and who had given his "informed consent" to the procedure. During a later neuropsychological examination he wanted to confirm his understanding of the procedure, and said, "This is something *nuclear,* right? Like *the bomb,* right?"

Examples of well-meant yet misjudged attempts to convey the nature of medical problems to children are also present in the literature. Whitt, Dykstra, and Taylor (1979) mentioned the potential iatrogenic harm that

may come from such casual statements as "the doctor will inject some 'dye' ..." (thus effectively raising the possibility of imminent "death") or "epilepsy is excess 'electricity' in the brain" (summoning up parental admonitions regarding wall sockets, shocks, and terminal consequences). Similarly, Perrin and Gerrity (1981) have written on the young pediatric patient's assumption that when the doctor says "there's edema in your belly," the "demon" was sent there to punish him or her for wrongdoing; the notion of a "demonic" brain could evoke even more primitive fears.

The pediatric literature advises that healthcare professionals consider the child's level of cognitive development (typically in a Piagetian sense) when conveying information regarding disease processes, medical procedures, and health maintenance (Brodie, 1974; Campbell, 1975; Mechanic, 1964; Neuhauser, Amsterdam, Hines, & Steward, 1978; Palmer & Lewis, 1976). The goals of such consideration include improved regimen compliance, reduced anxiety, and enhanced understanding and acceptance of the condition by the affected child and, if also afforded developmentally appropriate explanations, by healthy peers.

According to stage theorists, children functioning at a preoperational level of cognitive development (normally between ages 2 and 7) center on single external events, which are viewed from the child's own perspective without generalization to other situations and without the application of logical operations. Illness prevention and recovery may thus be associated with sets of rigid rules surrounding immediate perceptual experience and concrete action (avoiding the touch of sick friends; staying in bed) (Perrin & Gerrity, 1981; Whitt et al., 1979). Bibace and Walsh (1979) proposed refinements to this general category of cognitive development, as well as categories described below. For instance, preoperational explanations of disease are divided into the categories of *phenomenism* (illness caused by single inappropriate, external, and spatially remote sources, i.e., "people get colds from the sun") and *contagion* (reliance on single causes of contagion transmitted through mere proximity and manifest in a single symptom, i.e., people get colds when someone else gets near them). Siegal (1988) has suggested that familiarity with a disease results in more advanced conceptual understanding, so that

one might expect a preschooler to apply more sophisticated causal reasoning concerning a cold than a neurological illness with recent onset.

At the stage of concrete operations (normally between ages 6 or 7 and 11 or 12), the child's thought becomes less egocentric and perceptually bound, and reasoning becomes more logical. Specification of relationships among events or objects, categorical classification, and transformation comprehension become possible. Illnesses at this time may be defined by the child as a set of multiple concrete symptoms, and are often believed to be caused primarily by germs. From such a perspective, diseases may impinge on the body unless sick people are avoided, and cures may consist of passively allowing medicines to act on the body. A clear appreciation of the self-healing aspects of bodily functioning is presumably lacking in the concrete operational child. Unlike the preoperational child, the concrete operational child can more clearly distinguish between internal and external events, though the focus remains on the latter. Subdivision of this stage by Bibace and Walsh includes *contamination*, in which there is recognition of multiple disease symptoms caused by concrete sources such as germs, dirt, or bad behavior. The *internalization* subdivision of concrete operational thought is characterized by the ways in which illnesses are internalized: swallowing or inhaling germs or other contaminants. The body's own recuperative powers become recognized, and reversibility (the sick person can become well, and vice versa) is characteristic.

With the emergence of formal operations in late childhood and early adolescence, illness may be conceptualized as having complex, interrelated, and multiple causes that affect multiple internal systems and result in multiple external symptoms. Bibace and Walsh decompose the explanation of illness in the formal operational stage into two subdivisions: *physiological* and *psychophysiological*. In the former, illness is defined by the child in terms of internal organs and structures whose malfunctions are manifest in multiple external symptoms and there is a clear departure from previous reliance on concretely perceptible reality. In the psychophysiological category, psychological events are included as disease symptoms as well as causes of internal dysfunction. The etiologies of a headache, for instance, may at this developmental point include too much worry.

Based on this six-stage developmental sequence, Bibace and Walsh contend that not only do conceptions of illness shift in characteristic ways, but there is also a corresponding developmental increase in the perceived control the child has over illness, with a concomitant decline in the sense of personal vulnerability. For example, older children in the *internalization* phase may believe that there are things they can do to maintain bodily health, whereas young children in the *phenomenistic* phase may believe themselves to be vulnerable to disease causes that are spatially remote and uncontrollable. These points are elaborated on by Maddux et al. (1986) in an article on developmental issues in child health behavior that focuses on prevention of illness and injury, and on health promotion. It would be erroneous, however, to suggest that feelings of control and reduced vulnerability are inevitable accompaniments of older age or later stages of cognitive development. Once again, children's conceptualizations of their neurological disorders are likely to evolve over time, with general stages of cognition interacting with particular informational content and numerous other cognitive and affective variables.

The suitable selection of words of explanation and due consideration of the nature of the child's beliefs about disease may still be insufficient to enable children to understand neurological disorders, if only because neuropathological processes are so often without visible referents. The use of metaphor, perhaps aided by drawings, to provide appropriate explanations of medical events may be particularly beneficial for children who have not yet attained formal operational thought and/or who are not likely to have a sense of the pathophysiology of the unseen nervous system. For example, in the case of seizure disorders the analogy of a telephone system has been suggested (Whitt et al., 1979). In condensed form, a discussion with the child might refer to the notion that the brain is like a telephone that sends messages to all parts of the body, and just like a telephone, the brain sometimes gets a "wrong number" by sending messages to the ___ (substitute relevant perceptual cues, perhaps those related to the aura). In some cases it can also be pointed out that just like a telephone after a wrong number, the brain works fine again.

The same authors have also provided metaphor for other neurological conditions. For instance, the body can be analogously described as a large city made up of many people (cells) with important jobs (e.g., telephone cells, garbageman cells, doctor cells, carpenter cells, police cells), and cancer cells may be described as outlaws in the system. Treatment may then be presented as a means of helping the body's police and medical forces to establish law and order. Built-up pressure in a garden hose with blocked outlet may serve as a metaphor for children with hydrocephalus, and the swelling and potential bursting of a balloon may foster a better understanding of aneurysms (though we personally find this last example too likely to result in fears of imminent catastrophe to be used with most children).

In considering the process of aiding children and their families to better comprehend their neurological or other medical disorder, it should be remembered that the sophistication of children's concepts of illness may differ from their concepts involving different content. Perrin and Gerrity (1981) reported that in a sample of normal children, illness–causation concepts (e.g., "How do children get sick?") were slower to develop than concepts to explain physical causality (e.g., "Why does night come?"). Moreover, older children may indeed be able to provide more sophisticated explanations of illness than younger children, but in a conditional sense: Younger children with a history of poorer health have the least sophisticated concepts, whereas older healthy children may have less sophisticated concepts than peers of the same age who have been ill more often (Campbell, 1975). In addition, the value of providing illness explanations to healthy peers in order to facilitate acceptance of children with chronic illness has been questioned (Potter & Roberts, 1984). As expected, when groups of healthy preoperational and concrete operational children were provided with either symptom descriptions or metaphorical explanations of diabetes and epilepsy, those receiving the analogous explanations demonstrated significantly more general comprehension of the illnesses, and perceptions of personal vulnerability were reduced. However, these illness explanations did not significantly facilitate ratings of acceptance of a hypothetical child with these diseases.

In some cases, the trail of misunderstanding is so confused as to be impenetrable. For instance, when one latency-aged boy was asked if he knew what might be the reason for his seizures, he speculated vaguely that it was "because something was wrong"; when pressed for a specific possibility, he could only guess "AIDS?" Note that clarity of information will probably be helpful in a case like this, but perhaps not in all instances: Brewster (1982) speculated that retention of magical beliefs in illness causality and responsibility may be an important defensive function. It has also been persistently curious to hear in interviews with caring and well-informed parents that they often have no idea what their child might believe about her or his illness at this point in the child's development. For those interested in helping to communicate concepts to children with neurologically based learning and behavioral difficulties, books by Mel Levine (1990, 1993) prove especially helpful.

The presence of disease conditions may also alter the normal pattern and pace of cognitive development (Mearig, 1985). Obviously this could be the case in those with brain dysfunctions that change cognitive integrity, and it may also occur in those with chronic illnesses whose intellectual functioning is relatively intact. Myers-Vando, Steward, Folkins, and Hines (1979) reported that although children with congenital heart disease manifest lower levels of cognitive performance on conservation tasks compared with healthy peers (presumably because of the disruptive "intrusive stress" of the illness), some of the ill children were capable of thinking formally in the content domain of illness causality, possibly because of the greater affective salience of the topic or greater opportunities for direct education and experience with illness. On the other hand, Carandang, Folkins, Hines, and Steward (1979) reported that healthy siblings of diabetic children failed to perform at the expected cognitive level in conceptualizing illness causality and treatment when compared with children without ill siblings matched on demographic variables and measures of Piagetian cognitive development.

In conclusion, conflicting data in the literature suggest that children's cognitive understanding of a neurological disorder is not likely to be entirely predictable simply on the basis of their age or measures of their level of

intellectual/cognitive development in nonillness content domains. Attempts should be made to integrate such information with their historical experience with the disorder.

Facts Are the Enemy of Truth—*Man of La Mancha*

Quite apart from the strictly cognitive aspects of comprehension, a child's construction of the personal "meaning" of neurological disorder, and thus reactions to it, is likely to involve processes that blend cognition and affect, and that incorporate both past and current experience. Perhaps a clinical anecdote can illustrate this point. A large and powerful adolescent boy with a vague history of seizures entered a children's psychiatric hospital with a diagnosis of paranoid schizophrenia. Precipitating the hospitalization were social isolation, paranoid ideation, verbal threatening, and dangerous behaviors such as jumping out of trees and leaping before slow-moving cars.

During the course of therapy, two primary themes emerged sequentially. First, he believed his seizures to be a pervasive and primitive loss of bodily and self-control, and that during these episodes he might unknowingly and unwillingly kill the small children for whom he frequently cared at home. Later a history of physical abuse by the father was revealed. After one incident during which the boy secretly wished his father dead, the father promptly *did* die of a cardiac arrest. The boy was simultaneously overwhelmed by a sense of omnipotence—he believed he had actually caused his father's death—and by his perception of an organically based lack of control necessary to prevent harming those he most loved in the future. He projected great menace onto his environment, and then attempted to prove that he himself could not be killed by engaging in (but surviving) potentially injurious behaviors. His behavioral symptoms, therefore, seemed indicative of dynamic issues influenced by the objective and subjective realities of seizures and past experience. At issue, then, are the interactions between the ways in which children and adolescents react to and understand neurological disorder, with the ultimate targets of interest being their construction of meaning and daily coping and adjustment.

Defense or Coping?

If it is assumed that the onset or diagnosis of neurological disorder represents a threat not only to cerebral integrity but also to the child's self or ego in a fundamental manner, then it can be assumed that attempts will be made to control, contain, or minimize that threat. Such actions often lead to distortion, illusion, or self-deception (inaccurate reality testing), and may thus be considered classical defense mechanisms; they may thus seem contrary to mental health. For a review of empirical studies of defense mechanisms in children, see Schibuk, Bond, and Bouffard (1989). Yet there can be a psychologically positive side to these actions as well, and a number of early papers anticipated current trends in social psychological research in this area. Goldstein (1952) distinguished between protective and defense mechanisms, suggesting that although both may be employed to protect one from fear and anxiety, the former may arise in a neurologically impaired individual from an inability to function in a shifting environment, whereas the latter may develop in response to psychodynamic conflict. Kroeber (1964) categorized and paired ego defense mechanisms (e.g., isolation, projection, repression) with parallel coping mechanisms (e.g., objectivity, empathy, suppression).

Both coping and defense mechanisms may be rooted in common attempts to deal with painful reality, though defenses would be cast in more negative terms reflecting poor adaptability, whereas coping mechanisms may represent active, flexible, and effective attempts to deal with conflict. For instance, if an early adolescent girl hospitalized for diagnostic tests is playing with dolls, she may be employing mechanisms of time reversal by recapturing experiences, feelings, and ideas of the past. The behavior is not necessarily indicative of the defense mechanism of regression (i.e., age-inappropriate behavior to avoid responsibility, aggression, or unpleasant demands), but rather of the analogous and healthy coping mechanism of playfulness (utilizing feelings and ideas from past experience that are not directly ordered by the immediate elements of the situation). Similarly, the 9-year-old girl with little manifest anxiety during a neuropsychological evaluation on the day prior to surgery for an enormous left frontal tumor was perhaps not refusing to face painful thoughts,

percepts, or feelings as in the pathological sense of denial (or exhibiting frontal lobe signs, as the evaluation itself indicated). Instead she may have been able to recognize and then set aside disturbing thoughts and feelings in order to concentrate on tasks at hand. For a discussion of repression as a defense against health-related stress, see Gill (2005). The point, then, is that some of the behaviors and thoughts of those facing extraordinary levels of disruption in their lives may not be as psychopathological as they might superficially appear. Our evaluation of their actions to contend with severe stress needs to consider the degree (focal or pervasive, flexible or rigid, transient or chronic) of distortion as well as the temporal relationship between crisis moments and defense quality.

The role of denial in the coping process has perhaps been most clearly explicated. As Lazarus (1983) suggested, the paradox of self-deception being both adaptationally sound and psychopathological may be resolved by asking the more sophisticated question: "What kinds of self-deceptions are damaging or constructive, and under what conditions?" Lazarus initially distinguishes between classical denial, e.g., the negation of some internal impulse, feeling, or thought, or of an external reality, and avoidance or plain ignorance of threatening events. He then describes a family of denials. Partial denial, or the temporary and tentative suspension of belief, often takes place among the seriously ill in the context of reassuring social relationships with concerned friends, family, or healthcare providers. Such a situation is quite common among healthy young children who easily suspend the reality of the moment, particularly when that reality is unpleasant. In addition, Lazarus recommends that psychologists shift their emphasis from considering denial and other coping mechanisms as static states of mind to recognizing them as ongoing processes that are often not fixed or consolidated defense mechanisms and that depend on both internal events and the social context.

Perhaps most relevant are some of the conclusions Lazarus reaches on the costs and benefits of denial. If direct action to change the relationship between person and environment is adaptationally necessary, denial and subsequent inactivity will be destructive. On the other hand, when direct action is irrelevant to the outcome, denial may reduce distress and afford the individual the possibility for good morale and hope. Note that this position to some extent contrasts with many of the cognitive or rational treatment approaches employed with clients who are neurologically impaired. An additional time-related principle is that denial may be beneficial early in disease or immediately after severe injury when individuals are actually unable to participate in their own care. Later on, during extended treatment, rehabilitation, or education, it may be more important to contend directly with the insult and to struggle in a problem-focused manner. As an aside, it should be clear that reference is being made here to secondary reactions to neurological events. The existence of neurologically based forms of inaccurate perception and reality testing is not denied, nor is their significance in case management diminished.

Perception of Competence

Forms of denial may be related to other cognitive and conative attempts to cope with neurological insult. Duchenne muscular dystrophy (DMD) is a neuromuscular disease beginning in early childhood and resulting in relentlessly progressive muscle wasting and weakness, and eventually in death by late adolescence or early adulthood. In part, an understanding of the psychological functioning of children with DMD may be derived from their performances on intellectual and neuropsychological measures (Dubowitz, 1977; Karagan, 1979; Knights, Hinton, & Drader, 1973); however, the literature in this area remains conflicting (Mearig, 1979; Sollee, Latham, Kindlon, & Bresnan, 1985; Whelan, 1987). While we are continuing to research the intricacies of brain–behavior relationships in this population, we are also exploring other aspects of their psychosocial functioning. In this context, one motivational variable, perceived control of events, appears to affect a wide variety of psychological conditions. Indeed, perceptions of personal control, especially inaccurate perceptions, have been seen as central components of problems ranging from depression to paranoia to underachievement (Weisz & Stipek, 1982).

Although the conceptualization and measurement of the control dimension have been approached from the perspectives of social learning and attribution theories, the theory

and concepts of intrinsic motivation are also important. Competence motivation theory assumes that humans naturally strive for effective interactions with their environments. Successful mastery of a problem produces pleasurable feelings of efficacy of competence, which, in turn, reinforce and lead the individual to seek out and attempt to master additional tasks (Stipek & Weisz, 1981). Harter (1978) claims that in order for children to experience a feeling of efficacy, they must perceive themselves as responsible for their successful performance. Moreover, she reasons, failures perceived to be caused by a lack of competence or self-worth can lead to anxiety in mastery situations and thus decrease the child's mastery motivation. Children's expectancies and perceptions of efficacy may consequently be particularly important to consider because they may determine whether coping behavior will be initiated, how much effort will be expended, and how long it will be maintained in the face of obstacles and aversive experiences (Bandura, 1977).

Certainly, children with DMD experience a particularly acute and reality-based loss of motor control. Their perceptions of motoric, academic, and social competence, and general self-worth have been subjected to empirical investigation (Whelan, 1986). The Perceived Competence Scale for Children (Harter, 1979), which measures perceptions in the four mentioned domains, was administered to 31 boys with DMD. With regard to the central tendencies of the data, mean scores on the scales of cognitive and social competence and on the scale of general self-esteem were approximately at the normative mean. Scores on the scale of physical competence (referring primarily to athletic skills) were about one standard deviation below the mean for normal children (Whelan, 1986).

On the surface, these results might suggest that children with DMD maintain relatively accurate perceptions of their own areas of competence and disability, or that the existence of a neuromuscular disorder resulting in motor dysfunction and a reduced sense of efficacy in that domain have not substantially generalized to other measured domains. However, scores on the scale of perceived physical competence were not significantly correlated with any of the neuropsychological measures used in this study including measures of motor performance. This suggests that perceptions of physical competence or, conversely, of physical disability may vary widely in this population, with little relation to the objective reality of assessed motor performance. That is, some of the mildly physically impaired children may perceive themselves as severely limited, and others with greater actual motor disability may not perceive themselves as so seriously impaired.

Other data in this study may contribute to an understanding of the ways in which dystrophic children make sense of their condition. The magnitude of the correlations between scores on the scale of perceived physical competence and those on the scale of general self-worth (0.65) and social competence (0.39) was considerably higher than in the normative population. Together, these data may suggest reasons for the lack of a significant relationship between perceived physical competence and actual motor ability: Denial of physical disability in the service of preserving a sense of self-worth may be a prominent coping mechanism in children with neuromuscular disease.

An examination of perceptions of competence in other groups of children with suspected neurological disorder has also proved interesting. For instance, the factor pattern of the Harter scales for a sample of children with learning disability showed that the physical and social competence factors were retained as in the normal population, although cognitive and self-worth factors did not emerge as discrete entities. Instead, two cognitive—self-worth factors were obtained, the first composed of trait-like descriptions (e.g., being smart, liking yourself as a person) and the second composed of concrete and behavioral items (e.g., feeling it is easy to understand what one reads, thinking the way one does things is fine). Thus, the learning-disabled child's sense of self-worth seems directly tied to scholastic competence (Harter, 1985). Harter recommends that we treat self-concept as neither epiphenomenal nor as a static construct and concludes that "we cannot simply treat all children with intellectual deficits as a homogeneous group since clearly there are quite different processes influencing the structure and content of their self-perceptions" (p. 16). With necessary modifications, the measurement of domain-specific perceptions of competence and global self-worth in the neurologically impaired population of children may yield important data in

the future. For instance, we are interested in determining if the factor structure described by Harter for children with learning disability is truly representative for all those bearing that label. Certainly many investigators have recognized that such children may frequently have difficulty recognizing and interpreting social cues (Maheady & Maitland, 1982). Based on the subtyping literature (e.g., Rourke, 1985), it seems quite possible that some children with learning disability maintain accurate perceptions of their competencies and areas of disability, whereas others do not. Interventions with children who are accurately perceiving their abilities may consequently differ from those with children who are not. Moreover, the assessment of self-evaluative processes may be critically important to consider in the neurologically impaired population of children: If these processes are more amenable to change than structurally based abilities per se, then school and other performances might be indirectly enhanced through alternative interventions. Moreover, Luthar and Zigler (1991) have made a conceptual link between issues of vulnerability and competence, and extend these issues into the domain of resilience.

Attributions

If by definition the word *victim* applies to "anyone who suffers as the result of ruthless design or incidentally or accidentally," then the term may be broadly invoked in the context of various life crises, whether accidents, crimes, or diseases (Janoff-Bulman & Frieze, 1983). Because children with neurological impairment surely suffer physical and/or psychological alteration, they may justifiably be considered victims in this sense. Even the terms commonly associated with neurological disease or injury reflect this theme: cerebral *trauma* with *loss* of consciousness, brain *insult,* and vascular *accident*. Considerable research on the personal and social consequences of victimization has been conducted by social psychologists, and although there are few available reports concerning those with neurological disorder, the findings are generically relevant.

One relatively well-developed domain of research on coping with victimization concerns attributions of causality of undesirable events. In part, the impetus for these investigations

came from refinements of learned helplessness theory that were heavily based on attribution theory (Wortman, 1983). As part of the learned helplessness reformulation (Abramson, Seligman, & Teasdale, 1978), critical questions on the nature of coping with adverse circumstances shifted from the undesirable events themselves to individuals' interpretations of the events. For example, the type, intensity, and duration of a victim's coping responses in serious accidents may depend less on the precise physiological deficits and more on cognitions regarding the cause of the accident. One of the most relevant studies of this kind examined the relation between the attributions of causality made by adult accident victims with paralysis resulting from severe spinal cord injury and their subsequent coping patterns (Janoff-Bulman & Wortman, 1977). The findings suggested that those who tended to blame themselves for the accident were rated by medical and rehabilitation staff as coping better than those who blamed others and who felt the accident could have been avoided. Indeed, many respondents (e.g., passengers in cars, people accidentally shot) seemed to attribute more blame to themselves than might seem objectively reasonable. The authors interpreted the findings as reflecting attempts on the part of the victims to gain some control over their situations, for blaming oneself may be preferable to the conclusion that random harmful events may occur in a meaningless, chaotic world.

The results of the attribution literature concerning victims may be important in the field of clinical child neuropsychology because these and other forms of cognitive distortions may partially determine the quality of coping attempts. Moreover, "real world" findings may be counterintuitive at first glance; many psychologists might not consider, from an outsider's position, self-blame to be particularly adaptive or predictive of good progress in a rehabilitation program. The clinical utility of these forms of cognitions remains to be fully investigated, especially with children and especially over the long term.

Attribution theory has also been applied to other areas of child psychology: childhood depression and learning disabilities. According to the re-formulated learned helplessness model (Abramson et al., 1978), depressed individuals make more internal, stable, and global attributions for failure and more external, unstable, and

specific attributions for success than nonde-pressed individuals. Recent research has indi-cated that, like adults, depressed children have a more depressed attributional style than non-depressed children (Blumberg & Izard, 1985; Kaslow, Rehm, & Siegel, 1984), and that attri-butional style can be used to predict depressive symptoms 6 months later (Seligman et al., 1984).

A vignette may be illustrative here. A young man with a history of severe learning and atten-tional disorders was asked to make a videotape of his thoughts as he negotiated the transitions from childhood to adulthood, and he was remi-niscing about past depressive experiences: "When I made pottery or anything else like that, everybody else thought it was fine. But I was my own worst enemy, thinking this is good for other people but it's not good for me. So I would go home and give it to my mother and she would say, 'Oh, thank-you!' A couple of hours after that I'd get upset because it's not good enough, and 'd break it. ... and I said 'I'm sorry mom, it's not good enough ... *I'm* not good enough'."

With regard to learning difficulties, the attribution and learned helplessness literatures are also applicable (Thomas, 1979). It has been reported that children who attribute outcome to ability do not work as long or as hard as those who attribute outcome to effort (Dweck, 1975), and those who attribute failure to ability tend to be less persistent on learning tasks (Hiroto & Seligman, 1975). Diener and Dweck (1978) indi-cated that helpless children attribute failure to lack of ability, and nonhelpless children focused instead on self-monitoring and self-instructions. Compared with average and good readers, poor readers have been found to take less personal responsibility for success, and when they did make internal attributions for success, they were more likely to make effort rather than abil-ity attributions (Butkowsky & Willows, 1980). The potential importance of research in this area is that interventions designed to alter attribu-tional patterns (e.g., to shift attributions for fail-ure from insufficient ability to insufficient effort) may result in improved academic performance (e.g., increased academic task persistence and achievement) (Dweck, 1975; Fowler & Peterson, 1981; Schunk, 1983).

Taken together, these lines of theory and results suggest a convergence of information. Attribution patterns affect coping in affective and cognitive domains, and they seem important in adjusting to both acute insults or accidents and long-standing developmental difficulties. Equally importantly, it is possible to modify children's attribution styles through relatively brief interventions. Future research regarding the development and alteration of attributions among children with neurological disorder may consequently prove worthwhile. It may be important, for instance, not only to investigate children's cognitive understanding of the facts of the disorder, but also to explore their percep-tions of who or what is responsible for the situa-tion, why it happened to them, and to what they attribute their present successes and failures.

Issues in Psychotherapy

During the past decade, the neuropsycholo-gical literature on professional training models (e.g., Meier, 1981) and intervention procedures (e.g., Edelstein & Couture, 1984; Miller, 1984; Trexler, 1982) generally reflected the position that intervention with individuals with neurologic disorder is most commonly cognitive- behavioral in nature. Given the forms of neurological signs and symptoms, such procedures are often war-ranted, efficient, and effective. In addition, how-ever, some of the challenges to children's mental health described in this chapter might also be addressed within the context of a psychothera-peutic relationship. Moreover, there may be acute (hospitalization for diagnosis or surgery) and chronic (controlled epilepsy, minor head injury, learning disorder, neuromuscular dis-ease) situations in which there are no major behavioral difficulties but in which clients may benefit from, and psychologists may desire, a somewhat different style of intervention. Taube and Calman (1992) have provided a model for the psychotherapy of patients with complex par-tial seizures that might be useful to consider in this vein.

A number of general considerations to be kept in mind by the therapist have been provided by Christ (1978), Geist (1979), and Small (1973). Therapeutic goals may include the provision of nonconfrontal understanding, support, and feedback during periods of confusion, anger, anxiety, and depression. Strengthening of reality testing, learning to select areas of success and to avoid those of failure, and the improvement of relationships with others may also be

appropriate targets. Traditional psychotherapeutic emphases and processes may require modification, however. For example, the development of a therapeutic alliance may purposely be extended, allowing greater opportunities for clients to recognize and display their strengths. Primitive and fragile defenses may crumble with mild cognitive or affective stress, leading to catastrophic reactions that seem disproportionate to an outsider's appraisal of the stressor. It may thus be important to concentrate on building a defensive superstructure, using defenses that are more negotiable than frank denial or projection, such as displacement, rationalization, or intellectualization. The psychologist's concepts of client resistance must be modified in the face of slowly improving or impaired cognitive and integrative capacities, and the inability to recall may obviously reflect faulty memory and not repression of conflict. Finally, it should be remembered that those with neurological disorder do not work through a permanent disability as with a neurotic problem, nor do they "get over it" as with some normal developmental hurdles; instead, they must continually adjust to the dynamic nature of the disability itself and to its consequences at various levels in the systems hierarchy. For example, realistic limitations in adaptive abilities may prevent the adolescent from taking steps of autonomous action at the same age as most others. Indeed, true termination from therapy may not be desirable, and the option to return at developmentally stressful times may be a sensible alternative.

There is another therapeutic issue that deserves comment in order to provoke additional thought or research. A variety of sources suggest that it is important to instill a sense of realistic hope in clients with neurologic impairment. Travis (1976) recommended that those caring for children and adolescents with progressive muscular dystrophy establish a "context for security and an avenue for hope." Waddell (1983) discussed the hope that medical and familial people consign to children with life-threatening illnesses, and others considered the role of hope in the process of rehabilitation (Boone, Roessler, & Cooper, 1978; Heinemann, Geist, & Magiera, 1983) and psychotherapy (Erickson, Post, & Paige, 1975; Frank, 1968; Green, 1977; Smith, 1983).

Although *hope* is a term used frequently in everyday conversation, and although casual introspection suggests it is a pervasive human construct, there is very little related psychological research. Classical literature provides some insight into the concept. Hope was one of the evils contained within Pandora's box, and indeed, the Greeks viewed hope as an illusion and as mankind's curse because fate was seen as unchangeable. Such sentiment is reflected in lines from Antigone: "We are of the tribe that asks questions, and asks them to the bitter end . . . we are of the tribe that hates your filthy hope, your docile, female hope; hope your whore." On the other hand, the Judeo-Christian message is essentially one of hope, and in various cultures the symbol now written in most medical charts for "female" has meant eros, fertility, and hope (Menninger, 1963).

Perhaps because of the religious nature of historic tradition and because hope is a difficult construct to operationalize, psychologists may have left the study of hope to theologians and philosophers, and concentrated instead on hopelessness. Still, hope may rightly be classified as a coping phenomenon incorporating a future orientation, optimistic affect, expectant cognition, response to external stress, and resultant motivation (Petiet, 1983). Although multidimensional, and although the cognitive and developmental prerequisites of hope remain to be specified for children, the idea that hope is a desirable state during medical recovery and rehabilitation has been investigated with adults (Boone et al., 1978; Brackney & Westman, 1992; Brody, 1981; Dubree & Voge'phol, 1980; Heinemann et al., 1983; Lillis & Prophit, 1991; Perley, Winget, & Placci, 1971; Rabkin, Williams, Neugebauer, Remien, & Goetz, 1990; Ruvelson, 1990), and could be explored with chronically ill children. And in something of a full circle, Gottschalk, Fronczek, and Buchsbaum (1993) have considered the neurobiology of hope and hopelessness.

Psychosocial Adjustment

Much ambiguity surrounds the issue of whether chronically ill children, including those with neuropsychological deficits, are maladjusted when compared with their "normal" peers; see Harper (1991) for historical research conceptualizations in childhood illness, disability, and rehabilitation. Findings are contradictory, and diverse methodologies make

comparisons between studies difficult. It is generally accepted that children with chronic illnesses are at one and one-half to three times greater risk for behavioral, social, and psychological maladjustment than healthy peers (Perrin, 1986; Pless, 1984). Rutter, Graham, and Yule (1970) reported that the occurrence of psychiatric disorders among the general population of children and adolescents was 6.6%; for children with nonneurological chronic disease, 11.6%; those with epilepsy and no other pathology, 37.5%; and children and adolescents with epilepsy associated with organic brain disease, 58.3%.

