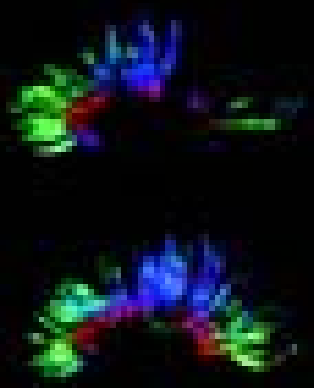
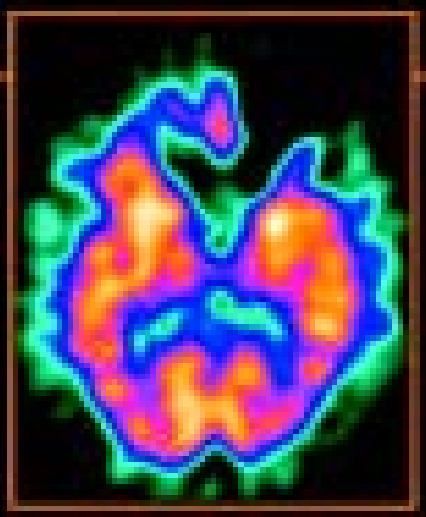


Pediatric Neuropsychological Intervention



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Pediatric Neuropsychological Intervention

Pediatric neuropsychology is the practice of understanding and elucidating brain–behavior relationships as applied to children and adolescents. This volume examines current trends in the assessment and treatment of common disorders including traumatic brain injuries, brain tumors, epilepsy, and autistic spectrum disorders. Its primary aim is to help practitioners and researchers identify and understand the evidence to support interventions with a range of acquired or congenital neuropsychological disorders.

The text is divided into three sections. Section one provides a foundation by considering general issues relevant to assessment and treatment in pediatric neuropsychology. Section two guides practitioners in their approach to the use of interventions in a range of conditions and disorders, and the book closes with a section focusing on medical and experimental initiatives with an emphasis on interdisciplinary issues.

This book is essential reading for pediatric neuropsychologists, child clinical psychologists and school psychologists, as well as pediatric neurologists and psychiatrists.

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Pediatric Neuropsychological Intervention

A Critical Review of Science & Practice

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To the patients and their families with whom I have had the opportunity to work, who have guided my thinking about practice and science.

Scott J. Hunter

With love to my children, Corey and Laura, and with gratitude to the many pediatric patients who have been an inspiration over the last 20 years.

Jacobus Donders

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Section I

Fundamentals of pediatric neuropsychological intervention

1

Introduction

Scott J. Hunter and Jacobus Donders

Pediatric neuropsychology is the science and practice of understanding and elucidating brain-behavior relationships as applied to children and adolescents. This specialty has advanced significantly in a relatively short period of time. Once merely a downward extension of general adult-based neuropsychology, the assessment of complex neurocognitive and behavioral difficulties in children and adolescents has become a comprehensive, independent arena of practice and research in its own right. This has been reflected in several recent published works about common neuropsychological disorders in children and adolescents (Dewey & Tupper, 2004; Yeates, Ris & Taylor, 2000) and comprehensive norms for assessment instruments that can be applied with such persons (Baron, 2004). However, with few exceptions (Farmer, Donders & Warschausky, 2006), there is a dearth of comprehensive reviews of methods of intervention from a pediatric neuropsychological perspective.

The move from diagnosis to recommendations is one still fraught with uncertainty for many practitioners. We live in a time when we are able to make use of many sophisticated approaches to diagnosis, but there are increasing demands for interventions for which there is firm empirical evidence as to their efficacy and cost-effectiveness. Research-informed data concerning the most appropriate and efficacious interventions for childhood neuropsychological disorders is scarce. Given this situation, the primary purpose of this volume is to help practitioners and clinical researchers better identify and understand the empirical evidence that is available that supports various interventions with a range of congenital or acquired neuropsychological disorders in children and adolescents.

It is the intention of this book to present what we know about intervention for developmental and acquired neuropsychological deficits, and how to best apply that knowledge when developing effective recommendations in reports, and when translating that information for use in educational and social environments. Additionally, because the state of the science remains quite variable in terms of

efficacy studies, it is our hope to redirect investigations within pediatric neuropsychology toward the domain of intervention. At a time when we are expected to demonstrate the effectiveness of our interventions with regard to clinical practice, to in effect show that we are practicing evidence-based neuropsychology, it appears appropriate to appraise where the science exists to support our clinical approaches and recommendations. Hence, we have sought recent and accumulating information to support the field's goals of defining the best means for remediating, supporting, and accommodating children and adolescents with developmental and neurocognitive disabilities.

All of the authors included in this volume are pediatric neuropsychology experts, with specializations in the areas about which they are writing. Through their own research, or their appreciation and integration of studies supporting their area of interest, these authors attempt to direct professionals in the field toward the "best practices" available at this time. Additionally, each author makes suggestions about where s/he believes the research needs to focus within the domain or disability being addressed; to guide the field toward a better elucidation of how to best intervene, and to help identify areas needing further research.

This text has been divided into three sections. The first section has been organized to provide a foundation for considering general issues that are relevant to intervention in pediatric neuropsychology. These include general developmental, cultural, and policy aspects of this specialty practice.

Section two has been developed to guide the practitioner in her or his approach to intervention across the more common presenting childhood disability conditions and disorders. Each of the chapters included in this section is designed as a review and critique of the current state of knowledge concerning common neuropsychological disorders and their associated interventions, with an emphasis on what needs to be done to improve efficacy and practice through empirical research.

The third section provides a review of experimental and medical interventions, as well as a discussion of how to approach assessment, diagnosis, and intervention from an interdisciplinary format. Each of these chapters provides the viewpoint of experts about the development and application of these methodologies and how they are best regarded given the current state of knowledge we have about these techniques and applications. The final chapter serves as a guide for the future, based on a synthesis of the information provided in the preceding chapters of the book.

We hope that this book will serve both as a reminder of where we have come from, and as a stimulus for further investigation and application of pediatric neuropsychological intervention. We anticipate that it will be of interest to not

only pediatric neuropsychologists but also to medical, allied health, and education professionals who are interested in providing evidence-based interventions to children and adolescents with congenital or acquired brain-related disorders.

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2

A developmental approach to pediatric neuropsychological intervention

Tara V. Spevack

The field of pediatric neuropsychology maintains a unique role in helping children with developmental, acquired, and degenerative disorders involving the central nervous system. Significant advances in assessment paradigms have promoted an understanding of the associated cognitive, behavioral, social, and emotional sequelae of these conditions. An understanding of treatment strategies to mitigate adverse consequences and optimize outcome is less complete, but emerging, as will be addressed in subsequent sections of this volume. Setting the stage for those examinations, the objectives of this chapter are to (1) offer a general review of neuropsychological development, (2) provide a rationale for adopting a developmental approach to clinical practice, and (3) introduce key concepts related to pediatric neuropsychological intervention.

Neuropsychological development

An appreciation of normal brain function and neuropsychological development is critical for informing age-appropriate intervention strategies in children. This knowledge serves as a foundation on which to base coherent approaches to clinical activity. Although a side-by-side review of corresponding structure–function relationships at each age would be ideal, efforts to correlate structural brain changes with concomitant cognitive and behavioral progression are still in their infancy (Majovski, 1997). For the purposes of this chapter, development is considered first from the perspective of central organizing principles and then from the perspective of functional neuroanatomical domains.

Organizing principles

Eight organizing principles of brain structure and function, adapted from Berninger and Richards (2002), provide a useful framework from which to approach the study of neuroanatomy.

1. *Neurons*. The primary functional unit of the central nervous system is the neuron. Neurons are varied in morphology and function. Collections of neurons with similar structure form unique cytoarchitectonic regions throughout the brain. In some areas, these neuronal congregations are organized into distinct layers of cortex.
2. *Communication*. Neurons communicate with each other by way of two types of projection fibers: *axons* carry messages away from each cell; *dendrites* receive messages from other cells. Single axons are bundled into collections of axons (i.e. *tracts*). These pathways serve to form sequenced connections between neurons, and on a larger scale brain regions, for purposes of transmitting electrical and chemical signals.
3. *Axes*. Communication in the brain occurs along three dimensions. Firstly, vertical axes allow for bottom-up and top-down communication across multiple projection pathways. Secondly, horizontal axes allow for interhemispheric communication across right-to-left and left-to-right commissural pathways that connect homologous structures on either side of the brain. With several exceptions, a *crossing principle* applies, in which each hemisphere responds to sensory stimulation from the opposite side of the external world and controls motor movement on the contralateral side of the body. Thirdly, horizontal axes also allow for communication between the back and front regions of the brain. In this sense, the posterior neocortex is conceptualized as processing primarily sensory information, and the anterior neocortex as processing primarily motor information (Kolb & Whishaw, 2003). Thus, posterior-to-anterior axes transfer sensory information from the external and internal environments to the neocortex for higher-level processing, while anterior-to-posterior axes transmit information necessary for purposeful motor responses.
4. *Hierarchies*. The brain is hierarchically organized according to its degree of direct connection to the outside world. *Primary projection areas* serve as a direct interface with the environment by receiving information from sensory input pathways and sending information to motor output pathways. Each primary projection area processes a unique type of data. Specifically, the primary projection areas in the occipital, parietal, and temporal lobes are specialized for processing visual, auditory, and body sense/tactile information, respectively, and the primary projection area in the frontal lobe is specialized for processing olfactory and motor information. Next, this information is sent to *secondary association areas* where it is converted into symbolic content. Secondary association areas then transmit information to *tertiary association areas* for higher-level polymodal integration which is necessary for language, attention, memory, and executive functions (Kolb & Whishaw, 1996; 2003). In this way,

information moving through these functional neuroanatomical tiers becomes progressively more abstract, and less directly influenced by sensory and motor information (Fuster, 2003).

5. *Specialization*. The brain is comprised of various structures and regions, each of which is specialized to perform a unique function. Certain functions are subserved by homologous regions in each hemisphere. In the case of lateralization, however, one or the other hemisphere is specialized to mediate a given function (Witelson, 1985). For example, behaviors involving sequential operations (e.g. language) are associated with the left hemisphere, and behaviors involving simultaneous operations (e.g. visuospatial processing) are associated with the right hemisphere. Specialization, though, is hardly absolute. A single neural structure may participate in more than one function, and even in the case of lateralized behaviors, the ''non-dominant'' hemisphere often is involved. In short, multiple neural networks mediate almost every human behavior, which implies some level of redundancy and an allowance for reliance on alternative pathways. In this way, there is some insurance that the developing brain can respond flexibly to the changing environment and continue functioning in the event of damage.
6. *Systems*. The various components of the brain are interconnected and organized into functional systems that operate in tandem, as well as independently. These systems change over the course of development, reflecting a process of continuous neural ''remodeling'' that enables greater behavioral efficiency and complexity as maturation progresses (Merzenich *et al.*, 2002). Thus, the structures and brain regions involved with a given function may be quite different at various points in the lifespan. Related to this, as development unfolds there are sensitive periods in which a particular type of environmental stimulation is especially important for normal organization of a specific brain region or function to occur (Greenough *et al.*, 1999; Kolb & Gibb, 2001). During these periods, certain external experiences seem to allow for ''growth spurts'' and refinements in a neural system. Without such input, development may be disrupted, resulting in abnormal functional organization (Courshesne, Townsend & Chase, 1995).
7. *Plasticity*. Plasticity refers to the capacity for modification of brain structure and function as part of normal development and learning, and in response to neural insult. Efforts to fully understand this phenomenon have resulted in considerable debate. In general, there is consensus that the developing brain is more plastic than the mature brain, and possesses greater potential for alternative organization following damage (Elbert, Heim & Rockstroh, 2001; Stiles, 2000). The capacity for plasticity, however, is far from linear. Plasticity depends, at least in part, on the timing, site, and extent of an injury, all of which

ultimately contribute to neurobehavioral outcome. Thus, significant functional devastation can occur as a consequence of brain perturbations that occur during particular developmental neural events. For example, neurological insult during neurogenesis has been shown to result in poorer functional outcome than neurological insult during neuronal migration and active synaptogenesis (Kolb & Gibb, 2001; Kolb & Cioe, 2004). Similarly, specific brain regions have "temporal windows" within which substantial neural regeneration can occur, and outside of which regeneration is limited or absent (Kolb & Gibb, 2001). With regard to lesion site, correspondences between the location of brain damage and functional impairment are stronger in adults than in children, which is consistent with greater plasticity in the developing brain. In a general sense, the extent of an injury has ramifications for functional outcome; however, there is not always a correlation between the extent of brain damage and amount of recovery of function (Lebeer, 1998). For example, substantial neurobehavioral restoration can occur in the face of massive brain damage, and significant functional impairment can result from a relatively small lesion. Although there is a high degree of unpredictability related to outcome following neural insult, the potential for sparing or recovery of function holds particular promise for intervention efforts.

8. *Resilience.* The degree of functional sparing, or resiliency, following neurological insult cannot be explained by plasticity alone. It appears that there are other intrinsic, biological mechanisms and extrinsic, environmental mechanisms at play. These influences, which collectively serve to ameliorate or compound neurological dysfunction, are referred to as *reserve* (Dennis, 2000; Geller & Warren, 2004). Each brain, then, shaped by innate influences and life experiences, is unique. Consequently, variation in brain structures and functions across individuals is the norm (e.g. Caplan, 2003).

Brain development

The organizing principles elucidated in the previous section are evident from the very beginnings of central nervous system development. A primitive brain has formed by 3 weeks gestation, is human in appearance by 14 to 15 weeks gestation, and looks similar to the adult brain by 40 weeks gestation (Kolb & Cioe, 2004), but continues to develop well after birth. This transformation involves seven stages:

1. *Neural tube.* A sheet of cells at one end of the embryo rolls up to form a neural tube that surrounds a ventricle. The top end of the tube will become the brain while the bottom end will become the spinal cord (Berninger & Richards, 2002).

2. *Neurogenesis*. Neurons are formed along the ventricular wall. By 4 months gestation, the majority of neurons have been created (Berninger & Richards, 2002) and by 6 months gestation, the process of neurogenesis is complete (Spreen, Risser & Edgell, 1995).
3. *Neuronal migration*. Once formed, neurons migrate outward along specialized filaments to genetically predetermined locations. The ultimate destination of a neuron plays a role in determining which neurotransmitter it will release. During the migrational process, neurons aggregate with similar subtypes of neurons to form cortical layers. In the cerebrum, the innermost layer is formed first, with subsequent layers forming in an inside-out direction, ultimately creating six cortical layers by gestational week 24 (Majovski, 1997). In the cerebellum, migration occurs in an opposite, outside-in fashion (Spreen *et al.*, 1995). Most neurons have migrated to their final location by 2 years of age (Kolb & Fantie, 1997).
4. *Differentiation*. During neuronal migration, rapid formation and growth of axons starts. Axons may extend to subcortical or other cortical regions, and within or across hemispheres. Dendrites typically begin developing only after neurons have reached their destinations, forming single extensions that later branch out and become progressively more complex (i.e. arborization). In contrast to axons, dendritic development is relatively slow and continues long after birth, making it particularly sensitive to environmental influences. A notable increase in the complexity of dendritic arborization occurs between the ages of 2 and 12 years (Kolb & Fantie, 1997), but final differentiation of the outer cortical layers continues through the second decade, and perhaps beyond (Majovski, 1997).
5. *Synaptogenesis*. Connections between the axon of one neuron and the cell body, dendrites, axons or synapses of another neuron begin forming during gestation (Berninger & Richards, 2002; Kolb & Fantie, 1997). Although synaptogenesis is genetically driven, environmental influences play a reciprocal and key role in determining the actual neural connections that are made. Thus, brain development represents a complex interplay between intrinsic biological programs and extrinsic events.
6. *Pruning*. During development, the brain produces many more cells and connections than are needed. Selective death (pruning) of neurons, axons, dendrites, and synapses in response to genetic blueprints and competition for resources allows for refinement of neural systems. Multiple periods of proliferation and pruning take place, with evidence to suggest that synapse elimination has a greater role than cell death in sculpting more complex functional systems (Huttenlocher, 1990). The rate of pruning redundant or unused neurons and synapses depends upon the specific brain region, but in

general begins at 7 months and 2 years, respectively. Continuing well into adolescence (Berninger & Richards, 2002; Kolb & Fantie, 1997), pruning allows the environment to exert significant influence on cortical organization (Neville & Bavelier, 2002).

7. *Myelination.* Myelination is the process by which designated cells (i.e. oligodendrocytes) wrap around neuronal projections to form an insulating sheath that allows for more rapid and efficient transmission of signals (Berninger & Richards, 2002; Kolb & Fantie, 1997). Although myelination starts at roughly 16 weeks gestation, the process becomes most vigorous postnatally and continues into adolescence, if not beyond (Kolb & Cioe, 2004; Kolb & Fantie, 1997). Myelination of a tract is concomitant with the tract becoming functional (Majovski, 1997). Thus, regions of the central nervous system that are necessary for viability (e.g. spinal cord, brain stem) and basic functions of the newborn (e.g. primary sensory and motor areas) begin to myelinate before birth (Berninger & Richards, 2002; Kolb & Fantie, 1997). The parietal and frontal association areas are the last regions to become myelinated, respectively (Neville & Bavelier, 2002).

Development of function

The human newborn enters the world with a range of primitive motor reflexes necessary to sustain life, and a basic, though comprehensive, sensory awareness of the environment. These motor and sensory functions serve as the building blocks of voluntary behaviors (Majovski, 1997). As central nervous system development proceeds, neural systems are continually reorganized, especially as new motor, attention, memory, language, visuospatial, and executive skills are mastered and become more automatic. Moreover, interaction occurs among these overlapping and interrelated functional domains (Diamond, 2002). Although the field of developmental neuroscience has begun elucidating the intricate anatomical changes underlying maturation of function, this line of research is still in the very early stages (e.g. Huttenlocher & Dabholkar, 1997; Johnson, 2001; Munakata, Casey & Diamond, 2004). The following section provides a broad overview of brain-behavior relationships in terms of functional systems. Since this information is based on investigations of animals and human adults, caution must be exercised in extending these findings to children.

Sensory systems

Each of the five sensory modalities (vision, hearing, touch, taste, and smell) has a unique receptor cell that specializes in detecting a specific kind of energy (light, sound, mechanical, and chemical) and converting that energy into neural activity (Nolte, 1993). This neural activity travels along a sequenced pathway of three to

four neurons that converge in the brainstem, and then (with the exception of olfaction) in the thalamus, which serves as a relay to the cortex. At the level of the cortex, sensory representations are grossly divided among the lobes, with vision represented in the occipital lobe, sound in the temporal lobe, olfaction in the frontal lobe, and taste and touch in the parietal lobe. Touch is just one component of the somatosensory system, which also processes information related to pressure, temperature, pain, position sense from muscles and joints (kinesthesis), and internal body systems (interoception) such as blood pressure.

Motor systems

In its broadest sense, the motor system sends top-down commands from the brain to the muscles of the body. Motor nerves in the peripheral nervous system then execute these commands, and sensory feedback from the environment back to the central nervous system allows motor actions to be appropriately modified. Various conceptual models of the motor system have been proposed and continue to be debated. One prominent model with important clinical implications highlights two distinct, but interacting, groups of motor pathways (Spreen *et al.*, 1995). The *pyramidal system* is dedicated to volitional, skilled motor movements, and the *extrapyramidal system* serves to modulate and adjust the movements of the pyramidal system. It is important to note, however, that the distinction between pyramidal and extrapyramidal systems, although clinically useful, is overly simplistic, in part because the systems are inextricably linked (Nolte, 1993).

From an anatomical perspective, pyramidal pathways originate in the primary motor cortex of the frontal lobe, which is arranged topographically in the form of a homunculus, such that each muscle from the opposite side of the body is represented. Thus, damage to this region results in motor deficits (paralysis or weakness) on the contralateral side of the body. Descending fibers from the motor cortex constitute part of the internal capsule, a subcortical white matter structure. The fibers then continue their descent through the midbrain to their final destination in the spinal cord. In contrast, the extrapyramidal system refers to motor circuits involving parts of the basal ganglia, cerebellum, and brainstem. A more detailed examination of the components of the motor system reveals many interconnections and mechanisms for regulation and feedback. For example, the primary motor cortex is regulated and influenced by the anterior premotor cortex, which has connections with subcortical regions of the brain (thalamus, hypothalamus, limbic).

The *basal ganglia* are a collection of subcortical gray matter structures. They form part of a circuit, composed of multiple cortical–subcortical loops, that links the motor cortex with other cortical regions by way of the midbrain, hypothalamus, and thalamus. Although the principal function of the basal ganglia

is control of complex movements, involvement in higher order cognitive activity also has been demonstrated (e.g. Rektor *et al.*, 2005); therefore, it is not surprising that these cortical–subcortical circuits involving the basal ganglia always include connections to the frontal cortex. In contrast, because there are no direct links between the basal ganglia and spinal cord, influence over motor movements is achieved by modulation of descending motor pathways (Nolte, 1993). Damage to the basal ganglia is associated with unintentional and non-purposeful movements that occur unexpectedly, and disturbance of muscle tone.

The *cerebellum* serves an important role in maintaining balance and postural control, and coordinating voluntary movements. Like the basal ganglia, the cerebellum does not connect directly to the spinal cord. Rather, its elaborate interconnections, which include projections to and from subcortical regions and the prefrontal cortex, make it possible to assemble separate motor acts into complex, unitary behaviors, and to assure precision, timing, and accuracy of movements. Also involved with motor and cognitive learning, the cerebellum is part of a coordinated circuit that includes the prefrontal cortex and is active when confronting activities that are unfamiliar or difficult, that require rapid responding and concentration, or that involve changing conditions and parameters (Diamond, 2000). Cerebellar damage typically is associated with tremor and incoordination during intentional movement (ataxia), impaired rapid alternating movements (dysdiadochokinesia), overshooting when reaching for an object (dysmetria), nystagmus, or awkward posture and gait.

The *brainstem* and *spinal cord* make up the lowest neuroanatomical level of the motor system, and are connected by pathways responsible for activating many reflexes, and executing complex movements such as walking and orienting to visual targets. In addition, the brainstem is involved with controlling body temperature and the sleep–wake cycle, and regulatory behaviors such as feeding, drinking, and sexual activity (Kolb & Whishaw, 2003).

Attention systems

Attention is a multidimensional construct that refers to both involuntary and voluntary focusing of consciousness on environmental information for the purpose of bottom-up and top-down processing (Harris, 1998). Although multiple theories and models of attention have been advanced, there is general agreement regarding three basic anatomical components that subserve attentional processing (Ponsford & Willmott, 2004). Firstly, the midbrain reticular formation and limbic structures play a key role in maintaining vigilance; modulating basic arousal, motivation, and affective tone; and assessing the salience of information. At a cortical level, this attentional system is predominantly controlled by the right hemisphere (Aimola Davies, 2004).

Secondly, occipital-parietal and occipital-temporal pathways make up a *posterior attentional system* that receives general information about perceptual and emotional aspects of the internal and external environments for higher-level processing (Turner & Levine, 2004). The occipital-parietal pathways are responsible for visual orienting; spatial attention; and engaging, disengaging and shifting of attention. The occipital-temporal pathways select objects and features of objects upon which attention will be focused (Kolb & Whishaw, 2003).

Thirdly, the frontal lobes, basal ganglia, and anterior cingulate gyrus are part of an *anterior attentional system* that receives projections from the posterior attentional system. The anterior system is responsible for detecting and selecting the information that ultimately becomes the focus of attention; implementing strategies for managing attentional demands; and switching and inhibiting attentional responses. It also is posited that the anterior system activates the selective attention mechanisms of the posterior system (Stuss *et al.*, 2002). An important aspect of the attentional system is its within-hemisphere specialization. Not only is each hemisphere responsible for shifting attention to the contralateral side of the environment, but the right hemisphere is involved with processing global aspects of information, while the left hemisphere is involved with processing more specific features (Harris, 1998).

Memory systems

Multiple conceptual models explicating the stages, subtypes, and anatomy of memory have been proposed. In terms of stage theories, there is a general agreement that memory involves at least five levels of processing, wherein information is initially registered, consolidated, stored, maintained, and later retrieved as needed. Stage models also tend to incorporate mechanisms for holding information in mind for rehearsal or manipulation (i.e. working memory; Baddeley, 1986), and for employing active strategies for encoding and retrieving information (Anderson & Lajoie, 1996), which presumably involve executive functions.

With regard to memory subtypes, several predominant models, which are not mutually exclusive, have been advanced (for a review, see Bauer, Grande & Valenstein, 2003; Tulving, 1987). One widely cited model posits an *episodic* memory system involving specific events and autobiographical experiences, and a *semantic* memory system necessary for language and involving factual knowledge, concepts, and vocabulary (Tulving, 1972). A second model makes a distinction between *declarative* memory, which is a conscious process involving the formation, storing, and recollection of life events, semantic knowledge and facts (i.e. ''knowing that''); and *nondeclarative* memory, which is an unconscious process involving skill learning and access to procedural knowledge (i.e. ''knowing how''; Cohen & Squire, 1980). A third model distinguishes

between *explicit* memory, which involves conscious and deliberate recollection, and *implicit* memory, which involves non-deliberate learning, unintentional retrieval, and indirect effects on memory such as priming (Graf & Schacter, 1985). Interactions among these memory systems can, and do, occur (Bauer *et al.*, 2003).

An understanding of the development of memory has only recently started to emerge. Most notably, early assumptions that young children do not possess the capacity to remember have been discounted by a growing corpus of research over the past few decades demonstrating that multiple memory systems exist in early infancy (Meltzoff, 1990; Temple, 1997). Moreover, age-related improvements in all aspects of memory functioning take place throughout childhood, including increases in working memory capacity, the length of time that information can be retained, the amount of detail that is recalled, and the intentional use of mnemonic techniques (Anderson & Lajoie, 1996; Bjorklund & Douglas, 1997; Ornstein & Haden, 2001). For example, a dramatic gain in memory skills occurs around the age of 18 months, when children start speaking. It is at this time that children begin recounting past events and using rudimentary strategies to facilitate remembering (Ornstein & Haden, 2001). By the age of 3 years, children can provide more detailed narrative accounts, and possess a greater number of deliberate memory strategies that are used more capably. This developmental trend in the maturation of memory functions continues throughout childhood and adolescence, and is concomitant with underlying neural changes, including myelination of frontal regions.

From a neuroanatomical perspective, memory is subserved by extensive neural networks with interconnected cortical and subcortical components (Fuster, 2003; Glisky, 2004). Although medial temporal regions, including the hippocampus, are essential for forming and encoding new memories, top-down and bottom-up influences in the brain related to the motivational and emotional significance of information also play a key role. In addition, circuits involving the frontal cortex, basal ganglia, and cerebellum mediate implicit memory and action sequences. The temporal cortex is associated with the process of storing information, with the left hemisphere specialized for verbal content and the right hemisphere specialized for visual–spatial content (Glisky, 2004), but memory stores involve associative networks encompassing the entire cortex (Fuster, 2003). It follows that memories can be accessed at different cognitive and perceptual hierarchical levels, with retrieval being activated and driven by bottom-up processes involving hippocampal and subcortical input, or top-down processes originating in the frontal cortex. Finally, of no less importance, the prefrontal cortex mediates executive functions related to verbal and visual working memory, and management of memory processes.

Language systems

Language involves multiple input and output modalities, including aural reception of speech by the ears, visual reception of the speaker and printed text by the eyes, oral expression by the mouth, and written expression by the hand (Berninger & Richards, 2002). Although the left hemisphere serves a dominant role in the reception and expression of language in the majority of people, the right hemisphere also is highly involved. In general, the left hemisphere is specialized for structuring sentences syntactically and sequencing syllables, and the right hemisphere contributes to auditory comprehension and prosody (Kolb & Whishaw, 2003).

With regard to underlying anatomic substrates of language, the primary auditory cortex functions as the principal linguistic processor and is located bilaterally in the temporal lobes, with specialization of the left hemisphere for speech sound perception, and the right hemisphere for processing non-speech sounds. Following speech sound perception by the left auditory cortex, information is transmitted to a posterior language center in the left temporal lobe (Wernicke's area) involved with comprehension of spoken language (i.e. language reception by the ears). From Wernicke's area, information is conducted along a white matter pathway (*arcuate fasciculus*) to an anterior language center (Broca's area), located in the left frontal motor association cortex and involved with expressive language. The information then travels to the face and hand areas of the motor cortex, which produces language (i.e. language spoken by the mouth and written by the hand). Subcortical and cerebellar structures also play a role in expressive language functions (Gout *et al.*, 2005), and left parietal-temporal and occipital-temporal regions are highly involved in reading (i.e. language by the eyes; Shaywitz & Shaywitz, 2005).

Although there are merits to conceptualizing language in terms of interconnected subcomponents, models involving strict structure–function relationships, often used as a basis for explaining circumscribed aphasia syndromes, have not been supported by research, particularly when considering developing language in children. Indeed, significant variability in language localization and organization seems to be the norm rather than the exception (Caplan, 2003). Further complicating the picture is evidence that the anatomical organization of language functions changes with age and in response to experience. For instance, the anterior and posterior regions of both hemispheres are active during word comprehension at 13 months of age, but by 20 months of age only temporal and parietal regions in the left hemisphere are active in typically developing infants with average vocabularies (Neville & Bavelier, 2002).

Visuospatial systems

Visual information related to color, form, and motion is first processed in the occipital lobe. From there, a ventral stream projects to the inferior temporal cortex where object and color perception takes place, and to the superior temporal sulcus where spatial aspects of an object are processed, making object recognition possible. In addition, a dorsal pathway projects from the occipital lobe to the posterior parietal cortex, where information about the spatial location of an object in space is processed and then used to guide visual exploration and movement (Farah, 2003). The ventral and dorsal streams are therefore referred to as the ''what'' and ''where'' pathways, respectively.

The parietal lobes play a central role in spatial processing, particularly within the right hemisphere. Specifically, damage to the right parietal lobe can be associated with neglect of the left side of the body and left extrapersonal space. Damage to the left parietal lobe is rarely associated with a similar impairment. One explanation for this finding is that the right parietal cortex contains a representation of the external world from the view of the observer (Kolb & Whishaw, 2003). A second explanation is that the right hemisphere is involved in sustaining non-directional vigilance and attention, and, in turn, influences the posterior system which mediates attention in space. In addition, the right hemisphere is responsible for directing global processing of spatial locations, while the left hemisphere focuses on more specific features of a spatial configuration (Aimola Davies, 2004). As such, damage to the right hemisphere adversely impacts both non-directional attention and directional spatial attention. The result is that attention is not spontaneously directed to the left side of personal space, and global representations are no longer available (Aimola Davies, 2004). The parietal lobes are also important for spatial aspects of math, reading, and mental rotations.

The frontal lobes are the destination of occipital-temporal and occipital-parietal visual streams and influence spatially guided behavior including looking, reaching, and walking, particularly when memory is involved (Kolb & Whishaw, 2003). Another important anatomical structure implicated in spatial functions is the hippocampus, which has bidirectional connections with the ventral and dorsal visual pathways and is thought to be involved with spatial mapping of the external environment and pathfinding (Kolb & Whishaw, 2003). This theory of hippocampal function, however, does not have universal support.

Executive systems

The term *executive functioning* refers to a wide range of higher-level cognitive processes, and emotional and behavioral regulatory processes, some of which have been detailed in previous sections. This system also mediates expression of emotion, self-awareness, insight, initiation, planning, organizing, establishing

goals, implementing effective strategies for achieving goals, monitoring performance, problem-solving and reasoning, sequencing, flexibly shifting cognitive and behavioral repertoires based on changing demands, using knowledge and previous experience to guide actions, using judgment, and controlling impulses. Clearly, executive functioning involves significant coordination and direction of other functional systems.

No single neuroanatomical or functional model of executive functioning provides a complete account of the various aspects of this construct, but there is agreement that the frontal lobes, and prefrontal cortex in particular, play a central role. Although material specificity is apparent in the frontal lobes, such that the right side subserves global and affective processing and the left side subserves sequential and language processing (Turner & Levine, 2004), multiple hierarchical representations of functions involving the whole brain and inter-hemispheric communication are involved (Fuster, 2003). Moreover, the frontal lobes have extensive and reciprocal connections with other brain regions (Turner & Levine, 2004) that include cross-linkages with the reticular activating system related to arousal, and with the limbic system related to motivation and emotions. Within the limbic system, the amygdala mediates physiological aspects of emotion and perception of interpersonal signals such as facial expressions, making its input important for social cognition (Harris, 1998). The extensive interconnections between the frontal lobes and numerous other subcortical and cortical structures result in an elaborate interplay of neural processes. Damage along any of these pathways, or to the structures themselves, can be associated with deficits in executive functioning.

In terms of structure−function relationships within the prefrontal cortex, the dorsolateral region appears to be intricately involved with cognitive aspects of executive functioning, whereas the orbitofrontal and anteromedial regions are considered particularly important for behavioral and emotional processes, and personality (Cummings, 1993; Mesulaum, 1986). Damage to the medial frontal area can be associated with lack of initiation, a slow behavioral tempo, blunted affect, and apathy. In contrast, damage to the orbitofrontal region can be associated with social disinhibition, irritability, aggression, and poor impulse control (Cummings, 1993). The clinical manifestations of frontal damage, however, typically do not fit neatly within such delineations and this model has been criticized as oversimplified (Mesulam, 1986). In short, executive functioning represents a complex cortical-subcortical system, in which the frontal lobes play a vital, though not solitary, role. Viewed through a developmental lens, maturation of the frontal lobes, and prefrontal cortex in particular, is the most protracted of any brain region, beginning in infancy and extending into early adulthood, with corresponding improvements in higher-level cognitive functions (Diamond, 2002).

Neuropsychological models for pediatric assessment and intervention

Having reviewed the framework for brain–behavior relationships in the developing child, theoretical approaches to pediatric assessment and intervention can be critically evaluated. Here, these approaches are divided into two broad conceptual categories, the first involving extrapolation of adult neuropsychological models and the second involving incorporation of developmental models.

Extrapolation of adult models

Pediatric neuropsychology has its roots in adult neuropsychology, reflecting several convergent historical realities. On a practical level, the field of adult neuropsychology was established first. Thus, an initial understanding of brain–behavior relationships was based only on adult populations and applied successfully to the creation of assessment measures. In its beginnings, pediatric neuropsychology relied on these available resources for adults due to a paucity of knowledge about the complexities of brain–behavior relationships in, and the lack of assessment measures designed specifically for, children. Contributing to this state of affairs, early research suggested that, during childhood, the brain was more resilient to insult due to plasticity. As a result, the need for intervention in the pediatric population was not deemed particularly pressing.

Subsequent research and experience demonstrated that the application of adult models to the assessment of children was often based on untested assumptions (Baron, 2000; 2004; Baron, Fennell & Voeller, 1995; Fletcher & Taylor, 1984). Specifically, adult instruments were assumed to measure equivalent skills in adults and children, and similar cognitive deficits in adults and children were assumed to reflect the same underlying neuropathology (Fletcher & Taylor, 1984). A further assumption was that scientific methods for dissociating intact versus damaged neurobehavioral processes in the relatively static brain of the adult could be used to understand insult to the developing, dynamic brain of the child (Karmiloff-Smith, 2002).

It has become increasingly clear that these assumptions do not withstand critical investigation when applied to children. Firstly, the organization of brain systems underlying specific functions is sculpted and refined in the course of normal development. In the event of injury, the age at onset of a brain injury may be equally as important in determining the consequences on development as the location of the injury (Dennis & Levin, 2004). Moreover, the full impact of a brain insult in the child may not be immediately evident (Courchesne, Townsend & Chase, 1995; Dennis, 2000). Only as the child encounters increasingly complex demands for learning and adaptive functioning may it become apparent that necessary skills to successfully navigate these challenges are not developing

properly (Frampton, 2004). In short, one might describe the brain as a "moving target." A brain that is developing normally is not directly comparable to a brain that is developing following an insult, much less to a brain that has achieved adult status (Beaulieu, 2002). For these reasons, making inferences about the location of underlying brain damage in the child, and predicting and describing the effects of that damage across time as is done with adults, is often fraught with difficulties.

Additional pitfalls of applying adult neuropsychological models to children include that assessment measures and therapeutic tasks designed for adults may not be appropriate (let alone appealing) to children, and may demand skills that have not yet developed (Sohlberg & Mateer, 2001). For example, adult-oriented materials may pertain to functioning in the adult workplace rather than at school (Sohlberg & Mateer, 2001). A further difficulty is that adult test batteries often do not consider, much less incorporate, child-friendly strategies for addressing the more variable attention span, endurance and task persistence of children, or take into consideration the impact of these influences on task performance (Farmer & Muhlenbruck, 2000). Moreover, adult models are not geared toward advancing an understanding of the multidimensional environmental influences that may be impacting development (Bernstein, 2000; Farmer & Muhlenbruck, 2000). Based on these considerations, efforts have since been directed at formulating more developmentally appropriate neuropsychological models.

Developmental models

In the practice of pediatric neuropsychology, development must be considered an integral part of the clinical approach to children, not just a backdrop (Bernstein, 2000). For this to happen, the pediatric neuropsychologist must possess several core competencies (Farmer & Muhlenbruck, 2000). Firstly, patients must be approached with a solid understanding of normal developmental trajectories as a frame of reference (Denckla, 1997; Harper & Peterson, 2000). This knowledge serves as a template for determining the presence, nature, and extent of a problem, as well as developing appropriate recommendations for subsequent intervention. Secondly, a firm grasp of the potential direct and indirect effects of a given neuropsychological disorder, and the ways in which these variables may interact in a given child, is paramount (Dennis, 2000). Not only do these consequences include the physical and cognitive sequelae of a disorder, but also their psychosocial impact (Harper & Peterson, 2000). Thirdly, the age at onset and duration of the disorder must be considered. The disruption to development caused by a neurological insult is not static and depends, in part, on both the time at which the insult occurs and its chronicity (Dennis, 2000; Prigatano, 1999). Fourthly, consideration must be given to the psychosocial milieu of the child, which interacts with multiple biological factors (Bernstein, 2000). For example, the

advantages that can be conferred by family resources have been well documented (Dennis, 2000). It is, then, the ''life history of the neurons of the central nervous system'' that is central to an understanding of overall development (Nowakowski & Hayes, 2002, p. 58).

For pediatric neuropsychology in general, both stage and social–interactionist theories of child development, put forth by Jean Piaget and Lev Vygotsky, respectively, have been influential (Piaget, 1971/2002; Vygotsky, 1978; Ylvisaker & Szekeres, 1998). Neither model, however, fully incorporates concepts related to the brain. When neurological underpinnings of behavior are integrated into theories of development, an ideological shift often is necessary, since development is not characterized by absolute stages, nor is it entirely sequential. Moreover, the many operations of the brain, including those related to executive control, are present in the very young child, even if in a ''simple'' or rudimentary form (Johnson, 2000*a*; Ylvisaker & Szekeres, 1998). Taking these findings into account, maturation represents a continuous process in which neurobehavioral functions develop simultaneously, but not in parallel, with considerable interaction and interdependence among them (Johnson, 2000*b*; Ylvisaker & Szekeres, 1998), and ongoing influence from genetic and environmental factors.

Key concepts for pediatric intervention

For most children presenting with neurological disorders, cure is not possible. This reality has created a need for treatment methods that involve accommodation and remediation to promote the greatest possible level of adaptive functioning, independence, well-being, and social acceptance possible. With an understanding of anatomy and child development as its anchor, the field of pediatric neuropsychology is making notable advances in its ability to prescribe and help implement interventions. In general, ongoing efforts to develop evidence-based treatments for children have adopted a three-pronged approach aimed at ameliorating deficits, helping children to compensate for residual impairments, and establishing environmental supports (Farmer & Muhlenbruck, 2000; Mateer, Kerns & Eso, 1997). The reviews that follow will include scholarly examinations of current trends in the treatment of a range of childhood neurobehavioral disorders and identify important considerations for future research. Eight guiding principles for the practice of pediatric neuropsychological intervention serve as a preface for those reviews.

1. *Developmentally appropriate.* The rationale for adopting a developmental approach to intervention with children has been detailed in the previous section. To summarize, the practice of using adult-oriented therapies in

children is based on unfounded assumptions. Developmentally tailored treatment strategies that are based on knowledge of normal cognitive, social, and emotional maturational trajectories; informed by an understanding of the typical deviations that occur as a result of specific disorders; and sensitive to the unique needs of children, have the greatest chance of facilitating meaningful improvements in adaptive functioning.

2. *Functional.* The hallmark of an effective intervention is that it improves functioning in real-world settings (Mateer *et al.*, 1997; Ylvisaker & Szekeres, 1998). Efforts should be made to ensure that progress in a controlled therapy setting will be generalized and maintained at home, in the classroom, and in the community.
3. *Individualized.* That each child will respond differently to intervention is a certainty (Sohlberg & Mateer, 2001). Central to pediatric intervention is the emphasis on individualizing treatment so that it is meaningful and effective for, and capitalizes upon the unique strengths of, a particular child (Dunn, 2000; Sohlberg & Mateer, 2001).
4. *Longitudinal.* The consequences of neurological and medical disorders in the developing child change with time as new challenges are encountered. For treatment to be effective, both immediate and anticipated longer-term issues and needs must be addressed. In this way, it is possible for future problems to be ameliorated, if not avoided altogether (Bernstein, 2000; Frampton, 2004).
5. *Systems-based.* A child is part of multiple interacting systems that include the family and school, as well as community and healthcare organizations. Each of these entities can impact functioning and outcome, making it crucial that collaborative relationships exist among them to facilitate integrated treatment efforts. Thus, the importance of helping parents, teachers, and other adults in the child's life to be cooperative in their efforts to implement therapeutic strategies in natural settings cannot be underemphasized (Beaulieu, 2002; Sohlberg & Mateer, 2001). When resources in these systems are lacking, facilitating access to supports through available agencies may become a focus of intervention (Conoley & Sheridan, 1997).
6. *Family-centered.* Truly effective intervention involves building partnerships with families (Sohlberg & Mateer, 2001). Families benefit from honest and understandable information about their child's condition, strengths and weaknesses, and anticipated challenges and needs (Semrud-Clikeman, 2001). Equally important is culturally sensitive support and therapeutic intervention to families as they adjust to their child's disabilities and related stressors and losses. For this alliance to be meaningful, families must be afforded opportunities to provide input regarding treatment decisions and goals. As part of this process, empowering families to feel confident in their expertise

about their child and to become active participants in the intervention process may be necessary. In addition, teaching families interventions that can be used at home and at school to maximize a child's functioning can be an essential aspect of treatment. In short, a defining feature of family-centered care is the emphasis not only on strengths of the child, but also on strengths of the family (Conoley & Sheridan, 1997).

7. *Transdisciplinary*. Just as a child is part of a community, so too is the pediatric neuropsychologist who works with that child. Particularly in a rehabilitation setting, effective treatment necessitates developing shared goals and collaborating with other professionals involved in the child's treatment, rather than assigning separate objectives according to discipline (Sohlberg & Mateer, 2001). Here, the pediatric neuropsychologist can make valuable contributions to treatment planning based on results of the neuropsychological assessment and a well developed understanding of the brain-behavior relationships impacting the multiple facets of a child's functioning. The pediatric neuropsychologist is also uniquely qualified to integrate information from multiple professionals to form a comprehensive and balanced view of the child (Bergquist & Malec, 2002; Farmer & Muhlenbruck, 2000). Barriers to adopting a transdisciplinary approach to intervention include time limitations and negative group dynamics, such as conflicting personality styles, turf issues, and underlying stress related to providing patient care (Prigatano, 1999). An awareness and understanding of these obstacles allows them to be more effectively addressed, resulting in a more positive working alliance (Prigatano, 1999).
8. *Scientific*. Not only should intervention involve clearly defined and measurable goals, but it also should be theoretically driven and scientifically sound. Research aimed at demonstrating the efficacy of available treatment strategies, delineating the active ingredients of successful therapies, and guiding future efforts to improve outcome is paramount. To date, published findings are based largely on case studies and small, cross-sectional samples; however, results from larger scale, longitudinal investigations are beginning to emerge.

Conclusion

Significant advances in pediatric neuropsychological assessment have promoted an understanding of the cognitive, behavioral, social, and emotional sequelae of developmental, acquired, and degenerative disorders involving the central nervous system in children. These paradigms are the basis for determining an individual child's strengths and challenges. Because the development of effective, and disorder-specific, treatment methodologies to mitigate the consequences of these neurobehavioral conditions is in its early stages, frustrating limitations on the

recommendations that can be made, and interventions that can be offered, to address identified needs and optimize outcome exist. The chapters that follow represent an effort to critically examine state of the art interventions and emerging innovations, with an emphasis on empirically supported strategies that are true to the guiding principles of the practice of pediatric neuropsychology. Opportunities for further advancing the science and practice of pediatric neuropsychological intervention are also highlighted.

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3

Empirical bases for assessment and intervention

Elizabeth P. Sparrow

Complex neurocognitive disorders are challenging to diagnose and treat, particularly when they occur in the developmental context of childhood. Pediatric neuropsychologists have a wealth of background knowledge and expertise that contribute toward a better understanding of a child[1] who has a neurocognitive disorder. Pediatric neuropsychological assessment[2] is important for accurate diagnosis, effective treatment planning, and conflict resolution among parents, teachers, and others who work with the child.

At the most basic level, an intervention is an action that leads to change. In the context of pediatric neuropsychology, the primary goal of an intervention is to effect a change in the child. This can be accomplished through direct intervention with the child, or by altering the child's environment in some manner. At times, interventions require changing those who work with the child, including caregivers (parents, guardians, family members), childcare providers (after-school, nannies), teachers (general education and special education), therapists (mental health, speech-language, physical, occupational), and medical professionals.

A pediatric neuropsychological assessment can guide intervention by establishing the need for services or funding, providing general and specific treatment recommendations, assessing change in the child, and informing treatment decisions made by other professionals. In some ways, the assessment *is* a form of intervention, as the neuropsychologist may reframe perceptions, adjust expectations, motivate interveners, and address caregiver emotions. The assessment can also be conceptualized as an intervention, in that it may prevent development of secondary disorders.

[1] "Child" is used throughout this chapter to refer to children and adolescents.

[2] "Assessment" is used throughout this chapter to refer to the process of receiving a referral, completing a diagnostic interview, observing the child, administering tests as needed, interpreting results, and providing feedback in oral and/or written format. See Fernández-Ballesteros, De Bruyn, Godoy, *et al.* (2001) for further discussion of the terms "assessment", "evaluation", and "testing".

In clinical practice, we assume that the pediatric neuropsychological assessment is important for intervention. We make this assumption based on clinical experience and intuition. Unfortunately, there is limited research on the efficacy of assessment. In today's climate of restricted access to services, it is critical to establish the incremental validity of neuropsychological assessment for children with neurocognitive disorders. (For a review of "incremental validity," see Hunsley & Meyer, 2003; also Johnston & Murray, 2003.)

Pediatric neuropsychological assessment

A child is typically referred for an assessment because there is a concern about his or her functioning in a given setting. The assessor's goals are to identify the problem, describe factors that cause or sustain the problem, and provide recommendations for how to eliminate or decrease the impact of the problem. Beyond these shared goals, assessments vary widely. They can be brief, lengthy, focused, or comprehensive. They may involve standardized tests, structured interviews, rating scales, questionnaires, structured observations, and/or informal measures. Different professionals (e.g. speech-language pathologist [SLP], occupational therapist [OT], physical therapist [PT], special educator) conduct different types of assessments, describing various but sometimes overlapping aspects of functioning and deficits.

When complex neurocognitive disorders are present, it is likely that a child will be evaluated by more than one provider. It can be difficult for parents, teachers, and therapists to see how all of these specialist reports fit together to describe the whole child. It can also be challenging for individual evaluators to find a way to develop a comprehensive treatment plan for the child (see Prigatano & Naar-King, this volume, for discussion of the interdisciplinary team concept).

The background and training of a "pediatric neuropsychologist" provide a unique perspective from which to understand complex neurocognitive disorders. The term "neuropsychologist" refers to a specialist in brain–behavior relationships (please see Hannay *et al.*, 1998, for a more complete description of the background and training that are required for specialty practice in the area of clinical neuropsychology). A neuropsychologist has obtained pre- and post-doctoral education in brain anatomy, brain function, and brain injury/disease, as well as practical experience working with people who have had problems involving the brain, including assessment, diagnosis, and treatment of social, emotional, and behavioral issues. As discussed by Spevack (this volume), a "pediatric" neuropsychologist has training in human development. This developmental background provides the context for determining if behaviors/symptoms are age-appropriate, and identifying when absence of a behavior represents

a developmental deficit. As discussed in greater detail by Maegden and Semrud-Clikeman (this volume), most children and adolescents receive education, so pediatric neuropsychologists must have knowledge of school systems and procedures such as Comprehensive Family Service Plan (CFSP), Individualized Education Plan (IEP), and educational law (e.g. Individuals with Disabilities Education Act (IDEA)). This combination of training and experience in developmental, neurologic, psychological, and educational issues produces a professional who is uniquely qualified to assess a child in order to inform diagnosis, guide treatment planning, and resolve conflicts. These three aspects of a neuropsychological assessment subsequently impact intervention.

The neuropsychologist's background and training contribute toward accurate *diagnosis*, even before any standardized tests are administered. Careful analysis of the pattern of symptoms, including onset and course, can establish reasonable hypotheses about the child's diagnoses. Understanding of the child's medical and developmental background provides part of the context for interpreting presenting symptoms. Academic successes and failures can suggest cognitive strengths and weaknesses. General clinical factors, such as social, emotional, behavioral, and adaptive functioning, can be part of the child's presentation. Consultation with the referral source, record review, diagnostic interview, and clinical observation by a neuropsychologist can result in a realistic list of differential diagnoses to be considered. At times, these sources of information may be adequate for a neuropsychologist to make a diagnosis.

For example, if a child is referred for difficulty following directions, the neuropsychologist might first attempt to establish whether this problem is pervasive or variable. If the child demonstrates ability to follow directions in individual tutoring sessions, this provides useful information about possible variables that impact the symptom (e.g. distractions, background noise, redirection, complexity of instructions, relationship with tutor). Exploration of these factors in interview might help eliminate diagnoses from a list of differentials such as Attention-Deficit/Hyperactivity Disorder (ADHD), Central Auditory Processing Disorder (CAPD), or Oppositional Defiant Disorder (ODD).

When a neuropsychologist cannot rule out or confirm diagnostic hypotheses with available information, administration of standardized and informal tests can provide additional data. Specific measures are often chosen based on initial diagnostic hypotheses. In the previous example, the neuropsychologist might choose to administer tests of directed attention (e.g. visual cancellation tasks), sustained attention (e.g. continuous performance tests or CPTs), and receptive language (e.g. phonological processing, comprehension of instructions). During the testing session, the neuropsychologist has the opportunity to observe the child's response to test items (e.g. reaction to difficulty or boredom, types of

errors), as well as his response to the examiner (e.g. challenges authority, eager to please). The comparison of the child's raw test scores with normative data provides quantitative data about areas of deficit. These qualitative and quantitative findings, in conjunction with data from the child's background, can be interpreted within the context of the neuropsychologist's professional background to reach an appropriate diagnosis.

Identifying the primary diagnosis and any comorbid diagnoses is of some benefit. Practically speaking, determination that a disability exists[3] is a necessary step to access many services (e.g. federally- or state-funded programs such as school-based treatment) or access funding (e.g. insurance coverage). Labeling a cluster of symptoms provides a shortcut for communication among professionals (although diagnostic labels can also result in overgeneralization and reduced specificity of treatment programming). For parents, it can be helpful to have a name for the difficulties that their child is experiencing. A label can convert vague concerns into concrete issues, and can guide further education and understanding. Knowing a specific diagnosis provides a framework for learning about the associated features, course, and validated treatment options.

Although a diagnosis is often necessary, it is not sufficient. Simply labeling a problem does not make it go away. Thus, the second reason to complete a neuropsychological assessment is to inform *treatment planning*. Results from an assessment should lead to treatment recommendations, including general recommendations based on knowledge of the diagnostic group and individualized recommendations based on the specific needs of the child. Given the child's profile, the neuropsychologist can specify an effective means of responding to his or her needs. For example, a child with language impairment is unlikely to benefit from traditional ''talk'' therapy for his anxiety, but may do well with visualization techniques and hands-on, behavioral treatment modalities. It is important to use results from an assessment to identify potential barriers to treatment response, so that treatment plans can be developed to maximize benefit and minimize failure. An assessment also contributes toward prognostic statements, including description of factors which will limit long-term outcome and factors that suggest more positive long-term outcomes (e.g. early ability to imitate is associated with fewer long-term social communication deficits in autism; Charman, 2003).

Finally, data from neuropsychological assessments can be useful to *resolve conflicts* among different people involved in the child's life. Conflict is generally

[3] Different school districts use varying terminology when discussing diagnosis and service provision to students with disabilities. Throughout this chapter, the term ''disability determination'' is used to refer to the initial referral for services. In some school districts, ''consideration of Special Education eligibility'' is used to describe a similar step in the process.

caused by a combination of two factors: variable motivation and imperfect information. Parents, school staff, and other professionals often consider different motivating factors when analyzing cost-benefit ratios. Some participants in the process may want to conserve resources, including professional time, money, and materials, while others may wish to maximize the child's success at any cost. A neuropsychological assessment can help to prioritize needs and increase the effectiveness of treatment. This can help to stabilize the cost–benefit discussion by identifying ways to optimize a specific child's outcome while allocating a system's available resources. This, in turn, can help different participants to reach a successful compromise, regardless of their sources of motivation.

Another source of conflict is imperfect information (e.g. about specific student needs, diagnoses, appropriate services). Parents and teachers may have different perceptions about a student's actual needs, which impacts what services they believe would be appropriate. For example, although a parent might describe behaviors as "oppositional," and a teacher might attribute difficulties to poor memory, neuropsychological data could reveal that the underlying deficit was poor comprehension of directions. Identification of the actual problem in this example gives parents and teachers a common ground for treatment planning, as well as guiding treatment efforts toward speech-language therapy rather than time-outs or memory training.

In some cases, neither parents nor teachers have a full appreciation of the student's actual needs, because neither party has a framework within which to understand the symptoms. A neuropsychological assessment provides an objective means to identify needs and describe appropriate services to address those needs. This establishes a more reasonable estimate of actual need, which can provide a common ground for further discussion about how to respond to the student's need. By correcting imperfect information, disparate perceptions of the same student can be resolved as understandings begin to converge. Accurate information may lead to more effective intervention.

Overall, when children present with complex referral questions that suggest neurocognitive impairment (e.g. autism, executive dysfunction), or when known neurocognitive issues are present (e.g. traumatic brain injury, brain tumor, seizure disorder), it is crucial to gain a perspective that integrates multiple sources of information about various domains of functioning. The pediatric neuropsychologist is uniquely qualified to meet the needs of children with neurocognitive disorders, given cross-disciplinary training and expertise. The pediatric neuropsychological assessment clarifies diagnosis, informs treatment planning, and aids in conflict resolution. By doing so, the assessment guides intervention efforts, and may even serve as a form of intervention.

Assessment guides intervention

Although funding sources such as insurance companies may make a distinction between assessment and intervention services, neuropsychological assessment is clearly necessary when developing effective intervention plans for neurocognitive disorders. By identifying the need for services, making general and individualized recommendations, monitoring progress, and making appropriate referrals, the pediatric neuropsychologist can guide intervention.

Before any child can receive intervention services, a need for services must be established. Disability determination is a necessary component of accessing funding for services, including insurance coverage, school-based services, government funding such as Social Security Disability (SSD), and private organization funding. Accurate and specific diagnoses can lead to identification of services, supports, or funding streams that are reserved for individuals with a certain disorder. Therefore, one way in which assessment guides intervention is by documenting the *need for services and funding.*

A pediatric neuropsychologist's understanding of brain–behavior relationships, specific disorders, and human development informs *general treatment recommendations* for immediate and future interventions. Interpreting testing results within a neuropsychological framework allows a specific pattern of findings to be generalized to other areas that are not directly assessed. Consider a child whose pattern of results indicates deficits in executive functioning, such as poor inhibition of response on a computerized CPT. His mother reports good ability to form friendships, but difficulty sustaining friendships. Although the neuropsychologist may not have directly observed the student's social interactions with peers, it is reasonable to offer a hypothesized connection to the parent. It is possible that the student shows poor inhibition of response in his social interactions, leading him to be perceived as "rude" or "hurtful" when he blurts out what he is thinking. This understanding of the underlying deficit guides more appropriate treatment intervention (e.g. work on better inhibitory control rather than acquisition of social knowledge).

A neuropsychologist's knowledge of specific disorders, including associated features, comorbidities, and treatments, contributes toward intervention planning and recommendations. For example, a pediatric neuropsychologist would examine possible symptoms of ADHD in a child who presented with features of Obsessive-Compulsive Disorder (OCD), given research documenting increased rates of ADHD among children with OCD (Geller *et al.*, 2002). This information would lead to more appropriate treatment recommendations. Knowing that children with pervasive developmental disorders (PDDs) often experience symptoms of anxiety (Gillott, Furniss & Walter, 2001), the neuropsychologist might

proactively refer the child to a therapist to learn effective relaxation techniques, potentially preventing development of an anxiety disorder. Recognizing certain dysmorphic features in a child with mental retardation might lead to a genetic consultation. Understanding the research literature about effects of treatment on the developing brain also guides intervention planning. For example, awareness that some medical treatments for childhood brain tumors are associated with later white matter lesions and cognitive decline (Fouladi *et al.*, 2004) might lead to education of parents and school personnel about how to recognize symptoms of white matter damage as neurologic in nature (rather than falsely attribute these symptoms to motivational issues).

Based on the knowledge of child development within the context of the traditional American educational system, a pediatric neuropsychologist can make predictions about future areas of difficulty. This can allow the student to learn compensatory strategies before he or she is in crisis. As an example, consider a second-grade student who has just been identified as having ADHD with significant executive deficits. Although he is not yet expected to write essays, it is reasonable to predict that he will have difficulty with organization of information in written language. He will benefit from learning a structured writing approach now that will become a good habit for use later. Thus, due to the neuropsychologist's integrated knowledge of brain-behavior relationships, specific disorders and related issues, and child development, a pediatric neuropsychological assessment can inform general recommendations for intervention.

Specific information obtained during a pediatric neuropsychological assessment guides *individualized recommendations*. Knowledge of a student's relative strengths and weaknesses can inform what specific treatment options will be most effective. Consider four students who are referred for ''memory'' deficits. John has specific deficits in attention. Because he is not attending to instruction, the information does not enter his awareness to be stored in his memory. Susan has specific deficits in language comprehension. Because she does not understand what the teacher is saying, she cannot process the information for memory. Tom has adequate attention and receptive language, but his executive deficits impact the organization of information in his memory. Although he can attend to and understand the information, he cannot retrieve specific facts when they are needed. Mary has intact attention, language, and executive functioning, but her specific memory deficits mean she cannot remember the knowledge. Although all four students in this example were referred for ''memory'' problems, their individual test results indicate very different needs, leading to different intervention recommendations. Relative strengths can be used in developing compensatory strategies to work around areas of weakness. For example, a student with intact visuospatial skills but deficient adaptive functioning skills might benefit

from using cue cards that illustrate step-by-step procedures to successfully complete a domestic task such as cleaning his room. (For a review of research on use of individualized reports and recommendations, and including strengths in assessment reports, see Brenner, 2003.)

After establishing a neuropsychological baseline it can be useful to complete reassessments at certain intervals to guide treatment plan revisions. Reassessment can document progress made in treatment and identify emerging areas to be addressed. A reassessment can also reveal areas that are showing little progress and suggest different intervention approaches that might be more effective. Reassessment may identify an area in which the student has reached his limits. At times, reassessment may lead to adjustments in expectations for the child (e.g. a child whose IQ score was previously in the intellectually deficient range, but who is now performing in the average range after seizure stabilization). Reassessment after a period of intervention may clarify diagnostic questions, such as whether attentional deficits were secondary to anxiety or due to a primary diagnosis of ADHD.

Medical professionals often consult with pediatric neuropsychologists when planning interventions. The usefulness of neuropsychological assessment has been acknowledged by major medical organizations including the American Academy of Neurology (Therapeutics and Technology Assessment Subcommittee, 1996), the American Medical Association (American Medical Association Press, 2005), and the Social Security Administration (Social Security Administration, 2005). For disorders that change over time, neuropsychological assessment can be invaluable in documenting progression or stabilization. In fact, medical doctors rely on neuropsychologists to identify early signs of cognitive deterioration in diseases such as HIV (Pearson *et al.*, 2000) and adrenoleukodystrophy (Riva, Bova & Bruzzone, 2000), which then alters intervention plans.

Neuropsychological assessment serves an important role in determining whether it is appropriate to proceed with some forms of medical intervention. For example, results from memory and language testing might influence a pediatric neurosurgeon's decision to use psychosurgery for seizure control (Lee *et al.*, 2003; see also Blackburn, Zelko & Shurtleff, this volume, for more on this subject). At times, physicians consult with pediatric neuropsychologists to evaluate the cognitive effects of prescription medications, such as methylphenidate for ADHD.

Assessment is intervention

If an intervention is anything that changes a behavior, then a neuropsychological assessment is an intervention in and of itself (see Kubiszyn *et al.*, 2000 for a review

of this concept in psychotherapy; see Reznick & Schwartz, 2001 for a study showing change after assessment). The pediatric neuropsychologist, using assessment as a tool, can reframe perceptions, adjust expectations, motivate interveners, and address parental emotions (see Fulmer, Cohen & Monaco, 1985 for further discussion of the impact of assessment results on psychotherapy; see also Brenner, 2003 for review of the importance of establishing therapeutic relationships during the feedback session). It is possible that a neuropsychological assessment may even prevent future psychiatric symptoms in some cases. By directly changing the child's environment (including those who work with the child), a neuropsychological assessment serves as a form of intervention.

During a diagnostic interview or feedback session, the pediatric neuropsychologist has the opportunity to *reframe perceptions* of the child. This paradigm shift can be accomplished through Socratic questioning or explicit education. For example, when parents are complaining of low energy levels in their daughter who has epilepsy, they might begin thinking about her fatigue differently when the neuropsychologist asks, "Does she seem more tired after she has a seizure?" The neuropsychologist can also use these parent meetings to explicitly link related behaviors, providing relevant educational information for the parent. In the case of a student with ADHD, parents might benefit from learning that variability in performance is more likely to be related to cognitive factors such as attention and fatigue, and less likely to be due to motivational factors (see Castellanos *et al.*, 2005). Explicit statements about core features of disorders and their associated features can also be included in the written report. This provides education for not just parents, but for anyone who reads the report (such as teachers, therapists, and pediatricians). This information may give the reader a different framework within which to understand the child's issues, thus resulting in more effective intervention.

In some instances, a feedback session may be used to *align expectations* with the child's level of functioning. For example, if an adolescent's skills are all in the severely impaired range, his or her parents might benefit from thinking about relevant life skills rather than entrance exams for post-secondary education. Expectations may need to be shifted in the other direction, as in the case of a young boy with severe language impairment who was placed in a life skills program, despite his intact reasoning skills. Inappropriate expectations, whether too high or too low, typically result in increased frustration for the child and those attempting to intervene. Guiding appropriate expectations is a way that the neuropsychological assessment can provide intervention.

Lack of *motivation* can be a barrier to intervention. In order for an intervention to be successful, the intervener must be motivated. First, the intervener must believe in the credentials of the recommender. When the pediatric

neuropsychologist is able to explain the child's specific problem in the context of brain–behavior relationships, this demonstrates useful knowledge that can help persuade the intervener that it is worth listening to the intervention plan. Once the intervener believes in the expertise of the neuropsychologist, he must be convinced that the child has a need for intervention. This can be facilitated by making test results meaningful to the intervener, such as showing how they will impact the child's functioning with that person. For example, although a football coach might not be interested in "working memory deficits," he will be likely to care about helping the child to follow directions for executing a maneuver on the field. When expertise and a need have been established, the intervener must understand what to do. The pediatric neuropsychological assessment goes beyond labeling a problem, by providing specific treatment recommendations that are based on an understanding of the disorder or the individual. These specific recommendations tell the intervener exactly what to do.

After understanding the intervention, the intervener must believe that he or she is capable of implementing the plan. In the case of parents, the pediatric neuropsychologist can empower them to try this new plan, even though past efforts may have seemed unrewarding. Finally, it is important to provide interveners with the necessary supports to follow through with an intervention plan, such as case managers, support groups, or appropriate resources to aid in implementation. Through establishing expertise, demonstrating a need, explaining what needs to be done, empowering the intervener, and providing appropriate supports, the neuropsychologist increases the motivation of the intervener. A motivated parent, teacher, or other provider will be more effective in implementing the intervention plan.

When possible, parents and others should be given a full understanding of the actual need, and how the intervention plan directly addresses the need. This connection between need and recommendation provides the necessary information to engage in active problem-solving to modify an intervention that is not succeeding or that is not functional in the given setting. For example, if a teacher sees the recommendation, "Give Jimmy preferential seating in the classroom," she may put him in the front row without much success. If the same teacher were provided with an explanation, "Give Jimmy preferential seating in the classroom. It is important that he is seated away from distractions and close to the teacher, so that we can optimize his attention to instruction," she could problem-solve and move him away from the open door, open window, and pencil sharpener that are in the front of the classroom. Thus, the assessment can provide understanding that directly impacts intervention.