Professionals and individuals involved with children with neurologic impairment should not be misled, however, by the temptation of such figures. For any particular child, the presence of neurological disorder does not necessarily imply lowered psychosocial adjustment. Individual reactions to disability are diverse, and specific disabilities have not been found to be related to specific personality types (Bronheim & Jacobstein, 1984; O'Dougherty, 1983; Pless & Nolan, 1991; Roessler & Bolton, 1978). Also, as Garrison and McQuiston (1989) pointed out, there are reasons to consider both individual-specific (Cadman, Boyle, Szatmari, & Offord, 1987) and disease-specific (Stein & Jessop, 1982) approaches to understanding the ways in which children adjust to their illnesses. For information regarding a measure of social functioning in children with chronic medical conditions, see Adams, Streisand, Zawacki, & Joseph (2002).

Psychiatric Symptomatology

The range of psychiatric symptoms displayed by children with neuropsychological disorders is similar to the behaviors of their nonhandicapped peers. Results from large-scale epidemiological studies of children with chronic illnesses suggest that these children experience lower academic achievement, greater absenteeism and truancy, and increased behavioral difficulties, nervousness, and aggression (Pless & Roghmann, 1971; Rutter, Tizard, & Whitmore, 1970). In addition, emotional dependence, poor social adjustment, low self-esteem, depression, anxiety, difficulties in sexual adjustment, embarrassment, regression, poor body image, excessive shyness, lifelong feelings of failure and inadequacy, immaturity, exaggerated self-consciousness, shame, and fearfulness have all been used to describe the various experiences of children with spina bifida, epilepsy, muscular dystrophy, cerebral palsy, cancer, and closed head injury.

A word of caution is necessary. Although it is true that discrete symptoms or symptom clusters may be manifest by individual children, it should not be construed that this laundry list of psychiatric symptoms uniformly affects ill children with neurological handicaps. All children, including those at high risk for developing psychiatric sequelae, will be individually influenced both by neurophysiological constraints of the disease and by events external to the presence of disease, such as premorbid coping style, family support, and social reaction to disease presentation. For example, social adjustment may be affected when children with spina bifida who are incontinent of bladder and bowel are avoided or teased by their peers because of their "outhouse syndrome" of smells (Bronheim & Jacobstein, 1984; Shurtleff, 1980). Similarly, the social stigma of epilepsy can increase embarrassment, feelings of shame, and a vigilant need for secrecy for some epileptic children (O'Dougherty, 1983). Depression, which is experienced by some children in all disease categories, may be exacerbated in muscular dystrophy around the time the child becomes wheelchair bound and the relentless nature of the disease becomes less deniable (Lindemann & Stranger, 1981; Pierpont, LeRoy, & Baldfinger, 1984). Expression of psychopathology, then, should be considered in context. Finally, the presence of behavioral symptoms that might be considered pathological in the healthy population may be appropriate or even adaptive in those with chronic illness (Drotar & Bush, 1985; Van Dongen-Melman & Sanders- Woudstra, 1986), and resiliency may be more impressive than psychopathology (Bachanas et al., 2001; Noll, Vannatta, Koontz, & Kalinyak, 1996; Stabler, 1988). Boekaerts & Roder (1999) provided a review of the literature concerning stress, coping, and adjustment in children with chronic diseases, and see Miller & LaGreca (2005) for a review of adjustment to chronic illness in girls. Gender effects on coping among children with chronic illness were also studied by Hampel, Rudolph, Stachow, Lab-Lentzsch, and Petermann (2005).

Self-Concept and Self-Esteem

As empirical studies on the effects of patho-neurological involvement on children's self-concept and self-esteem are sparse, the literature on chronically ill children suggests an equivocal response to this issue. Many studies offer findings of lowered self-esteem and poorer self-concepts (e.g., Lineberger, Hernandez, & Brantley, 1984; Tropauer, Franz, & Dilgard, 1970). In contrast, other researchers (e.g., Kellerman, Zeltzer, Ellenberg, Dash, & Rigler, 1980; Simmons et al., 1985; Tavormina, Kastner, Slater, & Watt, 1976) report no significant differences between various groups of chronically ill children and healthy peers. Anecdotal reports often emphatically suggest that impaired self-concept and self-esteem are intrinsic to the experience of chronic illness (Geist, 1979). Christ (1978), for example, suggested that children with neurologic impairment in psychotherapy view themselves as different, weird, or defective, at least from the time peer comparisons are first made in grade school or preschool. In general, greater agreement exists that children with neurological involvement or deficits are at increased risk for poorer self-concept and lowered self-esteem than their healthy peers (Lindemann & Stranger, 1981; Rutter, Graham, & Yule, 1970).

Although it is not yet clear precisely why these children may be at increased risk for poorer adjustment, perhaps an understanding can be found in the nature of the relationship of neurological deficit to the development of self-identity. The key question here may be, how does altered brain integrity affect the development of self-concept and self-esteem? For example, administration of a standard measure of perceived competence to a group of educable children with mental retardation suggested that these children did not make the same categorical distinctions of self-competence and general self-worth as children in the standardization samples evidenced (Harter, 1982).

At one extreme such a question implies that because of physiological limitations, some children do not develop self-concepts in the same manner that their normal peers do, reflecting perhaps a physiologically based lack of or unique processing of information. This notion is suggested by parents and teachers who are unsure of how much to expect from their handicapped child and wonder whether the child's behaviors reflect biological limitations. Yet, although brain integrity may indeed affect formation of self-concept, the lack of findings correlating one specific emotional or social pattern of behavior with a specific disease or deficit suggests that the relationship between brain functioning and self-concept is complex, mediated by environmental and biological variables, and cannot be subjected to unqualified reductionism.

Socialization

Although undoubtedly some people are arrantly satisfied living in relative isolation from family, friends, and community, most of us recognize the immeasurable importance of our relations with other people. Indeed, it is notable that children who are withdrawn or elect not to participate with their peers are considered by many to be maladjusted.

The relative importance of peer interactions increases with age and growing autonomy. For both normal children and those with neurologic impairment, the peer group has been described as instrumental in providing confirmation or disconfirmation of children's growing sense of competence and self-esteem, meeting dependency needs, a reference point for growing beliefs about sexuality, and a means of role rehearsal where dimensions of cooperative, competitive, and aggressive behaviors can be expressed (Battle, 1984). Additionally, peer groups are seen as a major source of communication and support, conversation and companionship, and fun and socializing for most adolescents (Resnick, 1984).

The importance of peer groups may even be greater for children with a handicap. For example, adolescent cancer patients have reported that spending time with their friends is of primary importance in their ability to cope (Zeltzer, LeBaron, & Zeltzer, 1984). Based on a study of survivors of childhood cancer, O'Malley, Koocher, Foster, and Slavin (1979) reported that a decrease in the number of social relationships during diagnosis and treatment had a negative impact on subjects' future adjustment. Minde, Hackett, Killou, and Silver (1972) reported that almost 50% of children with cerebral palsy who did not have a nonhandicapped friend were labeled psychiatrically deviant whereas less than 10% of those with nonhandicapped friends were so labeled. This finding is even more

striking when one considers evidence suggesting that nonhandicapped children, especially boys, who initiate contact with a handicapped child generally have less social experience, are more isolated, and adhere less to peer values (Battle, 1984).

Although diminished interactions with one's peer group can deprive children of valuable pleasure and experience in their preparation for adulthood, for some children with neurological disorders, gaining access to and acceptance by their peer group can be a formidable task. Hospitalization and requisite medical treatments for some diseases take time away from school attendance and peer activities (Zeltzer et al., 1984). At other times, peers' superstitions and misunderstanding about the nature of the disease can result in cruel teasing and unwarranted ostracism, especially when unfounded fears of contagion are involved (Isaacs & McElroy, 1980). Children who experience a loss of mobility may also face social isolation as their opportunities to participate in the normal activities of childhood and adolescence are restricted.

In contrast to the external influences that may limit a handicapped child's full participation in peer group activities, for some children, social isolation and withdrawal are means of coping with their disease. Children who are frightened and embarrassed by a loss of control during a seizure, for example, may consciously or unconsciously remove themselves from the influences of peers in attempts to reduce feelings of being different, unattractive, or socially rejected (Ozuna, 1979). Others have noted that wheel-chair-bound children and children with progressive muscular weakness can become isolated and withdrawn, relying heavily on fantasy and imagination (Lindemann & Boyd, 1981; O'Dougherty, 1983). Meijer, Sinnema, Bijstra, Mellenbergh, and Wolters (2000) reported that both physical restrictions and pain were associated with restricted social activities but not with other measures of social peer interaction.

Although children with obvious physical limitations can face rejection from peers because of their visible differences, visible handicaps may also at times be addressed and accepted more openly than deficits with few noticeable manifestations. Indeed, children whose disabilities are less obvious or are better controlled may suffer as much or more than their severely disabled counterparts (Hertzig, 1983; Pless, 1984). They may be teased for being slow, clumsy, or different, and often face the dilemma of trying to pass as normal peers, meeting the expectations of behavior and ability that such normalcy involves, or choosing to separate from the peer group, enduring consequent ridicule and isolation (O'Dougherty, 1983).

Independence and Autonomy

Emotional separateness and independence is recognized as a significant goal of childhood and adolescence, and a hallmark of adult adjustment. Although being special may be a plausible role for some people with a handicap, U.S. society expects individuals with a disability to strive maximally toward independence and autonomy (Parsons, 1964). The influences of neurological disorder, however, can run counter to goals of individuation, as illustrated in this case description quoted by Resnick (1984):

> While his age cohorts were arguing with parents over the length of their hair, he needed help washing his; while they were resisting doing assigned chores, he was unable to perform any; while they were battling curfew, he needed not only permission, but physical assistance in order to be out. Instead of sharing his peers' increased independence from parents and others, symbolized by mild acting out behaviors, this patient could merely fantasize his acting out, with his illness providing a constant reminder of his chronic dependent status. (p. 302)

Though not all children with neurological handicaps exhibit the same degree of physical limitation, they all share in an increased dependence on parents, medical staff, and sometimes siblings for physical, financial, and emotional support (Zeltzer et al., 1984). Although disorders that demand large amounts of time and care from parents and family might appear to encourage emotional dependence compared with other diseases, the critical issue remains how to foster developmentally appropriate independence and responsibility within the context of a child's neurological deficit. For "normal" children, autonomy invariably increases with age, and parental control usually decreases proportionally. Although the progression toward adulthood may not always be as smooth as many parents and children would prefer, in most cases autonomy and responsible adult

action are considered birthrights. For children with neurological disorders, however, both the pathway to autonomy and the children's right to eventually assume traditionally adult responsibilities may be questionable (Kopelman, 1985). Physical and mental abilities that have been compromised by presence of disease may in some cases realistically limit a child's ability to assume such adult activities as driving a car or making important decisions regarding medical treatment. With adults, an assumption is made that everyone over a recognized legal age is competent to make decisions for themselves, unless proven otherwise, and implicit in this supposition is the attainment of a certain, unquantified level of maturity. For children with neurological disorders, the issue of emotional maturity becomes inextricably linked with physical disability.

The physical and other limitations that some neurological disorders impose incite some parents to become overly protective of their handicapped child. Such overprotection can be detrimental to the child's quest for autonomy and can too easily create an atmosphere that encourages children to remain overly dependent, both emotionally and physically, on others. At one extreme, children may become complacent, passively accepting the ministries of others. In contrast, overly demanding, noncompliant, acting-out, or intentionally guilt-provoking behaviors may represent attempts to separate from parental domination and establish self-responsibility, while also satisfying certain emotional needs (O'Dougherty, 1983). This secondary gain that many children experience from their dependent roles can be reinforced when parents are reluctant to expect or demand independence from their handicapped child (Resnick, 1984).

Noncompliance with medical procedures can become a difficult issue when children and adolescents are unable to assert their autonomy in appropriate ways. Similarly, changing needs during illness can also complicate the process of separation and autonomy. For example, Zeltzer et al. (1984) reported that immediately following diagnosis and during times of disease relapse, adolescents with cancer prefer a more passive, dependent role, being less involved with the management of their disease than parents and physicians wish them to be.

Impact on the Family

Nowhere is systems theory perhaps more useful than in investigating the family. As a unit the family is affected by the presence of chronic illness, whether the illness is of neurological origin or not (for a family systems and social-ecological model of adaptation and change in families of children with chronic illnesses, see Kazak, 1989). One is reminded of John Steinbeck's *The Pearl,* the story of a poor fisherman who found a pearl so inordinate in its beauty and consequences that the lives of the entire village were altered. The birth or diagnosis of a child with neurological disorder is not unlike Steinbeck's description that time had changed and everything hence would be either before the pearl or after the pearl. Although it is perhaps ubiquitous that a neurological disorder will alter the lives of the family and individuals close to the handicapped child, it is also the case that not all families are similarly affected. Some families report being strengthened by the continuing challenge; other families cannot withstand the stress and become dysfunctional or disintegrate, and Wallander et al. (1989) have discussed multidimensional disability parameters affecting the adaptation of physically handicapped children and their mothers. Presently, no direct cause-and-effect occurrences have been identified that would fully explicate or predict the interaction of chronic illness and family dynamics; rather, the influences are mosaic.

Stages of Family Growth

Various theorists have proposed different stages of family growth and development, including marriage, childbirth, early child rearing, child schooling and increasing independence, departure of children from home, and integration of loss as parents adjust to problems associated with being alone and growing older. This model is influenced both by family subsystems and by groups external to the nuclear family, such as extended family, friends, and community. Stage theories depicting special times of stress may inadequately portray the family of a child with a neurological disorder who must deal with burdens unlike those of their average counterparts, and additional crisis points have been suggested for families of

chronically ill children: when parents first become aware of the child's handicap; when the child first becomes eligible for special educational services; when the child leaves school; and when parents are aging and can no longer assume responsibility for the care of their child (Bailey & Simeonsson, 1984).

Stage models of family development are useful in that they provide a framework with which to understand family dynamics; however, variability of family structures resulting from single parenthood, and ethnic, social, and financial differences makes generalizations about the consequences of chronic childhood illness, including neurological disorders, on family life a dangerous task at best. For example, it has been suggested that the birth of a child with a handicap is more devastating for lower socioeconomic status families than for middle and upper class families; yet, little data are currently available on class-related coping characteristics of parents (Schilling, Schinke, & Kirkham, 1985). Similarly, anecdotal reports suggest the importance that a family's ethnic background can have on family coping and adjustment, and on medical compliance (Hobbs, Perrin, & Ireys, 1985). Although systematic investigation of socioeconomic—ethnic variables is sparse, such influences cannot be extricated from the daily lives of children with neurological impairment and must not be forgotten in our quest for greater understanding.

Stages of Parental Adjustment

The diagnosis of a chronic illness or neurological disorder marks the beginning of a stressful and confusing time for parents. Even when there has been some suspicion of illness, diagnosis represents an immediate confirmation of parents' fears and a removal of hope. Although each parent may not feel each of these emotions, fear, shock, horror, numbness or detachment, relief, helplessness, denial, sadness, anger or rage, anxiety, depression, and guilt are all likely to be experienced at various times (Drotar, Baskiewicz, Irvin, Kennell, & Klaus, 1975; Hobbs et al., 1985; McCollum, 1981). Regarding relationships between parental distress and children's adjustment, see Thompson, Gustafson, Hamlett, and Spock (1992), Thompson, Gustafson, George, and Spock (1994), Thompson, Gill, Burbach, Keith, and Kinney (1993) and Thompson et al. (1994).

During the initial period of diagnosis, many parents experience shock and bewilderment and sometimes feel the situation is unreal, that it must either be a dream or happening to someone else. They may discuss their child as if he or she were a textbook case rather than their own child (McCollum, 1981). Parents will often have many questions, such as: "How will my child's life be affected?" "Is there a cure?" "Will my child's life be shortened?" "What does the disease do?" "Could I have done something to avoid this?" Paradoxically, in their emotional turmoil many parents are unable to remember what professionals say and, although forgetting may be an understandable defense against emotional pain, its consequences can be exacerbated when parents view it as a sign of their own inadequacy. Embarrassed, they may turn to friends or books for information rather than repeatedly question professionals. Of course there is a healthy side to seeking information from others who have negotiated the same trials, and the blossoming "chat rooms" or "discussion groups" found on computer networks are testimony. At the least there have been ongoing supportive sessions for those with epilepsy, neuromuscular disease, pervasive developmental disorders, and trauma and psychiatric symptoms, and affected individuals may share their clinical situations and affective reactions for the very first time in the privacy of their homes. However, some sources of information, although well intentioned, may be highly inaccurate, and misconceptions about their child's disease can linger for years, at times to the detriment of effective treatment (Whitten, Waugh, & Moore, 1974). During this initial period parents may also refuse to believe the diagnosis and a period of "shopping around" for second medical opinions may ensue.

Sadness, anxiety, and grief, from its raging anger and tears to its heavy numbness and pain, frequently occur next as parents begin to fully experience the unjustness of the situation (Blacher, 1984). Parents grieve for the feared loss of their child through death, for the loss of their "normal" child, and for hopes and aspirations for their child that have been relinquished (Mattsson, 1972). The intensity of emotions experienced and the isolating effects of grief can cause some parents to wonder if their reactions are normal. Customary sources of comfort

and solace, such as one's spouse, may be unavailable because they too are grieving. Anger can become a prominent emotion and parents may vent their anger at each other, at other healthy children, at hospitals, physicians, and psychologists, at their church or their God, and at times, their ill child (McCollum, 1981). Worry and anxiety may also increase as both the demands of care and the family's limitations become more evident. The stress and anxiety of this time may be associated with physical illness or symptoms in the parents and can cause parents to fear they too are sick. Inevitably, their child's illness confronts parents with their own mortality and eventual death (Isaacs & McElroy, 1980).

Progression to final stages in this coping model suggests parental acceptance of the child's handicap, an ability to emphasize positive aspects of the situation, and attenuation of the intensity of earlier feelings (Hobbs et al., 1985). The ability to master guilt, fear, and self-accusatory feelings of responsibility has been suggested as critical in determining parents' acceptance of their child's illness or handicap (Mattsson, 1972). Additionally, Mattsson suggested that the awareness of and ability to verbalize feelings indicates that parents are ready to accept the reality of the illness. Parental coping and acceptance are further facilitated through their use of various defense mechanisms, including rationalization; displacement and projection of feelings onto others such as medical professionals; intellectualization, including educating themselves about medical, physiological, and psychological aspects of the disease; identification with other parents of seriously ill children; and denial and isolation of helplessness and anxious feelings, especially during medical crises. The use of any of these defense mechanisms may at times be exasperating to people who are in contact with the ill child's parents, as is most obviously the case with angry and obstreperous parents. It is important to realize, however, that such "defense" mechanisms may be quite appropriate at different times in the course of the illness. Furthermore, there is some evidence that families with children with some chronic illnesses may function relatively normally, and that the family environment may buffer stress caused by illness (Soliday, Kool, & Lande, 2000).

Although useful as a structure for understanding family adjustment, the utility of stage theories is limited in specific applications. The attendant feelings of a parent toward a chronically ill child may ebb and flow chaotically, and even without apparent crisis or problem they may experience many feelings simultaneously. Parents' grief and the need for coping may reoccur as their ill child reaches chronological and developmental milestones (Schilling et al., 1985). Some parents report that although they may have learned to live with their child's illness, they do not feel they will ever accept it (Hobbs et al., 1985).

The consequences of unresolved guilt, or the inability of parents to adequately accept and cope with their child's chronic illness, can negatively affect their relationship with their ill child and other relations within the family. At one extreme, parents may reject or severely neglect their disabled child by denying the presence of illness or the need for treatment, or by blaming abandoned careers, financial ruin, and much inconvenience on their ill child (Hobbs et al., 1985). More frequently, prolonged parental overconcern leads to indulgence and overprotection. Family members become more loving toward the ill child, and normal rules and discipline are suspended. Although allowances need to be made according to the realistic limitations imposed by the disease or illness, changes in family attitude can be confusing and sick children are likely to gain a sense of their own vulnerability through the fears and reactions of their parents and siblings (Mattsson, 1972). Mattsson described four situations that may predispose parents to overprotection or rejection: the child is afflicted with a hereditary disorder found among relatives; the child was unwanted; the child was not expected to live at birth or as an infant; and emotional conflicts around the death of a close relative are aroused by the child's illness.

Parental Differences in Coping Style

There are some adaptive tasks that may be common for nearly all families with a child with a chronic illness, but allocation may vary. The coping styles of parents may differ according to gender. Findings suggest that women tend to employ interpersonal and cognitive coping strategies and men more frequently use cognitive coping patterns. Using their own health inventory, McCubbin, McCubbin, et al. (1983) factor analyzed the scaled responses of 100 families of

children with cystic fibrosis. Mothers' coping efforts were directed at the interpersonal dimensions of family cohesiveness, support, and expressiveness; fathers placed more emphasis on maintaining the family through cooperation and minimizing conflicts in family interaction through the use of rigid rules and procedures. Similar coping profiles were reported by McCubbin, Nevin, et al. (1983) in a study of parents of children with cerebral palsy. Such findings are consistent with available research on developmentally disabled children that suggests that parents of handicapped children tend to be more traditional in terms of sex roles than other families.

Within traditional families the father's role is most frequently as provider first and parent second, and for mothers the reverse is true (O'Donnell, 1982). In a Colorado statewide survey by Linder and Chitwood (1984), fathers of handicapped infants and preschoolers reported that their time with their handicapped child was limited by job and other family demands, even though they desired to become more involved with their child. Mothers were found to be the primary source of information about their child for fathers, though fathers indicated that newsletters or training in working with their child would be helpful. Additionally, survey replies indicated that fathers were least interested in "someone to talk to about my child" as a means of information or source of comfort and solace. Such responses are consistent with findings in other studies, and may be partially comprehensible when one considers that husbands tend to rely on their wives for intimate support, whereas wives report turning to other women and friends for support. Women in general report more dissatisfaction with family life, less freedom and opportunity to develop self-interests, worse health, and less positive moods. This is perhaps not surprising as wives and mothers are called on to balance the needs of their handicapped or ill child, unaffected children, and spouse, with their own needs.

Dyadic Relationships

It has already been suggested that the diagnosis of chronic illness or handicap in a young child may contribute to maternal overprotection (Mattsson, 1972). Such overprotection may result in the formation of an intense dyadic relationship, usually between mother and affected child, that isolates the dyad from other family interactions (Shapiro, 1983). This relationship then becomes an axis around which other family relations develop, especially other children's resentment of the special closeness between mother and handicapped child. Paradoxically the handicapped child may also develop feelings of being outside the family, participating primarily as an observer who is never fully accepted by other siblings or is fully a part of family life. Although such an intense relationship may represent a mother's conscious or unconscious efforts to atone for the guilt she may feel, its effects on the family can be severe. Psychodynamic theory clearly posits the insult to emergent self-identity and resultant psychopathology in response to prolonged and stage-inappropriate affective symbiosis. Spousal and sibling jealousies can also arise within the family system, and consequent emotional alliances that demarcate the family may actually only represent attempts at emotional connection and survival between members excluded from the dyad. For example, the birth of a chronically ill second child may leave the mother little time for her first child who soon may exhibit a clear preference for the father. Such alliances can readily exacerbate an already stressful family or marital situation.

Siblings

Some reports indicate that siblings of chronically ill children are more likely to have adjustment, behavioral, and academic difficulties (Allan, Townley, & Phelen, 1974; Lavigne & Ryan, 1979). Others suggest that although general mental health may remain stable, social adaptation may be compromised. Still other studies report no significant differences between comparison groups on measures of adjustment or sociability (Drotar, Crawford, & Bush, 1984). Guite, Lobato, Kao, and Plante (2004) compared sibling and parent reports of sibling adjustment to chronic illness and developmental disabilities. Again, although generalizations are to be made with caution as methodologies, patient groups, developmental levels, and comparison groups vary across studies, it may be reasonable to suggest that, like their siblings, brothers and sisters of neurologically impaired children are at increased risk for psychosocial maladjustment.

In some families the needs of healthy children can take second place to those of the ill sibling, especially during times of stress and crisis, and throughout the course of the illness parental adjustment and coping styles will directly influence healthy siblings. For example, depleted emotional reserves and lowered ability to communicate may make parents seem unavailable or rejecting. Younger children who are not yet cognitively able to interpret their parents' feelings or understand what is happening with their ill sibling will tend to effect individual interpretations of the family situation. They may feel guilty, or blame themselves for their sibling's illness. Children may also fear they are susceptible to the same fate, and older children may wonder if they are potential genetic carriers (McCollum, 1981). Distribution of labor may change in the family and researchers have suggested that older female siblings perform a disproportionate share of extra chores. In other comparisons, younger male siblings have been reported to be more sensitive to peers' comments about the illness (Hobbs et al., 1985).

Discussion

It has been assumed in this chapter that the human organism is a complex web of interaction, with normal and pathological developments taking place at multiple levels, from the biological to the social. Under this assumption, the understanding and significance of neurologically based changes in sensorimotor functioning, in cognitive and executive capacities, or in emotion and behavior are enhanced by placing these alterations in a social and historic context. When neuropsychologists listen to their clients, they may hear expected questions about the brain and the consequences of its disorder. Yet in our experiences, these questions do not often end with anatomy and physiology, or with strict brain–behavior relationships per se. Instead, the concerns of clients, both children and adults, extend to attempts to make sense of their condition and to the ramifications of their neurological disorder in the context of family, school, and social settings, and in terms of past experience and future expectations. Consideration of these temporal and ecological dimensions may thus lead to a richer understanding of the implications of neurological disorder in the lives of children, and may suggest additional directions for assessment and intervention in clinical child neuropsychology. Some of the topics included here have been selected for their utility in provoking additional research. In most instances, the topics purposefully suspend the trend toward reductionism in the social sciences and advocate the application of theory and methods from other domains of psychology to the field of neuropsychology.

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Child Forensic Neuropsychology: A Scientific Approach

ROBERT J. MCCAFFREY, JULIE E. HORWITZ, AND JULIE K. LYNCH

Child Forensic Neuropsychology: A Scientific Approach

In the early part of the 20th century, Binet and Simon began work on what would become the Binet–Simon scale, published in 1905 (Binet & Simon, 1905). Binet and Simon's efforts focused only on determining the child's current intellectual status and specifically ignored the issues of etiology and prognosis.

> Our purpose is to be able to measure the intellectual capacity of a child who is brought to us in order to know whether he is normal or retarded. We should therefore, study his condition at the time and that only. We have nothing to do either with his past history or with his future; consequently we shall neglect his etiology, and we shall make no attempt to distinguish between acquired and congenital idiocy; for a stronger reason we shall set aside all consideration of pathological anatomy which might explain his intellectual deficiency. So much for his past. As to that which concerns his future, we shall exercise the same abstinence; we do not attempt to establish or prepare a prognosis and we leave unanswered the question of whether this retardation is curable, or even improvable. We shall limit ourselves to ascertaining the truth in regard to his present mental state (Binet & Simon, 1905, as cited in Dennis, 1948, p. 412).

ROBERT J. MCCAFFREY • Department of Psychology, University at Albany, State University of New York, Albany, New York 12222 and Albany Neurological Associates, Guilderland, New York 12084-1522. **JULIE E. HORWITZ, AND JULIE K. LYNCH.**

A century later, the field of child clinical neuropsychology is no longer content to determine the functional status of a child. Etiology and prognosis are squarely in the forefront of the questions that child clinical neuropsychologists grapple with daily in both their clinical and forensic practices. The issue of etiology may bear directly on treatment options, availability of special educational opportunities, and other services, while the issue of prognosis encompasses all of this within the context of what will be required for the child to achieve his/her maximal level of functioning across an array of life skills. Our clinical ability to address issues of the etiology of a child's current biopsychosocial functioning and the impact of these etiological factor(s) on the child's prognosis frequently results in our involvement in legal proceedings where the issues of causation and long-term consequences are of paramount importance.

Clinical neuropsychological practitioners conduct evaluations based on referrals regarding clinical as well as legal questions. There are many similarities between the clinical and forensic neuropsychological evaluation of a child. In both types of evaluations, the neuropsychological test findings are interpreted in light of multiple sources of data, including but certainly not limited to information concerning the child's family history, medical history, psychiatric history, home/school environment, and the child's behavior during testing. In both contexts, the practitioner is concerned with documenting the child's neuropsychological strengths and

weaknesses and ultimately making a diagnosis and arriving at a prognosis. Effort is made to obtain an in-depth medical, developmental, psychological, and educational history of the child, as well as information regarding family medical, psychological, and social history as is relevant to understanding the child's clinical presentation and/or the issues at hand. In both evaluations, interviewing either a parent or guardian is essential in order to obtain a more complete history of the child with which to either include or exclude other factors that may have influenced the child's neuropsychological test performance. The use of archival records to assist in the assessment of the child's condition may be part of a clinical examination, but it is absolutely necessary in the context of a forensic evaluation where causal issues and the child's ultimate prognosis are the foci. While there may be a high degree of overlap in terms of the procedures utilized by the clinical neuropsychological practitioner, the contexts of the clinical and forensic evaluation are quite different. Our legal system operates on an adversarial premise which may impact both the child being evaluated and his/her parent or guardian, as well as the clinical neuropsychological practitioner. Litigation stress and other motivational factors can be very prominent and may color the entire evaluation process. The clinical neuropsychological practitioner must maintain his/her objectivity and utilize all available debiasing techniques, such as gathering background information in a systematic way by using a structured history questionnaire and systematically "thinking through" alternative explanations for the neuropsychological test data, in order to be of maximal benefit to the trier of fact (Williams, 1997). The importance of considering reasonable alternative explanations for the neuropsychological test findings cannot be overemphasized when working within the forensic arena.

Clinical neuropsychological practitioners are well versed in the process of differential diagnosis. Nowhere is this skill more extensively and intensively tested than in cases in which a child's current deficiencies in his/her cognitive, behavioral, and emotional status are attributed to environmental exposure to a toxin, particularly lead. For a variety of reasons, these evaluations are perhaps the most challenging that the clinical neuropsychologist will encounter. In the situation of childhood lead exposure, the majority of children are from disadvantaged backgrounds, a circumstance accompanied by many developmental risk factors. In addition, because of the early age at which children typically are exposed to lead, there is often no premorbid baseline (e.g., educational records) for comparison with the child's current functioning and test performance. In most situations, the child or adolescent manifests long-standing cognitive and/or behavioral difficulties, and the diagnostic question is whether these difficulties are due to early lead exposure and/or other factors. A further complication in the determination of the role of the exposure in the child's current presentation is the absence of a neuropsychological or behavioral profile specific to lead exposure. As a result of all of these factors, the determination of a causal link between a history of elevated lead levels and intellectual, cognitive, and/or behavioral deficiencies relies heavily upon a comprehensive and careful review of medical, family/genetic, and psychosocial background information in order to rule out other etiologies as plausible explanations for the child's current difficulties.