Portions of the neuropsychological assessment can be very therapeutic to parents, by addressing their *emotions*. Parental anxiety can be significantly

reduced by reassurance that the assessment will result in a better understanding of the problem, and specific recommendations about how to make things better. This can be especially important when working with parents of a child with a neurocognitive disorder, as they may have consulted a number of professionals without feeling that anyone has understood their child or how to help. A parent may benefit from validation of her observations, and recognition that she has been working very hard to help her child. The clinical skills of a pediatric neuropsychologist are often required when parents exhibit feelings of guilt or blame about ''causing'' the problem. Parents may need direct discussion about possible hidden feelings of inadequacy. At times, it is helpful for a parent to hear that his parenting approach is appropriate for most children, but that his child's special needs require a special kind of parenting. Many parents of children with disabilities experience grief that may go unrecognized. They may be mourning the loss of the ''normal'' child. The pediatric neuropsychologist can intervene by acknowledging such feelings, and normalizing them. Addressing these parental emotions is a form of intervention.

Finally, the neuropsychological assessment can serve as a form of *preventative treatment*. As a recent federal government report stated, ''New understanding of the brain indicates that early identification and intervention can sharply improve outcomes'' (President's New Freedom Commission on Mental Health, 2003). Children whose deficits go unidentified and untreated show higher rates of psychiatric disorders in adulthood. For example, several studies have found that children with ADHD who did not receive appropriate interventions in childhood were more likely to engage in substance abuse as adults, relative to those who received treatment (Wilens *et al.*, 2003). Thus, by identifying a child's needs and making appropriate recommendations, the pediatric neuropsychological assessment may serve as an intervention to prevent secondary diagnoses.

In summary, the pediatric neuropsychological assessment is not just a guide for intervention, it is also a direct intervention. Using the interview, feedback session, and written report, the neuropsychologist can shift perceptions, change expectations, motivate those who work with the child, and work therapeutically with parent emotions. Through identification of needs and appropriate services, a pediatric neuropsychological assessment may even help to prevent development of secondary issues.

Research on assessment

Research on psychological and neuropsychological assessment has focused on test-specific details, such as reliability, validity, sensitivity, and specificity (for a review,

see Meyer *et al.*, 2001). While these details are important, we have neglected the bigger picture of the efficacy of assessment. This deficit was noted in the realm of personality assessment and psychotherapy in 1987: ''To date, the role of treatment utility has been buried by conceptual confusion, poorly articulated methods, and inappropriate linkage to structural psychometric criteria.'' (Hayes, Nelson & Jarrett, p. 973).

Even in the broader literature of clinical psychology, research on the efficacy of assessment is limited. One review summarized the research on how well standard psychological measures predict functional behavior, health outcomes, and healthcare utilization patterns (Kubiszyn *et al.*, 2000). Another review paper described studies of the utility of psychological assessment, meaning primarily personality and social functioning measures (Nelson-Gray, 2003). In a recent special section of the *Journal of Clinical Child and Adolescent Psychology*, there was a call to develop guidelines for evidence-based assessment of child and adolescent disorders (Mash & Hunsley, 2005). This issue included suggestions for specific guidelines related to the assessment of a number of pediatric issues, such as anxiety (Silverman & Ollendick, 2005), depression (Klein, Dougherty & Olino, 2005; Youngstrom *et al.*, 2005), ADHD (ADHD; Pelham, Fabiano & Massetti, 2005), conduct disorder (CD; McMahon & Frick, 2005), learning disorders (LD; Fletcher *et al.*, 2005), and autism spectrum disorders (Ozonoff, Goodlin-Jones & Solomon, 2005). The concluding article in this special section raises useful points about how to assess progress in psychological treatment (Kazdin, 2005). But even these articles about evidence-based assessment focus primarily on which tools have adequate psychometric properties, rather than how assessment lends incremental validity to treatment planning.

The majority of studies use neuropsychological assessment as a way to measure treatment efficacy (e.g. did this intervention lead to change in neuropsychological test scores?). Studies that ask the opposite question, whether pediatric neuropsychological assessment itself is efficacious, are clearly needed.

At this time, information about the efficacy of pediatric neuropsychological assessment is based largely on clinical vignettes. Those that are published are typically in the broader field of psychological assessment. For example, Fulmer *et al.* (1985) published three case vignettes about the impact of assessment for learning disabilities upon further family therapy. A few published studies describe the utility of test data in predicting services or deficits. For example, a recent study showed that neuropsychological test data greatly improved prediction of which children received special education services at one and two years after traumatic brain injury (Miller & Donders, 2003). A study of children with ADHD documented that deficits on certain tests were associated with real-world deficits (Lawrence *et al.*, 2004). An interesting Spanish study showed a correlation between

cognitive profiles and automobile accidents involving newly licensed drivers (Martin & Estevez, 2005). Demonstration that neuropsychological assessments help to improve prediction of outcome or needs is an important first step in examining how neuropsychological assessments provide incremental validity for intervention efforts. For example, Hale *et al.* (2005) found that neuropsychological test data predicted response to medication in children with ADHD. This study shows that pediatric neuropsychological assessments can directly inform intervention.

In sum, research on pediatric neuropsychological assessment has focused on the psychometric properties of specific measures. Some studies have used assessment to determine if an intervention produced change. A handful of published studies have demonstrated that neuropsychological test data are useful predictors of future needs in certain populations. Few studies have considered the utility of assessment, much less pediatric neuropsychological assessment.

Summary

In conclusion, children with neurocognitive disorders are often complex, making it difficult for parents and professionals to understand their needs and develop appropriate intervention plans. The integrative approach of the pediatric neuropsychologist informs accurate diagnosis and effective treatment planning. Neuropsychological findings provide a common ground for various people in the child's life, correcting misinformation that leads to conflicts and supporting cooperative efforts for intervention. In some ways, a pediatric neuropsychological assessment is a form of intervention, in the sense that it changes aspects of the child's environment by educating interveners, increasing motivation, and addressing interfering emotions. A neuropsychological assessment can be viewed as an intervention given research on better outcome in children who are accurately diagnosed and appropriately treated. Research on the efficacy of pediatric neuropsychological assessment is scarce. A few studies have begun to ask important questions such as, ''Does test performance predict treatment response?'', or, ''Does this test score mean anything in the real world?'' Further research on the efficacy of pediatric neuropsychological assessment is critical for future advancement of the field.

Future directions

While it is important to continue evaluating test-specific details such as reliability, validity, and normative samples, it is even more critical to conduct further

investigations of the broader meaning of assessment. We must establish the efficacy of pediatric neuropsychological assessment in terms of guiding interventions and serving as an intervention. Neglecting this aspect of applied research may have severe consequences for survival of the pediatric neuropsychologist, given trends in managed healthcare (Eisman *et al.*, 2000). Given the inconvenience of obtaining pre-authorization for assessment services, we need to present supporting data to convince neuropsychologists that it is worth the effort and the cost (Kubiszyn *et al.*, 2000).

Important questions remain to be asked and answered. Is there an advantage to having a pediatric neuropsychologist involved in assessment and treatment planning? Does the integrative approach to interpreting test results in the context of brain-behavior relationships, specific disorders, and human development improve the long-term outcome for a child? Do our test scores inform meaningful recommendations for helping a child? Is there incremental validity for neuropsychological reassessment, whether in the context of monitoring treatment, development, or a progressive disorder? Does the very act of completing a neuropsychological assessment change any aspect of a child's life?

Other topics for future research include evaluation of whether specific test results can predict response to intervention, not just medical interventions such as medication and neurosurgery, but also interventions like cognitive–behavioral therapy, phonics-based, instruction, and memory training. It would be useful to establish predictive validity of test data in informing choice of interventions. Ecological validity is another related topic, such as whether test scores are correlated with real-life strengths and weaknesses, and whether there is any relationship with real-life functioning or quality of life. Cost-benefit analyses of pediatric neuropsychological assessment might include variables such as immediate cost of the assessment, lifetime cost of treating a child with a neurocognitive disorder, and whether the assessment changes the lifetime cost.

These are questions that are challenging to answer. They require abstract thinking and novel problem-solving skills. Research of this sort also requires careful methodology, including how to assess outcome (for some suggestions based in the general psychology context, see Kazdin, 2005; Finn & Tonsager, 1997; Hayes, Nelson & Jarrett, 1987), what types of statistical analyses are meaningful (e.g. for incremental validity studies, see Hunsley & Meyer, 2003; also Johnston & Murray, 2003), and how to analyze costs and benefits (for a recent analysis, see Yates & Taub, 2003). As the field of pediatric neuropsychology grows, it is important to engage in more intentional research to validate the importance of neuropsychological assessments in intervention.

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4

Multicultural aspects of pediatric neuropsychological intervention and rehabilitation

Julie K. Ries, Brian S. Potter, and Antolin M. Llorente

It is important to examine the precursory roots and historical foundations of neuropsychological rehabilitation in order to foster greater appreciation of our present state and future direction as a field, providing a better context for multicultural perspectives. This rich history spans across cultures and includes views of disability and interventions. José León-Carrión (1997) provides a partial yet eloquent chronology. He notes that some of the oldest discoveries of treatment for brain damage date back to the Mesolithic Age. Skulls were discovered with holes on their left side that appear to be a form of surgical intervention called trephination. Egyptian sorcerers utilized "supernatural" techniques to rid the body of ailments and demons. Hippocratic physicians noted brain-behavior connections underpinned by the brain housing one's intelligence, regulating a majority of body functions, allowing one to experience emotion and make judgments. In keeping with tradition, Hippocratic physicians used trephinations for the treatment of selected mild brain injuries.

The first hospitals and convalescence homes for the treatment of physical lesions were founded in 499 to 429 BC Greece, which demarcates an important shift in the treatment of illness in Western societies. Previously, children born with deformities were displayed in public places, or were thrown off Mount Taigeto. In Imperial Rome, it was acceptable to take the life of children who were born with any physical lesion, abandon them, or release them into the River Tiber in flower baskets.

In the second century BC, Galen was among the first to require a detailed clinical examination of all patients, noting all symptoms in order to provide diagnostic information and treatment. Through simian anatomical dissections, he provided detailed findings regarding the anatomy of the nervous system and brain trauma. The Middle Ages was marked by debates regarding scientific doctrine, notably the location of various functions within organs. Despite advances in science and medicine, individuals with physical disabilities were thought to bear

a curse as punishment by God, and were subsequently ostracized in European societies. The Renaissance was marked by attempts to prolong life (Paracelsus), the Inquisition, and a social revolution in which the "law of the poor" was approved in England in 1601 to assume responsibility of giving assistance to the ill and poor. In France, Vincent de Paul founded the first charitable organization for the sole purpose of caring for children with disabilities to protect them from exploitation as a means of survival.

The eighteenth century marked a period of scientific curiosity which led to new hypotheses about functional anatomy. The French Revolution (1789) prompted equal treatment for the sick, whereas advances in science and medicine introduced the use of electricity for rehabilitation of hemiplegias (León-Carrión, 1997), as well as a greater understanding of the nervous system. Franz Joseph is credited with establishing multiple functions of the brain through his phrenology as well as data to support his hypothesis regarding the cortex and its anatomical structures and functions. The nineteenth century was marked by scientists' continuation of the discovery of localization of functions as well as systems within the brain. Most noteworthy were the discoveries of Paul Broca (1861) in France and Carl Wernicke (1874) in Germany regarding language, as well as the proposition by Ramón y Cajal (1889) of the neuron system and the discovery of chemical neuronal transmission.

In the twentieth century, the Russian psychologist Lev Semenovich Vygotsky noted appreciation for culture in human development (Vygotski, 1986). According to Vygotsky, culture separates humans from animals, as well as playing an important role in our history (LeFrançois, 1995). Vygotsky noted that "[humans] create cultures, and cultures have a vitality, a life of their own. They grow and change and exert a very powerful influence on their members," determining the end result of competent development. Although Vygotsky was not the first to appreciate the importance of culture in the understanding of illness and intervention, he provided a greater understanding of the impact of one's environment, and indirectly culture, on development. According to Christensen & Castano (1996), Vygotsky's colleague, Alexander Romanovitch Luria, also made significant contributions to the field of rehabilitation by establishing rehabilitative centers in the Soviet Union after World War II. His conceptual models, like Vygotsky's, were cultural–historical models (Luria, 1979). Other figures in the field also made significant contributions related to specific factors associated with traumatic brain injury (TBI) outcome and co-occurring disorders (Russell & Witty, 1952).

It should be patently clear that the history noted above is eurocentric in its perspective. For example, although eurocentric history tends to note the emergence of trephination in Egypt, it fails to note that in the "New World," the Chinchoros culture of Northern Chile, precursors of the complex Inca

State, perfected artificial mummification as a means to protect the body and soul in the afterlife. However, the Chinchoros perfected this process in the third millennium BC, most likely before or temporally concurrent with Egyptians (Mosely, 1993). This underscores the importance of attending to our cultural biases, even when addressing historical facts, an issue that should be taken into consideration when assessing or rehabilitating individuals from ethnic minority backgrounds.

Despite the aforementioned historical record, and concurrence with previous writings that brain injury, and possibly its rehabilitation, was well recognized and perhaps attempted by ancient civilizations (Courville, 1967), it is an accepted fact by most students in the field that the evidence-based history of modern neurorehabilitation had its humble beginning in the twentieth century in association with World War I, the emergence of the industrial revolution, and advances in technology and Western medicine. This was partly the result of pragmatic factors impacting intervention, including low survival rates of victims who had sustained brain or central nervous system (CNS) injury before that time, precluding rehabilitation to take place, and indirectly the investigation of rehabilitative methods (Gurdjian, 1973). Technological advances in the treatment of infections led to increased survival, and advances in technology itself played a major role (e.g. angiography), leading to the study of previously untreatable injuries or poorly understood CNS diseases (e.g. strokes) (DeJong, 1982). Although several programs of rehabilitation for wounded war or industrial accident victims were established in the earlier part of the twentieth century (Harris, 1919), particularly in England and France, modern neurorehabilitation owns a great deal of debt to early programs established in Germany (Camus, 1917/1918; Harris, 1919). Most programs established during the early part of the last century did not include neurorehabilitation but predominantly focused on physical and occupational rehabilitation (Camus, 1917/1918), partially as a result of significant advances in orthopedic medicine following the development of the X-ray and limited neuroscience. However, the programs that started in Germany were charter interventions, which included the rehabilitation of brain injuries in a comprehensive fashion, including the social reintegration of individuals with brain injuries (Poser, Kohler & Schönle, 1996). For example, Kurt Goldstein (1919; 1942), in collaboration with his student Frieda Fromm-Reichmann and colleagues (Goldstein & Reichmann, 1920), was responsible for the development and documentation of rehabilitative programs, which included the assessment and intervention of patients. Assessments were comprehensive in nature including several domains of functioning (e.g. attention, perception, and memory), similar to modern neuropsychological examinations. Rehabilitative programs also were quite advanced, including the use of techniques employing relatively preserved

cognitive strengths to address relative weaknesses, specific rehabilitative treatments for aphasias and other disorders, and an examination of specific outcomes of rehabilitation and social reintegration, including return-to-work, which employed the results of neuropsychological assessments as well as behavioral observations in the work setting (Goldstein & Reichmann, 1920). Most important, their empirical research revealed important data at that time, including which groups of patients enjoyed the best (farming industry) and poorest (mining industry) vocational outcomes after trauma, providing empirically-based outcomes measured by the percentage of patients who were able to return to their previous occupations post-injury. Their programs were the progenitors of modern rehabilitation programs throughout the world and led to eventual and modern collaborations by the European Union including the formation of the European Brain Injury Society in 1986, leading to modern standards of practice in Europe.

The information presented above is relevant to this chapter as it underscores the multicultural genesis of the science and practice of neurorehabilitation. However, prior to engaging in an examination of the literature investigating the impact of culture on aspects of pediatric neuropsychological rehabilitation in the US, it is crucial to understand why it is important to understand the effects of culture. An examination of culture, ethnicity, and inherent factors associated with such constructs, as well as epidemiology of injuries and its relation to ethnicity and patterns of American immigration, and their impact on neuropsychology, are proper places to start (Hall, 1997).

Epidemiology of brain trauma or acquired brain diseases and race and ethnicity

Although several categories of illnesses and diseases will be covered, major emphasis will be placed on traumatic brain injury due to its greatest prevalence and frequency as a researched condition. Although a close examination is beyond the scope of this chapter, a brief glance at the epidemiology of brain trauma or acquired brain diseases buttress the need to attend to cultural factors. For example, although partially confounding ethnicity with race, a comprehensive investigation conducted by the Centers for Disease Control and Prevention (CDC) revealed that deaths in the US attributed to TBI as a result of transportation accidents, including automobile accidents, was equivalent in White and African-American populations; yet, the same investigation showed that African-Americans had a higher rate of TBI than Whites subsequent to firearm injuries (CDC, 1999). Similarly, a previous report published by the CDC (CDC, 1998) noted that "cerebrovascular disease is twice as high among African-American men (53.1 per 100,000) as among white men (26.3 per 100,000) and twice as high among African-American women (40.6 per 100,000) as among White women (22.6 per 100,000)."

Although comparisons between ethnic minority groups and the dominant cultural group have revealed significant epidemiological differences, modern investigations also have revealed inter-ethnic differences in the epidemiology of TBI. For example, Kraus *et al.* (1986) found differential epidemiology rates of TBI in "Hispanics" compared with "African-Americans" and "Asians/Native Americans" related to median income in these groups.

Although many other examples could be provided for other ethnic groups, as well as for other injuries and disorders, it should be sufficient to state here that race grouping, and more important, ethnic differences, in conjunction with other variables (e.g. socioeconomic status(SES)), lead to variations in the incidence and prevalence of brain injuries or acquired diseases of the brain. Therefore, the close relationship between the epidemiology of acquired brain injury and ethnic minority status underscores the importance of ethnic factors capable of directly or indirectly impacting neuropsychological interventions and rehabilitation in the US.

The dynamic and diverse nature of culture in the United States

The term "culture" can be defined in several ways. It has been described globally by the American Psychological Association (APA, 2003) as "the embodiment of a worldview through learned and transmitted beliefs, values, and practices, including religious and spiritual traditions." Culture embodies and influences all facets of the individual, including cognition. "Differences in cultural background include not just language differences, but also differences in group identity, beliefs, and values" (Dana, 1993), all of which influence the use of services, the presentation of symptoms, the assessment techniques used, and all or most aspects of treatment including neuropsychological rehabilitation.

"Culture" and "ethnicity" unfortunately have been used interchangeably with the term "race." This has been a source of significant confusion as race and ethnicity are distinct constructs. Culture and ethnicity may be considered similar because specific aspects of these constructs may be learned and are flexible (Smedley, 1993). 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." Therefore, one's culture and ethnicity are similar as they are learned and passed down from generations, whereas race typically refers to cultural groups with permanent attributes which are not learned and cannot be changed (Carter & Qureshi, 1995). The subtle but significant difference in terminology appears trivial but it is important as it marginalizes the differences between groups.

As it relates to Hispanics, the term has been used to describe a very heterogeneous group, and as stated by Harris and Llorente (2004), it has been misused

because it has been used as a racial category rather than an ethnic label. Harris and Llorente also note that this "panethnic label" fails to "capture the unique attributes" of an individual including, oddly enough, his or her racial background in some instances. Even when referring to a specific Hispanic group, such as Mexican, there are several attributes to consider. For example, it is necessary to establish whether they are Mexican-American of Mexican descent born and raised in the United States, or Mexican immigrants born and raised in Mexico from dozens of possible ancestral backgrounds, including one or more of 50 aboriginal origins, when considering ethnicity. Similarly, level of acculturation to American society and dominant language should be taken into account (Harris & Llorente, 2004). These distinctions are critical if we are to understand specific triggers that lead to variations in rates of inter-ethnic TBI and its outcome, partly because it is possible that specific demographics (e.g. level of education, specific occupational predilections or opportunities) of each subgroup may be associated, or may moderate, inter-ethnic TBI rates.

Similar conclusions can be reached about the pan-ethnic labels "Asian" or "Asian-American" and "African-American" (Wong *et al.*, 2000). Most important, culture can have significant impact in brain injury rehabilitation and prospective outcomes whether addressing pediatric or adult populations (Yeates *et al.*, 2002; Uomoto & Wong, 2000).

With regard to treatment adherence, the literature suggests that multicultural clients are more likely to end treatment prematurely due to frustration, misunderstanding and role ambiguities of treatment (Sue & Zane, 1987). Sohlberg and Mateer (2001) note that identity and self-concept are influenced by culturally mediated norms about assertiveness, emotional expression, and individual goal attainment versus sacrificing for the greater good. Culture may also underlie beliefs about illness and disability, as well as its meaning. Whereas personal independence is highly valued in Western culture, it is not necessarily a goal in other cultures, which have different beliefs about a person's degree of responsibility and control over health and the role of family in dealing with illness (Watanabe *et al.*, 2001; Uomoto & Wong, 2000). It is also important to recognize that in our society, "the great American melting pot," these factors have been, systematically and incontrovertibly, moderated by patterns of American immigration which indirectly modulate the demographic variables of individuals. Such a modulation impacts the demographics of individuals in the US, in many cases, individuals undergoing clinical investigation or participating in standardizations of neuropsychological instruments used in rehabilitation (Llorente *et al.*, 1999; 2000). Therefore, a close examination of patterns of American immigration also is required to understand critical aspects of multicultural neurorehabilitation.

Over the past 25 years, there have been significant changes in racial and ethnic diversity in the US. During two decades (1980–2000), minority populations (non-White) have grown 11 times faster than the White population (US Census Bureau, 2001). Immigration and population growth has dramatically increased the racial and ethnic diversity with a 204% increase in the Asian and Pacific Islander population as well as 142% increase in the Hispanic population (US Census Bureau, 2004). The projected population in fifty years predicts striking changes in the racial and ethinic composition of the US. The Census Bureau predicts that in the year 2050 the percentage breakdown of population by race will be: 72.1% White, 14.6% African-American, 8.0% Asian-American and 5.3% all other races. The percentage of Hispanic origin jumps to 24.4%. These predictions note marked increases in all minority groups. Most notably, the Hispanic and Asian populations grow at significantly faster rates, nearly doubling their percentage in their share of the total population, and inhabitants of Hispanic origin are predicted to nearly half the number of inhabitants of Caucasian origin living in the US (US Census Bureau, 2004).

As it relates to pediatric neuropsychological intervention, patterns of American immigration, moderating demographic variables of large numbers of individuals, are not the result of 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, 1990). In addition, the proportion of immigrants from specific regions living in the US or from foreign countries may vary substantially over large periods of time, and even for specific groups of individuals, particularly in relation to their relative representation in the US, with significant impact on demographic variables (Llorente *et al.*, 1999; 2000). This inter- and intra-variability in immigration patterns is particularly important for demographic variables such as level of education, geographical allegiance within the US, and occupational allegiance because gravitation exists towards specific areas of the US and toward certain occupations and educational levels for specific groups of immigrants and their children (Llorente *et al.*, 1999; 2000). Most critical, it is important to note that ultimately, these factors moderate the utility of data obtained during the course of neuropsychological assessment to be used for neurorehabilitation. This important issue is addressed in detail below (Harris & Llorente, 2004; Rey *et al.*, 1999).

In summary, the predicted changes in ethnic diversity in the US population underscore the ever-increasing importance of understanding the dynamics between culture and pediatric neuropsychological intervention. 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 US Census Bureau. 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 or rehabilitation. Finally, it is important to recognize that culture may interact with other variables to create specific brain injury epidemiology.

Normative data and multicultural assessment and intervention

As was the case during the early part of the last century in Germany, neuropsychological assessment continues to be a significant component of empirically based neurorehabilitation. However, unless using an idiographic approach, neuropsychologists depend on normative data during the course of assessment to inform their pediatric research or clinical practice including the application of specific treatments. Normative data provides a context or empirical frame of reference for which test scores can be understood (Mitrushina *et al.*, 2005), and normative data is considered the "gold standard" by many practitioners as a way of comparing individual performance (Mitrushina *et al.*, 2005). In fact, the combination of sound clinical judgment and the use of appropriate normative comparison groups allow neuropsychologists to better understand individuals (Lezak *et al.*, 2004). Ideally, the normative reference groups should be as narrow as possible (representative of the individual being compared) as long as the norms on which they are based are stable and do not fluctuate significantly (Rorer & Dawes, 1982).

Unfortunately, the ideal process of comparison sometimes does not take place and while a normative reference group may reflect overall population statistics, the norms may not reflect the specific demographic of an individual from a given ethnic group (Harris & Llorente, 2004). Such issues merit significant attention because they can lead to inaccurate inferences and interpretations of the data with ethnic minorities unless measures are taken to reduce such potential biases. For example, modern tests (e.g. WISC-IV-Spanish, Wechsler, 2004) oversample ethnic minority populations in order to represent a specific minority group more adequately (Harris & Llorente, 2004; Prifitera, Saklofske & Weiss, 2005). Such over-representation also permits additional and supplemental statistical analyses capable of informing test publishers and those who use them in applied settings of potential limitations of their procedures.

Multicultural diagnostic considerations

The ever increasing racial and ethnic diversity of the US population emphasizes the need to account for the role of culture on diagnosis, assessment, and choice of interventions. Groce and Zola (1993) noted that an individual's culture is not

a diagnostic category, and that cultural heritage is incapable of explaining how an individual will think and act, but it is capable of assisting professionals to understand how and why families make specific decisions. Groce and Zola also have emphasized the importance of cultural awareness and its impact on expectations of a child's physical, mental, and psychological development, given the potential for variability in these expectations and a child's experiences within his or her own cultural environment. Cultural awareness and understanding clearly need to be considered an integral part of a clinician's knowledge base when s/he is called upon to diagnose or to provide consultation and follow-up care. Additionally, Groce and Zola caution that cultural belief systems may be approached in an oversimplified manner, or misinterpreted, which may lead to mislabeling this unique way of responding to the condition or intervention. They further suggest that when faced with a question of whether a behavior is a cultural norm for all patients, or unique to that patient with a disability, the practitioner should compare the treatment of a patient with disability to that of patient without the disability who is matched on age, gender, socioeconomic, and sociocultural backgrounds.

The *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (DSM-III-R; APA, 1987) was the first version of the DSM to acknowledge the impact of an individual's culture on diagnosis. Subsequent versions of this text (APA, 1994; 2000) provide a framework for clinicians to account for the impact of an individual's culture when assessing each of the DSM-IV axes, as well as a glossary of 25 culture-bound syndromes. According to the DSM-IV, a cultural formulation should supplement the axes and include factors such as the cultural identity of the individual, the explanation of the individual's illness from his or her cultural and psychosocial environment and level of functioning, cultural elements between the individual and the clinician, and overall cultural assessment for diagnosis and care (APA, 2000). DSM-IV-TR, Appendix I of the manual provides a glossary of culture-bound syndromes which are defined as ''recurrent, locality-specific patterns of aberrant behavior and troubling experiences that may or may not be linked to a particular DSM-IV diagnostic category.''

An example of a culture-bound syndrome noted in the DSM-IV-TR found in the Inuit community is ''*pibloktoq*.'' *Pibloktoq* is a sudden dissociative episode that occurs in conjunction with extreme excitement that lasts for up to 30 minutes and is frequently followed by seizures and coma lasting up to 12 hours. Guarnaccia, Lewis-Fernandez and Marano (2003) similarly studied the prevalence of the culture-bound syndrome ''*ataques de nervios*'' with a slightly modified Diagnostic Interview Schedule (DIS) (Robins *et al.*, 1982) in Puerto Rico. They interviewed 912 people of whom 16% reported having experienced an episode of *ataque de nervios* in their lifetime. *Ataque de nervios* was highly correlated with a range of

internalizing disorders. Research on culture-bound syndromes serves to help close the gap between cultural and clinical knowledge and provides insights into issues of diagnostic universality and cultural specificity (Guarnaccia & Rogler, 1999).

Groce and Zola's (1993) review of the multicultural literature suggested that three recurrent themes emerge:

1. The culturally perceived cause of a chronic illness or disability will play a significant role in determining family and community attitudes toward the individual
2. The expectations for survival of the infant or child with a chronic illness or disability will affect both the immediate care and future allocation of resources
3. The social role(s) deemed appropriate for children with a chronic illness or disability will help to determine the amount of resources which a family and community invest in an individual.

Groce and Zola found that in some cultures to this date, illness and disability may be viewed as a form of punishment or retribution as it was hundreds of years ago. For example, the beliefs of witchcraft are held in some African, African-American, Caribbean, Pacific Basin, and Native American societies as causes for illness or disability, and may be transmitted through one's associations. In contrast, if a child has an illness with a rapid onset, some Mediterranean and Latin American societies believe that the cause is due to the "evil eye" (Groce & Zola, 1993; see also Simpson, Mohr & Redman, 2000). Chronic illness and disability may be seen by some cultures as a unique gift. For example, some Mexican immigrants believe that their child has been singled out by God for the role because of their past kindnesses to a relative or neighbor with a disability.

Important consideration should be given to a patient, whether adult or child, and to his or her family acculturation as it may have important implications for treatment. Groce and Zola (1993) advocate the assessment of acculturation on an individual basis, particularly an individual or a family's belief system and social structure. The authors note that "it is important to remember that traditional attitudes about disability may hang on long after other cultural beliefs are gone," despite the fact that more acculturated individuals may have the sophistication to know that expressing specific beliefs (e.g. witchcraft) is unacceptable.

Multicultural aspects of neuropsychological intervention

Multicultural models

Blonder (1991) examines the concept of culture within the context of neuropsychological theories and research. Blonder noted that the effects of cultural

variations on linguistics impact the cerebral organization of language and reveal both organizing principles as well as the impact of neuroplasticity on the brain and language functions. He noted that in spite of variation in syntactic markers in languages, aphasic speakers show similar patterns of problems following lesions to Broca''s area. The grammatical endings are lost or used incorrectly, and words are produced in their uninflected form as stems or infinitives. Blonder proposes that language is a brain-mediated cognitive system proceeded from a limited set of structural features that underlie the world languages.

Condeluci (1997) has extensively studied the transition from rehabilitation to one's community for people with chronic or acquired disabilities. Rehabilitation focuses on returning individuals to their community. Condeluci challenges the deficit-based medical model of rehabilitation in which the physician is empowered to fix deficits, or if the deficits are unable to be alleviated or mitigated, to accept them. Patients and families following such a model may find themselves in environments which are less than optimal for the individual, particularly ones in which the patient may be labeled or stereotyped, lack privacy or control, become dependent on such a system, and subsequently lower his or her standards and expectations. In contrast, Condeluci proposes a community-based, interdependent model which identifies the individual's capacities and supports, and encourages empowerment of the person with the disability through choice and participation in decision-making (as appropriate to his or her age), in which the individual and/or family is in charge of the outcome. The interdependence model focuses on the culture and community as the more effective change agents than the individual. In this context, culture is defined as ''common rituals, rules, boundaries, and jargon.'' Several types of ''cultures'' may be relevant in rehabilitation, according to Condeluci, including family, spiritual, work, age, neighborhood, ethnic, gender or sexual orientation, and common interests. As the supportive systems of the person with a brain injury understand the diverse cultures and their influences, it will be easier for the patient to then experience ''culturation,'' an informal process by which the patient is appreciated and understood by the group. This process is critical for the successful re-entry of the patient into his or her environment. Based on Condeluci's interdependent model, integration of the patient within the culture and the community and empowerment of the individual to make decisions regarding his or her future course are paramount for successful recovery.

The American Psychological Association (APA, 2003) guidelines are focused on psychotherapeutic intervention: ''Cross-culturally sensitive practitioners are encouraged to develop skills and practices that are attuned to the unique worldviews and cultural backgrounds of clients by striving to incorporate understanding of a client's ethnic, linguistic, racial, and cultural background into therapy.''

Therefore, the neuropsychologist must extrapolate how to interpret these guidelines for specific interventions. Unfortunately, empirically-validated, culturally-sensitive neuropsychological interventions are rare and there is a need for increased research in this area (Christophersen & Mortweet, 2001; see Hall, 1997).

Multiculturally-sensitive neuropsychological intervention poses unique challenges to practitioners, given the limitations in our assessment tools that guide this intervention, as well as developing a greater understanding of the impact of culture on one's practice. Groce and Zola (1993) propose that this cultural sensitivity begins with self-reflection noting that "Everyone has a cultural heritage that influences his or her health beliefs and practices. It is thus not practical to learn in detail the infinite details of specific cultures." Instead, "it is more important for practitioners to be sensitive to the patient's heritage, to their own heritage, and to what happens when different heritages and belief systems come together."