Consider the following cases that were referred for neuropsychological evaluation to determine the presence and extent of cognitive, behavioral, and emotional difficulties allegedly due to a history of elevated venous blood lead levels. The neuropsychological test data are summarized in Table 1. We report the highest blood lead level since this was typically available and was the focus of the overall degree of alleged insult. These children had varying levels of lead exposure. In reviewing the data from the tables on IQ, memory functioning and neuropsychological functioning, it can be seen that the two children with blood lead levels above 100 μg/dl had average IQs and memory scores, and their overall neuropsychological functioning was well within normal limits on the Reitan-Indiana Neuropsychological Test Battery for Younger Children. The child with the lowest blood lead level (23 μg/dl) had the poorest test scores. These findings seem counterintuitive. Why would children with histories of extremely elevated blood lead levels perform so well on neuropsychological testing, while children with substantially lower levels of lead exposure perform so poorly?

Another seemingly perplexing aspect of these cases is that the two children with blood lead levels above 100 μg/dl were not manifesting

TABLE 1.   Neuropsychological Data of Four Children with Elevated Blood Lead Levels

	Male 12 yr	Male 7 yr	Male 8 yr	Female 7 yr
Peak Pb Level	23 µg/dl	50 µg/dl	124 µg/dl	150 µg/dl
WISC-III				
Full Scale IQ	68	104	99	100
Verbal IQ	67	93	89	95
Performance IQ	73	115	112	106
Index scores				
Verbal comprehension	69	95	92	99
Perceptual organizational	69	114	111	104
Freedom from distractibility	75	90	78	87
Processing speed	91	104	111	114
Test of memory and learning				
Composite indexes				
Verbal memory	75	96	97	94
Nonverbal memory	81	98	100	93
Composite memory	77	97	99	94
Delayed recall	80	95	97	98
Attention/concentration	82	90	88	90
Sequential recall	73	92	93	97
Free recall	75	98	102	87
Associative recall	76	103	97	97
Learning	83	100	103	100

Reitan-Indiana Neuropsychological Test Battery for Younger Children	Male 7 yr 50 µg/dl	Male 8 yr 124 µg/dl	Female 8 yr 50 µg/dl	Average Controls	Average Brain Damaged	Cut-off Score
Level of performance						
Motor functions	8	0	6			
Sensory-perceptual functions	2	0	0			
Visual–spatial skills	9	5	10			
Alertness, concentration, and memory	1	0	1			
Abstraction, reasoning, logical analysis	5	2	0			
Level of performance total	25	7	17	19.55	42.24	31/32
Right–left differences						
Motor functions	8	3	2			
Sensory-perceptual functions	2	0	0			
Both motor and sensory-perceptual functions	1	3	1			
Right–left differences total	11	6	3	7.21	17.21	11/12
Dysphasia and related variables	4	1	0	5.79	19.83	10/11
Total neuropsychological deficit scale score	40	14	20	32.52	79.28	54/55

TABLE 1. (*Continued*)

HRNB-Older Children: Neuropsychological Deficit Scale (NDS)	Male 12 yr 23 µg/dl	Average Non- Brain Damaged	Average Brain Damaged	Cut-off Score
Level of performance				
Motor functions	7	6.29	14.05	
Sensory-perceptual functions	6	5.05	10.77	
Visual–spatial skills	9	4.06	7.69	
Attention and concentration	5	1.91	3.78	
Immediate memory and recapitulation	6	2.23	3.31	
Abstraction, reasoning, logical analysis	4	2.23	6.03	
Level of performance total	37	22.27	45.63	33/34
Right–left differences				
Motor functions	6	2.61	6.29	
Sensory-perceptual functions	2	3.09	5.28	
Both motor and sensory-perceptual functions	3	1.09	2.17	
Right–left differences total	11	6.79	13.74	9/10
Dysphasia and related variables	5	1.37	7.97	3/4
Total NDS Score	53	30.43	67.34	43/44

any physical or neurological symptoms. Yet, according to the Centers for Disease Control (CDC) publication on lead poisoning (Centers for Disease Control, 1991), death occurs at a blood lead level above 100 µg/dl, and there are significant medical and central nervous system effects as blood lead level approaches 100 µg/dl (see Figure 1). The fact is, however, that organizations such as the CDC and the World Health Organization rely on epidemiological research in developing their human health guidelines. Epidemiology is concerned with the frequencies and types of injuries and illnesses in *groups of people and populations*. It is the study of the distribution and determinants of diseases and injuries in human populations. It is a relatively new science that emerged in the 19th century and was concerned with the study of epidemics, but which has expanded beyond the study of epidemics and is today concerned not only with epidemic diseases but with all forms of illnesses and bodily injuries (e.g., HIV/AIDS, heart disease, traumatic brain injury, substance abuse, mental health issues, etc.).

The focus of epidemiology is not on the *individual,* but rather on the *community*. The target of study of the clinical neuropsychological practitioner, however, *is* on the *individual*. Thus,

the findings from epidemiological research do not necessarily apply to the individual patient.

> Epidemiology is concerned with the incidence of disease in populations and does not address the question of the cause of an individual's diseases. This question, sometimes referred to as specific causation, is beyond the domain of the science of epidemiology. Epidemiology has its limits at the point where inference is made that the relationship between an agent and a disease is causal (general causation) and where the magnitude of excess risk attributed to the agent has been determined; that is, epidemiology addresses whether an agent *can* cause a disease, not whether an agent *did* cause a specific plaintiff's disease [italics added] (Green, Freedman, & Gordis, 2000, pp. 381–382).

By way of example, cigarette smoking is a "risk factor" for the development of lung cancer and other diseases. Nonetheless, only 10% of lifelong cigarette smokers will develop lung cancer. Similarly, the Centers for Disease Control (1991) publication on lead poisoning indicates that death occurs above blood lead levels of 100 µg/dl, and yet not every child with blood lead levels of this magnitude dies or is found to have a below-average IQ. The case presentations at the beginning of this chapter illustrate that the
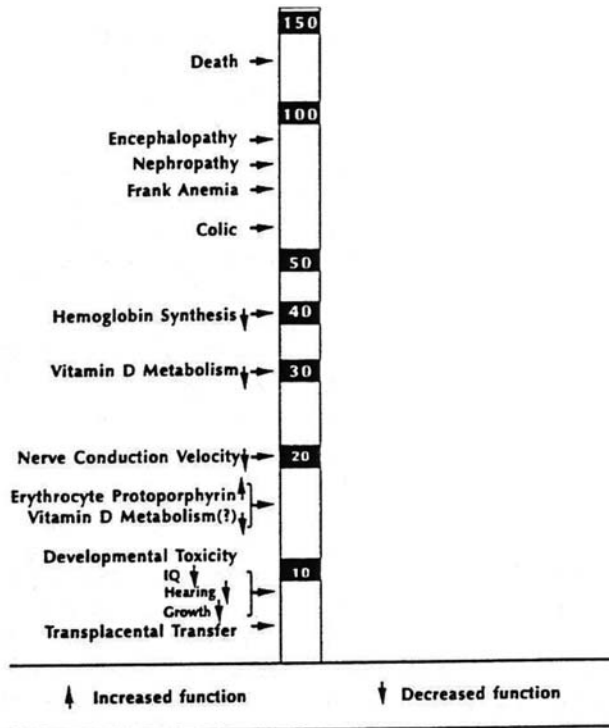
*Note: The levels in this diagram do not necessarily indicate the lowest levels at which lead exerts an effect. These are the levels at which studies have adequately demonstrated an effect.

Source: ATSDR, 1990.

FIGURE 1. Lowest observed effect levels of inorganic lead in children.

two young children with blood lead levels above 100 µg/dl demonstrated average intellectual and neuropsychological functioning. In fact, neither child's neuropsychological profile indicates the presence of cognitive dysfunction. Thus, while lead exposure has been associated with decline in neuropsychological and behavioral functioning, this is not always the case, even in the presence of extremely elevated blood lead levels. It is important to keep in mind the limits of epidemiological research when attempting to establish causation for neuropsychological and/or behavioral deficits. Determination of causation requires detailed analysis and consideration of known risk factors for cognitive and behavioral deficiencies. While epidemiological studies may reveal an association between the conditions in question and neuropsychological dysfunction, the individual child in your office may have a history of other factors which bear directly on his/her clinical presentation.

Table 2 provides a list of many important variables with known relationships to cognitive, behavioral, and psychological development. These are variables that have been routinely controlled for in studies of children who have a history of elevated blood lead levels because of their influence on the targeted outcome variable, which is usually, but not always, childhood IQ. Like the researcher, the clinical neuropsychological practitioner must factor these relevant variables into his/her conceptualization of the child's cognitive, behavioral, and emotional status.

The Scientist-Practitioner: Familiarity with the Scientific Research

In addition to being cognizant of variables relevant to a child's cognitive, behavioral, and emotional development, knowledge of the scientific research is important in both a clinical and

TABLE 2. Covariates Found in the Research on the Neurobehavioral Effects of Lead Exposure

Child's gender	Birth order
Child's race	Child's iron status
Family size	Parental education
Obstetrical complications	Maternal age at birth
Birth weight	Maternal/paternal intelligence
Gestational age	Maternal mental health
Prenatal care	Parental smoking habits
Prenatal alcohol, drug, and/or cigarette use	Child's medical history
Life stress/psychosocial stress	Socioeconomic status
Home environment (e.g., discipline, parental involvement, parental responsivity, availability of enriching activity, abuse/neglect,[a] domestic violence[a])	
Child/adolescent use of drugs, alcohol, and/or cigarettes	

[a]These variables have not been included in the lead research but are listed here as examples of other relevant home-related factors that can impact child development.

forensic setting. In reviewing the scientific literature on the neurobehavioral impact of childhood lead exposure, for example, it is clear that lead is a neurotoxin. High blood lead levels *can* result in encephalopathy, seizures, coma, and death. As a case in point, the CDC recently provided a report of the death of a 4-year-old child as a result of acute lead poisoning after apparently swallowing a metallic charm. His blood lead level was 180 μg/dl (Centers for Disease Control, 2006). Yet the amount of lead considered toxic is not entirely clear. Whereas highly elevated lead levels can lead to overt indications of lead poisoning (e.g., vomiting, stomach pain, fatigue, seizure, coma), lower elevations have been associated with adverse cognitive and behavioral effects. The CDC currently recommends that a child with a blood lead level of >10 μg/dl requires monitoring due to potentially adverse health effects (Centers for Disease Control, 1991). There has been recent concern expressed, however, about the adequacy of these criteria following research that has found negative associations between blood lead levels *below* 10 μg/dl and cognitive and behavioral development (Canfield et al., 2003; Canfield, Kreher, Cornwell, & Henderson, 2003; Coscia, Ris, Succop, & Dietrich, 2003; Wasserman et al., 2003).

In reviewing the research literature on childhood lead exposure, the weight of the research addresses the impact of elevated lead levels on intellectual functioning. There have been some peer-reviewed published reports that have not yielded findings of a significant relationship between elevated blood lead levels and intellectual functioning (Ernhart, Morrow-Tlucak, Wolf, Super, & Drotar, 1989; Pocock, Ashby, & Smith, 1987; Smith, Delves, Lansdown, Clayton, & Graham, 1983; Winneke & Kraemer, 1984). Nonetheless, a greater proportion of the research provides evidence of a statistically significant negative association. The magnitude of the association has been consistently small, with low to moderate elevations in blood lead levels usually explaining no greater than 7% of the variance in IQ scores. In many of the studies, the percentage of variance explained by a history of lead exposure ranges from 3 to 5%. These research findings indicate that between 93 and 97% of the variance in a child's IQ is due to factors other than lead.

There have been several studies that have reported elevated blood lead levels to have a greater association with specific aspects of intellectual functioning, but the findings from these reports have been inconsistent. For example, some research has found an inverse relationship between blood lead levels and Full scale IQ and Performance IQ but no significant association between lead and Verbal IQ. On the other hand, there has been research showing elevated blood lead levels to have a greater negative effect on verbal intellectual functioning than nonverbal intellectual abilities (Baghurst et al., 1992; Coscia et al., 2003; Dietrich, Berger, Succop,

Hammond, & Bornschien, 1993; McMichael et al., 1994; Wasserman et al., 1997, 2003; Wasserman, Liu et al., 2000).

The research on the effects of lead exposure on aspects of cognitive functioning beyond general intelligence is developing. Most of the research that has been completed shows a negative association between elevated blood lead levels and some aspects of neuropsychological functioning; however, the patterns of findings across the studies have not been consistent. Briefly, a history of elevated blood lead levels has been found to have an inverse relationship with visuoconstructive abilities, visuomotor integration, reaction time, attention, verbal memory, reasoning, language functions, and fine motor speed and dexterity (Faust & Brown, 1987; Ris, Dietrich, Succop, Berger, & Bornschein, 2004; Wasserman, Musabegovic et al., 2000; Winneke, Brockhaus, Ewers, Kramer, & Neuf, 1990). A recent study has found a negative association between very low lead levels ($<10\,\mu\mathrm{g/dl}$) and a child's knowledge of colors (Canfield, Kreher et al., 2003). As indicated earlier, a consistent pattern of neuropsychological deficits has not been found across the studies; therefore, the various neuropsychological domains above cannot be considered to represent the neuropsychological profile associated with elevated blood lead levels. It is also important to recognize that, as with IQ, the relationship between these neuropsychological domains and elevated blood lead levels is quite small. For example, Ris et al. (2004) found that childhood lead exposure explained, at most, 5% of the variance in neuropsychological functioning during adolescence. In the Winneke et al. (1990) study, a history of lead exposure that ranged from low to high elevations in blood lead level accounted for 0.8 % of the variance in performance on a measure of serial choice reaction time and 0.5% of the variance in performance on a measure of visuomotor integration. Faust and Brown (1987) found that children who had a history of moderately elevated blood lead levels for at least 1 year scored no greater than one-half standard deviation lower than children without a history of lead exposure on measures of verbal memory, language, higher level spatial abilities, attention, and reasoning. On a measure of fine motor speed, the lead-exposed children scored one standard deviation lower. Of note, none of the lead-exposed children in this study performed in the deficient range on any of the neuropsychological measures.

A history of elevated lead levels has also been associated with a number of behavioral problems. Specifically, exposure to low to moderate levels of lead has been associated with withdrawn behavior, inattentive behavior, destructive behavior, hyperactive behavior, and delinquent behavior (Dietrich, Ris, Succop, Berger, & Bornschein, 2001; Silva, Hughes, Williams, & Faed, 1988; Wasserman, Staghezza-Jaramillo, Shrout, Popovac, & Graziano, 1998). As shown in the research on the relationship between lead and intellectual and neuropsychological functioning, a history of lead exposure has been found to explain a very small percentage of the variance in these behaviors. Dietrich et al. (2001) found that a history of lead exposure explained 1–6% of the variance in delinquent behavior of adolescents, leaving 94–99% of the variance attributable to other factors. Silva et al. (1988) found lead exposure to explain 0.8–1.5% of the variance in inattentive and hyperactive behaviors of 11-year olds. Wasserman et al. (1998) found that a history of lead exposure accounted for 2–4% of the variance in withdrawn and destructive behavior reported on the Child Behavior Checklist. More recently, prominent lead researchers (Bellinger & Rappaport, 2002) have concluded that the current scientific literature provides "no compelling evidence that an EBLL [elevated blood lead level] increases a child's risk for attention-deficit hyperactivity disorder (ADHD)" (p. 81). This point is important because a history of elevated blood lead levels is often alleged to be the sole underlying cause of ADHD.

In summary, a review of the research identifies two important points that need to be considered when conceptualizing the basis of a child's neuropsychological test scores and behavioral functioning. First, there has not been a specific pattern of decline in either intellectual or neuropsychological functioning consistently associated with elevated blood lead levels. Therefore, the neuropsychologist will not be able to determine the etiology of the neuropsychological test findings based on a particular pattern of findings. Second, the potentially negative impact of a childhood history of elevated lead levels on development must be weighed in the context of other developmental risk factors. The association between lead exposure and

deficits in intellectual, neuropsychological, and behavioral functioning is quite small. This literature indicates that there are many other risk factors for adverse developmental outcome that have a greater relationship with child development than does elevated blood lead levels. In those studies where a statistically significant association has been reported between lead exposure and developmental outcomes, much larger associations have been identified between a child's intellectual, neuropsychological, and behavioral functioning and factors such as the child's home environment, parental intelligence, parental education, and socioeconomic status (Baghurst et al., 1992; Wasserman et al., 1997, 1998; Wasserman, Liu et al., 2000). As one example, Wasserman et al. (1997) found that the quality of a child's home environment accounted for 25–30% of the variance in childhood IQ. A history of elevated blood lead levels, however, explained only 4% of the variance in childhood IQ. Given these data, how can one rationalize or justify making a determination of causality without consideration of home-related factors that have been found to have a greater influence on the child's developmental outcome? Similarly, how can one come to any conclusions regarding the causality of the child's current cognitive, intellectual, and behavioral difficulties without considering parental education/intellectual functioning, as well as a host of other heritable conditions (e.g., learning disability) that have been found empirically to have a greater impact on the child's development than a history of lead exposure?

Consideration of the Other Sides of the Coin

When the question of etiology is paramount, as is the case with forensic evaluations, it becomes necessary to consider all of the other pertinent risk factors that may impact the child's development and to consider carefully the weight of these factors in the child's current status. The interpretation of evaluation findings within the context of the individual's medical, family/genetic, and psychosocial background is standard practice within the field of neuropsychology, but is not unique to the field, as medical specialists utilize this as an important source of diagnostic information regarding the individual patient. This practice is dictated by the scientific literature that has found that an individual's genetic history, sociodemographic background, and medical history are relevant to developmental outcome. Such information is essential in determining the etiology of cognitive or behavioral deficiencies documented during an evaluation. For example, the causal attribution between a cerebral injury and oppositional behavior would be different in a child with a prior history of such behavior versus a child without such a behavioral history. Similarly, findings of low intellectual functioning may reflect a decline in ability following a cerebral injury or may reflect the child's premorbid level of intellectual functioning. This determination is based on information obtained from clinical interview with the parent(s) and medical/educational records. In this situation, information regarding parental and sibling intellectual functioning would be relevant, particularly in the absence of a baseline for the child's intellectual functioning (Reynolds, 1997). As another example, the association between a cerebral insult sustained during infancy and low academic achievement and psychological difficulties during childhood would be less clear in the context of a home situation involving domestic violence, parental substance abuse, and/or parental mental illness.

Given the breadth of variables potentially affecting developmental outcomes, the clinical neuropsychological practitioner must undertake a thorough biopsychosocial history of the child in order to render an opinion regarding causation. For example, ascertaining information about any family history of mental illness, learning disabilities, developmental disabilities, mental retardation, attention-deficit disorder, conduct-related disorders, low intellectual functioning, and antisocial behavior alerts the clinician to a potential genetic vulnerability for intellectual, cognitive, and behavioral deficiencies in the child (Ingalls & Goldstein, 1999; Neisser et al., 1996; Spencer, Biederman, Wilens, & Faraone, 2002; Silberg et al., 1996, Simonoff, 2001). The medical history of the child, including information regarding prenatal and birth history, should also be reviewed for known risk factors for cognitive and behavioral deficiencies. Factors such as poor prenatal nutrition, prenatal drug or alcohol, preterm birth, and low birth weight have all been found to be associated with cognitive and

behavioral development (Howell, Lynch, Platzman, Smith, & Coles, 2006; Picard, Del Dotto, & Breslau, 2000; Singer et al., 2002).

Environmental factors must also be considered as potentially impacting the child's current presentation. For example, information regarding the home environment, examining such aspects as parenting style, discipline strategies, and the emotional climate of the family, is relevant, as these factors have been found to impact a child's academic functioning, intellectual development, and behavioral functioning (Bradley, Rock, Caldwell, Harris, & Hamrick, 1987; Espy, Molfese, & DiLalla, 2001; Sameroff, Seifer, Baldwin, & Baldwin, 1993; Veltman & Browne, 2001). Children who are severely maltreated, such as in the case of neglect or physical or sexual abuse, have a greater risk for poor academic achievement, behavioral difficulties, and psychological difficulties. Similarly, children raised in the context of domestic violence have a greater risk for behavioral difficulties, psychological difficulties, and school-related problems as compared with other children (Veltman & Browne, 2001).

A child's cognitive, intellectual, and behavioral development can also be adversely impacted by a home environment and caretaking that is *below par* but does not involve severe maltreatment of the child. A commonly used research instrument for assessing a child's home setting is the Home Observation for Measurement of the Environment (HOME) scale (Bradley & Caldwell, 1977). This scale examines six distinct aspects of a child's environment: maternal responsivity, restriction and punishment, organization of the environment, play materials, maternal involvement, and variety of stimulation. A study by Bradley and Caldwell (1980) found that organization of the home environment, availability of play materials, and maternal responsivity were significantly related to cognitive competence in girls, whereas play materials, maternal responsivity, and maternal involvement were significantly correlated with IQ in boys. Espy et al. (2001), using a sample of 105 children from rural areas, found that home environment had a constant and significant association with performance of young children on intellectual testing. In addition to intellectual development, children's early home environment (for ages 6 and below) and socioeconomic status have been found to be significantly associated with the development of reading abilities and performance on standardized measures of reading achievement (Molfese, Modglin, & Molfese, 2003).

The home environment is also relevant to a child's recovery from neurological injury. A number of studies have found that family functioning, including parental psychological adjustment and access to resources, influences child outcome following traumatic brain injury (e.g., Taylor et al., 1999, 2002; Yeates et al., 2001). For example, Taylor et al. (2002) found that among children with severe TBI, only those living in low-stress environments demonstrated short-term recovery of math function. Additionally, long-term decline in academic performance was only evident in those children from more socioeconomically disadvantaged backgrounds. Yeates et al. (1997) similarly found that deficits in memory and adaptive functioning associated with severe TBI in children were exacerbated by below-average family functioning. The authors also found that these deficits were buffered by above-average family functioning.

Sociodemographic factors are particularly salient in the neuropsychological evaluation of children with a history of elevated blood lead levels. A disproportionate number of these children are from socially disadvantaged backgrounds, which are generally accompanied by many factors that tend to have a greater adverse developmental impact than lead, as previously discussed. Poverty in particular can have a profound effect on cognitive development and neuropsychological functioning. For example, Korenman, Miller, and Sjaastad (1995) found that low income was associated with poorer scores on each of a number of neuropsychological tasks, especially those assessing vocabulary, math, and reading achievement. In his discussion of factors affecting normal cognitive development, Mirsky (1995) conceptualizes a "poverty pentad" consisting of five poverty-related environmental factors: (1) malnutrition, (2) disease, (3) toxic agents (particularly lead and alcohol), (4) perinatal injury, and (5) lack of intellectual–social stimulation. Each of these five factors represents a largely environmental influence on the child which can affect the development of his/her cognition in a number of different ways.

Malnutrition

A number of studies have found that poorer children are more likely to receive inadequate nutrition and that this poor nutrition is associated with lower cognitive abilities. For example, in a comparison of rural Guatemalan and urban American children, Cravioto, DeLicardie, and Birch (1966) suggested that poorer intersensory integration abilities among the rural children was due to malnutrition, and was specifically related to protein deprivation. In a discussion of the effects of nutrition on the nervous system, Balderston (1981) asserted that early protein-calorie deprivation in particular often has lasting effects on behavior, and that both mild and severe malnutrition likely affect learning. These effects may result from both chronic and acute deprivation (e.g., Levav, Cruz, & Mirsky, 1995). Additionally, results from a study of over 200 school-aged children in Ecuador suggested that the greater the level of malnutrition (classified as mild, moderate, or severe), the poorer the vocabulary score on the Peabody Picture Vocabulary Test (PPVT; Cruz et al., 1993, as cited in Mirsky, 1995). Similarly, Freeman, Klein, Townsend, and Lechtig (1980) found a significant association between nutritional status and cognitive competence, particularly language ability. With regards to associations between nutrition and attention, it has been suggested that the encoding element of attention in particular is affected by malnutrition (Mirsky, 1995). Taken together, these studies suggest that even mild levels of malnutrition may affect cognitive functioning, but that more severe malnutrition and inadequate nutrition earlier in life likely lead to worse outcomes. Additionally, certain neuropsychological domains may be more vulnerable than others to the effects of malnutrition.

In examining the association between malnutrition and cognitive abilities, it has been suggested that low birth weight, stunting (low height for age), and wasting (low weight for height) may partially mediate this relationship. These conditions, which are often elevated among poor children, have been found to be associated with worse performance on a number of neuropsychological tasks. For instance, a strong relationship has been found between stunting and poorer short-term memory (Korenman et al., 1995).

Disease

With regards to disease, one particular concern is that of parasitic infection. In the United States, the roundworm *Toxocara canis* has been associated with low socioeconomic status, and the tapeworm *Taenia solium* has been associated with immigrant populations (Schantz, 1991). Both parasites have been found to have effects on cognition; performance on effortful attention tasks in particular is thought to be ill-affected by parasitic infection (Mirsky, 1995). The extent to which parasitic infection affects neuropsychological functioning, however, is largely unknown. Some researchers have suggested that neuropsychological outcomes commonly associated with parasitic infection may be largely due to the effects of malnutrition or other related variables. For example, Worley et al. (1984) found that significant associations between *T. canis* infection and cognition and school achievement were no longer significant when accounting for confounding variables. Additionally, Levav, Mirsky, Schantz, Castro, and Cruz (1995) found interactions between level of nutrition and parasitic infection on results of the PPVT and Wechsler Memory scales, although only a main effect of nutrition level was found.

Toxic Agents

Children from disadvantaged backgrounds are at greater risk for exposure to environmental lead. In addition to lead exposure, exposure to drugs and alcohol prenatally carries significant risk for adverse developmental outcomes. Prenatal alcohol exposure has been associated with small decrements in IQ, poor achievement test scores, behavioral difficulties, and reduced neuropsychological functioning (Jacobson, Jacobson, Sokol, & Ager, 1998; Streissguth, Barr, & Sampson, 1990).

Perinatal Injury

There is also evidence that perinatal injury, particularly in the form of pregnancy and birth complications (including asphyxia), is associated with social class. For example, Chamberlain, Philipp, Howlett, and Masters (1978) found a correlation between social class and fetal death, which suggests that mothers in lower social classes may also be more likely to give birth to

children with undetected non-fatal brain injuries that may affect cognitive development (Mirsky, 1995). Auditory brainstem structures, including the inferior colliculi and the superior olives, are considered to be the areas most susceptible to insult as a result of asphyxia due to their high oxygen demand. Therefore, deficits in auditory information processing may be of particular concern among underprivileged populations (Kety, 1962; Mirsky, 1995).

Intellectual–Social Stimulation

Lower levels of parental education and reduced access to educational resources among poor children are two common factors resulting in decreased intellectual and social stimulation. In considering the impact that a lack of intellectual and/or social stimulation may have on cognitive development and performance on neuropsychological tests, one must be cognizant that some assessment measures are more prone to education effects than others (Ardila, 1995). For instance, language tests (Ardila, 1995), memory tests (Ardila, Rosselli, & Rosas, 1989), tasks involving the application of new problem-solving methods to abstract situations (Nell, 1999), and tests of arithmetic abilities (Geary et al., 1997) have been found to be sensitive to education effects, while tasks such as the Wisconsin Card Sorting Test have been found to be only minimally susceptible to educational factors (Rosselli & Ardila, 1993).

A number of variables have been examined as mediating factors in the relationship between brain insult and resulting cognitive ability, including gender, birth order, family size, poverty, and persistence of poverty. For example, children living in a state of persistent poverty have been shown to score lower on a range of cognitive tests as compared with children who spend less time in poverty (Duncan, Brooks-Gunn, & Klebanov, 1994; Korenman et al., 1995). Circumstances outside the home have also been investigated. For instance, Duncan et al. (1994) found that the presence of affluent neighbors was associated with higher IQ scores in a sample of 895 children. The absence of an association between the presence of poor neighbors and IQ scores led the authors to speculate that access to neighborhood resources and adult role models may have accounted for the beneficial relationship between affluent neighbors and IQ scores.

Additionally, the presence of behavior problems may be considered a mediating factor and should be taken into account in evaluating a child. Although a number of studies have also investigated and drawn conclusions regarding associations between race and various cognitive abilities, a word of caution is warranted in taking these conclusions at face value. For example, Duncan et al. (1994) found that race differences in IQ among children could be accounted for almost entirely by differences in maternal education, paternal presence, income-to-needs ratio, neighborhood income, and HOME scores. This finding illustrates the need to look to mediating variables rather than assuming direct correlations between cognitive abilities and factors such as race or ethnicity.

Within a Reasonable Degree of Neuropsychological Certainty

Causation

Unlike Binet and Simon, the clinical neuropsychological practitioner must address issues of etiology and prognosis. In the forensic arena, the child clinical neuropsychologist is ultimately faced with two questions: "Do you have an opinion with a reasonable degree of neuropsychological certainty?" and, if the answer is yes, then "What is that opinion?"

Legally, the phrase, "within a reasonable degree of neuropsychological certainty" translates to something akin to "the preponderance of the evidence," or $\geq 51\%$ likelihood that whatever the issue before the trier of fact was the "causative" or a substantially contributing factor to the plaintiff's alleged injuries. In conventional statistical terms, "within a reasonable degree of neuropsychological certainty" would equate to a research finding at a near chance level. The null hypothesis of no difference due to the experimental manipulation would be retained in most cases. Research findings that fail to result in the "rejection of the null hypothesis" would not be acceptable to the scientific community as evidence of a causal relationship, and yet this appears to be the legal standard. As scientist-practitioners, we have been taught that

reliable and valid experimental research findings must meet, at a minimum, the $p \leq 0.05$ level of statistical significance. In layman's terms, in order to establish "causality," the scientific "preponderance of evidence" must meet or exceed the 95% level of certainty.

While it is informative to understand the legal definition for neuropsychological certainty, we do not propose this as the standard by which clinical neuropsychologists should practice. Our scientific and ethical standards require that the clinical neuropsychologist undertake a comprehensive consideration of all possible alternative explanations as a prerequisite for rendering an opinion "within neuropsychological certainty."