Fadiman (1997) exemplifies what can occur if there is a lack of understanding of different cultures in the medical setting including the rehabilitation milieu. This book examines the potential cultural conflict between Western beliefs and individual culture when a seizure disorder is perceived as a gift within a specific culture, but as a disorder in Western medicine. The author provides some questions to ask to promote greater understanding of a patient's culture:

1. What do you call the problem?
2. What do you think has caused the problem?
3. Why do you think it started when it did?
4. What do you think the sickness does? How does it work?
5. How severe is the sickness? Will it have a short or long course?
6. What kind of treatment do you think the patient should receive? What are the most important results you hope he/she receives from this treatment?
7. What are the chief problems the sickness has caused?
8. What do you fear most about the sickness?

Li (2003) proposes a unique model that incorporates the dynamic interplay of culture and biology across the lifespan. He describes the reciprocal and dynamic process by which genetics and neuronal mechanisms interface with environment and culture to determine development. His framework highlights "how interactive processes and developmental plasticity at different levels are interconnected to each other and unfold across different time scales. Consequently, together they channel reciprocal cultural experiential influences on behavioral, cognitive, and brain development throughout the life span."

Empirically-validated models

Finally, attempts have been made to incorporate culture into specific models of rehabilitation as a moderating variable rather than as an independent variable. Such modeling has assisted investigators to better understand the role of culture in rehabilitation. For example, ethnicity has been hypothesized to be intricately related to SES, accounting for a portion of the findings that implicate ethnicity in TBI. In this regard, culture interacts, as a moderator variable, with SES to create a pattern of performance that is unique to a specific individual. Although related to race, not ethnicity, this is depicted in individuals who come from specific African-American pediatric populations in which the rates of TBI as a result of violence are greater than those for European-Americans, most likely as a result of lower levels of SES combined with other factors. In this case, TBI severity related to violence, for example, could be associated with SES, yet moderated by a specific ethnic background within a race construct (e.g. African-American), or other variable(s). Such methods of examining culture and other factors, as moderator variables, have been postulated by various investigators (e.g. Baron & Kenney, 1986; Holmbeck, 1997) and have received limited, yet sound empirical validation. In the case of children, for example, an investigation has shown that race (African-American vs. White) moderated differences between groups with, respectively, TBI and orthopedic injuries in family outcomes (Yeates *et al.*, 2002). Similarly, Collins *et al.* (2004) discovered that exposure to interpersonal racial discrimination represented an independent risk factor for preterm (and very low birthweight) delivery of African-American infants, while Lewis *et al.* (2004) noted that differences in language scores of four-year olds who were or were not exposed to cocaine inutero were more pronounced for children from ethnic minority backgrounds.

Although limited, in light of the dramatic increase in use of complementary therapies over the past 20 years, research has focused on the development of empirical models. One model incorporates Eastern medicine into traditionally Western medicine delivery systems. Wu (2004) developed a model for the use of complementary options to determine factors contributing to health care use among a cohort of Chinese-American families. The full and partial research models reveal that the factors contributing the most to their medical preferences were their acculturation level and health beliefs. Additionally, this culturally specific model showed that adding acculturation and health beliefs as enabling factors in the model, rather than predisposing factors, resulted in increased predictive power over predisposing factors for Chinese-American attitudes toward Western medical practices. Golomb *et al.* (2003) found that the combination of Eastern and Western medicine occurs frequently without knowledge. They studied the prevalence of use of Eastern medicine practices in first generation

Chinese-Canadian children with stroke and cerebrovascular disease. They found that over 53% of the children received alternative (Eastern) medicine (i.e. acupuncture, herbals) in addition to the Western medicine. Interestingly, Western doctors were unaware of most of the alternative medicine used until it was noted by a Cantonese-speaking clinician, who stressed the importance of the impact of culture and the role language has in the treatment of pediatric populations.

Although advances have been made in this area, a great deal of work remains to be done. For example, in the Yeates *et al.* (2002) and other studies (CDC, 1998), it is unclear who constituted the group labeled as African-American. Is it possible that specific subgroups of African-American families, from specific backgrounds (e.g. where violence is explicitly exhibited) or other demographic variables, are mostly responsible for such effects? In fact, to date, although we are aware that ''African-Americans'' have a higher rate of TBI as a result of violence, for example, understanding of the specific variables that moderate this relationship is limited. Clearly, factors such as acculturation, assimilation, education, and substance abuse may play a role on how violence is exhibited. These moderating influences must be examined within the African-American context, and within that of other cultures, in such investigations and in future studies in order to determine whether more precise intra-ethnic factors can lead to specific prediction. It is also critical to mention that such distinctions are important because they may reduce stereotypes that paint all ''African-American'' families (or other ethnic groups) with the same brush. Furthermore, it is critical to note that sometimes such investigations cannot be conducted as a result of small number of participants from different backgrounds within a specific ethnic group, and this issue plagues many studies, including our own investigations. Nevertheless, it is an issue that merits significant attention and resources.

Culturally-sensitive interventions and rehabilitation outcomes

Pontón, Gonzalez and Mares (1997) describe a cultural-based intervention used in the rehabilitation of a Hispanic population who experienced brain damage. Four well-grounded therapeutic techniques are utilized as intervention: *symptom validation, journal-keeping, structuring*, and *reframing*. *Symptom validation* is defined as the need to ''verbalize concretely the subjective experience of vague and diffuse symptoms and to make the patient feel understood.'' This technique involves active listening and informing the patient about the symptoms commonly experienced in brain injury rehabilitation. *Journal-keeping* involves recording symptoms and subjective experience (''How does the symptom make you feel?'') with reasonable frequency in order to define the symptoms, provide a baseline of symptoms, foster coping style, and to provide a concrete measure of progress.

Structuring involves establishing or returning an individual to a routine to increase his or her productivity and adjustment, constituting "a predictable, purposeful set of activities [which] allows patients to channel their energy productively." It gives them a sense of control over their immediate environment, provides them with positive feedback on their progress, and helps them achieve short-term realistic goals. Finally, the purpose of *reframing* is defined as, "shifting the perspective of the process – from tragedy to challenge, from future to present, from unmanageable issues to manageable issues." This technique involves paradoxical/cognitive behavioral interventions (e.g. guided imagery), as well as reframing of spiritual issues ("spiritualizing").

Unfortunately, the majority of the empirically-validated treatments have been based on European Americans, and do not reflect the cultural diversity of the United States. Christophersen and Mortweet (2001) note that lack of empirical data (e.g. base rates, treatment efficacy) on cultural diversity makes it difficult to estimate when and where cultural differences are important. The guidelines to improve cultural awareness and understanding that were created by the American Psychological Association (APA, 2003) recognize the importance of influences of the larger environment (e.g. social, political, historical, and economic) on an individual, encouraging psychologists to recognize "that, as cultural beings," patients "may hold attitudes and beliefs that can detrimentally influence their perceptions of and interactions with individuals who are ethnically and racially different from themselves." Psychologists also are encouraged to recognize the importance of multicultural issues in all aspects of their professional responsibilities, including research and education, and they are encouraged to use organizational change processes to support culturally informed organizational practices.

With regard to interventional outcomes, the literature supports the fact that racial and ethnic differences exist in outcomes. For example, in a recent study published by Hanks *et al.* (2003), data supported the fact previously reported that ethnic and racial minorities showed greater frequency of TBI associated with violence than Whites. In fact, they showed rates of violent TBI to be approximately twice as high in ethnic minorities (74%) compared with Whites (46%). Most importantly, these results suggested the presence of poorer outcomes in minorities as a result of violent TBI. It should be noted that this disparity is similar, for example, to that for strokes in African-Americans populations. One of the most comprehensive studies assessing TBI outcome to date was sponsored by the National Institute for Disability and Rehabilitation Research (NIDRR), Traumatic Brain Injury Model Systems, established in 1987. This organization demonstrates the benefits of a coordinated system of neurotrauma and rehabilitation care, conducts innovative research on all aspects of care for those who sustain traumatic

brain injuries, and establishes a national TBI database. In this study, a comparison was made again between the ethnic "minority" group (African-American, Asian/Pacific Islander, etc.) and Whites. This investigation revealed the presence of poorer outcome as measured by the Community Integration Questionnaire assessing role performance in the community, with the "minority" group scoring lower than whites after significant analyses were made to co-variate for various potential demographic and injury confounders including age, gender, and trauma cause and severity. In a study recently published from existing records (Stansbury *et al.*, 2004), the importance of appropriately documenting ethnicity was acknowledged as having high significance in stroke rehabilitation. More importantly, the authors noted the pitfalls associated with methodological issues when using ethnicity as a predictor with dichotomous response variables. Similar findings have been obtained for other outcome measures in other studies for various types of brain injury and its rehabilitation but their detailed examinations are beyond the scope of this chapter (Burnett *et al.*, 2003).

A brief word about language: the intersection between bilingualism and TBI

Although a detailed examination of this issue is beyond the scope of this chapter, it would be a travesty not to briefly address the impact of TBI on language in a manuscript addressing rehabilitation within the context of ethnicity and cultural factors, particularly given the fact that many individuals from such minority backgrounds may possess complete or partial fluency in more than one language. Therefore, a concise examination will be included to provide a hint into the complexity associated with this issue by briefly examining the effects of TBI in language in bilinguals and polyglots.

Although the literature predominantly presents single case studies and small samples, it provides convincing information suggesting that multilinguals, including children and adolescents, may show unique patterns of language recovery after TBI (Paradis, 1995). For example, differential degrees of improvement in one language versus the other, even after rehabilitation, have been observed in multilingual individuals who have sustained strokes (Junque, Vendrell & Vendrell, 1995). In some instances, partial recovery of one and complete recovery of another language; complete loss of one language but not the other, and other patterns of recovery after rehabilitation have been evidenced (Paradis, 1995). Although many factors are beginning to emerge as critical in recovery, including the language under investigation, the first language learned, age at the time of language acquisition, language most frequently used, and other factors, specific patterns of recovery are complicated and a great many questions remain, including issues associated with language localization and representation in multilinguals

(Hernandez *et al.*, 2001). It should also be noted that languages do not depend on the same mechanisms of representation. While some languages depend on phonemes, others depend on pictorial representations, and this issue also may impact recovery during rehabilitation in multilinguals from ethnic minority backgrounds (Paradis, 1995). Nevertheless, attending to language factors during the course of neurocognitive rehabilitation is important. Otherwise, erroneous assumptions and attributions may be used in explaining the recovery of specific language functions in multilingual individuals from ethnic minority backgrounds during the course of rehabilitation.

Summary

Neuropsychological intervention is in its infancy in understanding the impact of culture on assessment, diagnosis, and rehabilitation. However, it is critical for practitioners to be cognizant of epidemiological and demographic issues that impact their daily work with individuals from ethnic minority backgrounds, which, in the US, encompasses a large number of children. It is also important for multicultural models to guide empirically validated assessments and interventions, partly because individuals develop within their cultural context.

From a philosophical perspective, John Dewey (1938) stated that humans

> live from birth to death in a world of persons and things which is in large measure what it is because of what has been done and transmitted from previous human activities. When this fact is ignored, experience is treated as if it were something which goes on exclusively inside an individual's body and mind. It ought not to be necessary to say that experience does not occur in a vacuum. There are sources outside an individual which give rise to experience.

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5

Bridging neuropsychological practice with educational intervention

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Pediatric neuropsychologists are often looked upon to provide recommendations to the school system for the children and adolescents with whom they work. The purpose of these recommendations is generally to identify effective strategies, academic accommodations, and/or special education services that can be provided within the school setting, that are appropriate to the child's disability and functional limitations. Beyond the issue of efficacy of the recommendations being made is the issue of their legal viability and how well they conform to already established laws addressing educational placement. Unfortunately, clinicians often do not have much more than a basic understanding of legislation and statutes that determine the provision of special education services. This can lead to a lack of congruence between the recommendations being made and their effective application. Further complicating the issue is the reality that education laws are at times conflicting, and are often reinterpreted based on regionally relevant court decisions. The laws also dramatically differ in purpose and scope between the secondary and post-secondary setting (Gordon *et al.*, 2002; Murphy, 2004; Ranseen, 1998; Ranseen & Parks, 2005). In addition, the definitions set forth in disability-related legislation are often at odds with standard practices surrounding clinical diagnostic procedures. As a result, clinicians may find themselves confused when their recommendations are not incorporated within the elementary or secondary school environment or when the individual who they tested is deemed ineligible for academic accommodations in college.

The purpose of this chapter is to familiarize neuropsychologists with the laws and policies affecting the provision of accommodations in elementary, secondary and post-secondary settings, through a discussion of their scope and purpose, and how legislation has been interpreted by the courts and educational institutions. Issues related to the transition from secondary school to college and how this affects neuropsychologists who are working with incoming college students will also be reviewed. Finally, practical strategies relating to how clinicians can best work with school personnel and clients in kindergarten through

twelfth (K-12) grade and college settings will be considered, as well as a discussion of why neuropsychologists, by virtue of their training, may be especially well-suited to perform disability and education-related evaluations.

Relevant laws

There are three major pieces of legislation affecting the provision of accommodations and/or special education services in the educational environment in the United States. The *Americans with Disabilities Act* of 1990 (ADA) and Section 504 of the *Rehabilitation Act* of 1973 mandate the provision of reasonable accommodations to individuals with disabilities in higher education and the workforce. While these laws also apply to elementary and secondary schools, they are often overshadowed by the *Individuals with Disabilities Education Act* (IDEA), which makes state funding dependent on the mandate that children with disabilities receive a free and appropriate education in the least restrictive environment. IDEA was reauthorized in 2004 (P.L. 108−446). Changes in the law and definitions and issues related to ADA and Section 504 will be discussed within the context of K-12 and post-secondary education.

Laws affecting the K-12 environment

IDEA

The *Individuals with Disabilities Education Act* (IDEA; 1997, 2000, 2004) was originally passed by Congress as the *Education for All Handicapped Children Act* in 1975 (EACHA; 1975) and amended in 1986. Before this time, children with severe disabilities did not often attend school or were purposefully excluded from attendance; there were few programs for children with learning and emotional problems. Two important legal cases provided precedent for the passage of the EACHA and eventually IDEA: *Pennsylvania Association for Retarded Children (PARC) v Commonwealth of Pennsylvania* (1971, 1972) and *Mills v Board of Education of District of Columbia* (1972, 1980). PARC was filed by the parents of children with mental retardation who had been denied access to public education. The court ruling in this case provided access to a full education and mandated the additional training of children with disabilities toward self-sufficiency. In addition, the state of Pennsylvania was required to locate and identify all school-age persons excluded from public schools and to provide appropriate educational experiences. This practice was the basis of what is now known as the Child Find provision, which is designed to locate children who may qualify for special education services, but who are either not enrolled or are being served in another manner (such as home schooling). In Mills, the lawsuit was filed on behalf of

seven children with behavioral, emotional, and learning disabilities. The court's decision in this case required the schools to "provide each handicapped child of school-age a free and suitable publicly supported education regardless of the degree of the child's mental, physical, or emotional disability or impairment." The decision also required the schools to prepare a proposal that outlined the program for the child and set limits on disciplinary suspensions and expulsions. Both of these cases set the stage for the eventual passage of EACHA.

EACHA established that children with disabilities were entitled to special education and associated services designed to meet individual student needs (Altshuler & Kopels, 2003). The EACHA became the IDEA when it was reauthorized in 1990. The law was expanded when it was reauthorized in 1997, with new requirements in several areas, and the inclusion of categories of children covered by the law; these requirements and classifications can be found in Table 5.1. This expansion allowed for the inclusion of children with attention deficit hyperactivity disorder (ADHD) under "Other Health Impairment" if their difficulties adversely affect their academic performance (Altshuler & Kopels, 2003). The most recent revision of IDEA in 2004 (P.L. 108–446) contains changes in the way children with learning disabilities are identified, but retains the basic premise of the original EACHA and IDEA 1990. The six aspects defining IDEA include zero reject, nondiscriminatory evaluation, a free and appropriate education, least restrictive environment, due process, and parent/child education. Most of these aspects have evolved over the course of IDEA through practice and case law.

Zero reject requires that every child, regardless of severity of disability, must be educated. This requirement prevents a child being excluded for any reason, including toileting or feeding differences (*Irving v Tatro*, 1984; Prasse, 1995). For children with medical needs, a school nurse must be included in the child's

Table 5.1. Federal classifications of disabilities in IDEA 2004

1. Mental retardation
2. Deafness/Hearing impairment
3. Speech/Language impairment
4. Blindness/Visual impairment
5. Emotional disturbance
6. Orthopedic impairment
7. Autism
8. Traumatic brain injury
9. Other health impairment
10. Specific learning disability
11. Deafness/Blindness

educational plan. Nondiscriminatory evaluation requires that an unbiased assessment of the child be conducted to determine the special education services that are appropriate. This aspect was designed to protect cultural and linguistic minorities from over-identification for special education. Under this mandate, a child who is a non-English speaker must be tested in his or her native language. Moreover, the evaluation needs to be multifaceted, and the result of several measures, both formal and informal, that can pinpoint the child's strengths and weaknesses.

The mandate that children with disabilities be provided with a free and appropriate education (FAPE) is an important aspect of IDEA; it ensures the appropriateness and benefit of the placement as well as the provision of services at no additional charge to the parent or guardian. Services provided can include any that the child needs in order to benefit from their education. These can include occupational therapy, physical therapy, speech and language services, counseling, adaptive physical education, and assistive technology. The portion of the law specifying what FAPE involves has been highly contested through the courts and schools. Two key components are used to determine what is an appropriate education — the least restrictive environment (LRE) and the Individual Education Plan (IEP).

The LRE is designed to provide students with access to assistance in the most inclusive classroom and peer environment. The goal is for the child to remain in his/her regular classroom setting for as much of the day as possible. LRE can range from residential treatment (a facility where only children with severe needs are placed and therefore generally away from the public school) to full inclusion, depending on the child's needs.

The IEP documents the school district's responsibilities toward an individual child and outlines services necessary for the child to benefit from education. The IEP is developed by a team of individuals — usually the special education teacher, regular education teacher(s), a school administrator or district representative, the parent(s), and the student (as appropriate). It consists of specific goals and objectives, the names of specific individuals who are responsible for helping the child meet those goals, and the timeline for their completion. The services set forth in the IEP have also been contested in the courts. In *Hendrik Hudson District Board of Education v Rowley* (1982), the Supreme Court determined that the intent of IDEA was not to maximize the child's learning but rather to provide a reasonable opportunity to learn. In other words, the school does not have to provide the equivalent of a "Cadillac" in terms of instruction and support, when a "Ford or Dodge" would be sufficient. Thus, if the IEP is found to contain the necessary requirements as defined by IDEA, then it is generally regarded as an appropriate education.

Due process allows parents or the school to take established steps to ensure fairness in providing education to children with special needs (Jacob & Hartshorne, 2003), when the issue of fairness and appropriateness may be contested. A due process hearing is required when disputes cannot be resolved. The due process hearing allows for challenges to the assessment, identification, placement or the provision of FAPE. The decision from the hearing is final, but either party may appeal the finding to their State Educational Agency (SEA). The SEA then can conduct an impartial review and make an independent decision regarding whether the due process decision will stand. If the parent continues to disagree with the findings, he or she can pursue civil action.

Parent and student involvement is an important part of IDEA, specifically with regard to available funding provided for parent-school education. There are programs for infants, toddlers, and preschool children with special needs and their families. Additional requirements are for compensatory education for young adults up to 21 years (as long as they have not graduated from high school) and vocational and transitional services to assist students with special education needs in transitioning to living and working environments after secondary school.

Changes with IDEA 2004

IDEA was revised in 2004 and the period for public discussion about possible changes ended on September 6, 2005. The changes were ratified in 2006. The primary changes of importance for neuropsychologists include those involving the identification of a learning disability and the education of children with emotional disorders. For children with emotional disorders, it is now required that a functional behavioral analysis (FBA) be completed. FBA requires observation as well as recording of a child's behavior within the classroom and other ancillary environments. This addition is important for determining the extent to which a child's behavioral difficulties relates to the environments in which they occur.

The major changes regarding diagnosis of learning disabilities have occurred in the definition of how a child qualifies for services (see Wills, this volume). In the previous version of IDEA, a learning disability was defined as a discrepancy between measured ability and achievement that was not due to cultural or ethnic differences, or a result of poor instruction. With the revised IDEA, the emphasis has moved from determining the discrepancy based on a simple subtraction or regression method, to instead determining whether a child's presenting level of academic achievement is commensurate with his or her age or ability. In addition, new emphasis has been placed on both implementing and evaluating the success of scientifically supported, research-based interventions in the regular

education class, as part of the evaluation process (Skalski & Klotz, 2005). This procedure, also known as Response to Intervention (RTI), is designed to provide appropriate intervention to a child prior to their possible identification as having a learning disability. As such, RTI requires the use of intensive intervention with empirically validated approaches for learning difficulty, in order to determine whether the child will make effective gains. When success is deemed to have occurred, the evaluation ceases and no further classification is warranted. If the child does not make progress with intervention, then further evaluation is recommended (Semrud-Clikeman, 2006).

This change to how learning disability is classified has drawn much controversy; many educational and psychology professionals have suggested that RTI has not been empirically validated across subject areas and age levels. Fuchs *et al.* (2003) found that RTI may not be as robust as its advocates suggest. When schools that have implemented RTI were evaluated as to the success of the program, Fuchs *et al.* (2003) found insufficient evidence for its effectiveness. The authors suggest that RTI still needs to prove its effectiveness for identification of children with a learning disability, particularly for older children and adolescents, and be refined in terms of its implementation and scope. The clinical neuropsychologist needs to keep updated as to the evolution of IDEA 2004 and should access websites published by the Office of Special Education and Rehabilitive Services (OSERS) or those of interested parties, such as the National Association of School Psychologists.

Section 504

Section 504 is part of the Rehabilitation Act of 1973. The law was designed to protect the rights of individuals with disabilities in any facility that receives federal financial assistance. As applied to schools, it prohibits denial of access to participation in the educational environment based on a child's disability. The definition of a disability under Section 504 is discussed in more detail within the context of higher education. At this point, it is important to note that it is an antidiscrimination statute designed to ensure that the needs of students with disabilities are met at a level that is commensurate with that provided to children without disabilities. Children who are not eligible to receive services under IDEA because their disability does not fall under one of the categories covered by that law, but who are *substantially limited* by their disorder, as discussed in later sections, may be deemed appropriate for a "504 plan."

In the K-12 environment, Section 504 does not require development of a formal IEP, but it does require development of an educational plan. In keeping with the overall intent of Section 504, the purpose of the plan is to ensure that an appropriate education is being provided, that is equivalent to one offered to

children without disabilities. A 504 plan contains several elements, including a description of the child's concern; the basis for determining whether a disabling condition exists; a description of how major life activities are affected; identification of any necessary medications required by the child; description of the recommended modifications and accommodations needed; a list of participants involved in the education of the child; and a review/reassessment date. Section 504 also allows for determination of building and program accessibility. Thus, when a child uses a wheelchair, bathrooms and physical education rooms must be accessible. There is no specified federal funding for the implementation of a Section 504 plan, so monies required for its implementation must come from regular education funding. Table 5.2 details the differences between IDEA and Section 504 in the K-12 setting.

Table 5.2. Contrast between IDEA and 504/ADA

	IDEA	Section 504/ADA	
	K-12	K-12	College/University
Funding source	Federally funded.	Funded by local school district monies.	School pays for the provision of accommodations, not personal aids or devices.
Legislative authority	US Department of Education.	US Office of Civil Rights.	US Office of Civil Rights.
Notice of placement/ services	Written notice of placement required.	Notification of placement required.	Students are approved for accommodations following documentation review, but generally must request these every semester.
Intent of the law	Insures a child with a disability a FAPE.	Federal laws that prohibit discrimination.	Federal laws that prohibit discrimination.
Disability categories covered	Specific categories receive support.	Individuals must meet the definition of a disability set forth in the legislation. Has a broader scope than IDEA and generally includes children with more general, less severe deficits.	Individuals must meet the definition of a disability set forth in the legislation.

Table 5.2. (*cont.*)

	IDEA	Section 504/ADA	
	K-12	K-12	College/University
Extent of coverage	Covers children aged 0–21 years.	Covers all qualified individuals from birth to death.	Covers all qualified individuals from birth to death.
Parental permission	Formal written permission required.	Notification required, but not written permission.	Federal privacy laws (e.g. FERPA) limit the information that can be shared with parents or outside agencies without student consent.
Assessment procedures/ eligibility	Formal assessment procedures required.	Review of existing material may be sufficient.	Students must self-identify to appropriate office and provide documentation that meets established guidelines.
Evaluation/ documentation	Is the responsibility of the school system. An IEP is developed for each student and reviewed every year. Re-evaluations are scheduled at regular intervals.	Is the responsibility of the school system. Students who are designated as "504 only" have a 504 plan, which is reviewed annually.	The cost of the evaluation is the responsibility of the student. Once a student is approved for accommodations, additional documentation generally does not need to be submitted unless there is a significant change in the student's functioning, accommodation requests, or the nature of the specific disability changes over time.
Notification of teachers, faculty; facilitation of accommodations	Services coordinated by team of individuals. Services may be provided by specialists, including Special Education teachers, depending on the nature of the disability.	Accommodations provided by regular classroom teachers who have copies of 504 plan.	Once a student is registered for services, he/she must formally request accommodation letters every semester. It is generally the student's responsibility to deliver these to the professors and discuss how they should be implemented in the course.
Mandates for physical accessibility	Accessibility not directly mentioned.	Detailed regulations for access to facilities to prevent discrimination.	Detailed regulations for access to facilities to prevent discrimination.

Laws affecting the post-secondary environment

ADA

The Americans with Disabilities Act (ADA) was signed into law on July 26, 1990. This legislation was designed to ensure equal rights for individuals with disabilities and stemmed from antidiscrimination laws in the workforce, and court rulings related to disability discrimination (Gordon & Keiser, 1998). Although its definitions and regulations are somewhat similar to those comprising Section 504, the ADA is much broader in scope in that it applies to all public entities whether or not they receive federal financial assistance.

Most of the litigation related to the ADA has focused on whether the individual seeking protection under the law should be considered an *individual with a disability* and thus entitled to the law's protection (Goodman-Delahunty, 2000; Ranseen & Parks, 2005). The definition of a disability under Section 504 and ADA is a "mental or physical impairment that substantially limits one or more major life activities." In order to be considered eligible for protection under the law, an individual must demonstrate (1) a mental or physical impairment (i.e. diagnosis); (2) substantial limitations related to that impairment; and (3) the affected activities must be central to daily life. The ADA affords protection from discrimination to individuals who, by virtue of this definition, either currently have a disability, have a record of having a disability, or are regarded as having a disability whether or not they actually have one. Using a job applicant as an example, a workplace cannot refuse to hire an individual who is *otherwise qualified* to perform essential job functions if they have a disability; have had a disability in the past (e.g. someone with a history of psychiatric hospitalization or prior treatment), or are regarded as disabled based on stereotypical assumptions (Goodman-Delahunty, 2000). The "otherwise qualified" clause is important because it means that the ADA and Section 504 only protect individuals who have the skills to perform necessary duties related to a learning or job setting. In higher education, the correlate is students with disabilities are generally admitted under the same admissions criteria as all other candidates.

Using these definitions, the ADA and Section 504 both mandate that individuals with disabilities who are otherwise qualified to perform requirements necessary to function in a learning or job setting be afforded reasonable accommodations in order to do so. The purpose of these accommodations is to provide equal opportunity to the individual with a disability, and not to instill an unfair advantage. One way to think about this is to consider the goal of accommodations as "leveling the playing field" for the individual with a disability as compared to others.

Several issues of relevance to higher education have come out of recent court decisions related to protection under Section 504 and/or ADA (e.g. *Bartlett v New York State Board of Law Examiners*, 2000, 2001; *Gonzales v National Board of Medical Examiners*, 2000). One of the most robust is the concept of the ''average person standard.'' This refers to the principle that, in order to be considered substantially limited under the law, an individual must be considered limited relative to the average person. This serves to distinguish a disability from typical variation seen in individuals, and attempts to prevent comparisons with an inappropriate reference group when considering job and educational requirements (Maedgen, 2002). Department of Justice regulations concerning ADA illustrate this principle with the following example: ''an individual who had once been able to walk at an extraordinary speed would not be substantially limited in the major life activity of walking if, as a result of a physical impairment, he or she were only able to walk at an average speed, or even at a moderately below average speed'' (as cited in Gordon & Keiser, 1998, p. 7).

The average person standard brings up several issues of relevance in the post-secondary education setting. One is that diagnosis is not sufficient in and of itself for the provision of accommodations to be approved. This is best illustrated by the following case study.

CASE STUDY

Jane was diagnosed with a reading disability when she was in elementary school. Under IDEA, she was found eligible for and received special education services, including specialized reading instruction, individual tutoring, books in an alternative format, extended time for examinations, and a test reader. She was re-evaluated while a junior in high school. Test scores at that time revealed above average to superior intellectual ability and average range reading fluency and comprehension. Her broad reading scores were significantly weaker than her assessed intellectual ability, and retained a reading disability diagnosis based on the discrepancy seen between her aptitude and achievement. She was encouraged to seek disability support services in college. Indeed, her evaluator wrote the following in the recommendations section: ''Based on the discrepancy between her reading scores and above average intellectual ability, Jane meets criteria for a Reading Disorder and is legally entitled to academic accommodations at the University.'' The evaluator then recommended a continuation of support services similar to the ones Jane received in high school, as well as flexible deadlines for large reading assignments, and the ability to take a reduced courseload in order to ''ensure Jane's continued academic success.''

After enrolling in college, and eager to set up support services similar to those she received in high school, Jane and her parents visited the University Disability Services Office the week before classes began. They were stunned when the disability services provider let them know that Jane would not automatically qualify for accommodations simply because she received them in high school. They were upset further when Jane was denied accommodations based on the lack of evidence of a functional impairment.

What this example exemplifies is that, using the average person standard, an individual who meets the clinical definition of a disability does not necessarily meet the legal definition of a disability set forth in Section 504/ADA if their scores and/or limitations are not below those expected in the average person. Although Jane did indeed display a significant discrepancy between her scores on measures of reading and her intellectual ability, her scores were not lower than those of the average person, and her seemingly successful compensatory skills related to her childhood reading problems belied the necessity of academic accommodations in college.

Although not all colleges and universities strictly adhere to the average person principle, most do abide by the definition of a disability set forth in ADA and Section 504 and look for evidence of substantial impairment. Further, they generally do not approve accommodations solely because an individual has a diagnosis or to ''ensure'' academic success. As discussed earlier in this section, the purpose of accommodations under ADA/Section 504 is to allow equal opportunity not guarantee a certain outcome.

Another issue related to the determination of whether or not an individual has a disability under Section 504/ADA and which has implications in higher education is whether or not the use of mitigating measures should be considered in the determination of services. The term ''mitigating measures'' refers to aids or devices that may ameliorate or lessen the effects of a disability. A common example is corrective lenses or spectacles to correct low vision. Several Supreme Court decisions in the late 1990s addressed this issue with rulings that allowed for the consideration of mitigating measures in determining whether or not someone has a disability (*Albertsons v Kirkingburg*, 1999; *Sutton v United Airlines*, 1999). For example, in *Sutton*, the Court found that twin airline pilots, whose vision was corrected by lenses, should not be considered disabled under ADA, because their corrected vision was not substantially limiting. Based on this logic, the Court also found that the sisters were not discriminated against when they were not allowed to work as global airline pilots, which requires 20/20 *uncorrected* vision.

In the academic arena, the use of mitigating measures arises mostly with regard to medication, specifically whether an individual whose symptoms are successfully controlled by that medication continues to be functionally disabled and thus eligible for accommodations. Although it has been the authors'' experience that few colleges or universities deny accommodations when evidence of impairment is identified from a diagnostic evaluation, the student who has subsequently started and effectively responded to treatment is likely to be denied services if no further evidence of impairment remains. For example, a student with a long history of ADHD, who responds effectively to stimulant medication, may show little

evidence of impairment on a neuropsychological evaluation. Even if the diagnosis, by history, is still deemed appropriate, if the symptoms are remediated by medication use, it is likely that the student would be denied academic accommodations in college, for reasons similar to the ones discussed previously: successful compensation or treatment has removed the need for accommodations, which are based on current, functional impact. Conversely, the side-effects of medication can be disabling and as a result, may warrant accommodation (Goodman-Delahunty, 2000). It has been the experience of the authors that the treatments or medications themselves often impose additional functional limitations (e.g. difficulty sleeping, concentration problems), for which accommodations are appropriate.

A third issue relating to the interpretation of ADA and Section 504, and the provision of accommodations is the issue of ''relevance,'' which has primarily been discussed in respect of professional licensing examinations (e.g. Ballard & Elwork, 2003; Ranseen, 1998; Ranseen & Parks, 2005), but may also be of importance for accommodation decisions in undergraduate and graduate programs, particularly those which involve a practical or clinical component. The issue refers to whether or not an individual with a documented disability, and clear limitations associated with it, should be granted accommodations on professional hurdles such as licensing examinations when their limitations may in fact be weaknesses which the examination is designed to detect. Ballard and Elwork (2003) present the example of an individual with a mathematics disorder who requests academic accommodations on an accounting examination; they argue that because facility with numbers is a required skill in accounting, attempts to accommodate difficulty in this area on such an exam are inappropriate and may defeat the validity of the examination. Although most colleges and universities will and should provide reasonable accommodations for a student with dyscalculia on a math test, clinicians and students should be prepared for disability service providers to consider the essential elements or integrity of an exam or course when determining whether requested accommodations are reasonable.

As is evident, the differences in the applicable laws pertaining to post-secondary education, and the absence of IDEA in the post-secondary setting, result in very different decisions being made with respect to who can and will receive supportive services. In addition, specific differences in the way services are provided unfold and these may surprise a family who is well versed in IDEA and the educational responsibilities of the secondary school district. As a result, it is important that these differences are discussed with families during evaluation feedback sessions and in transition planning meetings at schools. Several of these differences are outlined in Table 5.2, which can also serve as a useful guide for students, families, and school personnel.

The role of the neuropsychologist

Neuropsychologists, by virtue of their training and focus on cognitive and behavioral remediation, are often especially well-suited to perform disability evaluations and make associated recommendations for schools (Mapou, 2004). However, a primary stumbling block has been a lack of explicit experience with the scope and meaning of education laws affecting service provision. Many clinical psychology programs do not offer coursework pertaining to special education laws, the definition and diagnosis of disability, or the impact and meaning of the ADA. While school psychologists do receive some training in this area, it is typically focused on IDEA, not on the laws affecting service provision in higher education (Gordon *et al.*, 2002). Thus, it is believed to be quite important that practitioners become knowledgeable about the requirements which educational laws have concerning diagnosis, eligibility, and implementation of disability services.

Evaluations for services under IDEA

For children who have not responded to RTI, a comprehensive evaluation is recommended (Kavale *et al.*, 2005; Fuchs *et al.*, 2003; Telzrow, McNamara & Hollinger, 2000). However, due to time and personnel constraints, most children will be evaluated by their schools, often using the minimum amount of testing, which in turn provides a minimal amount of information. Child neuropsychologists, particularly those who have school experience, can therefore provide an invaluable service to the child and school. However, the evaluation must be useful within the school setting. A list of tests and results and a 20-page report that does not provide ''useful'' recommendations will not be seen as helpful or efficacious. Thus, the child neuropsychologist not only needs to be aware of IDEA and its revision, s/he also needs to be conversant with how interventions can be appropriately adapted for the classroom. Interventions should be tailored to fit specific difficulties.

Evaluation for services under ADA/504 in college

Because eligibility decisions based on the definition of a disability under ADA/Section 504 are dependent on the severity and degree of functional impact, a comprehensive neuropsychological evaluation which assesses factors such as attention, memory, and executive processes can be of tremendous relevance in determining whether or not a diagnosis is actually *disabling* and what types of academic accommodations are appropriate. Mapou's (2004) model of neuropsychological assessment for adult learning disabilities is a good example of how a thorough neuropsychological evaluation can both document the need for and guide accommodation decisions in higher education. The core features of the

model include (1) an evaluation of specific cognitive deficits (e.g. learning, memory, language, visuospatial functions, attention, problem-solving); (2) analysis of how ability/achievement discrepancies relate to everyday functioning; (3) a thorough developmental history to document early learning difficulties; and (4) personality and emotional assessment to help rule out other disorders as the primary cause of learning problems. The testing data is further categorized into global (composite indices that indicate a client's functioning and overall potential), foundation (determine successful input and output of information), modality-specific (modalities in which information is processed), and integrated (skills that require all other skills to function effectively) skills. Deficits in these areas can be related to demands in the academic setting and consequent need for accommodations.

Strategies in working with school personnel

Unfortunately, there is not a large quantity of empirical research regarding the most effective ways of working with elementary, secondary, or post-secondary school personnel in the area of disability issues. Although neuropsychologists and other service providers are adept at conducting evaluations, which have empirical support, and there is some support for the types of remedial services that should be applied, based on a child's disability, there is very little research on what should be recommended for college students and/or how these should be applied. In addition, although one can offer suggestions for how to work effectively with school personnel in both the K-12 and post-secondary settings, few of these have been empirically tested. The recommendations below are offered based on best practices in the consultation literature and the authors'' combined experiences. Applicable guidelines, when available, are also presented.

Within the elementary and secondary school settings, one of the difficulties which pediatric neuropsychologists often experience is initial resistance to entry into the school system. The school will often view a clinician called into a case by an irate or upset parent as either an advocate for the parent or a threat. Meeting with school personnel prior to conducting an evaluation (with appropriate parental permission) can be helpful in garnering administrative support and gathering information about the child's functioning. There is empirical evidence in support of entering the system through the associated psychologist and the principal (Gutkin & Hickman, 1990). In addition, Gonzalez, Nelson, Gutkin & Shwery (2004) found that teachers respond well to consultations when they have met the consultant and spent time with the professional. The information that can be gathered as to the type of work the child is expected to do, the classroom setting, the child's placement in the classroom, the child's in-class behavior, and the feelings the teacher has about the evaluation can be extremely valuable in later

determining useful recommendations. Best practice suggests that being reasonable about what is recommended will provide a better service to the client than a series of recommendations that will not be implemented because they are unrealistic (e.g. one-on-one assistance by individual teachers to a child). Gains in student performance have been found to be greatest when the interventions are developed in a reciprocal manner rather than through expert–nonexpert relationships (Sheridan *et al.* 2001). Similarly, the evaluation report should be written in a way that it is understandable to the school personnel and not full of neurological jargon. Sensitive material that is not germane to the school should be kept to a minimum.

With respect to college students, there have been a few studies examining clinicians'' knowledge of legal definitions and documentation requirements under the ADA (Gordon *et al.*, 2002) and disability offices'' use of psychoeducational reports (Ofiesh & McAfee, 2000). The former revealed that clinicians generally have limited, if any, formal training on ADA issues and may be confused about the intent of the law and the level of impairment necessary to qualify for services. This is despite the fact that psychoeducational reports serve as the basis for most eligibility and accommodation decisions for students with learning disabilities (Ofiesh & McAfee, 2000), a diagnostic category for which issues such as the average person standard and the clinical versus legal definition of a disability can easily arise. As Gordon *et al.* (2002) assert, it is paramount that clinicians understand the ADA and communicate accurate information to their clients who are seeking accommodations. In addition to being an ethical issue, clients frequently pay a great deal of money for evaluations and individuals should be given accurate information about the relative impact of their strengths and weaknesses (Gordon *et al.*, 2002).

In order to best serve the client, clinicians should seek out additional information about the ADA and accommodations in higher education and familiarize themselves with local college and university disability documentation guidelines (Mapou, 2004). Table 5.3 presents the Association of Higher Education and Disability (AHEAD)'s ''seven essential elements of quality disability documentation,'' from which most disability documentation guidelines are adapted. In a survey of college disability service providers, Ofiesh and McAfee (2000) found that the summary of cognitive strengths and weaknesses and subsequent recommendations were the sections typically viewed as most helpful; thus, these areas should be emphasized in reports. However, in doing so, clinicians should take care to make recommendations consistent with the functional limitations evidenced in the evaluation and to avoid the encouragement of unrealistic expectations regarding what will be approved. It is also useful to familiarize oneself with other services available on college campuses as potential resources for students

Table 5.3. Seven essential elements of quality disability documentation (AHEAD, 2004)

1. *Credentials of the evaluation* – Documentation should be provided by a licensed or otherwise accredited professional who has gone through appropriate and comprehensive training, has relevant experience, and does not have a personal relationship with the individual being evaluated.
2. *Diagnostic statement of disability* – Documentation should include a clear diagnostic statement that describes how the condition was diagnosed, provides information on the functional impact, and details the typical progression or prognosis of the condition.
3. *Description of diagnostic methodology* – Documentation should include a description of the diagnostic criteria, evaluation methods, procedures, tests, and dates of administration, as well as a clinical narrative, observation, and specific results. Diagnostic methods should be congruent with the particular disability and current professional practices in the field. Summary data and specific test scores (with the norming population identified) should be included.
4. *Description of functional limitations* – Documentation should include information on how the disabling condition currently affects the individual in order to aid the reviewing party determine that a disability exists and to identify possible accommodations. Documentation should be thorough enough to demonstrate whether and how a major life activity is substantially affected by providing information on the severity, frequency, and pervasiveness of the condition(s).
5. *A description of the expected progression and stability of the disability* – Information on how the individual's condition is expected to change over time and on any known or suspected environmental triggers to periods of exacerbation is helpful in determining appropriate accommodations and planning timelines for re-evaluation.
6. *History of current and past accommodations, academic support, and treatment* – Documentation should include a description of accommodations used in the past and current support services or treatment modalities (e.g. medications). It is helpful to document any side effects associated with medication regimens as these may warrant particular accommodations.
7. *Recommendations for accommodations and academic support* – Documentation should include recommendations for accommodations that are based on the individual's functional limitations. While the post-secondary institution does not have an obligation to provide accommodations recommended by others, those that are congruent with the individual's disability and fit with the university's programs and services may be helpful.

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who are unlikely to qualify for disabilities accommodations and/or as a useful adjunctive service for those who do. Consider Jane, the student who met criteria for a developmental reading disorder, but did not demonstrate current impairment and consequently did not qualify for accommodations. She would be likely to benefit from other support services typically available on larger campuses, such as a learning center, a writing center, and tutorial support. Having these recommendations on hand to offer clients can help them feel more comfortable about the transition to higher education even if they do not qualify for disability services.

Concluding comments

The goal of this chapter was to familiarize neuropsychologists with the laws affecting disability accommodations in education and to provide recommendations as to how to best conduct evaluations under the framework of IDEA, Section 504, and the ADA. The purpose of accommodations differs between the elementary/secondary and post-secondary settings and students who qualify for services under one rubric may not meet criteria under another. It is important for clinicians to consider the definitions of disability put forth in related legislation and to make recommendations that are appropriate under the law as well as feasible within the educational environment. Unfortunately, most clinicians do not have ample training in this area. In the survey of clinicians noted above, 85% reported that they felt that they needed additional education on this topic (Gordon *et al.*, 2002). We concur that additional training on the legal issues surrounding disability accommodations and services in both the K-12 and post-secondary settings is needed and should be incorporated into graduate training programs, internships, and postdoctoral fellowship education. School psychology programs should broaden their focus to include transition issues and the differences in laws and in the ways in which services are delivered between the secondary and post-secondary environments. Clinical programs should include coursework on school and disability-related legislation in general. Clinicians should be encouraged to visit the school systems to gain a better understanding of the educational environment

In addition to increased training, more research should be directed toward the types of accommodations recommended and whether or not these are effective. In the K-12 setting, where one of the goals of special education is to facilitate academic success, it will be important to continue research on what interventions help remediate problem areas and are the most efficacious and easily applied within the classroom setting. In higher education, where the goal moves from promoting success to preventing discrimination, there needs to be more research on the responses of faculty to students with disabilities, their perceptions, and students'' perceptions as to whether the approved accommodations were effective in meeting this goal. Unfortunately, data from the recent National Longitudinal Transition Study-2 (NLTS2) suggest that the rate of attendance of post-secondary education classes by individuals with disabilities is less than half than that of their peers in the general population (Wagner *et al.*, 2005). Only one-third of the sample who did attend colleges or universities received accommodations, primarily because they did not make their disabilities known to the organization. Thus, more attention needs to be paid to the issue of transition and whether students are getting accurate information about services, as well as to the variables interfering with disability disclosure. For those students who do request accommodations,

research is needed on whether some of the most commonly approved accommodations, such as extended test-taking time, are effective across disability categories, as well as on the factors which interfere with student retention.

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Section II

Managing neurocognitive impairments in children and adolescents

6

Traumatic brain injury

Jacobus Donders

Children can acquire traumatic brain injury (TBI) when they experience an acute, external force to the skull. Many cases of childhood TBI are preventable but unfortunately, various potentially effective protective measures such as bicycle helmets and car seats are not always used appropriately or consistently (Agran, Castillo & Winn, 1992; Marshall, Koch & Egelhoff, 1998; Thompson, Rivara & Thompson, 1996). About 180 per 100,000 children incur TBI every year, accounting for approximately 30% of all childhood injury deaths, and there is considerable long-term morbidity in the survivors of those with relatively severe injuries (Rivara, 1994; Kraus, 1995). Rates are higher for boys than for girls, and whereas falls are the most common cause in young children, motor vehicle accidents become increasingly prevalent in older children. This chapter will review the most common neurobehavioral sequelae of pediatric TBI, describe empirically validated approaches to assessment and intervention, and explore avenues for future research.

Pathophysiology and injury severity

TBI can cause cerebral impairment through a combination of primary and secondary mechanisms (Hackbarth *et al.*, 2002; Statler *et al.*, 2001). Primary injuries result from accelerating or decelerating forces, including linear displacements that cause focal lesions such as cortical contusions, and intracranial rotations that lead to diffuse lesions such as axonal stretching. Secondary lesions result from disruption of cerebral circulation and cellular homeostasis, including cerebral ischemia and edema, as well as neurotoxicity due to increases in excitatory amino acids. Prefrontal areas as well as subcortical white matter regions are often preferentially involved in children with long-term neurobehavioral sequelae of TBI, sometimes accompanied by relative increases in cerebrospinal fluid volume (Dennis *et al.*, 2001; Levin *et al.*, 2000*a*; 2004; Max *et al.*, 2005; Serra-Grabulosa *et al.*, 2005; Verger *et al.*, 2001).

Some "adult" classifications of severity of TBI such as the Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974) may not be applicable with very young children, and estimates of posttraumatic amnesia are unreliable when obtained retrospectively (Donders & Kuldanek, 1998). Focal neurological signs such as pupil reflex abnormalities as well as intracranial lesions on neuroimaging reflect more serious injury (Prasad *et al.*, 2002; Woodward *et al.*, 1999). The number of days until a child follows verbal commands (equivalent to a score of 6 on the motor subscale on the GCS) is a reliable and widely used indicator of length of coma (Massagli, Michaud & Rivara, 1996).

Mild injuries that are not associated with prolonged coma, intracranial lesions, or focal neurological signs constitute at least 80% of cases of pediatric TBI. Although many of these children may be symptomatic during the first 1–3 months post injury (Fay *et al.*, 1993; Mittenberg, Wittner & Miller, 1997; Yeates *et al.*, 1999), the vast majority of school-age children who sustain uncomplicated mild TBI have an essentially unremarkable long-term neurobehavioral recovery which is not different from that of children who sustain orthopedic injuries (Bijur & Haslum, 1995; Light *et al.*, 1998; Satz *et al.*, 1997). In contrast, long-term cognitive and psychosocial sequelae are likely with more severe injuries. Persistent symptomatology after uncomplicated mild TBI may, however, occur in children with premorbid neurological, psychiatric, or special education histories or with family problems (Ponsford *et al.*, 1999). At the same time, the mere provision of basic education and anticipatory guidance can help to prevent chronic symptoms after such mild injuries (Ponsford *et al.*, 2001).

Common sequelae of pediatric TBI

With increasing injury severity, TBI can result in a wide range of neurobehavioral sequelae in children. There is no unitary or invariant profile in this regard, and various distinct subtypes have been described in both cognitive (Donders & Warschausky, 1997) and emotional–behavioral domains (Butler *et al.*, 1997; Hayman-Abello, Rourke & Fuerst, 2003). Many commonly reported symptoms, such as difficulties with attention, are not specific to TBI and may also occur with various other conditions such as attention deficit/hyperactivity disorder (ADHD). At the same time, childhood TBI may exacerbate premorbid attention problems (Yeates *et al.*, 2005) or create "secondary" ADHD in children who did not meet criteria for that condition premorbidly (Max *et al.*, 2004). Currently, available research data are equivocal as to whether or not children with TBI who develop secondary ADHD have different levels or patterns of cognitive impairment than those who had preexisting ADHD (Gerring *et al.*, 1998; Slomine *et al.*, 2005). Review of prior academic and (when applicable) treatment records is essential

to evaluate the degree of additional neurobehavioral compromise in children with TBI who have prior complicating psychiatric or special education histories (Donders & Strom, 1997; 2000; Farmer *et al.*, 2002). With these reservations in mind, some sequelae can be identified that are relatively common after moderate–severe pediatric TBI.

Attention is not the only cognitive area that tends to be involved. Speed of information processing as well as novel learning are often compromised; and various aspects of executive functioning and higher-level communication skills may also be affected. Specifically, children with TBI often have difficulties with tasks that place a strong emphasis on rapid and efficient performance, involve the recall of new and complex information, and/or require some problem-solving as opposed to exclusive reliance on over-learned skills (Catroppa & Anderson, 2002; Hoffman, Donders & Thompson, 2000; Slomine *et al.*, 2002; Yeates *et al.*, 2002*a*). In addition, although they often perform well on standardized tests of basic language, children with moderate–severe TBI may have difficulties with processing pragmatics, making inferences, and/or summarizing the most important information from connected oral or written material (Barnes & Dennis, 2001; Chapman *et al.*, 2001; 2004).

With regard to psychiatric and psychosocial sequelae, affective instability and impaired social problem-solving are common (Bloom *et al.*, 2001; Janusz *et al.*, 2002; Max, Robertson & Lansing, 2001; Yeates *et al.*, 2004). Many of these children need special education-based supports and accommodations for extended periods of time (Arroyos-Jurado *et al.*, 2000; Ewing-Cobbs *et al.*, 1998*a*; Kinsella *et al.*, 1997), although they do not always receive adequate services (Taylor *et al.*, 2003). Knowledge of state special education guidelines and active parental involvement are essential, and since the needs of children with moderate–severe TBI tend to change over the years, special education plans may need to be reviewed more frequently (Ylvisaker *et al.*, 2001). Savage *et al.* (2005) provide a review of common challenges in providing educational services to students with TBI, along with some possible pragmatic solutions.

Substantial proportions of families of children with moderate–severe TBI experience high levels of burden and stress for several years after the injury, but open communication styles, lack of rigidity, and use of acceptance and humor as coping styles appear to be associated with better family adjustment (Benn & McColl, 2004; Hawley *et al.*, 2003; Rivara *et al.*, 1996; Wade *et al.*, 1998; 2001; 2002). Other studies have indicated that families need sufficient information about their child's TBI as well as the variety of treatment options that are available, in order to achieve better coping with the changes that have occurred (Hawley, 2003; Waaland, Burns & Cockrell, 1993). Recent attempts at providing families access to research summaries about the

effectiveness of specific rehabilitation services show promise in this regard (Teplicky *et al.*, 2005).

Social support and other interpersonal (e.g. community respite) resources may have a protective effect on family outcomes (Wade *et al.*, 2004*a*). Child and family adjustment after TBI affect each other in a reciprocal manner (Taylor *et al.*, 2001), and both are strongly affected by psychosocial and premorbid variables (Anderson *et al.*, 2005). Child behavior problems after TBI may also negatively affect sibling relationships and may contribute to sibling behavior problems (Swift *et al.*, 2003). With worsening functional outcome of the child with TBI, siblings may also display more symptoms of depression and lower self concept (McMahon *et al.*, 2001).

Recovery and moderating variables

Cognitive skills tend to show partial recovery within the first year after moderate–severe pediatric TBI, with a subsequent relative plateau (Yeates *et al.*, 2002*a*). However, recovery may be more favorable for cognitive than for behavioral and psychosocial adjustment characteristics (Taylor *et al.*, 2002), and long-term cognitive and behavioral/psychosocial outcomes may be determined by different factors (Anderson *et al.*, 2005; Anderson *et al.*, 2004). Moreover, the full implications of the injury may not become apparent until years later, when the prefrontal systems of the brain mature and when environmental demands on the child increase in complexity (Fay *et al.*, 1994; Gil, 2003; Max *et al.*, 1998).

A number of variables that may serve as moderators of recovery have been identified. Moderators specify the circumstances under which a particular condition, such as pediatric TBI, results in specific outcomes (Holmbeck, 2002). The most widely studied moderator variable is age, with consideration of age of onset, time since injury, and age at follow-up assessment. Moderate–severe TBI that is sustained early in life may interfere with vulnerable, rapidly developing skills and is therefore associated with an increased risk for long-term neurobehavioral deficits (Anderson *et al.*, 2005; Ewing-Cobbs *et al.*, 2004; Woodward *et al.*, 1999). At the same time, even with TBI that is sustained during the preschool period, it is clear that premorbid behavioral characteristics have a significant influence on outcome (Goldstrohm & Arffa, 2005). A particularly concerning issue with very young children is child abuse-related TBI, which tends to result in more severe injuries and is associated with poorer cognitive and behavioral outcomes (Barlow *et al.*, 2005; Ewing-Cobbs *et al.*, 1998*b*; Makaroff & Putnam, 2003). Recent research does suggest that a brief hospital-based education program, involving a 1-page leaflet and an 11-minute video, aimed at parents and provided

at the time of all infants' births, can be effective in reducing the incidence of child abuse-related TBI (Dias *et al.*, 2005).

A lower or complicated preinjury level of functioning is clearly a risk factor with regard to worse psychosocial outcome, for both the child and the family (Anderson *et al.*, 2005; Anderson *et al.*, 2004; Luis & Mittenberg, 2002; Ponsford *et al.*, 1999; Rivara *et al.*, 1996; Schwartz *et al.*, 2003; Woodward *et al.*, 1999; Yeates *et al.*, 1997; 2005). A post-injury family environment that is characterized by low levels of stress and greater adaptive interpersonal dynamics may act as a buffer regarding the impact of moderate–severe pediatric TBI (Anderson *et al.*, 2001; Kinsella *et al.*, 1999; Max *et al.*, 1999). In general, the moderating effect of family characteristics is greater on psychosocial than on cognitive outcomes (Taylor *et al.*, 2002). The timing of the follow-up interval is also important because factors that are associated with recovery within the first six months are not necessarily the same as those that determine outcomes at two years. In fact, psychosocial adversity factors such as lower socioeconomic status and family stressors tend to remain more predictive in the long run than injury severity or lesion location variables (Max *et al.*, 2005*a*; 2005*b*).

A number of studies have suggested that socioeconomic disadvantage and/or ethnic minority status may also be associated with worse outcome after pediatric TBI, after controlling for the effect of injury severity (Anderson *et al.*, 2004; Catroppa & Anderson, 2004; Schwartz *et al.*, 2003; Yeates *et al.*, 2002*b*). However, the extent of this moderating influence is not clear because many studies involving extended follow-up typically suffer from differential attrition, with proportionally more participants lost from lower socioeconomic strata. Furthermore, there are differences between ethnic groups in death and hospitalization rates associated with traffic-related TBI, particularly at younger ages, and it is not yet clear to what extent this is due to modifiable factors such as the use of seatbelts and child safety seats (Langlois, Rutland-Brown & Thomas, 2005).

Although TBI happens more to boys than girls, the possible role of gender with regard to outcome has not been widely studied. When socioeconomic and ethnicity factors are controlled, data are not consistent as to whether male gender is associated with worse neurobehavioral recovery (Donders & Nesbit-Greene, 2004; Donders & Woodward, 2003).

One area that has not yet received a lot of attention in the pediatric literature as far as a potentially moderating role in outcome after TBI is that of genetics. Research with adults has suggested that carriers of the apolipoprotein E epsilon 4 allele (APOE ε4) have an increased risk for complicated outcome after moderate-severe TBI (Crawford *et al.*, 2002; Friedman *et al.*, 1999; Waters & Nicoll, 2005). However, recent studies have not found this to be the case in children and teenagers (Blackman, Worley & Strittmatter, 2005; Millare *et al.*, 2003). At this

time, it does not appear that firm conclusions about a potential moderating role of genetic risk factors in sequelae of pediatric TBI can be made yet.

There have not been many studies that have examined sequelae of childhood TBI into adulthood. In a 23-year follow-up of 159 persons who had sustained TBI between the ages of 2 and 15 years, severity of TBI was the most predictive of long-term outcome (Klonoff, Clark & Klonoff, 1993). Nybo and colleagues (Nybo & Koskiniemi, 1999; Nybo, Sainio & Müller, 2004) reported on a smaller sample of persons with preschool TBI and found that only a third of their sample was employed full-time in mid-adulthood. Another study compared outcomes at 5 or more years post injury of children who had been sustained TBI before the age of 8 years and children who were 8–16 years at the time of injury, and found that those in the younger onset group had worse social and vocational outcomes (Asikainen, Kaste & Sarna, 1996). However, those findings were confounded by the fact that the participants who had sustained TBI earlier in life typically had more severe injuries. Similarly, although another investigation (Kieslich *et al.*, 2001) found worse neurological and intellectual outcomes in children injured before the age of 2 years as compared with children who sustained TBI at the age of 6 years or older, those findings were confounded by the fact that the younger children incurred their TBI more often as the result of physical abuse, which tends to be associated with worse outcomes than accidental injuries (Ewing-Cobbs *et al.*, 1998*b*). In general, a long-term developmental perspective is needed in the evaluation and management of children with TBI, because with severe injuries, the risk for sequelae that may extend into adulthood is considerable, and the prevailing problems may be more of a psychosocial than a cognitive nature (Cattelani *et al.*, 1998).

Evidence-based assessment and intervention

Comprehensive, evidence-based recommendations have been developed for the acute medical assessment and treatment of children with TBI, based upon exhaustive review of the available literature (Adelson *et al.*, 2003). None of these could be considered unequivocal treatment standards (reflecting an accepted principle of patient management based on a high degree of clinical certainty) but several of them met evidence-based criteria for guidelines (reflecting a moderate degree of clinical certainty). However, in the majority of areas covered, the recommendations reflected options (consensus agreements for potential remaining strategies for which there were unclear clinical certainties). Guidelines were offered in the following areas.

First, children with severe TBI should be transported to a pediatric trauma center, because treatment at such centers is associated with better chances

for survival. It should be noted that no data were available on whether this difference extended to functional or neurobehavioral outcomes in the years after survival. Another set of guidelines was that both hypoxia and hypotension should be avoided if possible, and corrected as soon as possible when they do occur. In relation to that, it was suggested that the child's cerebral perfusion pressure (a measure of cerebral blood flow, defined as the mean arterial pressure minus the intracranial pressure) should be maintained at >40 mg Hg. The latter guidelines were clearly aimed at the prevention of secondary injuries associated with TBI. There were insufficient data to support specific treatment guidelines with regard to other potential medical management strategies such as hyperventilation, temperature control, etc.

Neuroimaging is an important component of the assessment of children with TBI. Although CT scanning is still the most appropriate technique to use in the acute phase, MRI is the method of choice in the subacute and chronic stages (Bigler, 1999; Poussaint & Moeller, 2002). Day-of-injury scans do not always relate well to levels and patterns of neurobehavioral outcome past the acute stage (Anderson *et al.*, 2004; Donders & Nesbit-Greene, 2004) but in all fairness, that is not how they were intended to be applied. Instead, such scans are to be used primarily as techniques to help guide critical care interventions (Adelson *et al.*, 2003). Some of the most common structural abnormalities after pediatric TBI, such as cerebral atrophy and thinning of the corpus callosum, may not materialize until 3–12 months post injury, and those subacute finding are more strongly correlated with neurobehavioral outcome (Levin *et al.*, 2000*a*; Vasa *et al.*, 2004; Wilde *et al.*, 2005). There are also exciting new developments in the field of structural neuroimaging, such as diffusion-weighted and diffusion-tensor methods, as well as emerging applications of functional MRI and spectroscopy, that may play an increasing role in the assessment and ultimate management of children with TBI (for a review, see Bigler, 2005).

There is increasing interest in the use of pharmacological agents in the management of the long-term sequelae of pediatric TBI. Given the frequency of reported difficulties with attention, as well as the phenomenon of "secondary" ADHD, it is not surprising that attempts have been made at using stimulant medications. However, a recent review found only modest evidence in support of the efficacy of such agents (Jin & Schachar, 2004). Treatment effects were noted to be relatively stronger on behavior than on cognition, and there was also a trend for initiation of treatment sooner after injury to be associated with more favorable outcomes. Other recent studies have addressed the potential utility of Amantadine, a dopamine agonist (Green, Hornyak & Hurvitz, 2004). The most convincing study to date was a small randomized controlled clinical trial that found promising effects on children's daily behavioral functioning, as assessed

by rating scales which were completed by the parents, but less promising effects on cognitive measures (Beers *et al.*, 2005). Larger, randomized, controlled studies are needed to determine with greater certainty the potential effectiveness and safety of such agents in the management of sequelae of pediatric TBI.

With regard to mood disorders, there is considerable controversy regarding the use of selective serotonin reuptake inhibitors (SSRIs) and other psychotropic agents with children, particularly in light of conflicting reports about relative efficacy as well as increased risk of suicidal behaviors. The current consensus is that, with the possible exception of Prozac, SSRIs should not be considered a first-line method of intervention in children with depression and other mood disorders (Courtney, 2004; Weller, Tucker & Weller, 2005; Whittington *et al.*, 2004; Wong *et al.*, 2004). It should be noted that, except for some case studies, there are almost no data regarding the efficacy of SSRIs in children with TBI.

There are few "hard" guidelines regarding the neuropsychological assessment of children with TBI. Given the above-mentioned frequency of difficulties with attention, information processing speed, learning and memory, and subjective affect in these children, it is essential to include reliable and valid measures of those domains in any psychometric evaluation. Yet, the neurobehavioral sequelae of childhood TBI are not necessarily captured completely by the tests which are typically included in neuropsychological evaluations. Such assessments rely to a large extent on tasks that were administered in a highly structured environment without distractions or other challenging variables, which may actually compensate for some of the executive difficulties that these children often have (Silver, 2000). Therefore, it is advisable to supplement the evaluation with standardized rating scales regarding behavioral regulation and attention/organization skills in daily life, such as the Behavior Rating Inventory of Executive Function (BRIEF; Gioia *et al.*, 2000). This may offer incremental information about the functioning of children with moderate–severe TBI in the community, above and beyond what can be accounted for on the basis of laboratory tests alone (Mangeot *et al.*, 2002; Vriezen & Pigott, 2002).

A complete discussion of the reliability and validity of all possible psychometric tests that can be used in the evaluation of children with TBI is beyond the scope of this chapter. The reader is referred to Baron (2004) for this purpose. However, to provide an illustrative example, some studies pertaining to the construct and criterion validity of a commonly used test of learning and memory, the California Verbal Learning Test – Children's Version (CVLT–C; Delis *et al.*, 1994), will be reviewed.

The CVLT–C is a task where the child has to learn and remember a grocery list. As such, it is similar to requirements that children face on a daily basis in school and in the community. The CVLT–C has acceptable reliability, with average

internal consistency estimates ranging from 0.72 to 0.85 in the standardization sample, and has age-based norms for children from 5 to 16 years (Delis *et al.*, 1994). However, when using a psychometric test like this in practice with clinical populations such as children with TBI, research should be conducted to ensure that there is sufficient evidence that the instrument accurately measures the intended constructs in those children, and that performance on that test is meaningfully related to some kind of external criterion or benchmark (American Educational Research Association, American Psychological Association & National Council or Measurement in Education, 1999). The CVLT−C is actually one of the few instruments for which such kind of information pertaining to construct and criterion validity has been demonstrated, specifically in samples of children with TBI.

There is evidence from confirmatory factor analyses that the CVLT−C measures various distinct latent constructs in children with TBI (attention span, learning efficiency, delayed recall, and inaccurate recall) and that performance on this test after TBI can largely be interpreted along the same multidimensional lines as have been suggested for neurologically normal children (Donders, 1999; Mottram & Donders, 2005). Within a larger neuropsychological battery as applied with children with TBI, CVLT−C data also constitutes a distinct, robust, and meaningful declarative memory factor (Brookshire *et al.*, 2004). These findings support the construct validity of the instrument.

Several other studies have documented the sensitivity of CVLT−C variables to severity of TBI (Levin *et al.*, 2000*b*; Roman *et al.*, 1998), offering support for the criterion validity of the test. Much of this sensitivity to injury may be because this test makes significant demands on speed and efficiency of information processing, with the latter skills essentially mediating the effect of cerebral injury on learning and memory (Donders & Nesbit-Greene, 2004). Importantly, there is evidence that performance on the CVLT−C is very predictive of special education placement several years after injury, and that it accounts for more variance in this regard than can be explained on the basis of demographic and injury variables alone (Miller & Donders, 2003). This attests to the incremental value that some neuropsychological tests can play in the evaluation and management of children with TBI.