Prognosis

Clinical neuropsychologists are frequently called upon to predict both educational and vocational outcomes for individuals who have sustained some form of brain-related injury. We have often seen reports that utilize intellectual functioning as the basis for predicting a child's ultimate educational level and vocational opportunities. For example, a child with an IQ of 82 might be described as never being able to complete high school or attend college, and consequently as also having a reduced vocational potential. The underlying scientific basis for these prognostic statements is questionable. In an analysis of the range of IQ from adults between 20 and 74 years of age who were part of the WAIS-R standardization sample, Reynolds et al. (1987, as cited in Kaufman, 2006) reported IQ ranges for individuals with various levels of education (see Table 3) and for six occupational groupings (see Table 4). The data included in these tables do not support the notion that an individual with an IQ of 82 would be unable to obtain either a 2-year college degree and/or be employed in a professional/technical position. This is but one example of the importance of basing an opinion "within a reasonable degree of neuropsychological certainty" upon solid empirical evidence. The clinical neuropsychological practitioner must be familiar with outcome research and should not provide opinions that are based on clinical lore or speculation, neither of which would be considered to be valid and reliable ($p \leq 0.05$).

TABLE 3. IQ Range Based on Education Level

Education Level (Years of Schooling)	IQ
Some elementary education (0–7 years)	53–139
Completed elementary (8 years)	65–125
Some high school (9–11 years)	59–146
High school graduates (12 years)	63–141
Some college (13–15 years)	76–139
College degree or higher (≥16 years)	87–148

Note. Data from Reynolds et al. (1987, as cited in Kaufman, 2006).

TABLE 4. IQ Range Based on Occupation

Occupation	IQ
Not in labor force	55–146
Unskilled workers	53–126
Semiskilled workers	56–135
Skilled workers	72–131
Managerial, clerical, and sales	73–137
Professional and technical	81–148

Note. Data from Reynolds et al. (1987, as cited in Kaufman, 2006).

Concluding Remarks

The purpose of this chapter has been to comment on a scientifically based approach to the neuropsychological evaluation of children for forensic purposes. While we have used the example of lead, a similar approach should be utilized in all cases where the determination of causality is important. The scientific research and the process of exploring alternative and/or other contributory explanations for the evaluation findings is absolutely necessary, if an opinion made "within a reasonable degree of neuropsychological certainty" is to be of maximal benefit to the trier of fact. Information from all these sources needs to be integrated in conceptualizing the underlying etiology of the child's current cognitive and behavioral deficits. Given the child's overall history, what is the most plausible explanation for the current presentation? In any neuropsychological evaluation, it is important to interpret evaluation findings in the context of a child's medical, family, and psychosocial history; this is particularly imperative in a situation where etiology is the highest concern. Clinical neuropsychological

practitioners should not fall victim to the trap of inferring causality from relational data (Reynolds, 1999). Moreover, just because a child is identified as having a specific problem, the direct relationship of this problem to the basis of the alleged injury cannot be made without a careful analysis of all of the relevant biopsychosocial factors.

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Neuropsychology and Coma Management

JOAN W. MAYFIELD, LINDA PEDERSEN, AND FRANK MCDONALD

Stedman's Medical Dictionary-26th Edition (1995) defines a coma as "a state of profound unconsciousness from which one cannot be roused; may be due to the action of an ingested toxic substance or of one formed in the body, to trauma, or to disease." Functionally, a person is in a coma when he or she is unable to respond purposefully to stimuli in the environment. According to Shewmon and DeGiorgio (1989), trauma, drug overdose, and cardiac arrest are the leading causes of coma. It has been my experience that, as a general rule, most people have a limited understanding of coma. Many times, their knowledge is based on what they have seen on television. The movie starts, the person is hurt, taken to the hospital, and is described as critical and in a coma. The person in the movie lies quietly with their eyes closed. In the next scene, the actor opens his or her eyes and calls the name of the person who is holding vigilance by their bed. As I approach the parent of a child who is in a coma, I watch as they wait for their child to look at them and say those important words, "mommy and daddy." My role, as a neuropsychologist, is to explain to the family how the brain affects behavior and explain what a coma is and the emerging process. Initially, information is provided about how the level of coma is measured, different aspects of the emerging process, and how to provide an environment that does not promote over-stimulation. The purpose of this chapter is to provide information as to how a coma is assessed, the emerging process, medical management of a coma, prognosis following different diagnoses, and the importance of family education.

Levels of Consciousness

Coma—A person is said to be in a coma when he or she cannot be awakened and has minimal or no response to stimuli in his or her environment. The person may appear to be in a deep sleep and cannot be awakened.

Vegetative State (VS)—There is some discussion in the literature as to when a person is in a coma or a vegetative state. According to the American Congress of Rehabilitation Medicine (1995), the main difference is based on whether the person is in a sleep–wake cycle. If the person is described to be in a coma, his or her eyes do not open either spontaneously or to external stimulation, while his or her eyes would open spontaneously or after stimulation if the person was in a vegetative state. Jennett and Plum (1972) were credited as the first to use the term persistent vegetative state (PVS) and defined the person to be in this state when they were unable to mouth words, follow commands, demonstrate purposeful movement but were experiencing a sleep–wake cycle for a period of at least 1 month.

The Multi-Society Task Force on PVS (1994) set the following criteria for a diagnosis of vegetative state:

(1) no evidence of awareness of self or environment and an inability to interact with others;

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(2) no evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli; (3) no evidence of language comprehension or expression; (4) intermittent wakefulness manifested by the presence of sleep–wake cycles; (5) sufficiently preserved hypothalamic and brain–stem autonomic functions to permit survival with medical and nursing care; (6) bowel and bladder incontinence; and (7) variably preserved cranial nerve reflexes (papillary, oculocephalic, corneal, vestibule-ocular, and gag) and spinal reflexes (p. 4).

There seems to be some confusion between the words persistent and permanent when referring to a vegetative state. According to the Multi-Society Task Force on PVS (1994), a persistent vegetative state is applied when the vegetative state is considered to be a diagnostic term. This would be used when the person has been and is in a vegetative state for at least a month. The term permanent vegetative state refers to a prognosis and would be used when the physicians, with a high degree of probability, determine that the condition is irreversible. Wade (1996) recommends using the term "continuing vegetative state" or even the term "coma" for all persons during their first 12 months after the onset of their coma to avoid misuse of the term "persistent vegetative state."

Locked-in State (LIS)—There are times when a person can appear to be in a persistent vegetative state when, in fact, he or she is aware of his or her environment but is unable to communicate that through obvious means such as speech or gestures. It is possible to make this false positive diagnosis when the person has a "locked-in" state. This is a result of an injury caused by an infarct, hemorrhage, or trauma that affects the ventral pons. Additionally, bilateral injury to the corticobulbar and corticospinal tracks may result in this syndrome (Smith & Delargy, 2005). According to Smith and Delargy (2005), "Locked-in syndrome was first defined in 1966 as quadriplegia, lower cranial nerve paralysis, and mutism with preservation of consciousness, vertical gaze, and upper eyelid movement. (406)." Mutism was removed from this definition in 1986, with the intention of clarifying the definition, as mutism may be elective. This is a difficult diagnosis, as people can go from a coma status to a locked-in state. The hallmark characteristic to be aware of is the voluntary vertical eye movement, which may serve as a means of communication. Neurodiagnostic studies, such as computer tomography, magnetic resonance imagines, and positron emission tomography can be used to help distinguish the person with locked-in syndrome from one in a vegetative state. The person with locked-in syndrome would be more likely to have minimal cerebral cortical atrophy and would show nearly normal cerebral cortical metabolism of glucose and oxygen (Cranford, 1996).

Minimally Conscious State (MCS)—The term minimally conscious state was recommended for use in 1996 by the Workgroup of the Aspen Neurobehavioral Conference. According to Giacino and Kalmar (1997), MCS frequently occurs as a natural transition between a person being in a coma, vegetative state, or higher levels of consciousness. The Workgroup (1996) defined MCS as "a condition of severely altered consciousness in which the person demonstrates minimal but definite behavioral evidence of self or environmental awareness." The main difference between a vegetative state and MCS would be the lack of consciousness in the vegetative state and some level of partial awareness in MCS. Giacino et al. (1997) describe the following characteristics: eyes would open spontaneously with a normal or abnormal sleep–wake cycle; arousal would range from obtunded to normal; there would be inconsistent but reproducible evidence of perception, communication, or purposeful movement; tracking would be observed; communication abilities would range from none to verbalizations or gesturing to inconsistently responding to yes/no questions. This state may also be referred to as a minimally responsive state.

Akinetic Mutism (AK)—According to Wijdicks and Cranford (2005), akinetic mutism is a less common state of impaired consciousness. The name is a misnomer in that the patient is not akinetic in that many may move in response to pain, and he or she is not necessarily mute. Although some are mute, others say single words. Giacino and Kasler (1995) indicate that this state is a result of damage to the dopaminergic pathways in the brain characterized by minimal movement, little or no spontaneous speech, some verbal response to questions but no initiation to speak, eyes opening and tracking, and inconsistent response to commands.

Coma Assessment Measures

There are numerous instruments that are used in various settings to measure one's level of consciousness, monitor or observe the emerging process, and help provide a prognosis.

Glasgow Coma Scale—Emergency medical personnel frequently use the Glasgow Coma Scale (GCS) as they perform their initial assessment of the injured person in the field. It was developed by Jennett and Teasdale in the early 1970s and quickly rose to be "the gold standard of neurologic assessment for trauma patients" (Fisher & Mathieson, 2001, p 52).

The GCS was initially developed as an objective research tool to measure the level of consciousness of patients with severe head trauma and track trends of recovery (Teasdale & Jennett, 1974). By using an instrument such as the GCS, professionals would be able to communicate more accurately with other professionals about the status of their patient. The GCS became widely accepted in Scotland, and since Jennett and Teasdale had both worked in Glasgow, Scotland, they decided to incorporate the name of the city into the title of the scale. Since that time, the GCS has been accepted internationally and is used universally by trauma professionals (Fisher & Mathieson, 2001).

The GCS is used to assess one's level of consciousness by measuring his or her ability to open his or her eyes, communicate verbally, obey commands, and move his or her extremities.

The scoring system ranges from 3 to 15, with the higher the score the better the status of the patient. According to Rosenthal, Griffith, Bond, and Miller (1983), 90% of people with a score of 8 or less are considered in a coma, and those with a score of 9 or better are not. A patient is given a score of 15 when he or she is opening his or her eyes spontaneously, is oriented, and obeys commands. A patient is given an overall score of 3 when there is no response to speech or pain, and he or she is not verbalizing. In terms of eye opening, if the person opens his or her eyes spontaneously, he or she is given a 4. If that does not occur, the evaluator speaks to the patient. If the injured person responds, a 3 is given. A score of 2 is provided when the person opens his or her eyes when a painful stimulus is given. When no response is made, a score of 1 is provided.

The motor response is reported to be the most valuable component of the GCS and is least affected by trauma. The score of 6 is provided when the patient is able to follow commands. When the patient is not able to respond independently, a noxious stimulus is provided. If the patient is able to localize to the painful stimulus and moves his or her arms in an attempt to push the painful stimulus away, a score of 5 is given. When the patient pulls away without localization, a 4 is given. A score of 3 is assigned when abnormal flexions are observed. This would be characterized by flexions in the arms, wrists, and fingers. In the lower extremities, the legs would extend and there would be internal rotation with plantar flexion of the feet. A 2 is assigned when extensions are observed, such as adduction and hyperpronation of the upper extremities, the legs are extended with plantar flexion of the feet, and the head can have a backward extension with arching of the back. When no response is observed, a score of 1 is given.

In the area of verbal responses, a person is described as oriented when he or she is able to provide his or her name (person), where they are (place), and knows the current year, season, and month (time). A 5 is given when the person is oriented. If the person is confused, a 4 is provided. A 3 is assigned when the person uses inappropriate words. If the person is making incomprehensible sounds, a 2 is given. When no verbal responses are heard, a 1 is scored. See Table 1 for description of scoring criteria for GCS.

The GCS is quick and easy to administer and provides useful information about the neurological status of the patient. However, there are limitations of the scale. For example, if the injured patient has sustained a spinal cord injury, the accuracy of the GCS score would be compromised. Additionally, once the patient has been taken to the emergency room and sedation has been given or the patient has been intubated (resulting in the patient not being able to speak), the results of the GCS are no longer meaningful.

Moreover, if the patient is a pre-verbal child or an infant, then the GCS would not be a useful instrument. If a patient has been diagnosed with "locked-in" syndrome, the GCS would not be appropriate. This may be the result of a brain stem lesion which is generally characterized by a disruption of the corticospinal and corticobulbar pathways which results in quadriplegia and

TABLE 1. Glasgow Coma Scale	
Eye opening (E)	
Spontaneous	4
To speech	3
To pain	2
No response	1
Best motor response (M)	
Obeys	6
Localizes	5
Withdraws	4
Abnormal flexion	3
Extends	2
No response	1
Verbal response (V)	
Oriented	5
Confused conversation	4
Inappropriate words	3
Incomprehensible sounds	2
No response	1
Coma Score = E + M + V	

TABLE 2. Children's Coma Scale	
Ocular response (O)	
Pursuit	4
Extraocular muscles intact, reactive pupils	3
Fixed pupils or extra ocular muscles impaired	2
Fixed pupils and extra ocular muscles paralyzed	1
Verbal response (V)	
Cries	3
Spontaneous respiration	2
Apneic	1
Motor response (M)	
Flexes and extends	4
Withdraws from painful stimuli	3
Hypertonic	2
Flaccid	1
Coma Score = O + V + M	

anarthria. In this case, the person would only be able to respond with an eye blink (Begali, 1987; Majerus, Gill-Thwaites, Andrews, & Laureys, 2005).

The GCS scores are frequently used as predictors of outcome for persons who have sustained a traumatic brain injury. The GCS score is used with other predictors such as length of loss of consciousness and time of posttraumatic amnesia to classify the severity of the traumatic brain injury. A score of 13–15 on the GCS is described as a mild head injury, a score of 9–12 is defined as a moderate head injury, and a score of 3–8 is reported to be a severe head injury (Begali, 1987).

Sterm (1996) was more specific in his description of head injuries and provided five different categories. A minimal head injury had a GCS of 15 with no loss of consciousness or amnesia. A mild head injury was characterized by a GCS of 14 or 15 plus amnesia, or a brief <5 min loss of consciousness, or impaired alertness or memory. A moderate head injury had a GCS of 9–13, or a loss of conscious greater than or equal to 5 min, or a focal neurological deficit. A GCS of 5–8 was a severe head injury, and a GCS of 3–4 was a critical head injury.

Children's Coma Scale—Raimondi and Hirschauer (1984) developed the Children's Coma Scale (CCS) to assess consciousness in infants and pre-verbal children under the age of 3. Motor, ocular, and verbal domains are assessed. Scores range from 3 to 11, with the higher the score the better the level of consciousness. The CCS does not require speech or visual localization to a stimulus and therefore can be used with infants as young as 1 month. In comparing the Glasgow Coma Scale (GCS), a score of 11 on the CCS is equivalent to a GCS score of 9–15, a score of 8–10 on the CCS is equivalent to 5–8 on the GCS, and a score of 3–7 on the CCS equates to a score of 3 or 4 on the GCS (Raimondi & Hirschauer, 1984). See Table 2 for the description of scoring criteria for CCS.

Coma/Near Coma Scale

According to Rappaport, Dougherty, and Kelting (1992), "The Coma/Near Coma (CNC) scale (given in Table 3) was designed to provide reliable, valid, easy, and quick assessment of progress or lack of progress in low-level brain injured patients (p. 629)." This is an instrument that can easily be taught to parents or caregivers who can then monitor the emerging process. With this assessment tool, small clinical changes can be observed. For parents or family watching their child in a coma, being able to look for small changes provides a sense of joy and a feeling of "helping" the emerging process. Monitoring of the coma status can also help determine appropriate placement settings.

TABLE 3. Coma/Near Coma Scale—Levels of Awareness

Level	Range	Level of awareness/responsivity
0	0.00–0.89	NO COMA: consistently and readily responsive to at least three sensory stimulation tests plus consistent responsivity to simple commands
1	0.90–2.00	NEAR COMA: consistently responsive to stimulation presented to two sensory modalities and/or inconsistently or partially responsive to simple commands
2	2.01–2.89	MODERATE COMA: inconsistently responsive to stimulation presented to two or three sensory modalities but not responsive to simple commands. May vocalize (in absence of tracheotomy) with moans, groans, or grunts but no recognizable words
3	3.00–3.49	MARKED COMA: inconsistently responsive to stimulation presented to one sensory modality and not responsive to simple commands. No vocalizations
4	3.50–4.00	EXTREME COMA: no responsivity to any sensory stimulation tests; no response to simple commands. No vocalization

Care should be taken not to administer the CNC score when the person has just received medication. Additionally, if the patient is sleeping, the CNC score should be administered at a later time. "Awake" would be characterized by eyes opening, yawning, postural or motor movements, etc. Whether or not the patient appears to be receptive to speech, when approaching the patient, speak encouragingly and supportively. The examiner should explain to the patient that he or she will be asking him or her to make simple responses. Instructions indicate that you request that the patient try to make the same response before the 2nd, 3rd, or subsequent trials. Before beginning the administration, observe the patient. Be aware of eye blink patterns, spontaneous movements, repetitive movement of extremities, mouth smacking, and level of agitation. As the person emerges from a coma, more agitation will be observed as more stimulation is provided.

The CNC score is comprised of 11 items, which are divided into 8 parameters: auditory; command responsivity, visual, threat, olfactory, tactile, pain, and vocalization.

Each stimulus can be presented on each side of the patient's body up to 3–5 times. Scoring options include a 0, 2, and 4, resulting in a range of scores from 0 to 4. The lower the score the better. A score of 0 is given for purposeful consistent responses. A 2 is given for inconsistent or generalized responses. A 4 is given if there is no response to the specific stimulus. The score and coma level are determined by adding the individual scores together, and then dividing that total by the number of items scored. For example, if the patient has a tracheotomy, the olfactory and vocalization portions would be omitted, and the total score would be divided by 9 instead of 11. The same would be true if the person has visual, auditory, or motor impairment that would interfere with this ability to respond to the stimuli. All stimuli are presented separately so that the response can be observed as a direct result of the presentation of the stimuli. For example, the evaluator would not talk and touch the patient simultaneously because if a response was provided, then the evaluator would not be able to determine if the response was a result to the vocalization or the touch.

The auditory portion is administered by ringing a bell for 5 s at 10 s intervals. A response would include eye opening or orientation toward the sound. A score of 0 would be given if the patient responded 3 or more times. If he or she responded inconsistently one or two times, a score of 2 would be given. A score of 4 is given if the patient does not respond. Command responsivity includes following commands, such as open or close your eyes, open your mouth, or move your hand, finger, or foot. Care must be taken to ensure that the person has the capacity to respond. For example, if the patient has a dense hemiparesis on the left side, one would not ask him or her to move his or her left hand. Responding to two or three commands results in a score of 0, while tentatively or inconsistently responding would yield a score of 2. A score of 4 is given if no commands are followed. A grasp reflex would not represent a meaningful response to a request; however, if the patient is able to let go of the evaluator's

hand on command, that would represent a good response.

Visual stimuli include light flashes, threat, and tracking. The light flashes includes shining a light in the patient's eyes for 1 s presented 5 times in different visual fields—front, slightly left, slightly right, and up and down each trial. A score of 0 is given if the patient sustained a fixation or avoidance for 3 or more times. A partial fixation of 1 or 2 times would result in a score of 2. No response would elicit a score of 4. If the patient is able to track consistently, a score of 0 is provided. A score of 2 would be provided if partial tracking (1–2 times) is given. No tracking receives a score of 4. A threat is administered by quickly moving a hand forward to within 1–3 inches of each eye. A score of 0 is given if the patient blinks consistently (3 times) to the threat. An inconsistent response of 1 or 2 blinks results in a score of 2. No blinks would result in a score of 4. When a score is determined by a blink response, be aware of differences in blink patterns and present the visual stimulus immediately after the person has blinked. With this in mind, the evaluator will be able to determine if the response is a result of the stimuli or normal blinking.

Responses to touch and pain are also assessed. Touch is evaluated by tapping the shoulder briskly three times on each shoulder without speaking to the patient. Before administering this portion, it is important to make sure that there are no shoulder injuries. An appropriate response would include head or eye orientation or movement of the shoulder in response to the tap. A 0 is given for consistent orientation to the response, a 2 for partial or inconsistent response, and a 4 for no response. A light touch is assessed by taking a swab and lightly touching the entrance only of each nostril (3 times). A consistent response (which is observed within 2 s) of withdrawing, eye blinks, or mouth twitch would receive a score of 0. A delayed or partial response observed 1 time would be scored as a 2. No response is scored as a 4. Pain is evaluated by putting pressure on the fingernail bed with the wood of a pencil and a robust ear pinch/pull. Consistent withdrawal or responses (2 or 3 times) would receive a 0. Responses may be slowed. Allow up to 10 s for the response. The degree of withdrawal may be dependent on the amount of tone that the patient is experiencing. Generalized responses or nonspecific movement would be scored as a 2. A 4 is given for no response.

The ability to respond to olfactory stimuli is assessed by placing a container of ammonia one inch under the nose for 2 s. A consistent withdrawal or observed response directly related to the stimulus, which occurs within 3 s, would be scored as a 0. A delayed response or grimace observed one time would be given a 2. No response received a score of 4. Spontaneous language results in a score of 0, nonverbal vocalizations (moans or groans) would receive a 2. No language production would be scored as a 4.

Clinical Use of Medication in Disorders of Consciousness

Ongoing research seeks to identify the most appropriate interventions to maximize functional recovery of coma patients. To date, reviews of the effects of medication treatment on recovery from prolonged impairments of consciousness have been limited in scope—frequently failing to include control groups and consisting of small samples. Difficulty developing controlled group design studies has often been reported due to the heterogeneity of injuries, especially in the brain-injured population. This has led to a great deal of current literature consisting of single case, small group, or observational studies. Additionally, studies have difficulty controlling for possible drug interactions because many of the patients receive numerous medications either simultaneously or sequentially during the course of recovery. With these limitations in mind, several classes of drugs have been reported to improve outcome including dopaminergic agents, stimulants, lamotrigine, tricyclic antidepressants, and serotonin reuptake inhibitors.

A body of literature is accumulating which suggests that amantadine hydrochloride may improve recovery after brain injury. Amantadine hydrochloride is a water-soluble salt that is capable of penetrating the blood–brain barrier and is thought to facilitate brain recovery through its pre- and post-synaptic affects on dopamine. It was initially developed for use as an anti-influenza agent. Amantadine's influence on neurorecovery was initially studied through retrospective reviews and more recently in randomized controlled trials for patients with

traumatic brain injury (TBI) associated with diffuse axonal injury (DAI). Nickels, Schneider, Dobovy, and Wong's (1994) retrospective review suggested eight of nine "low-arousal subjects" displayed increased responsiveness to amantadine. Areas of improvement most consistently noted included increased orientation, purposeful movements, initiation, verbalization, and sequencing skills. Etiology was mixed for the low-arousal group with the majority of the cases resulting from trauma and two cases due to aneurysm. No definitive relationship was found between the time post-onset of injury that amantadine was initiated, nor was responsiveness affected by the speed with which amantadine was titrated. The authors noted minimal side effects with the majority of the cases. In a single case study (Zafonte, Watanabe, & Mann, 1998) of a TBI patient in a minimally conscious state for 5 months prior to initiation of amantadine, the patient demonstrated a dose-dependent positive response to the medication. However, some studies have found no significant difference between subjects receiving amantadine compared to those receiving placebo (Giacino & Trott, 2004; Schneider, Drew-Cates, Wong, & Dombovy, 1999).

In a pilot double-blind randomized trial of 35 DAI associated TBI patients, Meythaler, Brunner, Johnson, and Novack's (2002) findings suggest that patients seemed to improve more rapidly while they were on amantadine. A consistent upward trend was noted for more functional improvement no matter when, during the first 3 months after injury, amantadine was initiated. Limitations in interpreting the efficacy of amantadine in Meythaler et al.'s study were noted by Giacino and Whyte (2003) due to concerns with compromised differences in baseline prognosis between treatment groups and design construction. A multicenter study of the medication effects found that amantadine was associated with greater recovery in prolonged posttraumatic disorders of consciousness (Whyte et al. 2005). Participants ($n = 124$) were individuals with TBI who were in a vegetative or minimally conscious state 4–16 weeks after injury. Those patients who received amantadine demonstrated significant improvement as measured by Disability Rating Scale (DRS) scores during the week of or the week after administration was initiated. The authors propose that for those patients that do regain consciousness, amantadine may possibly influence the overall pace of recovery rather than the time of recovery. Studies of other agents such as levodopa (Haig & Ruess, 1990; Lal, Merbitz, & Grip, 1988) and bromcriptine (Passler & Riggs, 2001) have been associated with facilitation of initiation in a limited number of small case studies.

Psychostimulants have generated interest in the TBI population and are widely used for facilitating arousal, attention, and related neurobehavioral difficulties resulting from TBI (Whyte, Vaccaro, Grieb-Neff, & Hart, 2002). Methylphenidate is a psychostimulant medication that was originally used for the reversal of barbiturate-induced coma and is now primarily used to treat symptoms of Attention-Deficit/Hyperactivity Disorder. The exact known mechanisms of methylphenidate's behavioral effect on the brain are lacking. It has been hypothesized that amphetamines may provide neurostimulation by augmenting activity of injured neuronal tissue in the reticular activating system and inhibiting dopamine reuptake (Worzniak, Fetters, & Comfort, 1997). A majority of literature on methylphenidate's efficacy in the recovery of brain injury is related to the post-acute phase of recovery; it has also been associated with significant improvement in attention in adults after TBI (Kaelin, Cifu, & Matthies, 1996) and children after TBI (Mahalick et al., 1998); motor recovery after stroke (Walker-Batson, Smith, Cutis, Unwin, & Greenlee, 1995); and beneficial effect on cognitive processing speed and behavioral ratings of attentiveness after moderate to severe TBI (Whyte et al., 2002, 2004).

There is limited information regarding the influence of methylphenidate on patients in comatose or semicomatose states. Two cases of methylphenidate trials for minimally conscious patients with TBI are reported by Laborde and Whyte (1997). In one case, the drug was not found to demonstrate a positive effect and was discontinued, while in the other a positive drug response was reported for increased response rate to command-following tasks. Another study reported that methylphenidate appeared to improve rate of recovery but not the ultimate level of recovery (Plenger et al., 1996). A recent evidence-based review (Forsyth & Jayamoni, 2003) concluded that there was insufficient evidence to support routine use of methylphenidate

or other amphetamines to promote TBI recovery. These authors used the following criteria to examine the methodological quality of studies: baseline comparison of experimental groups, explicit diagnostic criteria, allocation concealment, and completeness of follow-up, blind outcome assessment and blind administration of the drug. It was noted that none of the studies met all aspects of inclusion criteria and that studies require replication in larger groups that address a broader range of severely injured patients and children.

A limited number of studies with lamotrigine, tricyclic antidepressants, and serotonin reuptake inhibitors (SSRI) have also been related to increased arousal and initiation. Emerging data from animal studies indicate that lamotrigine's blockage of sodium channels and inhibition of glutamate release may provide neuroprotection after cerebral ischemia (Schuaib et al., 1995). In an uncontrolled case study ($n = 13$), Showalter and Kimmel (2000) noted that lamotrigine appeared to stimulate consciousness and cognition in patients who were already indicated for an anticonvulsant. Tricyclic antidepressants are to varying degrees epileptogenic and should be utilized with caution in a brain injury population. Reinhard, Whyte, & Sandel (1996) reported improved arousal and initiation with three patients after initiation of tricyclic antidepressants. A small ($n = 11$) controlled, randomized study was inconclusive in establishing whether the SSRI sertraline improves arousal and alertness in patients with TBI and associated DAI (Meythaler, Depalma, Devivo, Guin-Renfroe, & Novack, 2001). Mild sedation through medically induced coma has been utilized for brain-injured patients at risk for intracranial hypertension. Barbiturate coma therapy is indirectly related to reduction of intracranial pressure and improved ventilation (Montes, Wong, Fayad, & Awad, 2000).

In addition to studying the therapeutic benefits of medication, several studies have reported adverse effects of medication on brain recovery. Most of these studies include animal data and focus on cerebral ischemic models that may not apply to other coma-related incidences (Whyte et al., 2005). Drugs with potentially negative effects to outcome included phenytoin (Brailowsky, Knight, & Efron, 1986), diazepam (Schallert, Hernandez, & Barth, 1986), and haloperidol (Feeney, Gonzalez, & Law, 1982).

Additionally, Whyte et al's (2005) longitudinal observational study of TBI patients points to dantrolene sodium as having potential negative influences on recovery.

Treatment Effects

There are limited evidence-based reviews of the effects of treatment on recovery from prolonged impairments of consciousness (Whyte et al., 2005). Studies have addressed the possible influence of sensory stimulation and deep brain stimulation. Sensory stimulation was introduced in the early 1950s as a means to provide synaptic rejuvenation by increasing environmental inputs through all five sensory pathways. By reducing "environmental deprivation," stimulation was purported to enhance the rate and degree of recovery (as cited by Lombardi, Taricco, De Tanti, Telaro, & Liberati, 2002; p. 465). Studies varied in the administration of stimulation, with some sessions involving all five modalities vigorously stimulated for a 20 min period (Johnson, Roething-Johnston, & Richards, 1993) to a cycle of intervention that lasted for a period of 60 min (Mitchell, Bradley, Welch, & Britton, 1990). In 1991, Wood proposed a sensory regulation approach that regulated the way stimulation was delivered. Wood suggested that controlling for an overabundance of noise in the patient's environment was important in the role of recovery from coma. However, in a systematic review, Lombardi et al. (2002) concluded that there is no evidence to support coma stimulation programs. In Lombardi et al.'s (2002) review, only 3 of 25 published articles met criteria for review as randomized and controlled clinical trials.

Deep brain stimulation (DBS) therapy involves a surgical implant of a medical device into a specific area of the brain that sends electrical impulses to the brain. Yamamoto and Katayama's (2005) review discussed the tracking for 10 years of 21 cases of individuals in a vegetative state who were treated by DBS therapy. Their findings discussed the potential that DBS may facilitate emergence from the vegetative state if patients are selected based on selected criteria. For two of the participants, the mesencephalic reticular formation was selected as the target for stimulation and in the other 19 the thalamic center complex was targeted for stimulation. The authors suggest that DBS also may

be useful in the emergence from the bedridden state by patients in a minimally conscious state. However, similar to other rehabilitation treatment studies, findings are limited by the lack of adequately sized random controlled trial studies.