Another important issue to consider in the context of neuropsychological assessment is the fact that when tests get updated or revised, they may yield patterns of performance and relationships to TBI variables that are different from previous versions. For example, on the WISC−III (Wechsler, 1991), a widely used test of psychometric intelligence, it was common to see decreased performance after moderate−severe pediatric TBI on both the Perceptual Organization Index, pertaining to visual perceptual and constructional abilities, and the Processing

Speed Index, reflecting rapid and accurate pencil-and-paper performance (Donders, 2001). However, in the revision of this test (WISC–IV; Wechsler, 2003), significant changes were made in terms of subtest content and requirements, including a considerable decrease in emphasis on speed in tasks associated with the perceptual organization factor (renamed "Perceptual Reasoning"; see Yeates & Donders, 2005 for a review of other changes).

To illustrate the effect that test modifications may have on pattern of performance after TBI, Figure 6.1 presents preliminary WISC–IV data from forty 6–16 year-old children with TBI (55% male; 80% White; median age 12 years, 2 months) who were consecutively referred over the course of 2.5 years and who were assessed within one year after injury (median elapsed time = 88 days). Children with complicating premorbid histories (e.g. learning disability, child abuse) were excluded. Of these 40 children almost half (45%) had coma ≥ 1 day, and about two-thirds (65%) had an intracranial lesion on neuroimaging. Inspection of Figure 6.1 indicates that these children actually did well on the Perceptual Reasoning Index whereas the only relatively depressed score was on the Processing Speed Index. In fact, of all the four index scores, only processing speed demonstrated a statistically significant correlation with length of coma, accounting for 12% of the variance ($r = -0.34$, $p < 0.05$). These findings indicate that caution is needed when using new or revised tests in the evaluation of children with TBI. Simply assuming that they measure the same thing, or that they are equally sensitive to injury severity as similar instruments or previous versions of the same one, may lead to erroneous diagnostic conclusions.

Attempts at cognitive rehabilitation of acquired cognitive deficits have proliferated over the past few decades. However, the empirical support for these interventions is equivocal at best, with the few available studies having significant

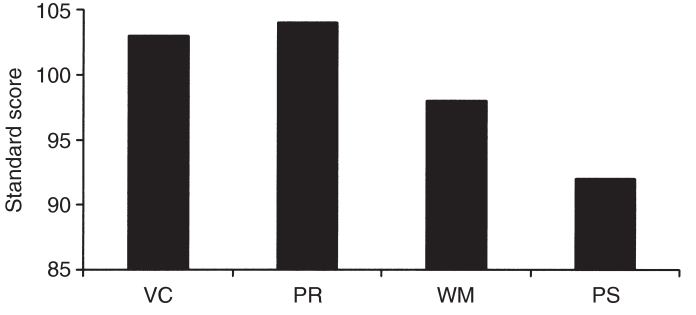

Figure 6.1 WISC–IV findings in 40 children with traumatic brain injury.
VC = Verbal Comprehension. PR = Perceptual Reasoning. WM = Working Memory. PS = Processing Speed.

methodological limitations (Limond & Leeke, 2005). Although there are exciting examples of the potential of systematic cognitive rehabilitation in children with other neurological conditions such as brain tumors (Butler & Copeland, 2002), these methods have not yet seen extensive systematic evaluation through randomized controlled trials in samples of children with TBI. An exception is a recent study with a heterogeneous group of children with various forms of acquired brain injury, but long-term follow-up data are still pending (Van't Hooft *et al.*, 2005).

Promising new avenues of research have emerged over the past few years in the utilization of electronic resources such as self-guided web-based instructional materials and videoconferencing for family problem-solving intervention after pediatric traumatic brain injury (Wade *et al.*, 2005; Wade, Wolfe & Pestian, 2004*b*). Most importantly, this is one of the few areas of applied intervention with this population that has seen the application of randomized controlled clinical trials. Although subject to replication with larger and independent samples, preliminary evidence suggests that an online, cognitive–behavioral problem-solving approach through videoconferencing is superior to the provision of standard care with internet access to written resources, in terms of improving both parental distress and child adjustment (Wade, Carey & Wolfe, 2006*a*; 2006*b*). This type of intervention could potentially be helpful for families living in remote areas who have limited access to healthcare systems. Another recent randomized controlled trial suggests and also supports the general idea that family-centered intervention can be associated with better functional outcomes for children with TBI than conventional clinic-based interventions (Braga *et al.*, 2005).

Future research directions

There continue to be several areas where additional research could potentially improve the evidence-based practice of pediatric neuropsychological assessment of, and intervention with, children with TBI and their families. To begin with, more information is needed with regard to the most effective ways to prevent various forms of pediatric TBI occurring in the first place. For the survivors, it needs to be determined specifically which acute care interventions are the most effective in not only saving lives but also preventing secondary neurological injuries. More prospective, longitudinal studies are needed to delineate predictors of variability in neurobehavioral recovery of TBI into the teen, adolescent, and adult years, and to identify potential moderating and mediating variables.

Current developments in the area of structural and functional neuroimaging are exciting but more data are needed to determine to what extent they will lead to interventions that are associated with improvements in outcomes.

In the area of neuropsychological assessment, more research is needed to determine the ecological validity and incremental value of laboratory tests and rating scales.

With regard to intervention studies, there is a need for more randomized, controlled trials, particularly with regard to the long-term effectiveness of pharmacological, psychotherapeutic, and cognitive interventions for children with TBI and their families. Diversity and cross-cultural issues will also need to be addressed in this context because there is insufficient information about how these variables interact with access to, and ability to profit from, various forms of treatment. With all these endeavors, it will be important to get a better understanding of the characteristics of both children and families who are at relatively greatest risk for complicated outcome, and also the child and family attributes which make certain types of interventions more likely to succeed than other ones. Eventually, this should result in a biopsychosocial model of pediatric TBI that incorporates genetic, medical, social, and demographic variables into a long-term developmental perspective.

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7

Neuropsychological sequelae in children treated for cancer

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Cancer is the leading cause of death by disease in children under the age of 15 years (National Cancer Institute Research on Childhood Cancers, Cancer Facts). Acute lymphoblastic leukemia (ALL) is the most common form of childhood cancer, comprising approximately 40% of all diagnosed cases (Margolin & Poplack, 1997). Brain tumors are the second most frequent malignancy of childhood and the most common of the solid tumors (Ries *et al.*, 2004). Brain tumors and other central nervous system (CNS) cancers account for approximately 20% of all childhood cancers (Sklar, 2002).

Given their higher prevalence amongst childhood cancers and their associated neuropsychological risk, most research into the neuropsychological sequelae of childhood cancer and its related treatment has involved the study of ALL and brain tumors. Such research has become increasingly important as neuropsychological morbidity has increased with the substantial increase in survival rates that has accompanied advances in detection and treatment over the last several decades. Estimated 10-year survival rates for children diagnosed with CNS tumors from 1995 to 1999 were approximately 70% (Brenner, 2003). Five-year survival rates for children with ALL under age 19 now exceed 70% (Ries *et al.*, 2004).

Treatment interventions and associated neuropsychological outcome

Treatment of childhood cancers involving or at risk of involving the CNS varies considerably and is dependent on such factors as tumor type, grade of malignancy, location of the tumor, extent of CNS involvement, and age of the child. The neuropsychological sequelae of childhood cancer extend into adolescence and adulthood and are not only associated with the cancer itself but the treatments employed, such as surgical intervention, chemotherapy, cranial/craniospinal radiation therapy (RT), or a combination of these treatments.

Beyond surgical biopsy for histological diagnosis, surgical interventions for brain tumors include tumor resection and other interventions such as shunt placement to relieve secondary cerebrospinal fluid flow obstruction. The neuropsychological risks associated with surgery vary, with some studies documenting minimal neuropsychological sequelae and others documenting more substantial evidence of cognitive and adaptive impairments (Beebe *et al.*, 2005; Moore, 2005). In general, however, the unique risks associated with surgery are much less than those associated with other treatments (e.g. radiation and/or chemotherapy; Mulhern *et al.*, 1999).

Chemotherapy is a primary treatment for ALL and is also commonly used in the treatment of brain tumors. With regard to brain tumors, chemotherapy has particular application as a means of delaying RT in young children, for whom the risk associated with RT is greatest. Identification of the unique neuropsychological risks associated with chemotherapy alone is complicated by its frequent use in combination with RT in children treated for brain tumors and, to a lesser extent, ALL. In general, while chemotherapy alone is viewed as having a less deleterious effect on neuropsychological outcome than RT, there does appear to be some neuropsychological risk (Buizer *et al.*, 2005). High dose intravenous cytarabine or methotrexate and intrathecal methotrexate have been most consistently associated with neurocognitive sequelae. Various agents have also been associated with other neurological complications, such as peripheral neuropathy and hearing loss, which themselves can impact a child's development, learning, and quality of life.

Radiation therapy has been one of the greatest contributors to improving the survival rates of children with varying types of CNS cancers. The indications for RT in the treatment of childhood brain tumors and the parameters for delivery are continuously evolving, with advances including a transition from whole brain radiation to greater reliance on hyperfractionation, conformal radiation models, and focal radiation (Merchant *et al.*, 2004). The benefits of RT notwithstanding, cranial RT has been associated with numerous neurologic and cognitive effects that vary according to the extent and location of CNS involvement, size of area irradiated, and total dose administered. Although the pathophysiology of these effects is not fully understood, it has been suggested that RT is associated with white matter changes (Fouladi *et al.*, 2004; Mulhern, White, *et al.*, 2004*b*). The functional implication of white matter changes is significant, as overall white matter volume and specific regional volumes of white matter in the prefrontal and frontal lobe and cingulate gyrus are associated with executive functions (e.g. attention, working memory) as well as processing speed and visual–spatial processing (Mulhern *et al.*, 2004*b*; Reddick *et al.*, 2003; Schatz *et al.*, 2000). In fact, global intellectual deficits in young children with brain tumors treated with RT can be at least partially explained by white matter pathology

(Mulhern *et al.*, 2001), with evidence of a mediating effect of attention in this relationship (Reddick *et al.*, 2003).

Current research on the long-term impact of CNS cancers and treatments documents an elevated risk for numerous neuropsychological sequelae. Much of this research has focused on global intellectual functioning, but there is an emerging literature documenting more specific areas of neuropsychological deficit. The heterogeneous nature of tumors, diverse treatment factors, and numerous possible complications of treatment create a challenge for researchers studying the associated neuropsychological outcomes. The major focus of outcome research has been on the sequelae of RT, as this has been shown to be the most critical determinant of outcome. Comprehensive reviews of the neuropsychological sequelae of CNS cancers and associated treatments are available in the recent literature (Moore, 2005; Mulhern *et al.*, 2004*a*). Only the most consistent findings will be discussed herein.

Intellectual functioning

Whole brain craniospinal RT has consistently been documented to have significant adverse effects on intellectual functioning (see Moore, 2005), but the impact of even reduced dose craniospinal RT (1800 cGy to 2300 cGy) is still substantial. Studies have strongly indicated that cognitive status declines with increasing time since RT. Additional risk factors for cognitive decline are younger age at time of treatment, higher dose of RT, and use of adjuvant therapies (Mulhern *et al.*, 2004*a*). Cognitive deficits begin to emerge on standardized tests as early as 1 year post RT, and a decline of 2 to 4 IQ points per year has been documented, with the greatest decline noted in the first few years following treatment (Spiegler *et al.*, 2004). The cognitive declines documented have been related to developmental stagnation (i.e. child's inability to acquire new skills and information at a rate comparable to same-age peers) rather than regression or loss of skills. In addition, children with higher baseline functioning have been found to exhibit greater decline in overall IQ (Palmer *et al.*, 2003; Ris *et al.*, 2001).

Neurocognitive functioning

There is no consistent neuropsychological profile that encompasses all childhood cancers or tumor types, treatments, and risk factors. However, attention, processing speed, and working memory deficits are most often cited as associated with cranial RT. In addition, declines in visual–motor integration, visual memory, verbal fluency, and executive functioning relative to intact verbal memory and language skills in children treated with RT have also been reported (see Morris *et al.*, 2000). Several researchers, most recently Anderson *et al.* (2000), have found the neuropsychological profile of children with CNS cancers treated with RT and

adjuvant chemotherapies to be similar to that of children with nonverbal learning disabilities.

Medical/surgical complications that can occur in children with cancer and treatments involving the CNS are associated with poorer intellectual and specific neuropsychological outcome (Mulhern *et al.*, 2004*a*; Palmer *et al.*, 2003), and less consistent findings suggest that female gender may also be associated with greater neuropsychological risk in this population (Ris *et al.*, 2001; see Waber & Mullenix, 2000). ''Stage of development'' at time of treatment has been associated with variability in associated neuropsychological sequelae. That is, abilities associated with early brain development, such as basic language and gross motor functioning, are typically only minimally affected, whereas skills that develop later or that have a more prolonged course of development (e.g. processing speed, executive functions) are more consistently impaired (Armstrong, Blumberg & Toledano, 1999).

Academic functioning

Children with CNS cancers are at increased risk for academic difficulties. In fact, 57% of children with varying types of brain tumors were found to have a specific academic deficit, and arithmetic deficits were identified in 3 out of every 4 such children (Buono *et al.*, 1998). Children whose cancer is complicated by hydrocephalus are at particular risk of performing poorly in math (Mabbot *et al.*, 2005). School-based special education services are often necessary. Treatment involving intrathecal methotrexate and cranial RT administered either alone or in combination significantly increases the likelihood for the need of special education services (Mitby *et al.*, 2003).

Due to the academic challenges experienced by children with brain tumors and other CNS cancers, many such children do not attempt post-graduate schooling. In the only available published data known to these authors, Hays *et al.* (1992) documented that 90% of childhood CNS cancer survivors graduated high school. However, only 10% obtained a bachelor's degree compared to 25% of individuals whose cancer did not involve the CNS. The long-term impact of CNS cancer also affects survivors' ability to maintain employment. In contrast to 86% of children with non-CNS cancer, only 54% of children with CNS involvement maintained employment at their usual jobs.

Socioemotional functioning

Research on adjustment to childhood cancer has documented equivocal findings. Most survivors do not exhibit clinically significant psychopathology, but mild withdrawal and social deficits have been found in a subset of children with brain tumors (Poggi *et al.*, 2005). Even for childhood cancer survivors without

psychopathology, there is evidence of significant parental distress and poor family functioning (Streisand, Kazak & Tercyak, 2003). Post-traumatic stress symptoms (PTSS) are present in family members of survivors and, less consistently, survivors themselves (Kazak *et al.*, 2001; Kazak *et al.*, 2004b). Factors predictive of poorer psychological outcome include low child IQ, single-parent family, higher family stress, moderate to severe disfigurement, low socioeconomic status, certain tumor locations, and severe functional impairment (Carlson-Green, Morris & Krawiecki, 1995; Mulhern *et al.*, 1993).

Intervention

Knowledge of the neuropsychological sequelae associated with childhood cancer and treatments involving the CNS is essential to the development of efficacious interventions for improving outcome, and there is now general agreement that intervention studies are an important next step in childhood cancer research. The Children's Oncology Group *Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers* (COG LTFU Guidelines) represents an initial effort toward a greater focus on intervention (Children's Oncology Group, 2004). This document provides professionals with a summary of the potential late-effects associated with various cancers and treatments, identifies those factors associated with the greatest risk of poor outcome, and summarizes basic guidelines for evaluation and intervention. Although this document specifically details recommendations for long-term survivors (2+ years post-treatment), the recommended considerations are often addressed in cancer treatment centers from the time of diagnosis and treatment.

The COG LTFU Guidelines serve as a helpful rubric in which to review common interventions for the neuropsychological sequelae of childhood cancer. For patients with CNS involvement, the guidelines include recommendations for neuropsychological evaluation, referral for educational resources/intervention via school liaison, referral for community disability services, and consideration of psychopharmacologic treatment. Guidelines for cancer survivors in general also include additional psychosocial interventions. Some of the areas recommended in the guidelines have been the focus of further study as an initial effort to provide empirical support for their inclusion in intervention plans. An additional intervention for which empirical support is being established is cognitive remediation, which is not yet included in the guidelines.

Neuropsychological evaluation

The COG LTFU Guidelines recommend comprehensive neuropsychological evaluation in survivors of childhood cancer with CNS involvement. Such evaluations

should encompass not only omnibus tests of IQ and measures of academic achievement that are traditionally included in assessing developmental learning disabilities, but also tests of processing speed, attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, and executive function and planning.

In an attempt to translate evidence-based research into recommendations for clinicians, Mulhern, Armstrong and Thompson (1998) formulated guidelines for the clinical neuropsychological evaluation of survivors of childhood ALL and brain tumors. They classified neuropsychological tests into practice standards, practice guidelines, and practice options, which respectively represent categories of practice recommendations in decreasing order of scientific evidence and clinical acceptance. Armstrong *et al.* (1999) further recommended that tests included in assessment batteries should have developmental norms derived from non-biased, large, and representative samples of children; the ability to detect differences between groups; and an established relationship to either objective measures of brain dysfunction or outcome following intervention. They also recommended re-evaluation at 12 to 18 month intervals in order to detect neuropsychological late-effects, emphasizing the use of identical tests or parallel forms across evaluations in order to detect change in both standard and raw score performance. Finally, local content-based assessment was also identified as important to more specifically direct intervention planning and program evaluation to the individual child. Curriculum-based measures have a number of advantages in this regard, including a greater level of sensitivity to short-term changes, direct relevance to the standards of achievement amongst the child's own school peers, and better utility when examining a child's progress in specific academic areas.

Educational interventions

Addressing the school experience of childhood cancer survivors is critical in any effective intervention program. Formal plans for continuation of school during treatment, effective school re-entry at an appropriate point during or after treatment, and implementation of appropriate educational interventions are important, particularly for those children whose cancer or treatment involves the CNS (Mitby *et al.*, 2003).

Specialized cancer centers often have established protocols and formal school re-entry programs. Though not standardized, these protocols typically involve not only components for maintaining education during treatment but also components such as educating parents and teachers about the educational needs and medical status of the child, providing basic education about cancer-related changes to school peers, and working with school educators to implement services appropriate for addressing the child's unique physical and learning needs.

School re-entry programs as described in the literature range from school personnel workshops to peer education programs to more comprehensive programs that involve these and additional components. Participants in school personnel workshops have reported increased knowledge about childhood cancer, greater confidence in dealing with children with cancer, and an increased level of concern about childhood cancer survivors and their families (see Prevatt, Heffer & Lowe, 2000; Rynard *et al.*, 1998). Participants in peer education programs have reported increased knowledge about childhood cancer, an interest in interacting with a peer with cancer, decreased personal worrying about cancer, and decreased concerns about ill peers (Benner & Marlow, 1991; Treiber, Schramm & Mabe, 1986).

Comprehensive school intervention programs typically involve school personnel and peer educational interventions but also ongoing consultation and therapeutic strategies to enhance family, social, and hospital collaboration. The programs are individualized, based upon the needs of a given child. Katz *et al.* (1988) described one such program that involved preparation of the child and family prior to school re-entry, school conferences, classroom presentations, and ongoing follow-up. Evaluation of this program utilizing standardized child, parent, and teacher ratings documented fewer internalizing behavior problems, more social competence and self-perceived social, cognitive, and physical competence, and greater levels of age-appropriate school behavior post-intervention. Evaluative ratings from parents and teachers were high (Katz *et al.*, 1992). None of the available studies exclusively included children with CNS involvement, despite the higher risk for poor school adjustment and performance in this group. In fact, Katz and colleagues actually excluded children with brain tumors because of the higher probability of learning problems.

School reintegration programs help to communicate recommendations for school-based accommodations and interventions to school personnel, and this is guided in part by neuropsychological evaluation results. The efficacy of commonly recommended school-based accommodations and interventions has been the focus of very little formal study. In a sample of children diagnosed with ALL and treated with chemotherapy and RT (18 Gy), Anderson *et al.* (2000) reported that those children who received higher degrees of educational interventions (i.e. verbal feedback plus recommendations and written report to family, telephone advice to school, and documentation of educational intervention by the school) demonstrated improved reading and spelling skills between initial evaluation at two years post-treatment and a follow-up evaluation three years later. This study thus provides some preliminary evidence of the benefits of neuropsychological evaluation and resulting recommendations.

F. D. Armstrong and colleagues (personal communication, November 10, 2005) conducted a clinical compensatory intervention study in which they tracked

outcomes of 10 children with medulloblastoma treated prior to age 6 years. All children were in special education programs. Following intervention, 9 of the 10 later graduated with regular high school diplomas, and 5 of the 10 entered college with accommodations. These investigators are now conducting a 5-year longitudinal study to evaluate outcomes following a compensatory intervention for children treated for either CNS tumors or ALL. Preliminary results with a small sample ($n = 45$) suggest a significant benefit for those children randomized to more intense monitoring of school-based interventions, and this benefit is observed across several areas of function. Statistical analyses of data from 22 participants collected during years 1 and 2 of the study indicate that children whose Individual Education Programs were monitored quarterly showed improvement on applied mathematics, whereas those monitored less intensively on an annual basis declined (Goldman *et al.*, in press).

Cognitive remediation

Cognitive remediation refers to systematic, therapeutic efforts designed to improve cognitive functioning after a CNS insult. Despite advances in our knowledge of the neuropsychological sequelae of childhood cancer and treatments, there has been relatively little attention given to the remediation of these deficits. This discussion will provide only a cursory review of the available studies of cognitive remediation in childhood cancer populations, as a more detailed discussion is provided by Butler in this text (see Chapter 16).

Penkman (2004) reported the results of attention training involving the "Pay Attention!" program (Thomson *et al.*, 2001) combined with instruction in meta-cognitive self-monitoring strategies in a 6-year-old child diagnosed with ALL and treated with RT, intrathecal methotrexate, and systemic chemotherapy. Following six months of training, the child improved on measures of attention and arithmetic but not on measures of visuomotor integration and receptive language, which were not targeted by the intervention. This provides support for the specificity of the training. Parent ratings of attention normalized post-intervention, providing evidence of the generalizability of the improvements.

The most extensive cognitive remediation in children with neurocognitive deficits associated with childhood cancer and related treatments has been conducted by Butler and colleagues though the Cognitive Remediation Program (CRP; Butler, 1998; Butler & Copeland, 2002). In their two published studies, Butler and colleagues have provided preliminary, empirical support for the use of the CRP in childhood cancer survivors, with consistent improvements documented in the area of attention. A randomized controlled intervention trial is now underway to further investigate the effectiveness of the CRP. Preliminary results

support academic generalization, which was not documented in the pilot study (Butler & Mulhern, 2005).

Psychopharmacologic interventions

Available research has documented the efficacy of methylphenidate (MPH), a stimulant medication, for addressing the attentional deficits which are present in childhood cancer survivors. Thompson *et al.* (2001) published evidence of the efficacy of MPH treatment in childhood cancer in a randomized, double-blind, placebo-controlled design. In their sample of 32 eligible school-aged children with a documented history of chemotherapy and/or RT for malignant brain tumor or ALL, the investigators reported significantly greater improvement on an index of sustained attention and on an overall index of attention with MPH (0.6 mg/kg) compared with placebo. There were no group differences in either ability to inhibit impulsive responding, reaction time, or other areas of cognition assessed.

A later study extended the Thompson *et al.* (2001) investigation by reporting on the results of a short-term (3 week), randomized ($n = 83$), placebo-controlled, double-blind trial of low dose (0.3 mg/kg) and moderate dose (0.6 mg/kg) MPH (Mulhern *et al.*, 2005). Statistically significant and clinically relevant improvements in attention and cognitive behaviors were reported by parents and teachers on standardized behavioral inventories, and teachers also reported improved social behaviors and academic competence. This study did not address whether benefits of MPH can be maintained over an extended time interval nor if they extend beyond parent and teacher perceptions to documented improvements in neuropsychological functioning and academic achievement.

Psychosocial interventions

Although findings are equivocal and suggest that associated risks may often be below psychopathology threshold and observed only within a subset of children, the existing evidence of socioemotional sequelae in childhood cancer survivors has been sufficient to lead to the development of interventions to improve outcome in patients and their families. The most developed programs have targeted three areas: maternal problem-solving, post-traumatic stress in the child and family members, and child social functioning.

Sahler *et al.* (2002; 2005) examined the degree to which problem-solving skills training (PSST) improves problem-solving and decreases emotional turmoil in mothers of newly diagnosed children. PSST is an 8-week, manualized intervention which involves the application of the cognitive–behavioral approach known as problem-solving therapy to individuals who are experiencing distress following a challenging life event but who do not have a diagnosable psychological condition.

It involves teaching five essential problem-solving steps and weekly homework assignments targeted to addressing specific problems that participating mothers identify as especially relevant to their individual situations.

In a multisite pilot intervention in 92 mothers of recently diagnosed patients who were randomized to either PSST or a standard psychosocial care intervention, Sahler *et al.* (2002) found that PSST led to greater reduction in maternal emotional distress. PSST also significantly decreased the mothers' tendency to adopt a negative problem orientation in which they pessimistically appraised a problem as unsolvable and threatening. The effect was greatest immediately after the intervention, with attenuation of the effect three months post-intervention.

In a follow-up, multisite, randomized trial in which 430 English and Spanish speaking mothers of recently diagnosed patients were randomized to PSST or standard psychosocial care, mothers in the PSST group demonstrated significantly greater improvement on all included measures of negative affect, and this was maintained three months post-intervention on two of the three measures (Sahler *et al.*, 2005). The PSST group also once again showed greater improvements on a measure of negative problem orientation as well as on a measure of avoidance style, which is a tendency to procrastinate or assign the responsibility for solving problems to others. These improvements were also maintained three months post-intervention.

With regard to interventions addressing symptoms of post-traumatic stress in both survivors and their families, Kazak *et al.* (1999) described the Surviving Cancer Competently Intervention Program (SCCIP) and presented a pilot study of 19 families of adolescent cancer survivors. Evaluation of this four-session intervention was conducted post-intervention through participant completion of a brief evaluation form as well as collection of data on measures of post-traumatic stress, anxiety, and family functioning pre- and post-intervention. Evaluative ratings provided by the adolescent survivors and their families were positive. In addition, symptoms of post-traumatic stress and anxiety improved for survivors and family members, but there was generally no change on measures of family functioning.

Kazak *et al.* (2004a) later conducted a randomized waiting-list control trial of the SCCIP intervention in 150 adolescent cancer survivors and their mothers, fathers, and adolescent siblings. Participants completed standardized assessment scales assessing emotional adjustment and post-traumatic stress symptoms at baseline and again 3 to 5 months post-intervention. The data were supportive of this brief intervention program, evidencing significant, post-treatment reductions in intrusive thoughts among fathers and in arousal among survivors.

A third focus of socioemotional intervention studies among childhood cancer survivors has been social skills. Varni *et al.* (1993) randomized 64 newly diagnosed childhood cancer survivors (brain tumor excluded) to either a social skills training group or a standard intervention group. The social skills training program supplemented routine school reintegration services with a manualized, individual program which addressed social-cognitive problem-solving, assertiveness training, and handling teasing and name calling across three, 1-hour sessions. The social skills intervention group demonstrated significantly fewer behavior problems and significantly greater perceived peer and teacher social support and school competence at 9 months post-diagnosis relative to pre-intervention. The standard care control group demonstrated no statistically significant change from baseline to the 9 month follow-up.

Barakat *et al.* (2003) presented a pilot study of the effectiveness of a manualized, group social skills training intervention for 13 school-aged children treated specifically for brain tumors. The intervention involved six, weekly parent and child group sessions as well as homework assignments which targeted a set of social skills. Although this study is limited by the absence of a control group, the data provide preliminary support for the effectiveness of the intervention. Significant improvement from baseline to a post-intervention follow-up (ranging between 6 and 22 months following the intervention) was found on child and parent ratings of social competence and on child ratings of internalizing behavior problems. Effect sizes ranged from small to medium, though some clinical significance was noted in that a subset of children improved from clinical to nonclinical levels of social and behavior problems.

Future directions

This review highlights the existence of a fledgling literature devoted to the treatment of the neuropsychological sequelae of childhood cancers in general. The literature devoted specifically to interventions following pediatric brain tumors and other cancers affecting the CNS is even less well-developed. These literatures describe a number of different intervention efforts targeting important neuropsychological sequelae, but the general lack of methodological rigor characterizing most of these studies limits empirical evidence of validity and efficacy. According to criteria reviewed by Chambless and Ollendick (2001), many of the current interventions would be considered ''experimental'' due to lack of sufficient empirical support, though certain interventions, such as use of MPH to address attentional deficits and interventions to address maternal problem-solving, could now be considered ''well-established'' or minimally ''probably efficacious'' treatments according to established criteria. While interest and focus on

intervention issues in childhood cancer is growing, there remain many potential directions for future research, and our discussion of this important topic is intended to highlight those we view to be particularly important as the field moves into the next phase of intervention research.

At the broadest level, there exists a need for a systematic approach that facilitates development of theoretically-based, standardized, and empirically grounded interventions. It will be important that such an approach allows professionals involved in treatment to systematically link our current and future knowledge of assessment with the interventions developed. Careful attention must be given to the degree to which the proposed interventions can be practically disseminated to, and implemented in, the diverse settings in which intervention occurs: childhood cancer interventions typically span medical, educational, home, and other community settings. Even within medical settings specifically, there is substantial variability in the resources and clinical expertise available. Thus, issues of dissemination and implementation, including demonstration of efficacy to justify funding through sources such as health insurance, school districts, grants, and governmental subsidies, are critical as intervention research in this population of children moves forward. Within the educational system, children with evidence of medical disabilities and documented educational needs are eligible for school-based interventions, such as those recommended through neuropsychological evaluation and school reintegration services, through funding under federal law (e.g. an Individual Education Plan through the Individuals with Disabilities Education Improvement Act or a Section 504 Plan).

We have previously proposed drawing upon the literature for treatment models pertaining to neuropsychological disorders and learning disabilities as a helpful next step in the systematic development of neuropsychological interventions in another childhood disorder with neuropsychological sequelae (Ris & Nortz, in press). We now submit this as a potential next step in childhood cancer research as well. Teeter and Semrud-Clikeman (1995; 1997), for example, developed a transactional model to assist in diagnosis and treatment of children and adolescents with various learning and neuropsychiatric disorders. They proposed that such a 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 and Semrud-Clikeman's eight-stage model requires expertise from various professionals, with Stages 1 though 4 (problem identification, behavioral-based intervention, cognitive child study, and cognitive-based intervention) typically conducted by school psychologists and educational professionals and Stages 5 through 8 (neuropsychological assessment, integrated neuropsychological intervention,

neurological and neuroradiological assessment, and medical and neurological rehabilitation) typically conducted by medical and other community professionals. This model is amenable to a neuropsychological orientation to remediation and to cross-disciplinary interactions. Such a model offers a promising orientation to guide future study and implementation of neuropsychological interventions in childhood cancer.

While an overriding, theoretical approach will be an important umbrella under which future intervention research can be conducted and implemented, further development of specific intervention methods is needed. Understanding the neuropsychological deficits associated with the various cancer conditions and treatments is an essential step in the development of efficacious interventions for minimizing or preventing late-effects. Ongoing neuropsychological outcome research is needed in order to more specifically identify vulnerable skills and cognitive processes that can be targeted for remediation and other interventions, particularly in more homogeneous patient populations, defined by variables such as tumor/cancer type and location, treatment type, age at diagnosis, time since treatment, and gender. Given that CNS involvement is consistently associated with greater risk among survivors of childhood cancer, intervention studies specific to this population will similarly be important. However, our review of the current literature found only a small number of such studies (Barakat *et al.*, 2003; Butler, 1998; Butler & Copeland, 2002; Mulhern *et al.*, 2005; Penkman, 2004; Thompson *et al.*, 2001). Furthermore, as investigations of neuropsychological sequelae identify the highest-risk patient groups within children with CNS involvement, follow-up intervention studies within these more homogeneous patient groups will be indicated.

Data generated from studies that address these issues will facilitate delivery of more efficacious interventions to those children at highest risk, and such studies represent a critical future direction in a healthcare market and public education system in which evidence-based care and/or cost-effectiveness are emerging as necessary standards for justification of intervention implementation/funding. To this end, future studies will also need to address issues of intervention timing. For example, do interventions implemented early following cancer diagnosis and treatment lead to better outcome (e.g. remediation of deficits, prevention of *late*-effects, better educational/vocational outcome, less associated socio-emotional maladjustment) than those implemented later after the emergence of late-effects? If so, is this observed even in the absence of documented deficits sufficient enough to justify acquisition of services according to current educational laws? This type of preventative approach is promoted within clinical practice, particularly for children at higher risk for emergence of late-effects, but it is often difficult to justify this need within an educational system

that is financially burdened and operating within a deficit-based rather than a prevention-based orientation. Empirical evidence in support of preventative interventions, whether they be offered through healthcare systems (e.g. cognitive rehabilitation, psychotherapy, and medications funded through health insurance or out-of-pocket expenses) or educational settings (e.g. special education services funded by the local school district through taxes and other government funding), will be necessary to justify this more intensive, early intervention approach. Moreover, the benefits documented will likely need to pertain to not only the individual child and family (e.g. higher academic achievement and educational/vocational attainment, reduced family stress), but also to society at large (e.g. reduction in health care, special education, and disability resource utilization over time).

Of those areas in which evidence-based intervention research is most advanced, opportunities for additional study nevertheless remain. Pharmacologic interventions need to be explored more fully to include studies of other psychotropics as well as additional psychostimulants and other medications which may result in attentional improvement. The impact of these interventions on additional variables, such as academic achievement in the classroom, socioemotional adjustment, and future educational and vocational attainment, should also be investigated. This applies to cognitive remediation research as well.

With regard to cognitive remediation more specifically, issues of broad implementation will need to be addressed given the professional training and funding needs involved. Development of training workshops, collaboration with special educators or school psychologists for implementation within school systems, and development of web-based models of implementation similar to those being explored in traumatic brain injury research (Wade, Wolfe & Pestian, 2004) are potential avenues of future investigation to address implementation issues. Finally, Butler and Mulhern (2005) have also proposed that future research investigate the influence of the family environment and resources, as factors such as family burden and adjustment have been shown to be important predictors of neurocognitive recovery in another neurologically involved patient population (Yeates *et al.*, 2001).

An additional direction of future research is in the area of ecological interventions. A major arena in which intervention for the neuropsychological sequelae of childhood cancer currently takes place is the schools, and a large part of our work as clinical neuropsychologists involves offering recommendations to be implemented in the school setting. However, the efficacy of these recommendations and of common interventions implemented within special education programs for addressing neuropsychological deficits is only now becoming the focus of formal study (F. D. Armstrong, personal communication,

November 10, 2005). More generally, the efficacy of school reintegration programs is also not well established, due in part to the potentially outdated nature of the available studies in the light of increasing neuropsychological morbidity associated with higher survival rates, the methodological limitations of the available studies (i.e. frequent absence of control group; lack of attention to important outcome variables such as school attendance, academic and social functioning, or graduation rates; heavy reliance on descriptive and anecdotal reports), and the fact that the protocols used by school re-integration programs are not standardized across centers. In fact, other than the COG LTFU Guidelines (Children's Oncology Group, 2004) and a lay literature that is emerging for parents and educators (Keene, 2003), there are few resources to guide educators and school re-entry personnel. Recommendations for school-based interventions are typically derived from knowledge of standard clinical and educational practice and from other sources, such as organizations and resources for children with learning disabilities. Thus, greater standardization of clinical practice for school re-entry programs, manuals or texts in which to disseminate this information, and formal investigation to provide empirical support for these programs and the special education strategies recommended is an important avenue for the future of neuropsychological intervention following childhood cancer. These advances will be likely to have particular benefit for families and professionals in rural areas or in areas where specialized cancer centers with formal school re-entry programs are otherwise not available.

Methodological avenues

Addressing methodological limitations, such as small sample sizes, a relative lack of well-controlled prospective studies, and poor selection of outcome measures, will be important for advancing our knowledge of empirically validated interventions for neuropsychological sequelae in childhood cancer survivors. Armstrong and Reaman (2005) discuss the role of cooperative group, clinical trial research in the study of psychological effects of childhood cancer. Although barriers to such research exist (e.g. cost and resultant need for prioritization of studies; standardization across multiple centers, authorship and productivity), this is a promising avenue through which issues such as sample size and the need for prospective research can be more adequately addressed.

The Psychology Discipline Committee of the Children's Oncology Group (COG) has developed a specific strategy for carrying out intervention research in the cooperative-group context. The cost, feasibility, and potential effectiveness of a proposed intervention are first evaluated in a small-scale rapid pilot intervention study conducted across three to four separate institutions. If continued investigation remains appropriate, a limited institution study within multiple centers

capable of enrolling sufficient numbers of children is next initiated. It is this mechanism that has heretofore contributed most to the establishment of empirically validated intervention approaches in childhood cancer, such as through the previously reviewed studies of psychostimulant mediations in the treatment of cognitive late-effects and of maternal problem-solving training. Investigation of the cognitive remediation of attentional deficits in children treated for cancer is also currently being conducted via this mechanism.

Once the effectiveness and feasibility of a psychological intervention has been demonstrated in the limited institution study, a group-wide trial across the COG institutions can be implemented. This represents translation research, moving the intervention from the experimental setting to the community setting of standard care. Modifications in the intervention's model become necessary at this level for practical implementation of the protocol across settings that are diverse with respect to resources and professional skills and training.

Despite the successful examples of multisite trials, there are potential liabilities of these studies. Kazak (2005) notes that newly developed interventions may be particularly difficult to deliver and test in multi-institutional studies unless sufficient resources are available for training and monitoring the interventionists. The costs involved would be above and beyond the usual cost barriers inherent in collaborative group studies. She thus proposes that a balanced portfolio of intervention studies for this population might best include a combination of large, collaborative studies of protocol-driven treatments with smaller, more intensive studies of innovative interventions targeting specific patient groups.

Summary

The field of neuropsychology plays an important role in childhood cancer research and clinical practice. Available studies have focused primarily on the neuropsychological sequelae of childhood cancer, with fewer investigations devoted to establishing empirically supported interventions. The most significant advancements thus far pertain to cognitive remediation, psychopharmacologic interventions, and socioemotional interventions, though the empirical support across even these areas ranges from experimental to well-established (Chambless & Ollendick, 2001). Clearly, intervention research in the field of childhood cancer is in its infancy, and there are many potential avenues of future investigation. However, the emerging literature as well as the establishment of avenues for conducting future studies suggests that the field is moving in a promising direction with respect to intervention research, and significant advancement in coming years is likely.

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8

Seizure disorders

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A diagnosis of epilepsy is made when a person experiences two or more unprovoked seizures, i.e. seizures without an immediate precipitating event such as fever, a blow to the head, active brain infection, or metabolic disturbance. Epileptic seizures result from abnormal electrical discharges which may be confined to a part of the brain or involve the entire cortex. The diagnostic classification system initially developed by the Commission on Classification and Terminology of the International League Against Epilepsy (1989) reflects both the manner in which the seizure begins (partial versus generalized) and the effects of the abnormal discharge (see Table 8.1).

Approximately 1% of children in the United States are diagnosed with epilepsy by age 20 (Epilepsy Foundation of America, 2002). The risk of developing seizures peaks during the first two years of life but declines over the childhood years (Camfield & Camfield, 1997). Epilepsy may develop as the result of or in association with a wide variety of medical conditions, as indicated in Table 8.2.

Typically, the diagnosis of epilepsy is based on behavior during the seizure and the characteristics of the electroencephalogram (EEG). For some children, the EEG will be abnormal only during the seizure event. An accurate description of the seizure by observers, and in some cases by the child experiencing the event, becomes essential in making the diagnosis. Medical and family history may facilitate identification of etiology. A genetic basis has been identified for five epilepsy syndromes and some forms of partial epilepsy (Winawer & Shinnar, 2005). Brain imaging studies such as MRI (magnetic resonance imaging) scans are used to investigate structural brain anomalies which might give rise to seizures.

Over the past 25 years, the number of anti-epileptic drugs (AEDs) available to treat epilepsy has more than doubled. AEDs are selected based on seizure type, with some working best either for partial seizures or for generalized seizures while other AEDs are effective for both. In a follow-up study of 613 children with new onset epilepsy, Berg *et al.* (2001) found that 74% obtained remission, defined as a two-year period of seizure freedom, in response to the first AED administered.

Table 8.1. Common seizure types in clinical practice

Seizure onset	Common clinical manifestations
Generalized	EEG onset at the same time in all parts of the brain. Loss of consciousness occurs during the event.
Absence	Staring, fixed gaze, rapid eyelid blinking.
Tonic clonic	Alteration of extension and contraction of muscles resulting in jerking appearance.
Myoclonic	Abrupt bilateral contraction of muscles, often involving arms and shoulders.
Tonic	Abrupt sustained increase in muscle tone, resulting in rigidity and falls.
Atonic	Abrupt loss of muscle tone resulting in falls.
Partial	Seizures onset limited to a single area in the brain, with possible progression to other areas as the seizure continues. Clinical manifestations represent the function of the area of the brain involved in the seizure. Partial seizures may spread to involve the whole brain (secondary generalization).
Simple	Patient reports experiencing a sensation such as a taste, odor, a sense of nausea, fearfulness, or seeing colors. Remains conscious.
Complex	May begin with sensations, progressing to alteration in consciousness such as being able to hear but not understand what is said. Often accompanied by automatisms (e.g. picking at clothing, repeated swallowing, lip smacking) or motor manifestations such as jerking involving only one side of the body.

The probability of gaining long-term seizure control decreased with each subsequent episode of breakthrough seizures requiring medication change (Berg *et al.*, 2004).

When medications fail to control seizures, other options are available. In addition to the removal of tumors, neurosurgical resection is often considered for individuals with cortical malformations, an area of focal brain injury, or when partial seizures arise from a single area of the brain (Duchowney, 2001). Pre-surgical evaluation in such cases is concerned with defining the seizure focus through use of video-EEG, functional imaging (PET, SPECT), and/or magneto-encephalography (MEG) (Knake *et al.*, 2004). The Intracarotid Amobarbital Procedure (IAP), functional magnetic resonance imaging (fMRI), MEG, and extra- and intra-operative electrocorticography (''brain mapping'') may be used to define eloquent brain cortex. The role of the neuropsychologist and neuro-psychological testing in this process will be discussed below. Surgical intervention

Table 8.2. Causes of childhood epilepsy

Changes in brain structure
Hippocampal sclerosis
Cortical malformations
Tumor
Late effects of brain insult
Traumatic brain injury
Infection
Hypoxic/Ischemic events
Stroke
Comorbid conditions
Tuberous sclerosis
Sturge-Weber syndrome
Neuro-degenerative disorders
Chronic infections
Genetic syndromes
Generalized epilepsy with febrile seizures plus (GEFS+)
Benign familial neonatal convulsions
Severe myoclonic epilepsy of infancy
Juvenile myoclonic epilepsy
Absence epilepsy
Autosomal dominant nocturnal frontal lobe epilepsy
Partial epilepsy with auditory features
Lateral temporal lobe epilepsy
Pediatric epilepsy syndromes with no known etiology
Lennox-Gastaut
Infantile spasms
Landau-Kleffner
Benign rolandic epilepsy
Electrical status epilepticus in sleep (ESES) also know as continuous spike wave in slow-wave sleep (CSWS)

can result in a ''cure'' for some children, allowing for the elimination of AED treatment. The likelihood of seizure control is estimated for each patient based on data collected in the pre-surgical evaluation.

The ketogenic diet (Freeman, Freeman & Kelly, 2000) is a highly restrictive diet, high in fat and low in carbohydrates, which has proved to be effective for some individuals with epilepsy. It can be particularly helpful in cases of intractable epilepsy which lack a focal origin. Because of the need for rigid adherence, including strict portion control, the ketogenic diet requires a high degree of motivation from parents and the child with epilepsy. Preliminary data regarding

the Atkins diet, a less restrictive regimen, suggests that this may be a more tolerable alternative for older children and adults while providing equal efficacy (Kossoff *et al.*, 2003).

The vagal nerve stimulator (VNS) is a surgically implanted device similar to a pacemaker which provides regular stimulation to the vagus nerve. It has been effective in decreasing seizure frequency and/or duration as well as in improving quality of life (Helmers *et al.*, 2001; Murphy *et al.*, 2003).

The neuropsychological consequences of childhood epilepsy

Epilepsy is not a single medical disorder, but rather represents a highly diverse condition. Any behavior mediated by the cortex may become part of a seizure and/or may be affected by epilepsy. As a result, epilepsy does not produce a single pattern of cognitive deficits. The resulting cognitive profile in a child with epilepsy reflects multiple factors, including age of seizure onset, seizure frequency, seizure type or syndrome, and treatment. The manifestation of symptoms will be further modified by psychosocial variables including the child's, family's, and community's reaction to the epilepsy. The neuropsychological consequences of epilepsy for an individual may fluctuate over time with changes in seizure frequency, treatment, and/or psychosocial context.

Cognitive consequences of childhood epilepsy

The cognitive consequences of childhood epilepsy can range from benign to catastrophic. Cognitive effects are more closely associated with epilepsy syndromes than with seizure type or EEG characteristics alone (Camfield & Camfield, 2002). Intellectual estimates for children with epilepsy in general fall within the average range, but below the standardization mean (Farwell, Dodrill & Batzel, 1985). Intellectual deficits are more common with generalized symptomatic epilepsies and early age of onset, as well as with markers for intractability such as high seizure frequency, presence of multiple seizure types, and treatment requiring multiple anti-epileptic drugs (LaJoie & Miles, 2002; Nolan *et al.*, 2003). Academic problems are common. Children with epilepsy are at greater risk for grade retention and special education placement than unaffected siblings (Bailet & Turk, 2000). There do not appear to be any learning profiles that are unique to childhood epilepsy (Aldenkamp, Overweg-Plandsoen & Arends, 1999), though mental slowing is common (Vermeulen *et al.*, 1994).

Difficulties with attention are the most common problem reported by parents (Dunn *et al.*, 2003). When DSM-IV criteria are applied, the primarily inattentive subtype of Attention Deficit Hyperactivity Disorder (ADHD) predominates and occurs more often than in the general population (Hesdorffer *et al.*, 2004).

Deficits have been reported on cognitive tasks of attention, though the poor performance of children with epilepsy on such tasks may be attributable to slow processing speed (Aldenkamp *et al.*, 2000).

Children with epilepsy often do poorly on tests of memory skills. Temporal Lobe Epilepsy (TLE), in particular, is associated with risk for memory deficits (Nolan *et al.*, 2004), which may progress over time (Hermann *et al.*, 2002). However, children with well-controlled seizures and without other psychiatric problems, tend to score at the same level as controls on memory measures (Williams *et al.*, 2001).

Syndrome-related outcomes

Seizure disorders beginning in infancy may range from benign to encephalopathic (Mizrahi & Clancy, 2000). West Syndrome has particularly poor outcomes, with high rates of mental deficiency (Czochanska *et al.*, 1994). So-called benign early epilepsies also may have adverse cognitive effects such as difficulties with attention and impulsivity (Shahar *et al.*, 2004).

Children with Benign Myoclonic Epilepsy may experience mild cognitive deficits (Mangano, Fontana & Cusumano, 2005), while Severe Myoclonic Epilepsy (SME; Dravet Syndrome) is typically associated with developmental arrest by age four. Outcomes in Myoclonic Astatic Epilepsy (MAE; Doose Syndrome) vary with success of seizure control (Guerrini & Aicardi, 2003).

Lennox-Gastaut Syndrome (LGS) is associated with high rates of mental retardation and behavioral disturbance, including autistic-like features (Besag, 2004). Children with LGS may initially demonstrate a period of average cognitive development, with cessation in cognitive development at or around the time of seizure onset.

Children with Landau-Kleffner Syndrome (LKS) often demonstrate receptive language deterioration, followed by impaired expressive communication and behavioral difficulties, including the development of autistic features. Functioning remains intact in other cognitive domains and in the ability to perform activities of daily living. Some cognitive recovery may be seen, though the prognosis is generally poor if the active phase of the condition lasts more than three years (Robinson *et al.*, 2001). Cognitive dysfunction in the related syndrome of electrical status epilepticus in sleep (ESES) is also common, though typically not limited to language skills (Scholtes, Hendriks & Renier, 2005).

Childhood Absence Epilepsy (CAE), which often resolves in adolescence, is typically thought to be benign with respect to behavioral and cognitive outcomes. However, mild deficits have been reported in CAE on tasks of general intelligence, visuospatial ability, and nonverbal memory (Pavone *et al.*, 2001).

Syndromes arising in adolescence include Juvenile Myoclonic Epilepsy (JME) and the Progressive Myoclonic Epilepsies (PME). Though intellectual outcomes in JME are typically felt to be favorable, difficulties with executive functions, memory, and emotional adjustment have been reported (Sonmez *et al.*, 2004). PMEs, while rare, carry a very poor prognosis and are often associated with progressive mental deterioration (Wheless & Kim, 2002).

The role of interictal discharges

Computerized tasks have been devised to study subtle disruptions of cognition in conjunction with brief EEG discharges. In a recent study, reaction times on a cognitive activation task during brief subclinical EEG discharges were found to be 35% slower than overall task responses (Aldenkamp *et al.*, 2005). Similar techniques have been used to demonstrate material-specificity of lateralized epileptiform discharges for verbal and visuospatial stimuli (Binnie, 1993). These methods have been used to address the question of transient cognitive impairment (TCI), the brief disruption of cognition during an epileptiform discharge without other clinical manifestations. Aldenkamp and Arends (2004) concluded that TCI is more likely to cause performance variability than to be a primary source of cognitive impairment. However, recent work using MEG technology suggests that persistent discharges may result in uneven skill development (Wolff *et al.*, 2005)

Anti-epileptic drug (AED) therapy side-effects

While AEDs are essential in supporting seizure control, medications often have an adverse impact on cognitive functioning and behavior. Parents and physicians face a balancing act, striving for optimal seizure control while minimizing cognitive and behavioral side effects. While research generated from medication trials necessary to gain FDA approval exists to guide this decision-making for adults, significantly less research is available for pediatric patients. Limitations in study design have often led to inconclusive results regarding the cognitive profiles for specific AEDs in children (Loring & Meador, 2004). Furthermore, the multi-factorial nature of emotional and behavioral problems in childhood epilepsy has complicated attempts to isolate the contribution of AEDs to these difficulties (Glauser, 2004).

The social and emotional consequences of childhood epilepsy

Childhood epilepsy is associated with significant risk for psychopathology, ranging from anxiety and depression to acting out behavior (Rodenburg *et al.*, 2005*b*). Seizure recurrence, gender (male), lower parental education, older age of

onset, and the presence of unrecognized seizure events prior to diagnosis have been cited as factors predicting behavior problems in children with new onset epilepsy (Austin *et al.*, 2001). Despite this risk, many children with psychiatric difficulties and epilepsy do not receive mental health services (Ott *et al.*, 2003).

Children with epilepsy and their families face a number of challenges to normal development. Much of the impact of childhood epilepsy upon quality of life (QoL) appears mediated by its effects upon parents and family (Williams *et al.*, 2003). Seizure events are often misunderstood and elicit anxiety from bystanders, increasing the likelihood that the child with epilepsy will be stigmatized (Austin, Shafer & Deering, 2002*b*). Parental anxieties focus on the seizure event and beyond it, focusing on the child's treatment and future life (Chapieski *et al.*, 2005). Parental anxiety can also have an inhibitory influence on the child's emerging mastery of adaptive skills.

Characteristics of the home environment such as family mastery and cohesion, marital conflict, discipline strategies, and parental support play a role in behavioral and emotional adjustment of the child with epilepsy (Austin *et al.*, 2004; Rodenburg *et al.*, 2005*a*). A study by Carlton-Ford *et al.* (1997) demonstrated the powerful interplay of psychosocial and family variables. They found an increased incidence of behavioral problems in children whose parents perceived epilepsy as limiting or thought their child would be stigmatized, as well as in children who perceived their parents as over-controlling.

The role of neuropsychological assessment

Neuropsychological assessment is viewed as a key element in the treatment of epilepsy (Buelow and McNelis, 2002), used to establish baselines for monitoring the impact of epilepsy and its treatment on cognitive development. Results directly impact medical care, affecting selection of medications and documenting need for further medical testing such as an EEG or evaluation for neurodegenerative disorders. In addition, neuropsychological assessment is used to tease apart the complex mixture of emotional, learning, memory and executive problems which may accompany epilepsy, serving as the basis for development of an intervention plan and referral to appropriate treatment sources. Because epilepsy is often misunderstood, the neuropsychologist's ability to provide information regarding epilepsy, in general, and the child's specific form of epilepsy to the child's teachers and/or mental health professional may be as important as the test findings.

In the evaluation of children as candidates for neurosurgical treatment of their seizure disorders, the neuropsychologist's role expands to include: (1) assisting with lateralization and localization of seizure focus, (2) assisting with lateralization and location of eloquent cortex such as speech, and

(3) determining the likelihood of producing memory or other cognitive or motor deficits (Bernstein, Prather & Rey-Casserly, 1995). In addition to the neuropsychological test battery, one or more of the following procedures may be used to achieve these goals.

The IAP involves selective unilateral injection of a fast-acting and short-lived anesthesia into the internal carotid artery followed by assessment of language and memory functions. The test materials and assessment protocol vary among epilepsy centers, contributing to varying reports of effectiveness (Meador & Loring, 1999). Functional imaging (fMRI, MEG) is another approach to localizing eloquent cortex. Some clinicians speculate that this tool may eventually replace the IAP, particularly for use with children, as it is a less invasive and confrontational method (Hertz-Pannier *et al.*, 2001). Cortical stimulation may also be used to map areas of eloquent brain cortex to minimize post-surgical declines (Ojemann & Dodrill, 1985). Successful mapping has been conducted with children both intra-operatively during the resection or extra-operatively following placement of a subdural grid which is also used for recording purposes to define the margins of the seizure focus (Ojemann *et al.*, 2003; Everett *et al.*, 2006).

The neuropsychologist can play an important role in the IAP, and with functional imaging and cortical mapping. Responsibilities include preparing the child for the procedures, both by educating the child and family about what will occur, and readying the child emotionally for the task demands. The rapport established during this process serves as the basis for maintaining cooperation during the procedure. Based on neuropsychological test results, the neuropsychologist also assists in identifying skill-appropriate stimuli, works with the medical team to modify protocols to fit the patient's skill level, and then interprets obtained responses.

Empirical validation of neuropsychological procedures

Epilepsy surgery

Neuropsychological assessment in the pre-surgical evaluation of patients for epilepsy surgery is an accepted standard of care. (The National Association of Epilepsy Centers, 2001). A considerable body of literature has demonstrated the role of neuropsychological test findings and IAP results in predicting surgical outcome for adults with temporal lobe epilepsy, though generalizing from this literature to pediatric patients may not be appropriate. Children may have different patterns of decline and recovery post temporal lobectomy than adults (Szabo *et al.*, 1998), and they are more likely to present with seizure foci outside the temporal lobe.

In a recent multicenter investigation of the role of IAP in pediatric pre-surgical epilepsy evaluation, a significant relationship was found between memory asymmetry scores and laterality of seizure focus, even for patients with foci outside the temporal lobe (Lee *et al.*, 2002). Accuracy of prediction for individual patients was related to location of focus (temporal/extra-temporal) and to site-specific IAP methodology. In subsequent studies, however, IAP methodology did not play a role. Patients whose memory asymmetry scores were consistent with the laterality of seizure focus were more likely to become seizure free as a result of surgery than patients showing either no asymmetry or a discordance between memory asymmetry score and laterality of the seizure focus (Lee *et al.*, 2003). With the concordant group, 75% became seizure free, while only 56% of the discordant group achieved seizure control as a result of surgery. Verbal memory outcome following surgery was also statistically related to IAP memory asymmetry scores (Lee *et al.*, 2005). No decline in verbal memory skills was reported for 77% of children with IAP memory asymmetries in the predicted direction, while verbal memory decline occurred in 80% without asymmetries. Post-surgical visual memory functioning was not predicted by IAP memory asymmetries.

Cognitive problems

While seizure control is the single most effective means for reducing the neuropsychological consequences of epilepsy, the attainment of seizure freedom is typically beyond the neuropsychologist's, patient's, or family's immediate control. The next best means of reducing the neuropsychological consequences of the child's epilepsy is to develop an integrated intervention plan based on findings from interview and testing. Intervention plans for children with epilepsy often involve elements of remediation and compensation, as well as psychological and/or psychiatric treatment.

Academic problems

Humphries *et al.* (2005) reported the results of a pilot project using a highly structured educational program (Direct Instruction) in a hospital-based classroom serving as a temporary placement for children with intractable epilepsy. While students made statistically significant academic gains in comparison to documented baseline skill levels, the failure to include a no-treatment control group and to obtain data regarding rate of progress over the months immediately prior to study entry limit conclusions regarding the relative efficacy of this procedure in comparison to standard educational instruction.

There are no studies available assessing the effectiveness of available reading and math remediation techniques in children demonstrating both learning disabilities and epilepsy. While the neuropsychologist may recommend remediation procedures based on the general learning disabilities literature, these recommendations assume that a learning disability in the context of epilepsy will respond in the same manner as a learning disability in an otherwise healthy child.

Memory and executive deficits

A similar situation exists with respect to interventions for memory and executive problems. At the present time, compensatory strategies used in other neurologically impaired populations are typically applied to children with epilepsy. However, there is no research to guide the neuropsychologist's selection of memory and executive deficit intervention strategies in the unique population of childhood epilepsy.

Emotional and behavioral problems

Attention deficit hyperactivity disorder (ADHD)

Stimulant medications and newer non-stimulant options such as Strattera have been shown to improve concentration in children with ADHD without seizure disorders. The safety of attention medications in children with epilepsy has been questioned, however, due to concerns that stimulant medication may lower the seizure threshold. Two studies using a double-blind crossover design have addressed this concern for methylphenidate, but there have been no controlled studies assessing the impact of other stimulant medications or Strattera.

In a small sample of children ($n = 10$), Feldman *et al.* (1989) found significant improvements on teacher ratings of hyperactivity and inattention in response to methylphenidate. There was no evidence of change in EEG abnormalities during treatment in comparison to baseline EEG. Gross-Tsur *et al.* (1997) assessed the impact of methylphenidate in groups of children with well controlled ($n = 25$) and poorly controlled ($n = 5$) epilepsy over a four-month period. EEG results, parent report, results of continuous performance tests (CPT), AED levels, and reports of seizure frequency were collected throughout the study. None of the children who were seizure-free at baseline developed seizures as a result of methylphenidate treatment. Three of the five children who had poorly controlled seizures experienced an increase in seizure frequency, while the remaining two children experienced a decrease in frequency. Seventy percent of parents reported improvement in ADHD symptoms while on treatment.

Group scores for the CPT demonstrated significant gains on measures of reaction time and time on task.

Mood and anxiety disorders

There are no controlled trials available to guide the physician in selecting medication for treatment of depression or anxiety in children with epilepsy. Shinnar (2005) noted that most psychotropic medications carry the risk of affecting seizure control, either directly by lowering the seizure threshold or indirectly through interactions between the metabolism of the psychotropic medication and AED.

The VNS has been approved for the treatment of medication-resistant depression in adults as well as for the treatment of epilepsy. Despite its apparent promise for the management of depression and seizures in childhood epilepsy, no research has been conducted to date on the impact of VNS treatment on depression in children with epilepsy.

Most psychosocial intervention research in childhood epilepsy has focused on the effectiveness of group therapy or educational programs to improve the social and emotional functioning of affected children. In most studies, a relatively brief intervention (4 to 10 weeks) is conducted, with efficacy determined on the basis of baseline to end-of-treatment change on parent- and patient-report measures.

Lewis *et al.* (1990) conducted parallel child and parent sessions focused on epilepsy information management, peer relations, and social decision-making. In comparison with a control group receiving general epilepsy education, children in the experimental group demonstrated improved ability to manage their seizures, reported an increase in perceived competence, and had fewer restrictions placed on social activities at the end of the program. Long-term gains from a child and family education program were demonstrated by Tieffenberg *et al.* (2000). Follow-up questionnaires at 6 months and 12 months after the program revealed retention of gains made by the children in knowledge, attitudes, and behavior. Parents also retained gains in knowledge, rated family life as less disrupted by the child's epilepsy, and noted improvement in their relationship with their physician. Following participation in the program, children had fewer emergency room visits and improved school attendance.

Recently, the Epilepsy Foundation of America has developed materials for an 8-week education program for the parents of adolescents with epilepsy (Epilepsy Foundation of America, 2005). While pilot groups are currently underway, recruiting sufficient numbers of parents to create meaningful groups has proven problematic, with an average of only 5 parents per group (Jones, M., personal communication November 28, 2005).

Hoare and Kerley (1992) provided some insight into the problems of recruitment for educational and treatment groups. Parents of children with epilepsy who had previously expressed interest in an education group were notified by mail of the availability of such a group ($n = 108$). Only 38 parents responded to the invitation to participate. Fourteen attended the first session, with an average attendance of two at subsequent sessions. Parents who followed through tended to have children with intractable epilepsy and other neurological or cognitive problems. Inconvenience of group sessions, lack of current problems, and good seizure control were most often cited as reasons for non-participation. Parents recommended that educational services and assistance with emotional and behavioral problems be provided in conjunction with the child's ongoing epilepsy medical care.

Future directions

Though epilepsy is a group of highly diverse conditions, previous research on cognitive and psychiatric outcome has often treated childhood epilepsy as though it were a single disease entity. In order to more effectively guide treatment, future research should investigate more homogeneous diagnostic groupings such as epilepsy syndromes or seizure types (e.g. absence, partial complex seizures arising from the temporal lobes or frontal lobes).

It is time for neuropsychological research to move beyond the definition of the incidence of learning problems in children with epilepsy. Studies conducted in collaboration with educators are needed to establish the effectiveness of currently available educational interventions for children with comorbid learning disability and specific seizure types or syndromes. Similar research is needed in collaboration with neuropsychologists in rehabilitation settings to investigate remediation techniques and compensatory strategies for the memory and executive deficits associated with some forms of epilepsy.

While we have well-standardized measures for office-based assessment in most cognitive domains, we know surprisingly little about their "ecological validity." This problem is particularly important in the domains of memory and executive functions. While parent, teacher, and self-report measures have been developed for executive functions which appear to have ecological validity, there is a paucity of such measures for memory. Ecological analyses of memory complaints have only recently been attempted (Kadis *et al.*, 2004). While parents rated the everyday memory skills of children with epilepsy to be poorer than controls, their ratings were unrelated to formal memory test scores, but instead correlated with parental ratings of attention. Further research is necessary to develop ecologically valid scales for assessing everyday memory "failures"

in children with epilepsy. The questionnaire developed recently by Drysdale, Shores and Levick (2004) may hold promise in this regard.

Neuropsychological testing is commonly used to establish a developmental baseline for use in evaluating the effects of AEDs and surgical interventions. While we are asked to document change, there are few data to guide us in defining reliable change (Sherman *et al.*, 2003). Research based on multicenter collaboration using data collected through repeat assessments of surgical as well as non-surgical epilepsy patients would be a means of collecting the sample size needed by age level for developing reliable change indices for intellectual and memory measures.

While seizure control will always be a primary focus of treatment in childhood epilepsy, the importance of factors contributing to quality of life is being increasingly recognized (Goldstein *et al.*, 2004). Quality of life is intimately related to emotional functioning. There is growing awareness of the high incidence of psychiatric problems in children with epilepsy, problems that often go undiagnosed. Ziegler *et al.* (2000) argue for a new standard of care for all epilepsy patients that integrates a psychosocial care team into epilepsy treatment. As a starting point, research is needed to develop methods for behavioral and emotional screening in the physician's office/consulting room that are accurate, time-efficient, and cost-effective (Wagner & Smith, 2006).

Once behavioral and emotional difficulties are identified, a key to enhancing quality of life is understanding treatment options. Medication has proven to be highly effective in addressing symptoms of ADHD, anxiety, and depression. Research similar to that conducted with methylphenidate is needed for the newer, non-stimulant options for the treatment of ADHD, as well as for commonly prescribed medications for depression and anxiety. Such research could serve as the basis for treatment guidelines possibly broken down by seizure type/syndrome and concurrent AED medication.

Preliminary research suggests that group approaches to education and treatment can be effective in reducing the adverse psychosocial impact of epilepsy. Involvement of both child and parent seems to facilitate the treatment process. However, it is difficult to engage families in this type of assistance. Education needs to be delivered in a manner consistent with current lifestyles. Future research should consider how existing technologies such as the Internet and teleconferencing might be used to enhance participation in group interventions (Austin *et al.*, 2002*a*). With better participation, it should be possible to determine what components of intervention are effective for what types of patients, allowing for refining of these interventions (Wagner & Smith, 2006).

The care of children with epilepsy is complicated by the fact that epilepsy continues to be misunderstood by the general public (Austin, Shafer & Deering, 2002*b*; Baumann, Wilson & Wiese, 1995). Research has documented the

persistence of stigma and the association of stigma with psychiatric comorbidity in epilepsy. Research efforts focused on the development and empirical validation of public education programs will therefore be an important endeavor for the neuropsychologist involved in the treatment of pediatric epilepsy.

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9

Autism spectrum disorders and social disabilities

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Autism was first described by Leo Kanner in 1943. He described 11 children with ''extreme autistic aloneness'' p. 242, failure to use language in a communicative fashion, and an obsessive desire for the maintenance of sameness. In the 60 years since this classic paper, there have been numerous studies on every aspect of autism, with the pace of research accelerating greatly in the last 15 years. Kanner's original description has held up remarkably well, and forms the basis for the three domains of diagnostic criteria found in DSM-IV-TR (American Psychiatric Association, 2000).