Neuroimaging and Electrophysiological Techniques

Neuroimaging techniques have been used for diagnostic consideration in some populations of comatose patients and may have a prognostic value (Stevens & Bhardwaj, 2006). Electrophysiological techniques have shown limited diagnostic capability but have emerged as a useful tool in the prognostication of comatose patients. The use of multiple brain-imaging techniques along with electroencephalography may offer an integrative view of the damaged brain and allow a clearer understanding of the underlying mechanisms of neurological disorders. Additionally, in the future these techniques may provide useful correlates of the differences between minimally conscious and vegetative states that are not evident from behavioral evaluations that will assist in the diagnosis, prognosis, and application of therapeutic interventions.

Computed Tomography (CT)

CT scans allow for the visualization of brain anatomy to determine structural differences, and the presence of focal lesions and tumors. CT of the brain is warranted in most cases of acute onset of unexplained coma but has been less beneficial in cases of hypoxic-ischemic or toxic-metabolic coma (Stevens & Bhardwaj, 2006). These authors caution that the benefit of information provided by CT should be weighed against the risks of transporting a critically ill patient outside of the intensive care unit.

Magnetic Resonance Imaging (MRI) and Functional MRI (fMRI)

MRI allows for noninvasive investigation and visualization of brain tissue with a clarity superior to that of CT scans. MRI is recommended in cases with unexplained coma and normal or unclear CT findings (Stevens & Bhardwaj, 2006). In terms of research, MRI

may be useful in identifying the structural boundaries of lesions that cause loss of consciousness. In a retrospective study where MRIs were obtained for 47 patients with brain stem stroke, Parvizi and Damasio (2003) observed differences between patients with coma and without coma. Of the 38 patients that did not have coma, damage was outside or limited to a small area of the tegmentum. Of the nine patients with coma, a majority showed bilateral lesions in the tegmentum and lesions were located primarily in the pons, or in the upper pons and midbrain.

Functional MRI (fMRI) allows for the mapping of cerebral blood flow or volume, as well as changes in cerebral blood volume, flow and oxygenation. It is a relatively new technique that is primarily used for research purposes. In a study that compared the fMRI maps of two male adults with brain injury leading to MCS and seven healthy participants, Schiff et al.'s (2005) findings suggest that functional imaging may provide evidence of distinct differences between the underlying physiology of the MCS brain and the VS brain. Activation patterns in the prefrontal, parietal, and occipital regions of the MCS brain suggest awareness that has been lacking in functional PET scans for those in the vegetative state. Because fMRI relies on several mechanisms that are generally abnormal under the pathological conditions of coma that result in a high failure rate, a negative fMRI scan should not be used as diagnostic proof of a vegetative state (Pickard, 2004).

Positron Emission Tomography (PET) and Functional PET (fPET)

Fluorodeoxyglucose PET scans allow for the visualization of brain metabolism. As glucose radioisotopes emit decay signals, the quantity is measured to indicate the level of brain activity in a given area. The overall cerebral metabolism is between 40 and 50% below normal levels in vegetative state and persistent vegetative state brains (Schiff et al., 2002; Laureys et al., 2004). It is unclear whether cerebral metabolic depression is due to irreversible structural neuronal loss or functional and possibly reversible damage (Laureys et al., 2004). When patients later recover awareness, there is improvement in cortical metabolism and connectivity of

previously affected cortical areas. A recent study has shown evidence that high-level residual auditory processing exists and remains persistent across time in a PVS patient (Owen et al., 2005). Boly et al. (2005) compared PET data for MCS and VS patients induced by auditory and noxious stimuli. In VS patients, no significant activation was found in higher order association areas for both pain processing and auditory processing. MCS patients, in contrast, showed activation similar to controls in response to stimuli. Locked-in patients appear to have near-normal cerebral glucose metabolism reflecting their conscious state (Levy et al., 1987).

Electroencephalography (EEG)

EEG is a tool that allows for continuous monitoring of the brain's functioning to be examined indirectly through the study of electrical activity as manifested in brain waves. Four waveforms have EEG patterns that have been studied in a few VS and MCS state patients with limited conclusive findings. A range of abnormalities has been noted with most patients in VS showing a significant slowing of delta rhythms that do no respond to sound, pain, and light stimuli (Hansotia, 1985). There is some evidence that improving alpha bands are associated with awareness; however, improving alpha and theta patterns and reduction in delta activity have not consistently correlated with clinical improvement. Because EEG provides a means to identify and monitor seizure activity, it may be beneficial in determining if control of seizure activity has been achieved in drug-induced coma (Young, 2000). It is also beneficial in monitoring subclinical seizure activity to reduce potential secondary brain injury in high-risk patients following head injury, ischemia, and meningitis/encephalitis (Jordan, 1999).

Significant variability has been found in EEG readings, especially in children and neonates. Limitations to EEG use include high sensitivity to electrical environmental noise, alteration by medical drugs, and an inability to test the brain stem. Because interpretation of raw EEG data requires specialized training and considerable time, the bispectral index (BIS) of the EEG may be as useful as a nonspecific measure of consciousness (Schnakers, Majerus, & Laureys, 2005). The BIS is a statistically derived variable of the EEG that is expressed as a score between 0 (totally suppressed EEG) and 100 (fully awake EEG). Schnakers et al. (2005) found that BIS values demonstrated a progressive increase as brain-injured patients went from coma to VS to MCS to emergence from MCS.

Evoked Potentials

Evoked potentials are similar to an EEG but examine discrete firing patterns of single cells or cell clusters. An evoked potential is recorded using electrodes connected to a microcomputer and amplifier. Because evoked potentials record direct responses to external sensory stimulation, they are considered to be relatively free from influence of the higher cortical processes believed to be necessary for awareness. Brain stem auditory evoked potentials (BAEPs) evaluate the functional condition of the brain stem, and somatosensory evoked potentials (SEPs) evaluate the primary sensory cortices. EPs can contribute to the identification of post-trauma cases that are primarily due to midbrain dysfunction (Guérit, 2005).

Event-Related Potentials (ERPs)

ERPs are long latency potentials that rely on a greater complexity of neural connections than do sensory-evoked potentials. These electrical waveforms are commonly associated with the associative areas of the cortices. P300 potentials are generally measured in patients with some degree of awareness but are not useful for diagnostic and prognostic indicators of VS (Laureys et al., 2004). Studies using P300 potentials have shown activation to auditory stimuli (Laureys et al., 2004; Perrin, et al., 2006). Similarly, the auditory system of MCS patients appears to be delayed but preserved in response to passive tones (Boly et al., 2004), language stimulation (Schiff et al., 2005), and semantic processing (Perrin et al., 2006). Perrin et al. concluded that a P300 response does not clearly reflect conscious perception or awareness and does not clearly differentiate locked-in state from MCS of VS patients. Mismatch negativity (MMN), one of the earliest and most robust ERP components is proposed as a viable measure of awakening because it does not require the voluntary attention of the patient (Fischer et al., 2006). MMN is an ERP that is generated in the

superior temporal plane and is generally accepted as reflecting a pre-cognitive response to a deviant sound in a repetitive sequence (Fischer & Luaté, 2005).

Prognosis

The prognosis for awakening and nonawakening is critical to facilitate treatment options and to provide families with accurate information. Current trends in ethical decision making also point to the need for accurate and timely prediction of reversibility of brain injury. Studies regarding the prognosis for awakening have provided information based on several clinical factors, which are discussed below. After reviewing published data on recovery, the Multi-Society Task Force (MTF) proposed that prognoses for recovering awareness only be expressed as probabilities with confidence intervals (Multi-Society Task Force, 1994). Additionally, the Aspen Neurobehavioral Conference Workgroup (1996) emphasized that the term "permanent vegetative state" refers to a prognosis that identifies a point after onset of coma in which the likelihood of recovery of consciousness is highly improbable but not impossible (Giacino et al., 2002).

Etiology. The underlying etiology largely determines the prognosis of coma outcome. Cause of injury is a strong predictor of outcome from VS and non-TBI patients demonstrating a greater severity of disability after 1 year and a shorter window for recovery (Giacino & Kalmar, 2005). The Multi-Society Task Force reported that of those patients with traumatic causes of coma, at 1-year post-onset, there is a 33% mortality rate, and approximately 15% are in a persistent vegetative state, 28% have severe disability, 17% have moderate disability, and 7% have good outcome (MTF, 1994).

In a study of 319 TBI patients with a broad spectrum of coma duration (from 0–225 days), Wong, Monette, and Weiner (2001) developed a mathematical model to express cognitive recovery. They found that the initial level of deficit in TBI is influenced by the severity of head injury as represented by days in coma. Verbal IQ was found to recover almost four times faster than Performance IQ; it takes 34.7 days for TBI patients to recover half of the initial verbal deficits and 131.7 days to recover half of the initial

visual–spatial deficits. Limitations of this study were that one third of the database were excluded, as they were unable to complete the intelligence measure.

The Multi-Society Task Force also reported poor outcomes for many patients with a hypoxic-ischemic coma. At 1 year after onset of coma, there was a 53% mortality rate, with approximately 32% in PVS and only 15% were reported to have awakened (MTF, 1994). In postanoxic coma patients, awakening is more difficult to predict than nonawakening (Robinson, Micklesen, Tirschwell, & Lew, 2003). Relatively few patients who lack pupillary and corneal reflexes at 24 h and have no motor response at 72 h will awaken (Booth, Boone, Tomlinson, & Detsky, 2004). Anoxic brain damage is frequently considered the most severe in terms of damage, decreased brain metabolism and poor prognosis. It is hypothesized that anoxia results in irreversible neuronal loss (Adams, Graham, & Jennett, 2000), while other etiological subgroups may experience decreased neuronal loss that results in partial regeneration of axons over time (Kotchoubey, 2005).

Coma status. The Multi-Society Task Force (MTF) concluded that the prognosis for recovering from vegetative state or non-traumatic (especially hypoxic-ischemic) coma is worse than for traumatic brain injury (The Multi-Society Task Force, 1994). The longer a patient remains in a vegetative state, the less likely they are to regain awareness. The MTF found that the probability of recovery of awareness is less than 1% after 3 months for a non-traumatic vegetative state or after 12 months in a traumatic vegetative state. Limitations to these findings include the small number of patients alive in a vegetative state after 12 months and evidence of cases where late recovery of awareness occurred outside of the MTF parameters. In addition, the MTF addressed life expectancy; however, limitations were noted due to the wide range of treatment given to patients. Mortality of the vegetative state was 70% at 3 years and 84% at 5 years. The MTF noted that many of the patients died of potentially treated causes but were not given the most aggressive life-sustaining treatment that, as argued by Shewmon (2000a), creates a potential for a self-fulfilling prophecy.

Few outcome predictors have been identified for those in a minimally conscious state because criteria for this condition were only

recently introduced (Giacino, 1997). Patients in MCS, relative to those in VS, appear to demonstrate improvement over a longer period of time and achieve a better functional recovery (Giacino & Kalmer, 2005). In a retrospective comparative analysis of outcome, 50% of MCS patients had "no disability" to "moderate disability" at 1-year post-injury on the Disability Rating Scale (DRS), while only 3% of VS patients received similar ratings (Giacino & Kalmar, 1997). Also, while none of the patients in the traumatic MCS group had scores in the "VS" or "extreme VS" categories, 43% of the patients in VS fell in this category 1-year post-injury.

The mortality rate for locked-in syndrome (LIS) was estimated at 60%, with risk being greatest in the first 4 months (Patterson & Grabois, 1986). The most frequent cause of death is respiratory failure, and mortality rate was higher with vascular insult. Re-emergence of horizontal pursuit of eye movement in the first 4 weeks increases the likelihood of a positive outcome (Chia, 1991). The mortality rate of LIS may be reduced by early rehabilitation and effective nursing care (Casanova, Lazzari, Latta, & Mazzucchi, 2003). Mortality was reduced to 14% at 5 years post-injury when patients began rehabilitation within 1 month of acute injury. Most survivors are severely impaired or in a chronic locked-in state (Smith & Delargy, 2005).

Clinical Signs. Time post-injury, current functional level, and rate of functional change are primary predictors of the return to consciousness (Whyte, et al., 2005). Giacino and Whyte (2005) report that the degree of long-term impairment lags behind current knowledge and ability to predict return to consciousness. While the visual pursuit behaviors are observed in both MCS and VS patients, the incidence was significantly higher in the MCS than the VS patients (Giacino & Kalmar, 1997). Of those VS patients with intact visual pursuit, 73% recovered other signs of consciousness by 12 months as opposed to 45% of those VS patients without pursuit. Rate of change in recovery has been shown to be predictive of outcome relative to static ratings (Giacino et al., 1991; Giacino, 2005; Whyte et al., 2005). Absent motor responses on the GCS, absent papillary responses, and absent corneal reflexes are predictive of death or VS (Zandbergen, de Haan, Stoutenbeek, Koelman, & Hijdra, 1998; Booth et al., 2004). Similarly, in children with severe diffuse brain injury, a combination of the GCS sum scores and horizontal oculocephalic reflex predicted poor outcome (Pillai, Praharaj, Mohanty, Sastry, & Kolluri, 2001). Shiel and Wilson (2005) noted that recovery of certain behaviors observed in the early stages of severe post-traumatic brain injury may be predictive of outcome. Time taken to achieve five behaviors may be predictive of overall outcome: obeying commands, watching someone move in the line of vision, looking at a person giving attention, turning head to look at a person talking, and focusing on a person talking.

Electrophysiologic Tests and Neuroimaging. CT patterns that have been shown to be predictive of poor outcome include lesions in the brain stem and diffuse axonal injury (DAI). Grade III DAI is associated with an increased probability of prolonged or permanent VS (Kampfl et al., 1998; Jennett, Adams, Murray, & Graham, 2001). MRI findings indicate that lesions in the corpus callosum and dorsolateral brain stem are strongly predictive of poor outcome (Kampfl et al., 1998). Currently, there is no established correlation between lowered brain metabolism and patient outcome (Laureys et al., 2004).

In patients with post-anoxic coma, EEGs with a burst suppression pattern are associated with poor outcome (Zandbergen et al., 1998). Also, somatosensory-evoked potentials (SEP) are predictive of outcome, especially poor prognosis. The absence of bilateral cortical SEP during the first week of anoxic coma was specific 100% of the time for identifying poor outcome (Zandbergen et al., 1998, Robinson et al., 2003). A further study refined this guideline to after a coma of at least 72 h, bilateral absences of early cortical response (N20 of the median nerve) in SEP appears to be the most reliable variable for predicting poor outcome in anoxic-ischemic coma (Zandbergen, de Haan, Koelman, & Hijdra, 2000). SEP has a weak prognostic value for awakening; however, the presence of mismatch negativity (MMN), the earliest component of event-related potentials, precludes comatose patients from progressing to a PVS (Fischer & Luaté, 2005), and is highly predictive of awakening (Fischer et al., 1999) in post-anoxic coma. However, Guérit (2005) argues that MMN evaluates brain function that is too primitive to provide information on residual cognition, and their absence is not sufficient to predict awareness. Bilateral absent cortical responses in adults

with traumatic coma predict a 2–7% chance of awakening, and approximately 1% of those patients have a better-than-severe disability outcome (Robinson et al., 2003).

Brain stem auditory evoked potential (BAEP) has primarily been studied with TBI patients. Attia and Cook (1998) noted that an absence of activity in the upper pons and midbrain was predictive of brain death or vegetative state. Poor outcome is prognosticated when BAEPs are abnormal (Fischer et al., 1999); however, normal values provide no prognostic information (Fischer & Luaté, 2005) and are not predictive of PVS (MTF, 1994). Shewmon's (2000b) comprehensive review of coma prognosis in children indicated that major abnormalities in the EEGs of neonates is predictive of a neurologic deficit or death while EEGs and EPs in children have a similar utility to that of adult prognosis.

Developmental Considerations. The risk for developing and recovering from VS differs in children from adults (Ashwal, Eyman, & Call, 1994), especially when consideration is given for the varying etiologies. With traumatic injury, in comparing children as a group to adults as a group, children appear to have a greater positive outcome than adults, given similar degrees of initial brain injury and depth of coma (Shewmon, 2000b). Additionally, improvement may continue over an extended period of time in comparison with adults (Boyer & Edwards, 1991). Some studies have shown that outcome in young children with TBI is poorer than in school-age children and adolescents (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2000), and for young children with inflicted TBI, the outcome is extremely poor (Prassad, Ewing-Cobbs, Swank, & Kramer, 2002).

The Multi-Society Task Force (1994) estimated the probability of recovery of consciousness and function in children who were in a vegetative state 1-month posttraumatic or nontraumatic injury. Additionally, probability was estimated at 12 months for those children who remained vegetative at 3 months and 6 months. For those children in VS 1-month posttraumatic injury, 24% had regained awareness by 3 months. At 1 year, 81% were alive of which 29% remained in VS. Children in VS due to non-traumatic injuries have a much poorer prognosis for recovery of consciousness and function.

For those children in a vegetative state due to progressive diseases or severe congenital brain malformations, it is unlikely that they will regain consciousness (Ashwal, 2005). The Multi-Society Task Force reported that of children in a vegetative state at 1-month post non-traumatic brain injury, only 11% had regained awareness by 3 months. At one year, of the 78% who were alive, 65% remained in a vegetative state. Shewmon (2000a) cautions against the MTF findings due to concerns regarding extrapolation of pooled data that was not specifically collected at the 3-, 6-, and 12-month intervals and further urges against the "lumping" of outcome categories and age groups when studying coma prognosis in children.

Other factors may also play a role in prediction of outcome and life expectancy in children. While life expectancy was not a factor in comparing children that lived at home with those living in an institution, life expectancy was slightly less for those children living in private hospitals and skilled nursing facilities (MTF, 1994; Ashwal, 2005). There appears to be an upward trend toward longer life expectancy in more recently diagnosed VS patients in children aged 2–10 years (Strauss, Shavelle, & Ashwal, 1999). Current literature is limited regarding the prognosis for children in MCS. Strauss, Ashwal, Day, & Shavelle's (2000) study suggests that mobility may be a better predictor of survival in children than the presence of consciousness, with 81% of mobile MCS patients surviving 8 years and a smaller percentage of immobile MCS and VS patients surviving over the same time period (65 and 62%, respectively).

Outcome Measures

Initially after an injury, the family is focused on whether their loved one will survive, and they wait cautiously and hopefully during those first 24 or 48 critical hours. Then as the time passes, the family becomes more focused on the recovery process. Several measures have been developed that allow the family to track the healing process and monitor recovery. The Rancho Los Amigos Scales, Disability Rating Scale, and WeeFIM System have been found to be helpful. All of the measures begin when the patient is in a coma and non-responsive and move through the

recovery process, ultimately exhibiting purposeful and appropriate behaviors independently.

Rancho Los Amigos Scales—The Rancho Los Amigos Level of Cognitive Functioning Scale was originally developed in 1972 by Hagen, Malkmus, and Durham at the Rancho Los Amigos Hospital in California. The measure was used to report progress of patients during this initial phase of recovery and was not intended to serve as a predictor of long-term outcome. The original scales consisted of eight levels, with Level 1 being the lowest and 8 being the highest. Many times, the patient will be in more than one level at a time. The speed at which one travels through these phases changes with the recovery speed of the patient. Levels 1–3 would be consistent with coma, vegetative state, and minimal conscious state. Level 1 is no response. In this level, the patient does not respond to voice, sound, light, or touch and appears to be in a deep sleep. Level 2 consists of generalized responses. In this phase, the patient has limited, inconsistent, non-purposeful responses. The patient may be in a sleep–wake cycle and initial responses will be to deep pain. In Level 3, the patient has more purposeful responses, although they may be inconsistent and automatic. The patient may begin to focus on objects or faces and inconsistently follow simple commands. As the patient moves to Level 4, he or she is observed to be highly agitated, confused, and disoriented. Aggressive behaviors may be observed. The patient remains confused in Levels 5 and 6. However, in Level 5, the patient may exhibit inappropriate non-agitated behavior that improves to appropriate behaviors in Level 6. In Level 7, the patient has automatic behaviors that allow him or her to perform routine activities with minimal confusion. The person may lack initiation, and have poor judgment, planning, and problem-solving abilities. Behaviors become more purposeful in Level 8. At this state, the patient is able to learn new activities and live independently. Problems with abstract reasoning and judgment may persist. Subsequently, Levels 9 and 10 were added. In Level 9, one is purposeful and appropriate. Although the person may be able to independently shift between two tasks and accurately complete them, low frustration may be noted and stand-by assistance may be required to help with problem solving, self-monitoring of behaviors, and determine appropriate consequences. By Level 10, the person is able to complete multiple tasks with modified independence.

Disability Rating Scale (DRS)—The Disability Rating Scale developed by Rappaport, Hall, Hopkins, Belleza, and Cope (1982) has been found to provide clinical usefulness in rating a patient's level of disability. It is divided into four categories: (1) arousability, awareness, and responsivity (including eye opening, communication ability, and motor response); (2) cognitive ability for self-care (including feeding, toileting, and grooming); (3) dependence on others; and (4) psychosocial adaptability. Scores range from 0 to 29 with 0 representing no level of disability and 25–29 representing an extreme vegetative state. Further breakdown of disabilities are as follows—DR Score 1: Mild; DR Score of 2–3: Partial; DR Score of 4–6: Moderate; DR Score of 7–11: Moderate Severe; DR Score of 12–16: Severe; DR Score of 17–21: Extremely Severe; and DR Score of 22–24: Vegetative State.

FIM-WeeFIM—The FIM was developed by a task force of the National Institute on Disability and Rehabilitation Research (NIDRR) and the American Congress of Rehabilitation Medicine (ACRM) in 1983. This 18-item instrument measures functioning ability in the areas of self-care, bowel and bladder management, locomotion, transfers, communication, and social cognition. The WeeFIM System (1998) is a functional assessment for use with children and adolescents with special health care needs. It is used with children who have functional and developmental delays from ages 6 months to 21 years of age. For non-disabled children, it is to be used with children from age 6 months to 7 years. Functioning skills are rated on a scale from 1 to 7, with 1 reflecting total assistance and 7 indicating complete independence. Use of the WeeFIMS allows parents and rehabilitation experts to communicate about a child's functioning level and chart progress.

Parent Education

Parent or caregiver education begins as soon as the patient has been stabilized. The more information that the caregiver is provided, the more equipped they are to make appropriate decisions. It should be noted that different people approach these difficult situations in different

manners, and care should be given to provide the information as they are able to process it. However, once the initial critical time is over, sharing of relevant information is important to be able to make appropriate decisions about care and follow-up. Once the patient is stabilized, caregivers remain hopeful that recovery will occur. As the time goes by and the patient remains in an altered level of consciousness, it becomes important to provide the caregivers with appropriate education to take care of their loved one and provide an appropriate environment. During this time, support is given to the caregivers from a multi-disciplinary staff who teach range of motion, physical care, medications, monitoring of coma status, and emotional support. Providing this information to the caregiver helps them feel that they are helping their loved one "get better" and is an important step in helping the family process their own feelings. As Lezak (1986, p. 247) describes, "Unlike a death, there are no social support or institutional rituals for this mourning." Additionally, with this training and information, caregivers are equipped to make long-term decisions about future care.

Conclusion

Having a loved one in an unconscious state or altered state of consciousness is difficult at best. This chapter has focused on the different levels of consciousness, with the hope of providing the reader with information as to the different states of consciousness, different tools that are available to measure levels of consciousness, the medication that can be helpful in the management, and the prognosis. With this information and family education, appropriate decision regarding care can be provided.

Ethical Considerations

Medically futile treatment has generally been accepted as treatment that would produce outcomes no better than VS, with no awareness achieved (MTF, 1994). It has been cited as the most common ethical issue involving unconscious patients (Young, 2000; Giacino & Whyte, 2005). Diagnostic inaccuracy has the potential to lead to "an overly pessimistic prognosis, limit accessibility to medical and rehabilitation services and inappropriately influence end of life decision-making" (Giacino & Kalmar, 2005, p. 166). While end-of-life decision making is beyond the scope of this chapter, it appears clear that prediction of neurologic outcome is a key concern in the management of patients with disorders of consciousness. Providing accurate prediction of the degree of long-term impairment for individual patients will facilitate early decision making regarding the aggressiveness of care. Additionally, research on treatment outcomes is limited but vital to providing evidence-based interventions to patients in need.

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31

Neuropsychological Aspects of Pervasive Developmental and Autism Spectrum Disorders

PRISCILLA A. BADE-WHITE, JOHN E. OBRZUT, AND PHILIP P. RANDALL

Autism is a complex pervasive developmental disorder (PDD) associated with substantial impairments in terms of social deficits, communication abnormalities, stereotypical and repetitive behaviors, and a wide range of clinical presentations (Cody, Pelphry, & Piven, 2002). The presentation of symptoms in autism varies greatly between individuals making differential diagnosis difficult. Furthermore, the uneven cognitive and behavioral profiles make it a unique and complicated condition. To facilitate better understanding of such complexities, researchers have focused on uncovering its etiological factors, identifying involved brain structures and processes, categorizing actual symptoms and its behavioral manifestations, and examining its neuropsychological basis. There is strong evidence from neuropathological studies that ASD originates in early prenatal life from abnormal brain development (Kemper & Rodier, 2002) and that atypical neurodevelopment continues to evolve throughout early life (Courchesne, Carper, & Akshoomoff, 2001; Zwaigenbaum et al., 2005). A substantial literature base exists on the neuropsychological underpinnings of autism albeit somewhat complex and

inconsistent (Dawson, 1996). With this in mind, this chapter reports on some of the neuropsychological findings on ASD and pervasive developmental disorders.

Diagnostic Criteria

Although the knowledge base of autism has expanded significantly, its etiology remains somewhat elusive. At present, no biological markers have been found for the disorder. As such, it is typically defined in terms of observed behavioral characteristics (Bryson & Smith, 1998). As a reflection of the expanding knowledge base, the diagnostic criteria for autism have changed over the years. Despite these revisions, two of the core features described by Kanner (1943) remain the same. These are (a) the "obsessive insistence" for sameness and (b) the characteristics of self-isolating behaviors (Happe & Frith, 1996). Currently, the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV, American Psychological Association [APA], 1994) delineates three primary diagnostic criteria, which include qualitative impairments in social relationships and reciprocal interactions, qualitative impairments in verbal and nonverbal communication, and the presence of stereotyped and/or repetitive behaviors. Further, these criteria must present prior to 3 years

PRISCILLA A. BADE-WHITE, JOHN E. OBRZUT, AND PHILIP P. RANDALL • College of Education, University of Arizona, Tucson, Arizona 85721.

of age and cannot be better explained by other PDDs. Although not a diagnostic requirement, up to three quarters of persons with autism have mental retardation (IQ scores below 70) as well as a variety of co-occurring medical (Lockyer & Rutter, 1970) and/or psychological conditions (APA, 1994).

Prevalence rates ranging from 2 to 20 cases per 10,000 individuals have been reported with males being 4–5 times more likely to develop the disorder than females (APA, 2000). This estimate, however, seems conservative given that the current estimate of preschool children with autism is 1 in 250 (Bertrand et al., 2001; Bryson & Smith, 1998; Chakrabarti & Fombonne, 2001). The reason for this increase in prevalence remains controversial (Centers for Disease Control [CDC], 2005); assertions include heavy metal toxicity (Wakefield, 1999), improved diagnostics, and increased awareness (Fombonne, 2003), or they remain unsure of the reason (CDC, 2005).

Differential Diagnosis

Asperger's Disorder

One year following Kanner's (1943) account of early infantile autism, Hans Asperger (1994/1991) published a study describing four boys who displayed similar behavior to Kanner's children. Asperger noted that the boys demonstrated fluent linguistic skills, but had irregular voice prosody, used unusual nonverbal communication, had an unbending desire for routine or sameness, and engaged in repetitive behaviors (Meyer & Minshew, 2002). However, it was not until the early 1990s when his research was translated into English that it began to gain attention (Morris, Morris, & Bade-White, 2005). Consequently, this pattern of behavioral manifestations, known as Asperger's disorder, was added to the DSM-IV in 1994.

The publication of Kanner's (1943) and Asperger's (1944/1991) studies sparked a long-running debate concerning the distinctiveness of the two disorders. Although most authorities agree that differentiating features distinguish the disorders, there has been no consensus as to what these are. It has been argued that individuals with autism who have IQ scores over 70 (high-functioning autism, HFA) are indistinguishable from persons with Asperger's disorder. It has also been argued that Asperger's disorder simply falls along a continuum of autistic-related disorders. Consequently, some authors have suggested that the label "autism spectrum disorders" (ASD) may better characterize and encompass both conditions (Meyer & Minshew, 2002).

The children in both the original Kanner (1943) and Asperger (1944/1991) studies demonstrated stereotyped patterns of behavior and resistance to change. Asperger's children were similar to Kanner's children in terms of social interaction deficits and restricted or obsessive interests but they differed in terms of the severity of language and cognitive impairments (Meyer & Minshew, 2002).

More recently, Manijiviona and Prior (1999) compared a large sample of children with autism to children with Asperger's disorder using a neuropsychological battery to assess executive function, brain lateralization, and intelligence. The authors were not able to differentiate the disorders in terms of laterality or executive function. They did, however, find that the group with Asperger's had overall higher IQ scores than the sample with autism. The authors also noted that both groups showed similar strengths on Block Design, a visual–spatial task on the Wechsler scales.

In another study, Miller and Ozonoff (2000) were not able to find significant differences between the two groups in terms of executive functions, visual–spatial abilities, intellectual abilities, or motor-skill deficits. The authors argued that the two disorders were largely inseparable. Although the debate remains unresolved, several studies have found that individuals with Asperger's disorder typically have no associated language or intellectual delays whereas both are common features of ASD (Rourke et al., 2002).

Pervasive Developmental Disorder, Not Otherwise Specified

Unlike autism and Asperger's disorder, pervasive developmental disorder, not otherwise specified (PDDNOS) does not have a specific set of diagnostic criteria. Generally this diagnosis is used to identify those individuals who, after 30 months of age, present with atypical or fewer symptoms necessary to meet the criteria for other PDDs (Tanguay, 2000). Many of these children, however, receive a subsequent diagnosis of autism in later childhood (Tsai, 2000).

Rett Syndrome

Rett syndrome (RS) is a pervasive developmental disorder identified by Andreas Rett, who in 1966 described young girls who were severely disabled with stereotypical hand-wringing movements (Hagberg, Aicardi, Dias, & Ramos, 1983). RS is a progressive neurodevelopmental disorder with normal prenatal and perinatal development for the first 6–18 months of life followed by regression in cognition and functioning (Mount, Hastings, Reilly, Cass, & Charman, 2003).

There are four stages of regression that progressively affect the individual's functioning. Hagberg and Witt-Engerström (1986) describe the four-stage model. The first stage starts with an age of onset between 6 and 18 months with symptoms including a disinterest in play and hypotonia. The second stage involves a rapid regression with autistic-like symptoms and irritability occurring between 1 and 3 years of age. The third stage occurs between 2 and 10 years of age with symptoms of severe seizures, mental retardation, hand-wringing, hyperventilation, aerophagia, and bruxism. The last stage of RS develops at about 10 years of age with symptoms including scoliosis, muscle wasting and rigidity, along with improved eye contact.

RS is caused by a genetic mutation of the MeCP2 gene that is located on the X chromosome (Amir et al., 1999). The protein encoded by this gene suppresses the genetic activation of neurons and leads to developmental delays and neurological disorders. RS is considered rare, occurring in one per 10–22,000 births (Jellinger, 2003) with survival age being 30–40 years (Glaze, 2004).

Childhood Disintegrative Disorder

Childhood disintegrative disorder (CDD) is a condition similar to autism with impairments in communication, social relationships, and adaptive behavior (Morris et al., 2005). However, these impairments are caused by a loss of previously acquired skills prior to 10 years of age (APA, 1994). Development appears normal for at least the first 2 years of life; then a marked regression in the individual's abilities becomes apparent (Dawson, 2000). After the regression, behavioral manifestations typically associated with autism develop (Dawson, 2000) such as qualitative impairments in social and communicative domains. Thus, the major difference between CDD and autism is the course of early development and the age of onset.

CDD is a very rare disorder with an estimated prevalence rate of 1.7 per 100,000 individuals (Fombonne, 2002). Researchers (Zwaigenbaum et al., 2000) conducted a case study on two half-brothers who shared a mother; one was diagnosed with CDD and the other with autism. They found that CDD and autism share a genetic mechanism, supporting the notion that CDD is a subtype of PDD and that genetic loading may be the result of maternal origin. However, these results are speculative at best.

The umbrella term "pervasive developmental disorders" encapsulates several complex conditions that vary in presentation and severity. In reference to the neuropsychological research, autism has been examined in more detail than the other related PDDs. Given that, the remainder of this chapter will mainly focus on the neuropsychological theories of ASD.

Neuropsychological Theories of Autism

Research has shown that autism affects a number of neuropsychological domains and functions within these domains. To help explain these impairments, a number of interrelated neuropsychological theories have been proposed in the literature, each emphasizing what researchers believe to be the defining feature of the disorder. The limbic system hypothesis, the weak central coherence hypothesis, and the executive function hypothesis have been most prominently featured in the literature (Joseph, 1999). A fourth theory, called the theory of mind, is closely related to the executive function hypothesis. These hypotheses have been primarily outlined by Tonn and Obrzut (2005) and will be summarized below.

The Limbic System Hypothesis

The limbic system links the social and communication deficits seen in ASD to the medial temporal and limbic brain structures (Joseph, 1999). A number of researchers have directly studied the link between autism and the limbic system. Boucher and Warrington (1976) found that individuals with damaged hippocampus and individuals with autism had similar long-term memory deficits, although subsequent studies have not supported these findings (Minshew, Goldstein, & Siegel, 1997). At present, more research investigating the

role of the limbic system in the development of ASD must ensue. Although there is no conclusive evidence, it is plausible that abnormalities in the limbic system may contribute to the rather specific memory deficits seen in persons with ASD and are thus an important area for subsequent research (Joseph, 1999).

The Weak Central Coherence Hypothesis

The major premise of the weak central coherence approach is that cognitive and perceptual difficulties often seen in individuals with ASD reflect sporadic processing of information stimuli as opposed to the more coherent processing seen in individuals without the disorder (Joseph, 1999). The basic idea is that individuals with ASD make relatively less use of context and pay preferential treatment to individual parts rather than wholes. While other neuropsychological theories primarily focus on the social and communicative deficits of ASD, the weak central coherence hypothesis is concerned with restricted and repetitive features of the disorder such as resistance to change and the preoccupation and exclusive focus on a singular part of an object (Joseph, 1999). It is not uncommon for individuals with ASD to have good rote memory, advanced jigsaw puzzle skills, and even savant abilities such as calendar and prime number calculation skills or superior music or drawing abilities (O'Connor, 1989). The weak central coherence hypothesis also addresses these abilities that are sometimes seen in individuals with ASD (Joseph, 1999).

It has been well documented that individuals with ASD typically perform better on Block Design than on the Comprehension subtest from the Wechsler scales. Shah and Frith (1993) investigated whether persons with autism were better at copying whole or segmented designs. They concluded that superior block design abilities often seen in persons with ASD are likely due to their unusual pattern of segmented processing as opposed to advanced visual–spatial reasoning skills.

Executive Function Hypothesis

The executive function hypothesis views autism as "a manifestation of primary deficits in executive control over behavior" and involves mental operations such as working memory, planning, inhibition of responses, as well as the maintenance and shifting of mental set (Joseph, 1999). Generally speaking, deficits in executive control are believed to be the result of damage to the dorsolateral area of the prefrontal cortex. However, in persons with developmental disabilities damage to the interconnected cortical and subcortical brain structures are believed to be involved as well (Joseph, 1999; Pennington & Ozonoff, 1996). Researchers (Klin, Jones, Schultz, Volkmar, & Cohen, 2002) surmised that this theory has great face validity given that individuals with ASD perseverate on inappropriate responses as well as have difficulty planning and within their organization of daily affairs.

Several studies have found evidence of executive function impairment in individuals with ASD (Hughes & Russell, 1993; Hughes, Russell, & Robbins, 1994; McEvoy, Rogers, & Pennington, 1993). Damasio and Maurer (1978) hypothesized that deficits found in individuals with frontal lobe injury and in ASD may be the result of damage to similar brain systems. Subsequent studies have found evidence of prefrontal cortical dysfunction in individuals with ASD (see Pennington & Ozonoff, 1996). For example, Hughes et al. (1994) presented individuals with ASD with two tests of executive function: The Tower of London planning task and the extra-dimensional set-shifting task. On each of the tasks the group with ASD performed poorer relative to controls. Furthermore, impairments were the most prominent in tasks that demanded the greatest executive control (Hughes et al., 1994).

Not all researchers agree on the executive function hypothesis. Questions have been raised about prefrontal impairment in children with ASD. In one study, Dawson et al. (2002) examined the performance of 3- to 4-year-old children on ventromedial prefrontal tasks and whether performance on such tasks correlated with joint attention ability. Three groups of children were matched on mental age: one group had ASD; one group of children had a developmental delay; and one group was developing normally. Results revealed no significant differences between the ASD group and control groups, indicating no autism-specific pattern of executive dysfunction for that particular age group. They did, however, find that ventromedial prefrontal task performance was strongly correlated with joint attention ability.

Theory of Mind Hypothesis

A now famous study conducted by Baron-Cohen, Leslie, and Frith (1985) examined the relationship between executive function and ASD. The researchers presented a story to children with ASD about a doll named Sally who placed a marble in a basket. When Sally left the room, another character removed the marble from the basket and placed it in a box. Upon Sally's return, participants were asked where Sally would look for the marble. The researchers found that individuals with ASD were often unable to infer Sally's response. Most respondents replied that Sally would look for the marble in the box, although the correct response would be that Sally would look for the marble where she had left it: in the basket.

The findings of this particular study along with subsequent variations of it led to the theory of mind hypothesis. The theory of mind hypothesis proposes, "the social and communicative abnormalities of autism derive from a specific inability to understand other people's minds and to interpret behavior in terms of underlying mental states" (Joseph, 1999, p. 311). In other words, the theory of mind hypothesis refers to the inability to take on the perspective of others' mental states (Baron-Cohen et al., 1985).

Other studies have examined the link between the theory of mind hypothesis and the executive function account for ASD (e.g., Ozonoff & McEvoy, 1994). In general, researchers have found that persons with ASD have deficits in both theory of mind and executive functioning, although executive function deficits are more widespread and prominent. It has thus been proposed that executive dysfunction is the primary deficit, which in turn, directly affects performance on theory of mind tasks (Joseph, 1999).

Neuropsychological Profiles of Persons with Autism Spectrum Disorder

Understanding autism at a neuropsychological level requires one to consider the relationship between brain structures and the behavioral functions they serve. There is overwhelming evidence that individuals with autism have neuropsychological impairments across a number of domains, which indicates that multiple regions of the brain are likely involved including the language, intelligence, memory, attention, and executive function domains (Dawson, 1996). However, not all brain functions within each domain are equally affected. It appears that certain functions are markedly impaired while others are not affected at all as indicated below.

Language Domain

Language and communication impairments are a cardinal characteristic of ASD. In fact, it has been estimated that approximately 35–40% of individuals with ASD do not develop functional, communicative language (Mesibov, Adams, & Klinger, 1997). Persons with ASD who develop language show impairments in pragmatics, prosody, and comprehension in addition to severe expressive and receptive language delays. Happe and Frith (1996) assert that children with ASD appear to have an absence in communication rather than a lack of language; even those whose language skills are intact often have difficulty communicating with others. Overall, however, there is a great deal of variance in language and communication skills in children with ASD (Dawson, 1996). For example, Kjelgaard and Tager-Flusberg (2001) examined the broad language abilities of children with ASD specifically measuring phonological and vocabulary production, semantics, grammar, and lexical comprehension. Results showed significant heterogeneity in their performance across receptive and expressive language domains with some children's language functioning within normal ranges while others functioned significantly below their age-level expectations.

Regarding receptive language, researchers suggest that individuals with ASD show dissociation between the mechanical recitation of written material and its comprehension (Minshew, Goldstein, Taylor, & Siegel, 1994). Further, studies have shown that these individuals have great difficulty in comprehending language that is grammatically complex or has metaphorical or analogical content (Frith & Snowling, 1983; Minshew, Siegel, Goldstein, & Nicholson, 1994; Whitehouse & Harris, 1984). Minshew, et al. (1994) investigated the characteristics of speech and language in participants with high-functioning ASD (defined as autism with FS IQ scores > 70). They found that compared to typically developing controls, participants with high-functioning ASD showed a significant

dissociation between basic mechanical and proce-dural language abilities, which were demonstrated to be intact, and the more complex or interpreta-tive language abilities, which were found to be significantly impaired. These findings may suggest that ASD is a generalized disorder of complex information processing with these language differ-ences illuminating the disproportionate involve-ment of comprehension in the pathophysiological process underlying ASD (Minshew et al., 1995).

Hermelin and O'Connor (1970) reported that when asked to memorize word lists, indivi-duals with ASD memorize the words in the exact order presented indicating that they did not actively reorganize the words into semantic categories, as did normal controls. However, research shows that this cannot be attributed to an inability to categorize. For example, Dunn, Vaughn, Kreuzer, and Kurtzberg (1999) mea-sured the reaction time and error rate in the auditory presentation of words according to superordinate category labels in normal and autistic groups matched on age and nonverbal IQ. They found that persons with ASD were slower in word classification and made more errors than normal controls, although only the prior finding was statistically significant. Together, these findings indicate multiple brain functions may be implicated in the processing of language in this population.

Event-related potentials (ERPs) may be use-ful in explaining linguistic-cognitive processes of children with ASD. Researchers (Dawson, Finley, Phillips, & Galpert, 1986) examined the relation between neuropsychological-linguistic profiles and ERPs in children with ASD. They found that the difference in the latency of the early negative auditory-evoked potential compo-nent N1 recorded over right and left hemispheres was related to language level. Differences in N1 were strongly related to level of receptive vocabu-lary and mean length of utterances. Moreover, they found that the latency of N1 was shorter in participants with ASD when compared to normal controls. Regarding ERPs, it has been shown that children with ASD process semantic information differently than typically developing controls (Dunn et al., 1999). Specifically, it appeared that in children with ASD, global context did not set up a selective activation of target words over words from other categories, meaning that words that did not fit with the context did not

appear to be deviant to the group with ASD (Dunn et al., 1999).

Brain lateralization may also be implicated in the development of impaired language and communication abilities in children with ASD. It has been shown that individuals with high-functioning ASD had diminished rates of lateral preference (Escalante-Mead, Minshew, & Sweeney, 2003) supporting findings from a pre-vious study that revealed a lack of cerebral dom-inance (Hauck & Dewey, 2001). However, this study did not focus on language. Regardless, Escalante-Mead et al. (2003) concluded that the association of dysmaturation in hemispheric spe-cialization suggests that language impairments in ASD may be linked to atypical development of left-hemispheric specialization for language.

Intellectual Domain

Individuals with ASD are known for their uneven cognitive profiles (Happe, 1994). It is common to see verbal, abstract reasoning, and sequential processing impairments with little visual–spatial or organizational deficits (Tonn & Obrzut, 2005). Further, it is estimated that approximately 75% of children with ASD have some degree of mental retardation (APA, 2000), although it is not a diagnostic criterion for ASD.

As shown on intelligence tests, cognitive profiles of persons with ASD indicate that these individuals generally perform better on nonverbal than on verbal tasks as shown by higher perfor-mance than verbal IQ scores (Lincoln, Courchesne, Kilman, Elsmasian, & Allen, 1998; Otha, 1987; Ozonoff, Rogers, & Pennington, 1991; Wechsler, Lincoln, Allen, & Kilman, 1995) with discrepancies decreasing with age in those with intact language (Joseph, Tager-Flusberg, & Lord, 2002). For exam-ple, Harris, Handleman, and Burton (1990) examined the cognitive profiles of children with ASD using the Stanford-Binet scales of intelligence. They found that children with ASD scored lowest on the Absurdities subtest and highest on the Pattern Analysis subtest. This performance could be attributed to the verbal nature of the Absurdities subtest and the nonverbal nature of the Pattern Analysis sub-test. Moreover, the Absurdities subtest requires abstraction ability whereas the Pattern Analysis subtest is more concrete in nature. Carpentieri and Morgan (1994) reported similar findings. They examined performance in children with ASD compared to

controls with mental retardation matched on age, gender, and composite IQ score. Like Harris et al. (1990), they found that children with ASD perform better on nonverbal tasks compared to verbal tasks. Moreover, in addition to scoring highest on the Pattern Analysis and lowest on the Absurdities, the participants with ASD also scored significantly lower on the Verbal Reasoning composite when compared to controls. In fact, it is generally accepted that children with ASD perform better on nonverbal versus verbal subtests of intelligence (Happe, 1994; Lincoln et al., 1998; Tonn & Obrzut, 2005; Venter, Lord, & Schopler, 1992), with the lowest subtest scores on tests requiring substantial receptive language abilities (Venter et al., 1992).

Given the diminished performance on verbal subtests of intelligence and subsequent significant discrepancy in verbal IQ versus performance IQ, researchers (Goldstein, Beers, Siegel, & Minshew, 2001) compared individuals with ASD to individuals with nonverbal learning disabilities, who have similar cognitive profiles on intelligence tests. They found that on the *Wechsler Adult Intelligence Scale – Revised* ([WAIS-R]; Wechsler, 1981), individuals with high-functioning ASD had different cognitive profiles than individuals with nonverbal learning disabilities. Specifically, they found that individuals with ASD perform poorly on subtests concerning social judgment and perception and perform relatively well on subtests requiring semantic memory, attention, and spatial-constructional skills. These findings support the assertion that high-functioning ASD and nonverbal learning disabilities are distinct diagnoses with varied abilities.

Rumsey and Hamburger (1990) found that individuals with high-functioning ASD and controls with dyslexia performed similarly on measures of tactile perception, motor speed and coordination, word fluency, and perceptual organization, which is indicative of nonimpaired performance in the experimental group. Individuals with ASD had difficulties on tasks requiring verbal and nonverbal reasoning, comprehension, and recalling complex visual and verbal information. However, the experimental group outperformed controls on auditory tasks of recalling simple information and on tasks of basic academic information. Other researchers have reported similar findings (Siegel, Minshew, & Goldstein, 1996). Siegel et al. (1996) found that individuals with high-functioning ASD performed well on nonsocial subtests and poorly on subtests requiring social judgment. These findings led Minshew and her colleagues to postulate that individuals with high-functioning ASD possess impairments in processing complex information. They tested this hypothesis and found that participants with high-functioning ASD had deficits in processing complex information, specifically in conceptualizing and organizing information (Minshew et al., 1997).

Researchers have believed that persons with ASD have a fundamental impairment in abstract reasoning ability. Boucher (1977) and Rutter (1978) found that persons with ASD displayed such deficits in abstraction abilities, which may support speculations by developmental psychologists who posit that individuals with lower-functioning ASD do not attain Piaget's formal operations stage of cognitive development. Lovaas (1987) developed the now famous behavioral intervention program to teach children with ASD; one aspect of that program was to teach the children to group items based on a variety of concepts including size, color, or function. The children were unable to generalize these principles to solve problems in different contexts illustrating this population has impaired abstraction skills. Jarrold, Boucher, and Smith (1996) investigated children's abstraction skills as it relates to play. They found that children with ASD had difficulties in perceiving play objects or situations in multiple ways and that the children's play activities were very repetitive and concrete characterized by little abstraction and lacking pretend play. Moreover, Minshew and her colleagues (2002) administered a variety of test batteries including the *Wisconsin Card Sorting Test* (WCST), *Trail Making Test Part B* (TMT-B), *Halstead Category Test* (HCT), *Goldstein–Scheerer Object Sorting Test*, the Absurdities subtests on the Stanford-Binet, to individuals with ASD who were not mentally retarded and to typically developing controls. They found significant differences between the experimental and control groups on all tasks requiring abstract reasoning. There were no significant differences on tasks requiring concept identification, except on the WCST. Using factor analysis, the researchers determined that the concept identification tasks and concept formation tasks were comprised of different factors for the group with ASD but not for the control group. They postulated that individuals with high-functioning ASD were able to

perform abstract reasoning tasks that required concept identification, but were impaired on tasks requiring concept formation abilities. They surmised that this was due to deficits in cognitive shift and the inability to consider feedback from the examiner while performing WCST tasks.

Cognitive shift is another aspect of cognitive functioning that appears to be implicated in ASD. In addition to the findings by Minshew et al. (2002), Ozonoff (1995) examined cognitive shift abilities in children with ASD using the WCST. When compared to typically developing controls, children with ASD had significantly impaired performance on this task. Ozonoff attributed the impaired performance to children with ASD having difficulty with cognitive shift. Ciesielski and Harris (1997) delved into examining the capacity of cognitive shift in persons with ASD. They administered the TMT-B, WCST, HCT, *Ambiguous Figure Test* (AFT), and the *Luria Motor Reversal Test* (LMRT). They found that individuals with ASD performed the worst on the AFT, which has very few rules to instruct performance, and the best on the LMRT, which has specific rules to instruct performance. They determined that the amount of rule-governing within the test demonstrated the need for the individual to shift his/her cognitive set. Further, the participants with ASD performed better on the WCST and HCT, which had the highest demand for concept formation abilities. The authors asserted that the rule-governing restraints had more influence on test performance than the participants' intelligence level.

Memory Domain

Within the memory domain, impairments have been found in both long- and short-term memory with some inconsistent results (Tonn & Obrzut, 2005). However, studies have shown that a variety of domains appear to be spared such as rote memory (Bennetto, Pennington, & Rogers, 1996; Dawson, 1996; Toichi & Kamio, 2002), cued recall, operant learning, and discrimination learning (Dawson, 1996) as well as object memory (Hauck, Fein, Maltby, Waterhouse, & Feinstein, 1998).

Regarding working memory, research has revealed differing findings for verbal and spatial working memory. For example, researchers (Williams, Goldstein, & Minshew, 2005) compared persons with high-functioning ASD with normal controls on various aspects of memory. They found no significant differences on measures of verbal working memory. These findings are in contrast with results from Bennetto et al. (1996), who found deficits in verbal working memory with this population. However, consistent results have been shown regarding spatial working memory in persons with ASD; specifically deficits in spatial working memory were found (Bennetto et al., 1996; Minshew et al., 2005). According to Minshew and her colleagues, the common theme for these deficits is the dependence on concept formation, which is considered a complex information processing ability.

Social and nonsocial memory has also been examined in children with ASD. In one study, researchers (Hauck et al., 1998) explored the processing of faces in children with ASD to mental age-matched, typically developing controls, using the Peabody Picture Vocabulary Test Revised (PPVT-R). They compared participants' performance on matching and memory tasks with performance on a variety of other measures. They found that children with ASD had significantly lower scores on tasks using face materials as the memory task. Other researchers have reported similar results (Boucher & Lewis, 1992; Williams et al., 2005) indicating that memory for faces may be impaired in children with ASD. Given that Boucher and Lewis (1992) have shown that persons with ASD are able to perform proficiently on tasks involving memory for complex stimuli, Williams et al. (2005) postulated that this impairment was the result of deficits in social perception and judgment rather than the task complexity.

Studies on long-term memory suggest that persons with ASD who do not have mental retardation seem to have relatively intact long-term memory (Bennetto et al., 1996; Minshew & Goldstein, 1993; Summers & Craik, 1994). However, others (Ramondo & Milech, 1984; Tager-Flusberg, 1991) have found that memory for verbal information that is semantically or contextually related is impaired. For example, performance on free recall was worse in individuals with ASD than normal controls when matched on ability for items to be remembered when arranged to make a meaningful sentence (Ramondo & Milech, 1984). In another study, researchers found that on free recall tasks, persons with ASD performed comparable to normal controls when the words were abstract and poorer than controls when the words were

concrete despite overall comparable performance (Toichi & Kamio, 2002). The authors asserted that although the groups did not differ in performance on abstract words, the participants with ASD may have reduced semantic encoding compared to normal controls that may be the result of a lack of dual encoding of verbal stimuli for concrete nouns. Other studies specifically examining the semantic and episodic memory patterns in children with ASD reveal contrasting findings to this assertion. Studies examining mnemonic functions in persons with high-functioning ASD reveal impairments in episodic memory (Bowler, Gardiner, & Grice, 2000; Gardiner, Bowler, & Grice, 2003), but not semantic memory (Minshew, Goldstein, Muenz, & Payton, 1992; Siegel et al., 1996). In a recent study, researchers (Salmond et al., 2005) examined children with ASD on multiple memory assessments including the *Rivermead Behavioural Memory Test* (Wilson, Cockburn, & Baddeley, 1991), *Children's Memory Scale* (Cohen, 1997), *Pyramids and Palm Trees Test* (Howard & Patterson, 1992), and the *Wechsler Intelligence Scale for Children III* ([WISC-III]; Wechsler, 1991). Results revealed that children with ASD perform significantly poorer than typically developing controls on episodic memory tasks, but performed relatively comparably on indices of recognition and semantic memory.

Attention Domain

Regarding attention, children with ASD show typical and atypical abilities. Orientation, selective attention, and attention shifting are often impaired while sustained attention is typically found to be intact (Dawson, 1996). On simple orientation tasks, children with ASD had more severe impairments on socially oriented stimuli than on other types of stimuli (Dawson, Melzoff, Osterling, Rinaldi, & Brown, 1998). Baron-Cohen and his colleagues (1997) used photographs of people's eyes to examine the ability of adults with high-functioning ASD and Asperger's to recognize complex mental states. They reported that compared to normal controls, both groups had significant difficulties with task completion.

In terms of selective attention, Burack (1994) compared the attention abilities of four groups including individuals with ASD, organic mental retardation, familial mental retardation, and a normal control group on a forced-choice task. Burack found that individuals with ASD had significantly impaired performance on focusing on a target object when exposed to extraneous factors. He postulated that this impairment contributes to the overarousal that individuals with ASD experience and may be attributed to cognitive and social dysfunction.

Pascualvaca, Fantie, Papageorgiou, and Mirsky (1998) also assessed the attentional abilities of children with ASD compared to chronological age-matched and mental age-matched controls. They measured the participants' abilities to focus attention, sustain that focus, and shift attention on tasks including the WCST, *Continuous Performance Test* ([CPT]; Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956), and the Digit Cancellation Task ([DCT]; Lifshitz, Kugelmass, & Karov, 1985). They found no significant differences in performance on the CPT and DCT indicating that children with ASD focused attention and sustained that focus relative to normal controls. However, they did find a significant difference in the children's abilities to shift their attention as evidenced by diminished performance on the WCST. The authors proposed that there may not be specific deficits in set shifting, but there may be problems in the coordinating attentional resources and in initiating motivation.

Another function commonly implicated in ASD is joint attention. Joint attention refers to the "ability to coordinate attention between interactive social partners with respect to objects or events or to share an awareness of the objects or events" (Dawson et al., 2002, p. 346; Mundy, 1995; Mundy, Sigman, Ungerer, & Sherman, 1987). In other words, it is the ability to share attention between other people and objects or events. Commonly appearing in the first year of life, joint attention is considered integral to language, social, and cognitive development and may be one of the earliest indicators of ASD. Children with impaired joint attention typically show abnormal eye gaze, point to ask for things but not to share attention, and fail to monitor the gaze of others to share experiences or to infer meaning from conversations (Meyer & Minshew, 2002).

In one study on joint attention, Dawson and her colleagues (2004) compared a group of children with ASD to children with nonautistic developmental delays and to typically developing controls matched on mental age. Researchers measured the participants' abilities on two tasks,

their ability to orient themselves to social and nonsocial cues and their ability to join their attention with the examiner who was experiencing distress or hurt. They found that children with ASD did not orient to any stimuli while children in both control groups did. Moreover, the difference was even greater on measures of social stimuli. Children with ASD made significantly less attempts to joining their attention and were less likely to respond to the examiner than were controls. There was also a significant difference in the ability of the children with ASD to attend to the examiner in distressed conditions. The authors contend that these impairments in social attention are the best diagnostic indicators in distinguishing children with ASD from other developmental disorders. Furthermore, researchers have suggested that social orienting is directly related to joint attention and indirectly related to language abilities (Dawson et al., 1998; Dawson et al., 2002).

Executive Function Domain

Executive functions involve mental operations such as working memory, planning, inhibition of inappropriate responses, and maintenance and shifting of mental set (Joseph, 1999). These skills are used to allow a person to maintain an appropriate problem-solving set in order to achieve a goal (Klin et al., 2002). Several studies have reported such executive function impairments in persons with ASD (e.g., Hughes & Russell, 1993; Hughes et al., 1994; McEvoy et al., 1993). Although research has shown that some functions are spared in other domains, it appears that all executive functions are impaired within the executive domain (Dawson, 1996), with cognitive set shifting considered to be the most affected skill (Ozonoff, 1997). Moreover, some researchers attribute the associated impairments of ASD to a cognitive shifting deficiency in the executive function domain (Ozonoff, 1997; Pennington & Ozonoff, 1996). However, in a later study, researchers (Griffith, Pennington, Wehner, & Rogers, 1999) examined children with ASD and reported intact abilities in most sub-domains of executive function with the exception of joint attention and made more perseverative errors on spatial reversal tasks.

In one study, researchers (Berger, Aerts, van Spaendonck, Cools, & Teunisse, 2003) investigated the relationship of central coherence and cognitive shifting with social skills in persons with ASD. Some participants were determined to have weak central coherence while others were found to have poor cognitive shifting skills. They measured social competence and social intelligences using a variety of assessment skills, including the *Vineland Adaptive Behavior Scale* (VABS), in a pretest–posttest research design over a 3-year period. They found that participants increased their social competence score on the VABS as a function of their initial cognitive shifting ability. Unlike weak central coherence, poor cognitive shifting was associated with lack of improvement in social adaptive functioning despite residential treatment over this 3-year period. Their findings support those of Ozonoff and Miller (1996) in that the social cognitive functioning performance improvements did not extend to improvements in overall social competence. It appears the cognitive shifting ability, an executive function, is implicated in the social skills impairments of individuals with ASD.

Gilotty and her colleagues (2002) examined 35 children with ASD using two parent reports of everyday functioning including the VABS and the *Behavior Rating Inventory of Executive Function* (BRIEF). They found negative correlations between most adaptive behavior domains and Initiate and Working Memory domains on the BRIEF. The Communicate and Socialization domains of the VABS were negatively correlated with a number of areas of executive functioning. In summary, these findings suggest that executive abilities are implicated in communication, play, and social impairments found in children who have ASD.

Some assert that there is a relationship between executive functions and theory of mind. For example, Frye, Zelazo, and Palfai (1995) posited that performance on theory of mind tasks can be reduced to executive function ability. Specifically, theory of mind is acting on a set of embedded rules and that many executive function tasks can be understood in terms of these rules. Furthermore, performance on executive function tasks predicts performance on theory of mind tasks, with the converse not being accurate (Hughes, 1998).

Dawson and her associates examined the executive functions of young children with ASD, developmental delays, and typically developing controls. They found that children with ASD and developmental delays have impaired executive function, but that ASD was not associated with a unique pattern of executive function impairment at a young age.

However, this may be attributed to development as executive functions are emerging during early childhood (Diamond & Goldman-Rakic, 1989). Thus, these impairments do not distinguish ASD from other developmental delays in early childhood. However, other studies in later childhood and adolescence have shown executive function impairments in participants with ASD relative to controls (Hughes & Russell, 1993; Ozonoff, 1995).

The Role of Lateralization in Autism

Some of the impairments common to individuals with autism may be a result of abnormal lateralization. Normal lateralization usually involves a relative right-hemisphere dominance for spatial processing and a relative left-hemisphere dominance for motor skills and language. However, research suggests that compared to other developmentally impaired populations, individuals with autism have higher rates of inconsistent lateral preference (Escalante-Mead et al., 2003). For example, one early study found that individuals with autism had a left ear preference in dichotic listening for both verbal and musical stimuli whereas typically developing children usually have a left ear preference for music and a right ear preference for verbal stimuli (Blackstock, 1978).

A recent study by Escalante-Mead et al. (2003) assessed cerebral dominance in a group of high-functioning autistic adults with early language developmental problems. Relative to normal controls, the researchers found that the group with the language delays had "significantly reduced rates of established left or right lateral hand preference" (Escalante-Mead et al., 2003, p. 541). The authors also found evidence of reduced lateral preference in individuals with autism who did not have language problems. However, some studies have revealed an increased rate of left-handedness in individuals with high-functioning ASD (Cornish & McManus, 1996; Soper et al., 1986) indicating anomalous cerebral lateralization. In one study, however, it was revealed that half of the children with ASD showed a clear preference for right-hand usage, but demonstrated no overall difference in skilled performance between hands whereas controls with mental retardation and those who were typically developing showed greater hand skills with the preferred hand (McManus, Murray, Doyle, & Baron-Cohen, 1992).

Although language impairments are often associated with dysfunction of the left hemisphere, the role of the right hemisphere in linguistic function should not be overlooked. Stroke studies have shown that persons with right-hemisphere damage have difficulty with pragmatic communication (e.g., Molloy, Brownell, & Gardner, 1990). Researchers began noticing that individuals with autism had deficits similar to right-hemisphere patients. Some of these similarities included literal and concrete use and comprehension of language, difficulty understanding the main idea of conversations, difficulty understanding figurative language, and the misinterpretation of others' intentions during conversations (Hough, 1990; Ozonoff & Miller, 1996).

Ozonoff and Miller (1996) illustrated these pragmatic deficits in a series of experiments with high-functioning adults with autism. The authors found that relative to normal controls, the group with autism had more difficulty identifying the correct funny ending of a joke. A previous study of right-hemisphere patients showed similar results, which suggests that both groups might have similar problems in cognitive flexibility (Brownell, Potter, Bihrle, & Gardner, 1986). Ozonoff and Miller (1996) also found their sample of individuals with autism to have more difficulty using context and meaning to understand details of a short story than normal controls. Similar findings were also noted in studies of right-hemisphere patients signifying the possibility of similar underlying deficits (e.g., Weylman, Brownell, Roman, & Gardner, 1989).

Neuropsychological Profiles of Persons with Other Pervasive Developmental Disorders

Asperger's Disorder

Although the DSM-IV recognizes Asperger's disorder (AD) as a separate and distinct category within PDDs, others believe it is a less severe form of ASD. The distinguishing feature of AD is the acquisition of language within the normal range of development (Tantam, 1988). In terms of intelligence, however, Ghaziuddin and Mountain-Kimchi (2004) compared a group of boys with high-functioning ASD to a group of boys with AD who were matched on age and IQ. They found that boys with AD had a higher

mean verbal IQ and a higher full-scale IQ than the boys with high-functioning ASD. Furthermore, the boys with AD demonstrated a significant Verbal IQ – Performance IQ discrepancy on the WISC-III, with the AD boys performing significantly better than the boys with HFA on the Information, Vocabulary, and Arithmetic subtests. No significant differences were found between groups on Block Design or Object Assembly subtests. This Verbal IQ – Performance IQ discrepancy has been reported in other studies as well (Miller & Ozonoff, 2000).

Gillberg (1989) investigated the gross motor skills of individuals with AD as measured by scores on the Griffiths test. It was reported that individuals with AD scored 15 points below their overall IQ. Similarly, young children with AD have diminished performance on both gross and fine motor tasks (Szatmari, Tuff, Finalyson, & Bartolucci, 1990). Klin et al. (1995) found that 90% of the participants with AD were found to have fine motor deficits compared to 32% of participants with high-functioning ASD. These findings indicate that motor development may be a critical feature in the differential diagnosis of AD from other PDDs.

Rett Syndrome

Regression is a distinctive feature of Rett syndrome (RS) with gait ataxia, apraxia, breathing anomalies, and hand stereotypies as hallmarks for differential diagnosis from other neurodevelopmental disorders (Glaze, 2004). It appears that the MeCP2 gene mutation is likely implicated in the abnormalities common in RS. For example, the onset of RS occurs during synaptic development (Glaze, 2004), suggesting it is a disorder of synaptic maintenance (Johnston, Blue, & Naidu, 2005; Johnston, Jeon, Pevsner, Blue, & Naidu, 2001; Zoghbi, 2003). Specifically, research has shown that the development of synapses and their modulation may be a crucial factor in the pathology of RS (Glaze, 2004). Additionally, seizures have been reported to occur in 50–80% of females with nearly 100% of individuals with RS having abnormal EEGs (Glaze, 2002). In one study, researchers used a mouse model with a MeCP2 mutation similar to RS (Shahbazian, Young, & Yuva-Paylor, 2002). They found that similar to persons with RS, the mice developed normal motor functions until 6 weeks of age but then showed a progressive deterioration including seizures and stereotypic forelimb movements.

Armstrong, Dunn, Antalaffy, and Trivedi (1995) investigated the selective dendritic abnormalities in RS. They found decreased dendritic territories in both apical and basilar branches of Layer 3 and Layer 5 pyramidal neurons. Others (Belichenko, Oldfors, Hagberg, & Dahlstrom, 1994) found a reduced number of dendritic spines and regions of bare dendrites in the frontal cortex of individuals with RS. They concluded that abnormal growth of dendrites might cause development of mental retardation in many genetic neurodevelopmental disorders, such as RS. Moreover, brain imaging studies have shown abnormal gray matter and neurons too densely packed which results in reduced dendritic connections (Armstrong, 2001).

Data collected from a multidisciplinary clinical assessment of 87 females with RS ranging from toddlerhood to adulthood have confirmed a number of findings and reported some trends (Cass et al., 2003). Over time, individuals with RS were shown to have increasingly poor growth, joint anomalies, and scoliosis in adulthood. Additionally, they found that characteristic hand stereotypies did not impede development of hand-use skills. Despite the profound limitations in cognitive and communication skills, there was little evidence of these abilities deteriorating with age. They surmised that RS is not a degenerative condition and increases in motor, cognitive, communication, and daily skills could be made.

Childhood Disintegrative Disorder

Similar to RS is CDD, which involves a regressive pattern of development. However, it differs from RS in that there is no known etiology (Rogers, 2004). In addition, the regression also occurs at a later age in CDD than in related PDDs (Rogers, 2004) with a pattern of continuous speech loss extending to 5 years of age (Shinnar et al., 2001). Overall the late timing of regression, loss of physical skills, and fearfulness differentiate CDD from ASD (Rogers, 2004).

In one study investigating the clinical validity of the DSM-IV CDD diagnosis, researchers (Kurita, Koyama, Setoya, Shimizu, & Osada, 2004) compared 10 children with CDD to 30 nonverbal controls with ASD. Results showed that children with CDD had significantly more frequent fear-ful behavior and epilepsy and, at

first visit, more stereotypic movement and invariant intellectual development compared to controls. Epilepsy has relatively consistently been shown to occur more frequently in this population (Malhotra & Gupta, 2000; Mouridsen, Rich, & Isager, 1998) suggesting greater brain dysfunction in the underpinnings of CDD (Kurita et al., 2004).

In the intellectual domain, mental retardation is a salient feature of CDD (Kurita et al., 2004). Longitudinal studies on intelligence reveal higher rates of mental retardation in CDD compared to ASD (Volkmar & Cohen, 1989; Volkmar & Rutter, 1995). However, in cross-sectional studies, it has been shown that the degree of mental retardation is less severe in CDD than ASD (Kurita et al., 2004). In one study, researchers compared IQ scores of young adult participants with CDD or ASD and found no significant differences (Mouridsen et al., 1998), although severe mental retardation was frequent in participants with CDD. Regarding evenness of intellectual abilities, when compared to children with ASD, children with CDD may show more invariant cognitive skills and are less likely to have relative strengths in rote memory and visuospatial skills (Kurita et al., 2004).

Malhotra and Gupta (2002) examined the profiles of individuals with CDD, including intellectual functioning. They reported the majority of participants scoring within the severe to profound range of mental retardation. Similar findings have been reported by other researchers (Malhotra & Singh, 1993; Volkmar & Cohen, 1989). However, it is important to note that all participants in Malhotra and Gupta's study were found to achieve all of their developmental milestones prior to CDD onset, which may be attributed to the regressive nature of CDD.

Summary and Conclusion

Although there have been some promising findings linking brain abnormalities with the behavioral manifestations of autism, the picture is far from complete (Happe & Frith, 1996). Understanding autism at the neuropsychological level is both challenging and complex. On one hand, there are distinct patterns of symptoms and behavioral features common to the disorder. On the other hand, the pattern of behaviors varies greatly. What is known about autism is that functions within several domains are affected, indicating the involvement of multiple brain regions (Dawson, 1996). Despite conflicting views regarding its differential diagnosis, defining characteristics, and the specific brain functions involved, most researchers agree that autism is a spectrum disorder that cannot simply be defined in terms of mild to severe (Kabot, Masi, & Segal, 2003). Although the limbic system, executive function, theory of mind, and central coherence hypotheses are helpful in conceptualizing the disorder, it is unlikely that any of them represent "mutually exclusive" abnormalities (Duel, 2002). Solving the many questions that remain about autism will undoubtedly require the integration of all the disciplines involved in its research.

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32

Using the Planning, Attention, Simultaneous, Successive (PASS) Theory Within a Neuropsychological Context

JACK A. NAGLIERI, CARA CONWAY, AND SAM GOLDSTEIN

Introduction

Neuropsychologists evaluate brain function by interpreting an individual's cognitive, emotional, social, and motor behavior. Standardized instruments with known reliability and validity have played an important role in the procedures used by neuropsychologists to collect information and derive inferences about brain function. Though these measures are efficient at providing data about functioning in comparison to sample populations, technology such as magnetic resonance imaging and computerized tomography have reduced the need for neuropsychological tests to assess and localize brain damage. Neuropsychological tests have, therefore, begun to plan an increasingly important role in the evaluation of the processes or abilities necessary for effective thinking, learning, and behaving. Many tests utilized by neuropsychologists may be described as atheoretical even though researchers have recognized the value of a theoretical perspective of brain function. A conceptualization of human cognitive functioning like the one described by A. R. Luria can guide the development of neuropsychological assessment tools.

Such tools could then be used to not only evaluate the underlying processes necessary for efficient thinking and behaving but also provide a foundation for prognosis and a guide for intervention. In this chapter, we will provide an overview of Luria's conceptualization of the basic psychological processes corresponding to the three functional brain units, one method by which it has been operationalized, a summary of the present literature on this method, and a discussion of its applicability as a critical part of a pediatric neuropsychological battery.

From Neuropsychology Theory to Assessment

A. R. Luria's (1966, 1973, 1980) research on the functional aspects of brain structures formed the basis for the Planning, Attention, Simultaneous, Successive (PASS; theory initially described by Das, Naglieri, and Kirby (1994) and operationalized by Naglieri and Das (1997a) in the Cognitive Assessment System (CAS). Das and Naglieri and their colleagues used Luria's work as a blueprint for defining the basic neuropsychological processes that underlie human performance (Naglieri, 2003). Their efforts represent the first time that a specific researched neuropsychological theory was

JACK A. NAGLIERI CARA CONWAY, AND SAM GOLDSTEIN • Department of School Psychology George Mason University, Fairfax, Virginia 22030.

used to provide an alternative conceptualization of human intelligence.

Luria proposed that human cognitive functions could be conceptualized as three separate but connected "functional units" that provide four basic psychological processes. The three brain systems are referred to as "functional" units because the neuropsychological mechanisms work in separate but interrelated systems. These brain systems are consistent with the four psychological processes identified by the PASS theory (Naglieri & Das, 1997b). Luria (1973) stated "each form of conscious activity is always a complex functional system and takes place through the combined working of all three brain units, each of which makes its own contribution" (p. 99). In other words, the four processes form a "working constellation" (Luria, 1966, p. 70) of cognitive activity. Thus, a child or adult can use different combinations of the four psychological processes in conjunction with their knowledge and skills to perform a task. Although effective functioning is achieved through the appropriate combination of all processes as demanded by the task, each process is not equally involved in every task. For example, reading comprehension may predominately involve one process, while reading decoding can be strongly dominated by another (Das, Naglieri, & Kirby 1994).

Three Functional Units Described

Luria (1973) provided considerable evidence for the psychological processes associated with each of the three functional units and their association with specific regions of the brain. These three functional units have been used by Naglieri and Das (1997b) as the basis of Planning (third functional unit), Attention (first unit), and Simultaneous and Successive (second unit) cognitive processes. The function of the first unit provides regulation of cortical arousal and attention, while the second unit codes information using Simultaneous and Successive processes. The third unit provides for strategy development, strategy use, self-monitoring, and control of cognitive activities.

According to Luria, the brainstem, the diencephalon, and the medial regions of the cortex are the primary locations for the first of the three functional units of the brain, the Attention–Arousal system (Luria, 1973). This unit provides the brain with the appropriate level of arousal or cortical tone, and directive and selective attention so that a person can focus on one dimension of a multidimensional stimulus array and inhibit responding to other (often more salient) stimuli (Luria, 1973). Luria stated that optimal conditions of arousal are needed before the more complex forms of attention involving "selective recognition of a particular stimulus and inhibition of responses to irrelevant stimuli" (Luria, 1973, p. 271) can occur. Moreover, the second and third functional units can operate effectively only after individuals are sufficiently aroused and their attention is adequately focused.

The occipital, parietal, and temporal lobes posterior to the central sulcus of the brain are associated with the second functional unit. Information from the external world is received, processed, and retained within this unit. The functions of this unit involve Simultaneous processing and Successive processes. Simultaneous processing involves arranging stimuli into integrated groups in order to comprehend the interrelationships among the components. For example, in order to construct a diagram correctly when given the instruction, "draw a circle above a triangle that is to the right of a square under a diamond", the relationships among the different shapes must be correctly understood. While Simultaneous processing involves working with interrelated stimuli, Successive processing involves information that is linearly organized and integrated into a chain-like progression. For example, Successive processing is involved in the decoding of unfamiliar words, production of syntactic aspects of language, and speech articulation. Following a sequence such as the order of operations in a math problem is another example of Successive processing. This is almost the inverse of Simultaneous processing, which involves integration of separate elements into groups.

The prefrontal areas of the frontal lobes of the brain are associated with the third functional unit (Luria, 1980). Luria stated that "the frontal lobes synthesize the information about the outside world ... and are the means whereby the behavior of the organism is regulated in conformity with the effect produced by its actions" (Luria, 1980, p. 263). This unit provides for the programming, regulation, and evaluation of behavior and enables the child to ask questions,

develop strategies, and self-monitor (Luria, 1973). Other responsibilities of the third functional unit include the regulation of voluntary activity, conscious impulse control, and various linguistic skills such as spontaneous conversation. The third functional unit provides for the most complex aspects of human behavior, including personality and consciousness (Das, 1980).

A particularly strong relationship exists between the first and third functional units. The higher systems of the cerebral cortex both regulate and work in collaboration with the first functional unit while also receiving and processing information from the external world and determining an individual's dynamic activity (Luria, 1973). In other words, the first functional unit has a reciprocal relationship with the cortex. It is both influenced by the regulatory effects of the cortex and influences the tone of the cortex. The ascending and descending systems of the reticular formation enables this relationship by transmitting impulses from lower parts of the brain to the cortex and vice versa (Luria, 1973). This connection between units also links the psychological processes that are routed in each of the functional units. For the PASS theory, this means that psychological processes of Attention and Planning are necessarily strongly related because Planning often has conscious control of Attention. In other words, one's limited attentional resources are dictated by the plan for one's behavior. However, Attention as well as the other PASS processes is influenced by many variables other than Planning. One of these influences is the environment.

Functional Units: Interactions and Influences

Luria's organization of the brain into functional units was not an attempt to map out the precise locations where specific areas of higher cognition took place. He states "...perception and memorizing, gnosis and praxis, speech and thinking, writing, reading and arithmetic, cannot be regarded as isolated or even indivisible 'faculties'..." (Luria, 1973, p. 29). That is, attempts to identify a precise "arithmetic" spot like a phrenologist are misguided. Instead, the brain should be conceptualized as a functioning whole comprised of units that provide purpose.

Luria (1973) describes the advantage of this approach:

> It is accordingly our fundamental task not to "localize" higher human psychological processes in limited areas of the cortex, but to ascertain by careful analysis which groups of concertedly working zones of the brain are responsible for the performance of complex mental activity; when contributions made by each of these zones to the complex functional system; and how the relationship between these concertedly working parts of the brain in the performance of complex mental activity changes in the various stages of its development. (p. 34)

Activities such as reading and writing can be evaluated and seen as constellations of activities related to specific working zones of the brain that support them (Luria, 1979, p. 141). This also means that since the brain operates as an integrated functional system, even a minor disruption in an area can cause disorganization in the entire functional system (Varnhagen & Das, 1986).

Luria's organization of the brain into functional units also accounts for the interaction of cultural influences and biological factors within higher cognition. Luria viewed a child's cultural experience not only as a significant influence on the functional units but also as a necessary foundation that aids the development of human cognition (Luria, 1979). Luria (1979) notes, "...the child learns to organize his memory and to bring it under voluntary control through the use of the mental tools of his culture" (p. 83). Kolb, Gibb, and Robinson (2003) also wrote that although "the brain was once seen as a rather static organ, it is now clear that the organization of brain circuitry is constantly changing as a function of experience" (p. 1). Similarly, Stuss and Benson (1990) recognize this interplay and especially in the use of speech as a regulatory function when they state the following:

> The adult regulates the child's behavior by command, inhibiting irrelevant responses. His child learns to speak, the spoken instruction shared between the child and adult are taken over by the child, who uses externally stated and often detailed instructions to guide his or her behavior. By the age of 4 to 4½, a trend towards internal and contract speech (inner speech) gradually appears. The child begins to regulate and subordinate his behavior according to his speech. Speech, in addition to serving communication

thought, becomes a major self-regulatory force, creating systems of connections for organizing active behavior inhibiting actions irrelevant to the task at hand. (p. 34)

Culture influences the development of higher cognitive functioning through a variety of different channels. Luria (1979) stressed the role of the frontal lobes in language, organization and direction of behavior and speech as a cultural tool that furthers the development of the frontal lobes and self-regulation. Cultural experiences actually help to accelerate the utilization of Planning and self-regulation and the other cognitive processes. Luria (1979) also points out that abstraction and generalizations are themselves products of the cultural environment. Children learn, for example, to selectively pay attention to items that are pertinent through conversations and playful interactions with adults. Even Simultaneous and Successive processes are influenced by cultural experiences (e.g., learning dances, poems, game rules). Naglieri (2003) summarized research that showed that the influence of social interaction on children's use of plans and strategies resulted in improvements in performance on academic tasks. Luria's concept of functional units and their relationship to the larger socio-cultural context provides the foundation for the PASS theory.

From the Three Functional Units to the PASS Theory

The four processes included in the PASS theory represent a fusion of cognitive and neuropsychological constructs such as executive functioning (Planning), selective attention (Attention), visual–spatial tasks (Simultaneous), and serial features of language and memory (Successive) (Naglieri & Das, 2005). These four processes are more fully described below.

Planning is a frontal lobe function. As one of the prominent capacities that differentiate humans from other primates, Planning is associated with the prefrontal cortex. The prefrontal cortex "plays a central role in forming goals and objectives and then in devising plans of action required to attain these goals. It selects the cognitive skills required to implement the plans, coordinates these skills, and applies them in a correct order. Finally, the prefrontal cortex is

responsible for evaluating our actions as success or failure relative to our intentions" (Goldberg, 2001, p. 24). Planning helps one to achieve goals through the development of strategies necessary to accomplish tasks for which a solution is required. Therefore, Planning is crucial to all activities that demand the child or adult to figure out how to solve a problem. This includes self-monitoring and impulse control as well as creation, assessment, and execution of a plan. Thus, Planning allows for the generation of solutions, discriminating use of knowledge and skills, as well as control of Attention, Simultaneous, and Successive processes (Das, Kar, & Parrila, 1996).

The essential dimension of the construct of Planning as defined by Naglieri and Das (1997b) is very similar to the description of executive function provided by others (see Naglieri & Goldstein, 2006). For example, O'Shanick and O'Shanick (1994) describe executive functions as including the abilities to formulate and set goals, assess strengths and weaknesses, plan and/or direct activities, initiate and/or inhibit behavior, monitor current activities, and evaluate results. This is very similar to the description provided by Hayes, Gifford, and Ruckstuhi (1996). Executive functions include abilities to formulate a goal, plan, carry out goal-directed behaviors effectively, and monitor and self-correct spontaneously and reliably (Lezak, 1995). These skills are essential for fulfilling most daily responsibilities and maintaining appropriate social behavior. A variety of assessment tools that have been proposed to assess executive functions often yield conflicting data, given the very broad definition of these functions (e.g., for a review of this issue in the assessment of ADHD, see Barkley, 1997). Planning in the PASS theory offers a more finite description that may be characterized as executive function.

Attention is a cognitive process that is closely connected to the orienting response. The base of the brain allows one to focus selective attention toward a stimulus over a period of time without the loss of attention to other competing stimuli. The longer the attention is needed, the more that activity necessitates vigilance. Intentions and goals mandated by the Planning process control Attention, while knowledge and skills play an integral part in the process as well. The attention work of Schneider, Dumais, and Shiffrin (1984) and the attention selectivity work of Posner and Boies (1971), which relate to

deliberate discrimination between stimuli, are similar to the way that the Attention process was conceptualized. Planning processes regulate a variety of other processes, including attention.

Simultaneous processing is a necessity for sorting information into groups or a coherent whole. The ability to recognize patterns as inter-related elements is made possible by the parieto-occipital–temporal brain regions. Due to the substantial spatial characteristics of most Simul-taneous tasks, there is a visual–spatial dimension to activities that demand this type of process. Conceptually, the examination of Simultaneous processing is achieved using tasks that could be described as involving visual–spatial reasoning found in progressive matrices tests like those developed by Penrose and Raven (1936), but Simultaneous processing is not limited to non-verbal content, as demonstrated by the impor-tant role it plays in the grammatical components of language and comprehension of word rela-tionships, prepositions, and inflections (Naglieri, 1999). This is most apparent by the inclusion of the Verbal–Spatial Relationship subtest included in the CAS (Naglieri & Das, 1997a). Typically, however, matrices tests have been included in so-called nonverbal scales of intelligence tests such as the Wechsler Nonverbal Scale of Ability (Wechsler & Naglieri, 2006), the Stanford-Binet Fifth Edition (SB5; Roid, 2003), the Naglieri Nonverbal Ability Test (NNAT; Naglieri, 1997), and the Kaufman Assessment Battery for Children Second Edition (K-ABC2; Kaufman & Kaufman, 2004) as a Simultaneous processing scale.

Successive processing is relevant when working with stimuli arranged in a defined serial order such as remembering or completing infor-mation in compliance with a specific order. However, the information must not be able to be grouped into a pattern (like the number 553669 organized into 55-3-66-9), rather each component can only be related to those compo-nents that precede it. Successive processing is typically an integral element involved with the serial organization of sounds, such as learning sounds in sequence and early reading. Further-more, Successive processing has been concep-tually and experimentally related to the concept of phonological analysis (Das, Naglieri, & Kirby, 1994). The concept of Successive proces-sing is also related to the concept of sequential processing included in the K-ABC2 (Kaufman &

Kaufman, 2004), and tests that require recall of serial information such as Digit Span Foard on the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV; Wechsler, 2003).

Traditionally, intelligence has been exam-ined through verbal, nonverbal, and quantita-tive tests, yet the PASS theory offers an alternative approach to intelligence. This theory not only broadens the idea of what "abilities" should be measured but also emphasizes the sig-nificance of basic cognitive processes. In addi-tion, the functions of the brain that encompass the PASS processes are considered the building blocks of ability conceptualized within a cogni-tive processing framework. While the theory may have its roots in neuropsychology, "…its branches are spread over developmental and educational psychology" (Varnhagen & Das, 1986), p. 130). Thus with its connections to developmental and cognitive processing, the PASS theory of cognitive processing offers an advantage in explanatory power over the notion of general intelligence (Naglieri & Das, 2002).

Operationalization and Application of the Theory

The PASS theory was operationalized by the CAS; (Naglieri & Das, 1997a). This instru-ment is amply described in the CAS Interpre-tive Handbook (Naglieri & Das, 1997b) and by Naglieri (1999). Naglieri and Das (1997a) gen-erated tests to measure the PASS theory follow-ing a systematic and empirically based test development program designed to obtain effi-cient measures of the processes for individual administration. The PASS theory was used as the foundation of the CAS, so the content of the test was determined by the theory and not influenced by previous views of ability nor developed from a factorial method.

There is a strong empirical base to support both the PASS theory and its operationalization in the CAS (see Das, Kirby, & Jarman, 1979; Das, Naglieri, & Kirby, 1994; Naglieri, 1999, 2003, 2005; Naglieri & Das, 1997b, 2005). The CAS measures the four basic psychological pro-cesses using 12 subtests (three for each of the four scales) and was standardized on a sample of 2,200 children aged 5–17 years who were representative of the US population on a num-ber of important demographic variables (see

Naglieri & Das, 1997b for more details). The CAS Full Scale score has a high internal reliability ranging from 0.95 to 0.97 for the different age groups. The average reliability coefficients for the scales are 0.88 (Planning), 0.88 (Attention), 0.93 (Simultaneous processing), and 0.93 (Successive processing).

Validity

As described earlier in the chapter, the neuropsychological work of A. R. Luria (1966, 1973, 1980, 1982) is the basis for the fundamental validity of the PASS theory. With Luria's three functional units serving as a foundation, Das (1972), Das, Kirby, and Jarman (1975, 1979), and Das, Naglieri, and Kirby (1994) began the task of figuring out methods for measuring the PASS processes. These efforts included extensive analysis of the methods used by Luria, related procedures used within neuropsychology, experimental research in cognitive and educational psychology, and related areas. Their work, which was summarized in several books (e.g., Kirby, 1984; Kirby & Williams, 1991; Das, Naglieri, & Kirby, 1994; Naglieri, 1999; Naglieri & Das, 1997b) illustrated that the PASS processes associated with Luria's concept of the three functional units could be measured. Their work also demonstrated that there was significant potential for the application of the theoretical conceptualization of basic psychological processes. The remainder of this section will provide a summary of relevant validity research on the PASS theory as operationalized by the CAS.

Relationship to Achievement

One of the purposes of an ability test is to determine a child's level of cognitive functioning that can then be used to anticipate performance in a number of contexts, such as school. Some have noted that the relationship between a test of ability and achievement is perhaps one of the most important aspects of validity (Brody, 1992; Cohen, Swerdlik, & Smith, 1992; Naglieri & Bornstein, 2003). For this reason, the relationship between ability and achievement has been examined by researchers for many years. The relationship between ability and intelligence has been found to be about 0.55–0.60 (Brody, 1992; Naglieri, 1999). It has been argued, however, that a portion of the correlation between

traditional IQ tests and academic achievement tests is due to the similarity in content that exists between these two types of tests (Naglieri & Bornstein, 2003; Naglieri & Rojahn, 2004). That is, it is well known that IQ tests often include measures of vocabulary, general information, and arithmetic as do tests of achievement. This raises the question: how well would a test built on the PASS theory correlate with achievement given that although it does include verbal subtests, it does not contain measures of vocabulary and arithmetic, for example? The relationship between the CAS and achievement has been studied.

Naglieri and Rojahn (2004) examined the relationship between the PASS processing scores of the CAS with the Woodcock Johnson-Revised (WJ-R) Tests of Achievement (Woodcock & Johnson, 1989) with a sample of 1,559 students aged 5–17 years. The sample was also part of the CAS standardization sample and closely represented the US population on gender, race, parental education, and geographic region. The correlation between the CAS Full Scale with the WJ-R Tests of Achievement was 0.71 for the Standard (all 12 subtests) and 0.70 for the Basic Battery score (eight subtests). These findings provide evidence for the construct validity of the CAS but more importantly demonstrate that basic psychological processes are strongly related to academic performance as measured by a standardized test of achievement.

Naglieri, Goldstein, DeLauder, and Schwebach (2006) compared the Wechsler Intelligence Scale for Children-Third Edition (WISC-III; Wechsler, 1991) to the CAS, and Woodcock-Johnson III (WJ-III) Test of Achievement (Woodcock, McGrew, & Mather, 2001) for a sample of children aged 6–16 ($N = 119$) who were referred for evaluation due to learning problems. The purpose of their study was to compare the WISC-III and the CAS correlations with the same achievement scores. The obtained correlations and those corrected for restriction in range between the WJ-III achievement scores with the WISC-III were 0.52 and 0.63. For the CAS, these correlations were 0.69 and 0.83. The study's results suggest that when the same children took the two ability tests, and those scores were correlated with the same achievement scores, the CAS Full Scale correlations were significantly higher (Naglieri, Goldstein, DeLauder, and Schwebach (2006).

The evidence briefly summarized here suggests that the PASS processes are strongly related to achievement and at least as related to achievement as traditional IQ test scores. This provides construct validity evidence for operationalization of this theory by the CAS. These findings are particularly important because the measures of the PASS processes do not include achievement-like subtests (e.g., vocabulary and arithmetic). This provides considerable advantage and is especially important for children who come from disadvantaged environments as well as those who have had a history of academic failure.

Relationship to Behavior

Though limited research studies have been conducted specifically examining the relationship of PASS processes to behavior, the hypothetical connection is not difficult to make. For example, Successive processing involving the ability to follow information in a linear organization or chainlike progression will exert a significant impact on a child's behavior. Following a sequence such as hanging up a coat, putting a book in one's desk, and sitting in your seat demands that tasks in their order be remembered. A child's behaviour will also be substantially influenced by Planning processing which allows the child to make decisions about how to do things, monitor the effectiveness of those solutions, and modify or select new behaviors as needed.

Several researchers have examined the relationships between behavioral problems seen in children with ADHD as they are related to profiles of PASS scores. For example, Paolitto (1999) was the first to study match samples of ADHD in normal children. Children with ADHD earn significantly lower scores on the Planning scale. Similarly, Dehn (2000) and Naglieri, Goldstein, Iseman, and Schwebach (2003) found that groups of children who met diagnostic criteria for ADHD earned significantly lower mean scores on the planning scale of the CAS. These results support the view that ADHD involves problems with behavioral inhibition and self-control which is associated with poor executive control (Planning) (Naglieri & Goldstein, 2006). These findings suggest that the PASS processing theory has utility for differential diagnosis of behavioral conditions,

intervention, as well as response to intervention for behavioral problems (Naglieri, 2003, 2005).

Fairness

As the characteristics of the US population continue to change, the need for fair assessment of children has become progressively more important. However, as discussed earlier, it is common for traditional IQ tests to have items that measure vocabulary, general information, similarities between two words, and math word problems. This content can create an unfair disadvantage for many children, such as those living in non-English-speaking homes. Reducing the amount of knowledge needed to correctly answer the questions on intelligence tests is a useful way to ensure appropriate and fair assessment of diverse populations. Some researchers have suggested that intelligence conceptualized on the basis of psychological processes, such as the PASS theory as operationalized by the CAS, has utility for assessment of children from culturally and linguistically diverse populations because verbal and quantitative skills are not included (Naglieri, Rojahn, Matto, & Aquilino, 2005; Naglieri, Rojahn, & Matto, 2007).

Researchers have typically found a mean difference of about 15 points between Blacks and Whites on traditional measures of IQ. Results for PASS processing tests have been quite different. The CAS scores of a sample composed of 298 Black children and 1,691 White children have been compared (Naglieri et al., 2005). Controlling for key demographic variables, regression analyses showed an estimated CAS Full Scale mean score difference of 4.8, which is smaller than that found with traditional IQ tests. Another finding was that correlations between the CAS scores and WJ-R Tests of Achievement were very similar for Blacks (0.70) and Whites (0.64) (Naglieri et al., 2005). Similarly, Naglieri et al. (2006) examined the utility of the PASS theory with Hispanic children by comparing performance on the CAS of Hispanic and White children. The study showed that the two groups differed by 6.1 points using unmatched samples, 5.1 with samples matched on basic demographic variables, and 4.8 points when demographic differences were statistically controlled. Also, it was shown that the correlations between achievement and the CAS scores did not differ significantly for the Hispanic and

White samples (Naglieri et al., 2006). These studies illustrate that the PASS cognitive processing approach provides a fair way to assess diverse populations of children.

Diagnostic Utility of PASS

Two major goals of diagnosis are to discern variations in characteristics that help distinguish one group of children from another and, subsequently, to determine if this identification can help with intervention decisions. With these goals in mind, one way to examine the diagnostic utility of the PASS cognitive profiles is through the analysis of the frequency of the PASS cognitive weaknesses found in children in regular and special educational settings. A second way to explore the diagnostic utility is by examining specific populations (e.g., ADHD and LD). Research that has examined the PASS cognitive profiles using these two methods is summarized below.

Naglieri (1999) defined three types of disorders that can be identified in one or more of the basic PASS processes. Using the ipsative methodology originally proposed by Davis (1959) and modified by Silverstein (1982, 1993), a relative weakness is a significant weakness which is low in relation to the child's mean PASS score. In contrast, a disorder in one or more of the basic psychological processes (termed a cognitive weakness) is found when a child has a significant intraindividual difference (using the ipsative method) *and* the lowest score also falls below some cut-off designed to indicate what is typical or average. Therefore, in comparison to a relative weakness, a cognitive weakness method uses a dual criterion based on having a low score relative to the child's mean and a low score relative to the norm group. Naglieri (1999) further suggested that a third type of disorder is a cognitive weakness accompanied by an academic weakness comparable to the level of the cognitive weakness. The children who have a cognitive weakness and an academic weakness should be considered candidates for special educational services if other appropriate conditions are also met (e.g., the child has had opportunity to learn and appropriate instruction was provided) (Naglieri, 1999).

Naglieri (2000) found that children with a cognitive weakness earned lower scores on achievement and the more pronounced the cognitive weakness, the lower the achievement scores were. Additionally, children with a PASS cognitive weakness were more likely to have been previously identified and placed in special education. Finally, the presence of a cognitive weakness was significantly related to achievement, whereas the presence of a relative weakness was not. Naglieri's (2000) findings support the view that the PASS theory could be used to identify children with cognitive and related academic difficulties for the purpose of eligibility determination and instructional planning. Naglieri (2003) and Naglieri and Pickering (2003) provide theoretical and practical guidelines about how a child's PASS cognitive weakness and accompanying academic weakness might meet criteria for special educational programming.

The PASS theory offers a way to define and measure a disorder in basic psychological processes that can be integrated with both academic performance and all other relevant information to help make a diagnosis. Although the PASS constructs play an important role in the identification process, the determination of a learning disability or any other disorder cannot be made solely on the basis of these constructs. Still, the connections between the PASS and academic instruction have also led researchers to begin an examination of the diagnostic potential of PASS profiles.

Diagnostic Utility in Specific Populations

The profiles of the PASS scores obtained from populations of children with ADHD, mental retardation, and reading disabilities have been examined in several studies (Naglieri, 1999). The finding among the various studies has been that differences between the groups have emerged in predictable and discriminating ways. That is, children with mental retardation earned low and similar PASS scores (Naglieri & Das, 1997b), while children with evidence of reading disabilities obtained average scores except for low Successive scores (Naglieri, 1999). In contrast, children diagnosed with ADHD earned average scores except in Planning (Dehn, 2000; Paolitto, 1999; Naglieri, Goldstein, Iseman et al., 2003; Naglieri, Salter, & Edwards, 2004). A brief summary of the PASS research examining children with ADHD and children with evidence of reading disabilities is provided below.

There is now a consistent line of research that suggests that ADHD-Combined Type can be viewed as a failure of self-control or Planning as defined by the PASS theory. Some researchers have described a Planning cognitive deficit as a distinguishing mark of ADHD (Naglieri & Goldstein, 2006). This interpretation of ADHD is consistent with Barkley (1997, 1998) who has suggested that ADHD is a failure of control related to frontal functioning intimately involved in regulating and self-monitoring performance, which fits directly with the Planning part of the PASS theory. Additionally, there is mounting evidence that suggests adults and children with ADHD also have Planning (e.g., executive functioning) deficits (Ellison, 2005, p. 473). This is relevant because, as noted earlier, the Planning process and executive functioning share many of the same qualities.

Children with ADHD have earned PASS profiles that are predictably similar to each other, but are also distinctly different from other populations. Naglieri, Goldstein, Iseman, and Schwebach (2003) reported that children with ADHD had a different PASS profile than those with anxiety disorders. Additionally Van Luit, Kroesbergen, and Naglieri (2005) found that Dutch children with ADHD earned their lowest score on measures of Planning. These findings are in contrast to profiles reported by for children with reading disabilities that were low on Successive processing and children with anxiety disorders that showed no PASS weakness.

Reading Disability

It has been suggested that a major cause of reading disability for children is the inability to engage in phonological coding (Stanovich, 1988; Wagner, Torgeson, & Rashotte, 1994). Reading research generally supports the idea that phonological skills play an important role in early reading. Wagner, Torgesen, and Rashotte (1994) argue that phonological skills are causally related to normal acquisition of reading skills. The relationship between pre-readers' phonological scores and their reading development 1–3 years later (Bradley & Bryant, 1985) adds support to the causal relationship between phonological and reading skills. A review by Share and Stanovich (1995) concluded that there is strong evidence that poor readers, as a group, are impaired in a very wide range of basic tasks in the phonological domain (1995, p. 9).

There is substantial evidence that one of the causes of learning disabilities is related to problems with certain types of information processing or an overdependence on one form of cognitive processing (Reynolds & French, 2005, p. 108). Studies examining children with reading disabilities have shown that they perform adequately on all of the PASS constructs except Successive processing (Naglieri, 1999). This is consistent with Das' view (see Das, 2001; Das, Naglieri, & Kirby, 1994) that reading failure is the result of a deficit in sequencing of information (e.g., Successive processing). Das, Naglieri, and Kirby (1994) suggest that a specific cognitive processing deficit that is involved in word reading and reading deficit underlies a phonological skills deficit. For example, the various central correlates of word decoding can be untied by Successive processing. Additionally, Successive processing's binding strength increases if the word is a pseudo-word and further if it is to be read aloud, requiring pronunciation. The correlates are speech rate (fast repetition of three simple words), naming time (for naming simple, short and familiar words arranged in rows, naming rows of single letters, or digits and color strips), and short-term memory for short lists of simple and short words. Of these tasks, speech rate correlates best with decoding pseudo-words. Whereas the correlation with naming time is the next best one, it has, however, a slight edge over speech rate in decoding short familiar words (Das, Mishra, & Kirby, 1994). Thus when discriminating between normal readers and children with dyslexia, it was shown that a test of strictly phonemic coding, such as phonemic separation, led to approximately 63% of correct classification, whereas two tests that involve articulation and very little phonemic coding (Speech Rate and Word Series, both Successive processing tests in the CAS) contributed nearly 72% to correct classification. In other words, the discriminant function analysis showed that the two tests, Speech Rate and Word Memory, were better at classifying normal and poor readers than a direct test of phonemic segmentation. Several studies on the relationship between PASS and reading disability have since supported the hypothesis that in predicting reading disability, PASS scores are as important as phonological skills (Das, Parrila & Papadopoulos, 2000).

The various studies involving special populations lead to the conclusions that children with mental retardation evidence minimal variation among the four PASS scales. In contrast, the LD and ADHD children profiles are quite disparate. The children with reading decoding problems evidence a successive weakness whereas the children with ADHD evidenced a Planning deficit. These findings are consistent with Das view (see Das, Naglieri, & Kirby, 1994) of reading failure as a deficit in sequencing of information (Successive) as well as Barkley view (1997) of ADHD as a failure in control (Planning) (also see Naglieri & Goldstein, 2006). As a group, these findings suggest that the PASS processing scores have utility for differential diagnosis, intervention, as well as predicting children's response to instruction (Naglieri, 2003, 2005).

Treatment Validity

There are several resources for applying the PASS theory to academic remediation and instruction. The PASS Remedial Program (PREP; Das, 1999) developed by J. P. Das is an option as is the Planning Strategy Instruction, also known as the Panning Facilitation Method, described by Naglieri andPickering (2003). Other resources include Kirby and Williams' 1991 book *Learning Problems: A Cognitive Approach* as well as Naglieri and Pickering's (2003) book *Helping Children Learn: Intervention Handouts for use in School and Home*. The first two methods are based on empirical studies, while the third and fourth resources, the two books, contain several reasonable approaches to academic interventions. The instructional methods in the books use structured and directed instructions based on PREP, as well as minimally structured instructions based on Planning Strategy Instruction. The books vary from much applied (Naglieri & Pickering, 2003) to more general (Kirby & Williams, 1991). Since the two books utilize the concepts of both PREP and Planning Strategy Instruction, only PREP and Planning Strategy Instruction will be discussed in further detail.

PREP

Based on the PASS theory of cognitive functioning (Das, Naglieri, & Kirby, 1994), PREP was developed as a cognitive remedial program and is supported by a line of research beginning with Brailsford, Snart, and Das (1984), Kaufman and Kaufman (1979), and Krywaniuk and Das (1976). These researchers demonstrated that students could be trained to use Successive and Simultaneous processes more efficiently, which resulted in an improvement in "their performance on that process and some transfer to specific reading tasks also occurred (Ashman & Conway, 1997, p. 169)." PREP aims at improving the information processing strategies – specifically Simultaneous and Successive processing – that underlie reading, while at the same time avoiding the direct teaching of word reading skills such as phoneme segmentation or blending. The tasks in the program teach children to focus their attention on the sequential nature of many tasks, including reading. This helps the children better utilize Successive processing which is a very important cognitive process needed in reading decoding. PREP is also founded on the premise that the transfer of principles is best facilitated through inductive, rather than deductive, inference (Das, 2001). The program is accordingly structured so that tacitly acquired strategies are likely to be used in appropriate ways.

Support for PREP has been established by studies that examine the effectiveness of the instructional method for children with reading decoding problems. Carlson and Das (1997) studied children who received PREP ($n = 22$) in comparison to a regular reading program (control $n = 15$). The samples were tested before and after intervention using the reading subtests Word Attack and Word Identification from the Woodcock Reading Mastery Test-Revised (WRMT-R; Woodcock, 1987). The intervention was conducted in two 50-min sessions each week for 12 weeks. Another study by Das, Mishra, and Pool (1995) involved 51 reading disabled children who were divided into a PREP ($n = 31$) and control ($n = 20$) groups. There were 15 PREP sessions given to small groups of four children. Word Attack and Word Identification tests were administered pre- and post-treatment. In both studies, PREP groups outperformed the control groups.

Boden and Kirby (1995) studied a group of learning disabled children who were randomly assigned to a PREP training and a control group that received regular instruction. As in previous studies, the results showed significant differences

between the two groups in reading decoding of real and pseudo-words. Similarly, Das et al. (2000) found children who were taught using PREP ($n = 23$) improved significantly more in pseudo-word reading than did a control group ($n = 17$). Another study by Parrila, Das, Kendrick, Papadopoulos, and Kirby (1999) was an extension of the above experiments except for three important changes. The first change was that the control condition was a competing program given to a carefully matched group of children. Additionally, the participants ($N = 58$) were beginning readers in Grade 1, which was younger than the participants in the previous studies. Lastly, the training was shorter in duration than in most of the previous studies (Parrila et al., 1999). The purpose of this study was to examine the possible efficacy of PREP in relation to a meaning-based reading program received by the control group. All of the participants were experiencing reading difficulties and were divided into two matched remediation groups of either PREP or the control condition. Results showed a significant improvement of reading (Word identification and Word Attack) for the PREP group; the gain in reading was greater than it was for the meaning-based control group (Parrila et al., 1999). Specific relevance to the children's CAS profiles was also demonstrated by the fact that those children with a higher level of Successive processing at the beginning of the program benefited the most from the PREP instruction, but those with the most improvement in the meaning-based program were characterized by higher level of Planning (Parrila et al., 1999).

All of these experimental studies of the PREP instruction "suggest that process training can assist in specific aspects of beginning reading" (Ashman & Conway, 1997, p. 171). Taken together, the above studies make a clear case for the effectiveness of PREP in remediating deficient reading skills during the elementary school years. Additionally, they illustrate the connection between the PASS theory and intervention.

Planning Strategy Instruction

The connection between Planning and intervention has been well illustrated by research that has examined the relationship between strategy instruction and CAS Planning scores. The studies have involved both math and reading achievement scores. These intervention studies focused on the concept that children can be encouraged to be more planful when they complete academic tasks and that the facilitation of plans positively impacts academic performance. The initial concept for Planning Strategy Instruction was based on the work of Cormier, Carlson, and Das (1990) and Kar, Dash, Das, and Carlson (1992). These authors taught children to discover the value of strategy use without being specifically instructed to do so. The children were encouraged to examine the demands of the task in a strategic and organized manner. They demonstrated that students differentially benefited from the technique that facilitated planning. Children who performed poorly on measures of Planning demonstrated significantly greater gains than those with higher Planning scores. These initial results indicated that a relationship between PASS and instruction might be possible.

Planning Strategy Instruction was shown to improve children's performance in math calculation by Naglieri and Gottling (1995, 1997). All children in these studies attended a special school for those with learning disabilities. In the investigations students completed mathematics work sheets in sessions over about a 2-month period. The method designed to indirectly teach Planning was applied in individual 1 on 1 tutoring sessions (Naglieri & Gottling, 1995) or in the classroom by the teacher (Naglieri & Gottling, 1997) about two to three times per week in half hour blocks of time. Students were encouraged to recognize the need to plan and use strategies when completing mathematic problems during the intervention periods. The teachers provided probes that facilitated discussion and encouraged the children to consider various ways to be more successful. More details about the method are provided by Naglieri and Gottling (1995, 1997) and Naglieri and Pickering (2003).

The relationship between Planning Strategy Instruction and the PASS profiles for children with learning disabilities and mild mental impairments was studied by Naglieri and Johnson (2000). The purpose of this study was to determine whether children with cognitive weaknesses in each of the four PASS processes and children with no cognitive weaknesses showed different rates of improvement in math when given the same group Planning Strategy Instruction. The findings from this study showed

that children with a cognitive weakness in Planning improved considerably over baseline rates, while those with no cognitive weakness improved only marginally. Similarly, children with cognitive weaknesses in Simultaneous, Successive, and Attention showed substantially lower rates of improvement. The importance of this study was that the five groups of children responded very differently to the same intervention. Thus, the PASS processing scores were predictive of the children's response to this math intervention (Naglieri & Johnson, 2000).

Haddad et al. (2003) assessed whether an instruction designed to facilitate Planning would have differential benefit on reading comprehension, and if improvement was related to the PASS processing scores of each child. The researchers used a sample of general education children sorted into three groups based on each of the PASS scale profile from the CAS. Even though the groups did not differ by CAS Full Scale scores or pretest reading comprehension scores, children with a Planning weakness benefited substantially (effect size of 1.52) from the instruction designed to facilitate Planning. In contrast, children with no PASS weakness or a Successive weakness did not benefit as much (effect sizes of 0.52 and 0.06, respectively). These results further support previous research suggesting that the PASS profiles are relevant to instruction.

Iseman (2005) examined Planning Strategy Instruction in children with learning disabilities and ADHD. Students in the experimental group engaged in Planning Strategy Instruction designed to encourage effective strategies in mathematics. A comparison group received additional math instruction by the regular teacher. Following the intervention, an analysis examined students with and students without a cognitive weakness in Planning on the CAS. Students with a Planning cognitive weakness in the experimental group improved considerably on math worksheets. In contrast, students with a Planning cognitive weakness in the comparison group did not improve. Students with ADHD in the experimental group with a weakness in Planning improved considerably on the worksheets. In contrast, students with ADHD in the comparison group without a cognitive weakness in Planning did not improve. Thus, individuals with cognitive weaknesses in Planning, with and without ADHD, benefited more from Planning strategy instruction than normal instruction (Iseman, 2005).

The results of these Planning Strategy Instruction studies using academic tasks suggest that changing the way aptitude is conceptualized (e.g., as the PASS rather than traditional IQ) and measured (using the CAS) increases the probability that an aptitude-by-treatment interaction (ATIs) is detected. Past ATI research suffered from inadequate conceptualizations of aptitudes based on the general intelligence model. That approach is very different from the basic psychological processing view represented by the PASS theory and measured by the CAS. The summary of studies provided here is particularly different from previous ATI research that found students with low general ability improve little, whereas those with high general ability improve a lot to instruction. In contrast, children with a weakness in one of the PASS processes (Planning) benefited *more* from instruction compared to children who had no weakness or a weakness in a different PASS process. The results of these studies also suggest that the PASS profiles can help predict which children will respond to the academic instruction and which will not.

Sample Cases

Case I: Ryan's Problem with Planning

Ryan is a friendly fifth-grade student who wants to please his teachers. If Ryan thinks a teacher is upset with him, he becomes noticeably anxious because he does not know how to improve the situation. Despite his desire to do well in school, Ryan does not participate in class discussions and often turns his assignments in late. He needs constant reminders to perform daily tasks such as putting his books away or cleaning up after himself. Ryan rarely asks for help with assignments that he does not understand. As a result, his work is usually late or incomplete. When his teacher offers help, Ryan does not even understand what he needs help with. Starting a new assignment is very difficult for Ryan because he does not know where to begin. Yet Ryan does very well when his teacher directs him through the process of the assignment. Unfortunately, Ryan becomes confused about what to do next as soon as his teacher leaves him to work on his own.

Math is difficult for Ryan, yet he has always tried to do well in the subject because he knows his older brother loves math. Despite a history of receiving poor grades in the subject area, Ryan continued to be enthusiastic about math until his class began to study word problems. No matter how many times Ryan's teacher tried to teach him how to work through a word problem, he felt overwhelmed. When his teacher helped Ryan through the word problems, she found that he had trouble keeping track of the different steps he needed to follow. However, if the teacher explicitly told him what to do, Ryan demonstrated that he had the mathematic knowledge-base to complete every aspect of the question.

Math is not the only area in school where Ryan struggles. It seems difficult for him to figure out how to solve any kind of problem, both inside and outside the classroom. This leaves Ryan in a constant state of anxiety because he feels like he does not know how to handle daily tasks. His social relationships have started to suffer because of this as well. Recently, Ryan's friends stopped including him in their daily game of ball. When the teacher confronted them about excluding Ryan, they said that Ryan only plays ball his way and acts like a baby if they want to play the game differently. According to Ryan, he does not understand how to play the game differently. More importantly, he does not know how to convince his friends to play with him again.

Ryan's parents are concerned with his overall performance at school and his increasing level of anxiety about his ability to do well in school. Ryan struggles to start his homework because he never knows how to do the assignments and, even if he tries, he believes that he will still get it wrong. Ryan has begun to doubt the quality of all of his work and often begs his parents to let him leave his work incomplete. Now due to his recent problems with his friends, Ryan is always upset about school and wishes he did not have to go.

Ryan's teachers met with each other and his parents on multiple occasions to try to think of ways to help him. A few of his teachers tried to give him simplified directions throughout the day. One teacher even had him plan out his daily assignments in a journal. Most of Ryan's entries in this journal were either incomplete or directly copied from the original entry the teacher wrote with him. In retrospect, the teacher

realized this was not the best solution for the problem since Ryan found it difficult to complete essays, or other tasks involving writing. The other methods to help Ryan also had limited success, so his teachers requested that the school psychologist conduct an assessment on Ryan's levels of achievement and ability.

The results (shown in Figure 1) indicate that not all of Ryan's scores on measurements of cognitive ability fell within the average range. Test results from the Cognitive Assessment System (CAS) showed that Ryan has a cognitive weakness in Planning processing. This finding goes along with Ryan's scores on measures of achievement. He also earned scores in the 70s and low 80s on tests of math calculation, math word problems, written language, and math fluency, all of which demand Planning processing. Whenever Planning processes played a substantial part in an achievement task, either on a formal test or in the classroom or at home, Ryan experiences considerable problems because he cannot manage the demands of the task. Ryan's problem with Planning processing is a vital piece of insight into why he has so much trouble completing projects, and figuring out how to work through multi-step problems, including resolving conflicts with his friends.

Ryan has problems whenever the task requires that he manage his own behavior and figure out *how* to solve a problem on his own; these things demand Planning ability. Planning is a cognitive process that provides children with the intellectual tools needed to manage their behavior in social as well as academic environments. Fortunately, children can be taught to better utilize planning processes (Naglieri, 2005; Naglieri & Das, 2005). In fact, in the last 15 years, there has been a series of research studies that have consistently shown that children can be taught to better utilize plans and strategies when doing lots of different things. The cognitive strategy instruction that teaches children to be more planful has been shown to improve academic performance. The initial work of Cormier, Carlson, and Das (1990) and Kar, Dash, Das, and Carlson (1992) taught children to discover the value of strategy use without being specifically instructed to do so. The children were encouraged to examine the demands of the task in a strategic and organized manner. These authors demonstrated that children who performed poorly on measures of planning

CAS Results	Standard Scores	Difference from Mean	Strength or Weakness
Planning	76.00	−19.25	Weakness
Attention	95.00	−0.25	
Simultaneous	108.00	12.75	Strength
Successive	102.00	6.75	
Mean	95.25		
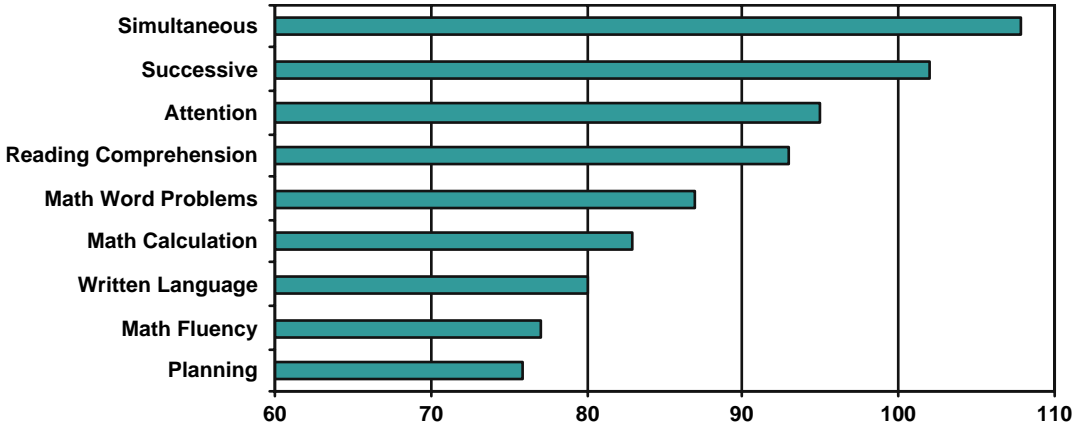
Figure 1. Ryan's PASS and selected achievemet scores.

demonstrated significantly greater gains than those with higher planning scores. Similarly, Naglieri and Gottling (1995, 1997) conducted two studies and showed that cognitive strategy instruction in Planning improved children's performance in math calculation.

Case II: Jessica's Problems with Simultaneous Processing

Jessica is a soft-spoken fourth grader who loves to help her teachers with small tasks, such as passing out papers and collecting homework. Despite her helpful nature, Jessica is shy and behaves awkwardly with her classmates. She hardly ever raises her hand to answer questions and even avoids eye contact with the teacher during class discussions.

Jessica's teachers are particularly troubled with how easily Jessica looses her direction when walking between classrooms. Jessica has been going to the same school for the last 2 years, but she still gets confused, and at times lost, in the hallways. The result is not only a seemingly unnecessary record of tardiness that Jessica cannot explain but also constant teasing from her classmates because of this odd problem.

During the school day, Jessica works diligently. She remains focused for long periods of time without letting the activities of the classroom distract her from the task at hand. Yet it is what she concentrates on that is the problem. Jessica does well with straightforward assignments such as filling in the blanks. However, she finds the more complex tasks that require integration of information from multiple sources almost impossible because she does not know how to pick out the important details. For example, each child had to create a poster that represented his or her interests in and outside the classroom. At first, Jessica was really excited about the assignment because she has so many different interests in animals, crafts, and music. However, when Jessica finished the poster, it did not reflect her broad

spectrum of interests. Instead, the poster only had pictures of her pet cat. When asked why she did not include any of her other interests, Jessica said that she was confused because she did not know how to include everything.

It has always been difficult for Jessica to make friends. When she does try to interact with her classmates, they often complain that she is annoying. When she first started going to this school, Jessica tried very hard to become friends with two of the girls in her class. Jessica followed them around and tried to imitate their behaviors. After a few weeks, the girls became tired of Jessica and tried to make it clear that they did not want her around. At first, they demonstrated their feelings through actions, such as hiding from her at recess. Jessica never picked up on the girls' feelings toward her, so finally they bluntly told Jessica that they did not want to be her friend. Jessica does not understand why she bothers her classmates so much, so she has learned to leave them alone altogether. She does not see the common pattern in her behaviors that irritates her classmates. However, her teachers have noticed Jessica's socially inept behavior and feel that she does not understand the social dynamics behind friendships.

Lately, Jessica has become frustrated with her poor grades. In her first few years of elementary school, her hard work resulted in good grades. Yet now she feels that she is working even harder and cannot understand why she is not doing well. She never recognizes the purpose behind her assignments and lately does not know why she should continue to work so hard. Both her parents and her teachers are concerned that eventually Jessica will stop trying. Due to both her academic and social problems, Jessica's teachers asked the school psychologist to meet with her.

Jessica's school psychologist conducted a thorough assessment that produced test scores consistent with her difficulties in the classroom. Jessica's scores on the CAS showed a significant weakness in Simultaneous processing (see Figure 2). This weakness helps to explain the

CAS Results	Standard Scores	Difference from Mean	Strength or Weakness
Planning	95.0	−2.5	
Attention	110.0	12.5	Strength
Simultaneous	83.0	−14.5	Weakness
Successive	102.0	4.5	
Mean	97.5		
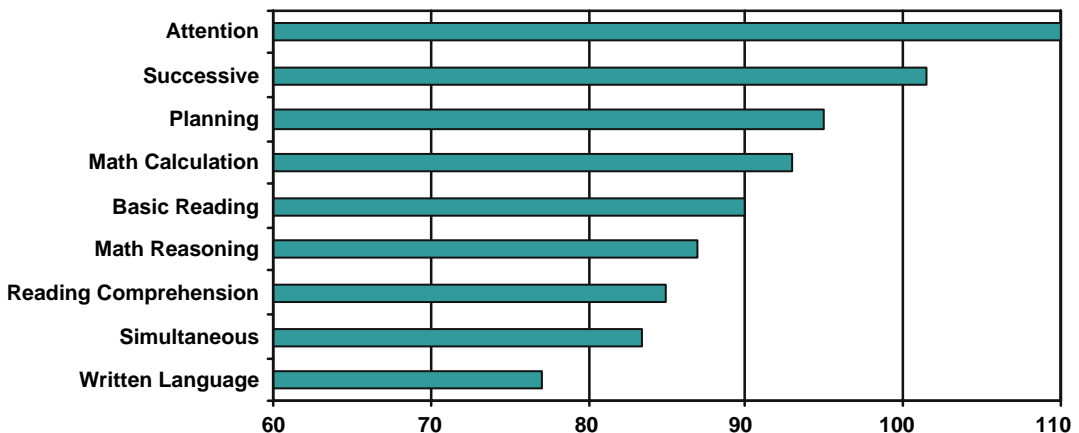
Figure 2. Jessica's PASS and selected achievement scores.

poor scores she earned on tests in reading comprehension, written language, and math reasoning. Jessica's CAS scores are very consistent with the problems Jessica is having in school. Simultaneous processing is used to recognize patterns, relate separate pieces into a whole, and understand relationships. Jessica's academic and interpersonal problems are directly linked to her weakness in Simultaneous processing. Due to this weakness, it is very difficult for Jessica to understand social dynamics, pick up on themes, figure out spatial relationships, and recognize the overall purpose behind assignments.

Jessica's weakness in Simultaneous processing should be managed by helping her see the relationships among, for example, behaviors exhibited by her peers. This could be achieved through diagrammatic representations like story maps (see Naglieri & Pickering, 2003, pp. 97–98) used in academic areas. Reading comprehension would likely be enhanced through the use of graphic organizers (see Naglieri & Pickering, 2003, pp. 51–52). These methods would help her see how things are interrelated. The behaviors that could provide insights into other student proficiency with Simultaneous processing will be any of those that require the child to get the big picture. Look for confusion about the goal of the classroom activity, the purpose of the project, or reasons why something does or does not make sense. Students who are good in Simultaneous processing have a good understanding of social relationships because they can easily see patterns in behavior. They are able to understand and relate the verbal and nonverbal forms of communication into a whole and extract the meaning, sometimes hidden meaning, behind interactions among people. They are sometimes described as people who are good with visual–spatial tasks which, of course, demand relating many parts into a coherent whole. Those who are poor in Simultaneous seem to miss the point of discussions, get lost easily, and have problems working in complex environments.

Conclusions

There is a growing need for neuropsychological measures to evaluate and explain function to facilitate prognosis and most importantly guide intervention. Luria's PASS theory offers a blueprint for defining the basic neuropsychological processes underlying human performance and behavior. Appreciation and application of this model as a framework for neuropsychological assessment provide pediatric neuropsychologists with the essential mindset necessary to not just understand children's learning and behavior but to guide and develop effective intervention.

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