Impairment in social relationships, the first domain, has four behavioral markers: (a) impaired nonverbal communication, including eye contact and gesture, (b) poor peer relationships, including lack of interest in peers when young, and odd, one-sided relationships later on, (c) lack of joint attention (pointing to indicate interest, bringing items to show others, following a point), and (d) lack of emotional reciprocity, such as failure to notice or share another's distress.

The second domain is *impairment in language and symbolic capacity*, and includes: (a) language delay, (b) impaired ability to carry on a two-way conversation (when there is sufficient language), (c) perseverative and repetitive language, such as repeating what others say or what the child has heard in commercials or videos, or repeating favorite phrases over and over, and (d) absent, delayed, or repetitive pretend play.

The third domain relates to Kanner's insistence on sameness, but includes other *repetitive behaviors*: (a) preoccupations with favorite objects or topics which are unusual for the child's age, (b) non-functional routines or rituals which cause great distress if prevented or interrupted, and insistence on sameness in the environment, (c) stereotypical movements (motor stereotypies) (rocking, hand flapping, spinning), and (d) absorption in parts of objects, or visual fascinations, such as lining things up, or staring at lights, shadows, water, or spinning wheels.

To meet the criteria for Autistic Disorder, an individual must have six of these twelve symptoms, including at least two in the social domain and one in each of the other domains. It will be obvious that with such a set of criteria, there will be a highly heterogeneous set of children who meet the diagnosis, from the nonverbal child with profound mental retardation who has no peer relationships and frequent motor stereotypies, to the highly intelligent child who tries to relate to peers in an ineffective fashion and perseveratively talks about electric appliances.

Other pervasive developmental disorders include Asperger's Disorder, Rett's Disorder, Childhood Disintegrative Disorder, and Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS). Asperger''s Disorder is a form of high functioning autism, in which social relationships are impaired and there are strong perseverative and obsessive interests, but in which language and cognition develop normally (American Psychiatric Association, 2000). Furthermore, Asperger's disorder and autistic disorder can often be distinguished by their neuropsychological profiles: individuals with Asperger's Disorder usually have relative strengths in verbal skills, combined with deficits in visuospatial and visuomotor ability, with the opposite profile usually seen in autistic disorder. Rett''s Disorder is a serious, genetic disorder of girls, in which a few months of normal development are followed by loss of skills, characteristic hand-washing or hand-wringing movements, and autistic behavior. The diagnosis of PDD-NOS is given to children who have some features of autism (including at least one symptom in the social domain) but do not meet criteria for another autism spectrum disorder (ASD).

Commonly associated, but not necessary, features are sensory disturbances – under-responsiveness or over-responsiveness to sensory stimuli, and repetitive behavior which seems designed to provide sensory stimulation, such as moving fingers back and forth in front of a light (Liss *et al.*, 2006). Also common are disturbances in sleeping, eating, and mood. Children on the autism spectrum often have trouble falling asleep, and may wake for long periods during the night (Williams, Sears & Allard, 2004). Children with autism are often very picky eaters, refusing food with certain textures or tastes and eating a very restricted set of foods. Although many children are described as generally happy, others are moody and irritable, and sometimes cry inconsolably, especially when they are young and communication skills are poor.

Children with ASD are at elevated risk for other psychiatric and cognitive disorders (Lainhart, 1999). As many as 50% of children with ASD have mental retardation (IQs below 70), with the prevalence of ASD increasing as one descends the IQ scale (the relationship between autism and mental retardation is reviewed by Muhle, Trentacoste and Rapin (2004).

Nonverbal Learning Disability (NVLD) is usually considered to be a "right hemisphere" analogue to language disorder, characterized by problems with spatial awareness, motor agility, attention, and social skills. Klin *et al.* (1995) and others have noted similarities in this picture and that of ASD, especially Asperger's disorder, and many children may meet criteria for both NVLD and Asperger's Disorder. Tourette's Disorder, characterized by vocal and motor tics that may be complex and resemble the stereotyped behaviors of autism, and Obsessive Compulsive Disorder, which may involve preoccupations and rituals similar to those in high functioning autism, have elevated comorbidity with ASD (Comings & Comings, 1991). The relationship of ASD to developmental language disorder remains controversial, but some children with ASD have deficits in phonology and syntax which resemble those of children with developmental language disorder (Kjelgaard & Tager-Flusberg, 2001). Attentional difficulties are so common in ASD that a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) is precluded by a diagnosis of ASD; nevertheless, the full syndrome of ADHD may be present in ASD and should be considered, and a recent paper (Fein *et al.*, 2005) describes children in whom the clinical picture evolves from ASD to ADHD. In adolescence, patients with ASD are at increased risk for anxiety and depression (Kim *et al.*, 2000).

Medically, children with ASD are at increased risk for seizures; Volkmar and Nelson (1990), for example, found an estimated 29% of patients with ASD to have seizures, with peaks of onset in early childhood and adolescence. Landau-Kleffner syndrome, marked by a regression in language and characteristic abnormalities on EEG, sometimes involves the development of autistic symptoms (Trevathan, 2004).

The epidemiology of autism is another area of debate. The gender distribution is about 4:1 boys to girls, but the incidence, and especially whether the incidence is increasing, remains controversial. There have been reports of significant increases in incidence (Newschaffer, Falb & Gurney, 2005), but Chakrabarti and Fombonne (2005) argue that much, if not all, of this apparent increase is due to factors such as changes in how the diagnostic criteria are used, and methodological variation in how incidence is ascertained. Current estimates of the prevalence of ASD are as high in 1/166 children (Chakrabarti & Fombonne, 2005).

A great deal of recent research has examined pathophysiology and genetics in autism, but findings are very inconsistent. There is general agreement, based on twin and sibling studies, that autism is highly heritable, and linkages have been found on many chromosomes; however, many linkages have been unreplicated across studies (see Muhle *et al.* (2004) for a recent review). The general conclusion is that autism is a set of polygenic disorders, with no one set of genes involved across children.

Similarly, brain anatomy has led to a highly inconsistent set of findings. One finding that does seem to be replicated across studies is that of increased brain volume (Piven *et al.*, 1996). Courchesne, Carper and Akshoomoff (2003) found that children with autism tend to have normal or small head sizes at birth, which then accelerate to unusually large sizes in early childhood, and then level off, suggesting abnormal brain growth in the first two years of life. Studies of which brain areas are responsible for the enlargement have led to contradictory results. Piven *et al.* (1996) found all lobes except the frontal lobe to be enlarged, while Carper *et al.* (2002) found only the frontal lobes to be significantly enlarged. Herbert *et al.* (2002) used a finer grained cortical parcellation technique and found volume differences specifically in language-related cortex. Casanova *et al.* (2002) examined frontal and temporal cortex in nine brains of persons with autism and found that the cortical minicolumns were smaller and abnormally organized. It has been suggested that this dysmorphology may be related to overgrowth of white matter, and functional disorganization and lack of integration. Such a lack of integration of processes might result in the lack of "central coherence" suggested by Frith (1989) or top-down processing (Schultz, Romanski & Tsatsanis, 2000). It is apparent from the inconsistent anatomical findings across studies that samples of participants must vary, and that some method for making them more homogeneous and better defined must be found, in order to replicate and refine anatomical studies.

Studies of brain chemistry in autism go back more than 40 years, but here again, findings of abnormal levels of neurotransmitter metabolites or abnormal levels of transmitters in plasma or cerebrospinal fluid (CSF) (e.g. oxytocin, serotonin) are highly inconsistent. The most consistent finding is that of increased levels of serotonin in plasma (Cuccaro *et al.*, 1993) and medications affecting the serotonin system are among the most widely prescribed.

Functional imaging studies, most recently and effectively using functional magnetic resonance imaging (fMRI), have been used in the past 10 years to better pinpoint areas of the brain that respond to or process stimuli in unusual ways. Several studies have reported hypoactivation of amygdala in the processing of social stimuli (Castelli *et al.*, 2002; Critchley *et al.*, 2000; Pierce *et al.*, 2001). Similarly, hypoactivation of the face processing area of the fusiform gyrus, on the inferior surface of the temporal lobe, has been reported (Critchley *et al.*, 2000; Pierce *et al.*, 2001) and Schultz *et al.* (2001) found the degree of hypoactivation to be related to the degree of social impairment. fMRI studies have also reported hypoactivation of medial prefrontal cortex (Castelli *et al.*, 2002) and dorsolateral prefrontal cortex (Luna *et al.*, 2002). Just *et al.* (2004) reported that language areas, while activated, were less coordinated in their activity, while adults with autism performed a syntax task, assessing this functional connectivity by correlating the

activation of language areas across time. The use of functional neuroimaging holds great promise for elucidating neural systems that function abnormally and the ways they function abnormally. These exciting methods are in their early stages, and in their application to autism, still in their infancy. The next decade will no doubt reveal much about brain functioning in autism through the use of these methods.

Role of assessment in documenting impact of treatment

Deficits in social skills are at the core of autistic symptomatology, and therefore should be a focus of assessment. Social behavior can be assessed through standardized observational measures, such as the Autism Diagnostic Observation Schedule (see below), as well as by asking parents to complete inventories of social skills, such as the Social Responsiveness Scale (Constantino, 2002). In cases in which differential diagnosis is a question, assessment of social problem solving is especially important in determining whether social deficits arise from a difficulty understanding social information, or whether the social deficits may be secondary to some other primary difficulty (e.g. social anxiety, ADHD, etc.).

Assessment of ASD should also include an assessment of adaptive functioning. This is important both for identifying co-occurring mental retardation, and because knowledge about a child's adaptive skills informs intervention planning. The Vineland Adaptive Behavior Scales (Sparrow, Cicchetti & Balla, 2005) is the most commonly used measure of adaptive functioning in the assessment of autism spectrum disorders. In contrast to children with mental retardation, who typically display a flat profile on the Vineland scales with delays across domains, individuals with autism typically display a highly variable profile, with the most pronounced deficits in socialization (Carter *et al.*, 1998). As a result of this scatter, special norms for the Vineland have been developed for individuals with autism (Carter *et al.*, 1998).

Diagnosis of autism

A diagnosis of autism based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000) requires an early history of impairment, particularly in the form of a language delay. Therefore, testing of a child's current ability alone is not sufficient to determine the appropriate diagnosis. Obtaining information regarding the child's developmental history is also necessary. As a result, an assessment to address the question of autism typically involves observation of the child's current

behavior (in the context of a structured play or verbal interaction) along with a parent interview to assess early developmental history. Cognitive, social, and adaptive skills are usually tested as well, in order to obtain a picture of the child's strengths and weaknesses, to determine whether a diagnosis of mental retardation is appropriate, and because estimates of adaptive skills inform intervention planning.

A number of measures frequently utilized in the diagnosis of individuals with autism spectrum disorders have obtained empirical support and will be discussed below. It should be noted that this discussion is not intended to be exhaustive, but rather a representative sample of some of the assessment measures commonly used in diagnosing ASD.

Interview measures

The Autism Diagnostic Interview – Revised (ADI-R; Rutter, LeCouteur & Lord, 2003*b*) has become the "gold standard" interview measure in the assessment of autism spectrum disorders. The ADI-R is a semi-structured parent interview which assesses symptoms in the areas of social interaction, communication, and repetitive and stereotyped patterns of interest and behavior, consistent with the DSM-IV-TR criteria for autism. The interview focuses on both present and past behaviors, with emphasis on the time period between the ages of 4 to 5, because older individuals with autism may not demonstrate impairments that were more apparent earlier in their development. Individual items are generally coded 0 through 2, with a score of 0 indicating no impairment, and a score of 2 representing marked impairment. Some of these items then contribute to the overall algorithm, which generates cut-off scores in each of the three areas of impairment. The advantage of having cut-offs in separate domains is that it provides a quantification of severity within each separate domain, and reduces the likelihood than an individual will meet the autism cutoff because of pronounced deficits in a single domain but not in the other domains. The ADI-R has demonstrated good reliability and validity (Lord *et al.*, 1997). Weaknesses of the measure include its lengthy administration time (2 to 3 hours), which limits its utility in clinical settings; the potential for bias in responding from parents; and the absence of cut-off scores for pervasive developmental disorders other than autism. In addition, the ADI-R may be overinclusive (Lord *et al.*, 1997) or underinclusive (Ventola *et al.*, 2006) in its classification of very young children or those with severe mental retardation.

Another semi-structured interview for use in the diagnosis of autism spectrum disorders, as well as other developmental or psychiatric disorders, is the Diagnostic Interview of Social and Communication Disorders (DISCO; Wing *et al.*, 2002). In comparison with the ADI-R, the DISCO covers a wider range

of behaviors, including adaptive skills and visual–spatial ability, and obtains greater detail with regard to sensory abnormalities and repetitive and stereotyped behaviors. In addition, whereas the ADI-R places emphasis on the 4- to 5-year age range, the DISCO emphasizes the age at which the most impairing behaviors were evident. The authors note that the DISCO was designed not strictly as a diagnostic instrument, but as a system for compiling developmental history from birth through present. Like the ADI-R, the DISCO has demonstrated high inter-rater reliability (Wing *et al.*, 2002).

Observational measures

The Autism Diagnostic Observation Schedule (ADOS; Lord *et al.*, 2002) is a semi-structured assessment of social interaction, communication, play and imagination, and repetitive behaviors and interests. The administration involves activities designed to press for social and communicative behaviors, and provides a standardized context in which to observe behaviors. The examiner chooses from one of four different modules, based upon the language level of the individual. The provision of separate modules was intended to minimize the potential bias introduced by differences in language ability. The ADOS provides cut-off scores in the areas of socialization, communication, and in total. No cut-off scores are provided for the repetitive behavior domain, as the observation period is thought to be too short a window in which to expect to observe these behaviors. Based on these cut-off scores, the ADOS provides classifications of autism, autism spectrum, or non-spectrum. The ADOS does not differentiate among autism spectrum diagnoses (Asperger's, PDD-NOS), because the authors found that the distribution of ADOS items did not cluster, but rather were continuous from autism to PDD-NOS, thus refuting the appropriateness of separate cut-offs for each diagnosis (Lord *et al.*, 2000). All four modules of the ADOS have been shown to have good inter-rater reliability, test–retest reliability, and diagnostic validity (Lord *et al.*, 2000). However, given the short time period provided by the ADOS administration, as well as the fact that it provides an observation only of current functioning, it is important that diagnosis be made not on the basis of the ADOS alone, but rather that the ADOS is used in tandem with a parent interview.

The observational measure that has been historically most widely used in the diagnosis of autism is the Childhood Autism Rating Scale (CARS; Schopler, Reichler & Renner, 1986). The CARS has good reliability and validity, and is both sensitive and specific in its classification of autism. The CARS was developed before the development of the current DSM-IV-TR triad of symptoms; therefore, it does not provide cut-off scores in each domain, but rather provides a single, total impairment cut-off score. As a result, Tidmarsh and Volkmar (2003)

have suggested that the CARS may be best suited as a measure of overall impression, rather than a descriptive measure. The CARS total score has been found to correlate with the ADI-R algorithm scores, although the CARS classifies more cases of autism than the ADI-R, which may be attributed to its use of a single domain, rather than requiring that the child meet criteria in multiple domains. Indeed, greater diagnostic agreement is reached between the CARS and ADI-R when a single ADI-R total score is utilized (Saemundsen *et al.*, 2003). The CARS has good agreement with clinical diagnostic judgment and with the ADOS in very young children (Dixon *et al.*, 2006). One limitation of the CARS is that it does not include standardized activities during which to observe the child. Another limitation is that the CARS may simply function to confirm pre-existing clinician impressions. Therefore, the CARS may best be used as a screening tool.

Screening instruments and questionnaire measures

Improvement in autism symptoms is most responsive to early intervention, and as such, the early detection of autism is of paramount importance. Screening devices are necessary in this regard. It should be emphasized, however, that screening devices are not sufficient as a substitute for a full diagnostic evaluation. Rather, they are useful in identifying children who are showing characteristics of a pervasive developmental disorder, and who should be referred for a full diagnostic evaluation which would include the diagnostic measures described above. Some commonly used screening instruments include the Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen & Gillberg, 1992), the Modified Checklist for Autism in Toddlers (M-CHAT; Robins *et al.*, 2001), the Social Communication Questionnaire (Rutter, Bailey & Lord, 2003*a*), the Social Responsiveness Scale (SRS, formerly known as the Social Reciprocity Scale; Constantino, 2002), the Screening Tool for Autism in Two-Year-Olds (STAT; Stone & Ousley, 1997), and the Pervasive Developmental Disorder Behavior Inventory (Cohen *et al.*, 2003). A full review of this topic is beyond the scope of this chapter; the reader is referred to a recent review by Dumont-Mathieu and Fein (2005).

A limitation of all diagnostic and screening instruments for autism is that, while they may differentiate ASDs from other developmental disorders, they typically do not differentiate well between the various autism spectrum disorders. This raises questions regarding the appropriateness of the current diagnostic classification system. Further research is necessary to determine the validity of the diagnostic system, and in turn, to develop diagnostic measures that can differentiate among diagnoses within the autism spectrum.

Neuropsychological profile

The autism spectrum is characterized by wide variation in cognitive ability, ranging from significantly delayed to superior range levels of functioning. In examining cognitive profiles of individuals with autism, no clear or consistent pattern emerges. A pattern of higher Performance IQ than Verbal IQ is sometimes, but not consistently, found, and a high degree of variability is found within individual cognitive profiles. The reader is referred to the special issue of *Developmental Neuropsychology* devoted to this topic (Akshoomoff, 2005).

There is also debate as to whether Asperger''s disorder can be differentiated from other ASDs on the basis of cognitive profile. Whereas autism has been associated with a VIQ < PIQ profile, Asperger's disorder has been associated with the opposite pattern (Klin *et al.*, 1995). Ghaziuddin & Mountain-Kimchi (2004) found that individuals with Asperger's syndrome had higher verbal IQ scores, but not performance IQ scores, than individuals with high functioning autism. However, the authors note that there were participants in each group who showed a pattern more typical of members of the other group. Studies have also found that overall IQ is higher in individuals with Asperger's disorder than in those with high functioning autism (Ghaziuddin & Mountain-Kimchi, 2004; Miller & Ozonoff, 2000), which is consistent with the DSM-IV-TR definition that Asperger's disorder cannot include a cognitive delay. Miller and Ozonoff (2000) suggest that the differences in cognitive profiles between individuals with Asperger's disorder and high functioning autism can be accounted for by differences in overall IQ.

Since communication impairment is characteristic of autism, a neuropsychological assessment should include evaluation of language. Some individuals with autism are completely nonverbal, and for those individuals, measures such as the Peabody Picture Vocabulary Test (PPVT; Dunn & Dunn, 1997) can provide an estimate of receptive language ability. A limitation of this measure, however, is that it assesses understanding of single-word vocabulary only, and therefore may inflate estimates of language ability in children whose single word comprehension is better than other aspects of comprehension. A more comprehensive assessment of language ability is therefore important, in order to identify areas of strengths and weaknesses across various aspects of language ability, and to inform speech and language goals. Although phonology and syntax are often spared, especially in high-functioning individuals with autism, this is not always the case (Kjelgaard & Tager-Flusberg, 2001); furthermore, although single word receptive and expressive tests may be areas of strength, the actual use of semantics may be abnormal, as manifested by odd word choices which preserve the literal meaning of words, but neglect the connotations or the social context. Therefore, a comprehensive battery of language functions, administered by a psychologist or speech/language pathologist, is essential.

Even among individuals with Asperger's disorder, who may not have demonstrated a language delay in their early development, impairments in the pragmatic aspects of language are commonly observed. Therefore, it is important that measures of pragmatic language, such as the Test of Pragmatic Language (TOPL; Phelps-Terasaki & Phelps-Gunn, 1992), be included in a neuropsychological evaluation of autism. Young *et al.* (2005) found that the TOPL differentiated individuals with an ASD from typically developing controls. However, it should be remembered that pragmatic language tests assess whether the children know what they are supposed to say in a given situation, but not what they actually do. Parents and teachers can be queried on this point.

Although not part of the diagnostic criteria for autism, neuropsychological testing may reveal deficits in executive functioning. A number of studies have identified such deficits in ASD, particularly in the areas of mental flexibility and planning (Ozonoff & Jensen, 1999). Kleinhans, Akshoomoff and Delis (2005) found impairments in switching and strategy use but not in inhibition. These findings have led some to posit that executive functioning may be an underlying "core" deficit in autism. However, some recent work has failed to support this hypothesis. For example, Griffith *et al.* (1999) failed to find executive functioning deficits in preschoolers and older children with autism. Similarly, Liss *et al.* (2001) found no differences in executive functioning skills between children with high functioning autism and developmental language disorder. While executive functioning was found to be related to adaptive functioning and autistic symptomatology in this study, these relationships disappeared when controlling for verbal IQ, suggesting that the executive functioning deficits found in ASD may be attributable to impairments in overall cognitive ability.

The theory of "weak central coherence," first proposed by Frith (1989), suggests that individuals with autism are impaired in their ability to integrate pieces of information into a meaningful whole, resulting in a bias for local over global processing. In neuropsychological testing, individuals with autism may demonstrate such impairments in their approach to tasks such as block design or in poor performance on categorization tasks. However, the weak central coherence hypothesis has received mixed empirical support (Jolliffe & Baron-Cohen, 2001; Mottron *et al.*, 2003).

With regard to attentional ability, individuals with autism are able to sustain attention but may be better able to do so when an activity is selected rather than imposed or when strong incentives are used (Garretson, Fein & Waterhouse, 1990). Individuals with autism display delayed orienting of attention (Townsend, Courchesne & Egaas, 1996), and are impaired in their ability to shift attention (Courchesne *et al.*, 1994). However, they have been found to be unimpaired at some tasks requiring shifting attention, which suggests that there may not be

a general deficit in shifting attention, but rather a deficit which is specific to some component of the shifting process (Pascualvaca *et al.*, 1998).

Findings with regard to memory skills in individuals with autism are also mixed. While verbal memory tends to be poor (Toichi & Kamio, 1998), visuo-spatial memory tends to be intact except for selective memory deficits for social material such as faces and social scenes (Williams, Goldstein & Minshew, 2005), and spatial working memory is also found to be impaired (Luna *et al.*, 2002). Source memory has been found to be impaired but may be dependent upon the type of context information to be remembered, and may be particularly weak when the source information to be remembered is social in nature (O'Shea *et al.*, 2005). Findings with regard to working memory are mixed, and Ozonoff and Strayer (2001) suggest that performance varies depending on the type of working memory task administered. Episodic memory has been found to be impaired among individuals with autism (Millward *et al.*, 2000), although the clinical literature has many examples of individuals with autism who show exceptional memory for details of events to which they were motivated to attend.

To summarize, no clear pattern emerges with regard to a neuropsychological profile that characterizes all individuals on the autism spectrum. Therefore, it is not valid to diagnose autism spectrum disorders on the basis of neuropsychological functioning. Rather, performance on neuropsychological tests can supplement other diagnostic measures in order to provide estimates of a child's strengths and weaknesses and to inform recommendations and treatment planning.

Target areas of intervention

The variability in the neuropsychological and clinical profile among individuals on the autism spectrum dictates that areas targeted for intervention vary from one child to the next. This section provides a brief overview of common areas of focus in intervention for children on the autism spectrum.

The appropriate educational setting for a child with autism varies greatly depending upon the individual needs of the child. Some children with autism spectrum disorders require a small setting with intensive one-to-one instruction for optimal learning. Other children may be successful in the mainstream environment with resource room time devoted to work on particular areas of weakness. Others may succeed in the mainstream environment with the provision of a one-to-one aide who can adapt the curriculum to meet the needs of the child. Regardless of the specific academic environment, it is important that the educational program offer structure, consistency, and predictability and emphasize generalization of skills across settings, with an emphasis not only on academic skills but on adaptive skills as well.

A primary target area for intervention for children with autism spectrum disorders is social skills. In remediating social deficits, it is useful to have as a framework a comprehensive social skills program, such as Skillstreaming (McGinnis & Goldstein, 1997) or S.O.S. Social Skills in Our Schools (Dunn, 2006). The specific focus of social skills interventions will vary with the age and developmental level of the child. In young children, social skill interventions typically target basic skills such as eye contact, social imitation, or simple reciprocal interactions (e.g. peek-a-boo). In middle childhood, skill development focuses on skills such as interactive play, awareness of self and others, reciprocal conversation, initiation of social interaction, and appropriate social responses. Once these skills are mastered, the focus of social skills intervention turns to fostering understanding of the complexities of social interactions, including abstract and subtle social cues, the emotions of self and others, appreciation of humor and sarcasm, and perspective-taking.

Speech and language therapy is generally considered to be an integral component of the treatment plan of children with ASD. Some evidence suggests that behavioral approaches to language intervention are effective, particularly when implemented in a naturalistic setting (Delprato, 2001). Much research in this area has focused on interventions targeting spontaneous communication (e.g. Kravits *et al.*, 2002). Additional research is needed to develop specific empirically validated approaches to improving other areas of language impairment for children with ASD, such as receptive language, narrative language, conversational skills, and social/pragmatic language. Speech/language therapy may also be beneficial in increasing semantic knowledge and inferencing ability, which in turn may improve reading comprehension, an area of weakness for many children on the autism spectrum (Nation & Norbury, 2005).

Given the difficulties with attention and organization often seen in children with autism spectrum disorders, supports in these areas are usually necessary. These strategies include classroom modifications, breaking down tasks into component parts, and providing the child with frequent breaks. It is common practice to present information in multiple modalities with the goal of increasing attention and comprehension of material. Particular emphasis has been placed on use of visual aids, central to the TEACCH approach (Treatment and Education of Autistic and related Communication Handicapped Children, discussed in more detail below), although these techniques require greater empirical validation. Finally, there is some evidence that incorporating a child's individual interests into academic material can increase motivation to learn (Jennett, Harris & Mesibov, 2003).

Psychiatric symptoms such as depression and anxiety are often associated with ASD (Lainhart, 1999), especially in adolescents (Kim *et al.*, 2000). These concerns

may be addressed through psychotherapy and pharmacological intervention. Although an extensive treatise of all potential pharmacological interventions is beyond the scope of this chapter, a recent review has been provided by McDougle and Posey (2003).

A final area of intervention concerns family members of individuals with autism spectrum disorders. Parenting a child with autism presents unique challenges that may result in increased parenting stress (Schuntermann, 2002). Parent support networks may be helpful to parents who become overwhelmed by the task of providing for the special needs of a child with autism. In addition, parent training has been shown to be beneficial in increasing a sense of self-efficacy among parents of children with Asperger's disorder (Sofronoff & Farbotko, 2002). Similarly, siblings of children with ASD may be at risk for feeling "left out," as much of the family's resources may be devoted to the child with autism (Khouzam *et al.*, 2004). Sibling support groups may address these concerns, although little empirical work has been conducted to investigate their effectiveness.

Intervention approaches

Currently, no treatment method completely eliminates the symptoms of autism and no specific treatment has emerged as the established standard of care for all children with autism. Given the pervasive nature of autism, interventions are typically needed to assist in the development of communication, social skills, cognitive skills, sensory and motor skills, adaptive behaviors, and for the reduction of problem behaviors. Outcome papers on a variety of comprehensive intervention programs have been published. Although outcome research is limited, there appear to be core elements that have empirical support which should be included in comprehensive programs for children with autism. These core elements are individualized supports and services for children and families, systematic instruction, comprehensible/structured learning environments, specialized curriculum content, functional approach to problem behavior, and family involvement (Iovannone *et al.*, 2003). Programs vary in their emphasis on behavioral strategies, developmental strategies, or augmentative and alternative strategies for building new skills.

The only form of treatment empirically validated as effective for children with autism is treatment based upon a behavioral model (e.g. National Research Council, 2001). The best studied programs are based on the principles of applied behavior analysis. These range from highly structured programs that are conducted in a one-to-one treatment setting to behaviorally based inclusion programs which include typically developing children as models. The systematic application of the principles of learning can lead to substantial gains in many

children with autism, particularly when interventions are introduced at a very young age.

The first comprehensive treatment programs developed by researchers to teach cognitive, language, and social skills to children with autism were highly structured, very intensive, one-to-one behavioral programs. This type of approach is often referred to as "Discrete Trial Training" because massed discrete trial methods are used to build up use of labeling vocabulary and simple sentences. Results by Lovaas and his colleagues suggested that this approach was highly effective for as many as half of the children enrolled (McEachin, Smith & Lovaas, 1993). However, there are a number of controversies associated with this approach (Schreibman, 2005). Children sometimes have difficulty generalizing the information they learn as they move into group and community settings. Other issues associated with discrete trial training include a lack of spontaneity, prompt dependency, slow progress, and the extensive amount of time involved.

To address these issues, researchers have developed and empirically validated less structured, more naturalistic teaching methods that can be implemented in both individual and school settings. These methods include Pivotal Response Training (Schreibman & Koegel, 2005), Incidental Teaching (McGee, Krantz & McClannahan, 1985), Fluency Training (Kubina & Wolfe, 2005) and Milieu Training (Kaiser, Yoder & Keetz, 1992). These methods teach behaviors in the environment where they would naturally occur and use the same principles as discrete trial training but with natural contingencies. The acquisition and generalization of new behaviors occur simultaneously, in the natural environment, rather than in an artificial environment that requires having to then move to the natural environment for generalization training.

In pivotal response training, the target behaviors are those "pivotal" behaviors that will have a greater impact on a number of other behaviors. Skills that can be taught include language, functional, symbolic (pretend) and sociodramatic play skills, social skills, and academic skills. An emphasis is placed on maximizing the child's motivation, which can be very difficult for children with autism. Motivation is maximized through child attention, child choice, reinforcing attempts, direct reinforcement, interspersing maintenance tasks, and shared control. Research on pivotal response training has shown that children with autism show greater generalization of skills than when using the discrete trial approach. Research has also shown that this approach is more easily adapted for use in parent education and training programs (Schreibman & Koegel, 2005). Approximately half of the children have good outcomes in these types of programs. Fluency training (Kubina & Wolfe, 2005) is another variant of behavioral teaching, in which the emphasis is placed on increasing accuracy, speed, and automaticity of behaviors which are taught, making them more

functional. Studies of inclusion models using naturalistic behavioral techniques report positive results for children with ASD, with as many as 50% of children mainstreamed into regular education (McGee, Morrier & Daly, 2000).

The Developmental Intervention Model or "Floor Time" (Greenspan & Weider, 1997) uses an interactive developmental approach. The focus is on socially interactive relationships. The home component involves intensive interactive floor-time work, where the adult follows the child's lead in play and interaction. The adult also presents specific small challenges designed to move the child forward in reaching more advanced developmental milestones. A review of case files indicated that about half of the children made strong gains (Greenspan & Weider, 1997).

Augmentative teaching strategies such as sign language, communication keyboards, or the Picture Exchange Communication System are frequently employed to assist nonverbal children with autism in acquiring communication skills. There is some evidence that these strategies may assist development (e.g. Bondy & Frost, 2001) but more research needs to be conducted to determine how these alternative methods may assist or detract the development of spoken language in children with autism.

The TEACCH program is based on a structured teaching approach. TEACCH emphasizes the use of strategies that teach to the strengths of children with autism, such as visual schedules, picture systems, and structured, independent and routine activities (Mesibov, 1997). There is limited empirical data available on the efficacy of the comprehensive TEACCH program, although some reports support treatment efficacy (Mesibov, 1997; Panerai, Ferrante & Zingale, 2002). The TEACCH program utilizes several specific interventions that have been empirically validated, such as naturalistic behavioral strategies, picture schedules, and parent training, lending credibility to this approach (Schreibman, 2005).

More research is needed to determine how the use of more than one treatment method compares to the use of a more focused approach, such as has been typically reported in the empirical literature. One recent study found that young children with autism had significantly greater improvement on standardized tests of cognitive, language and adaptive skills when enrolled in an intensive behavior program compared with children in intensive "eclectic" special education classrooms or non-intensive public early intervention programs (Howard *et al.*, 2005). However, individual child profiles were not compared, behavioral improvements beyond performance on standardized tests were not assessed, information provided regarding what was included in the eclectic programs was limited, and treatment fidelity was not assessed. There is some empirical support

for other model programs that include the systematic combination of treatments (Rogers *et al.*, 2000; Stahmer, Ingersoll & Koegel, 2004). Efforts have been made to transfer model programs to the community through the use of personnel preparation programs (Bryson, *et al.*, 2003; National Research Council, 2001). However, limited data is available on what is needed to maintain treatment integrity and the impact of individual modifications. There is great interest in designing empirical studies that focus on individualizing treatments for children with autism. One approach is to identify specific variables that help to determine which treatments will be most effective for individual children. Sherer and Schreibman (2005) identified a behavioral profile which predicted the effectiveness of pivotal response training for individual children with autism. It is important to note that after five weeks, treatment was stopped for the non-responders and they were referred to other programs. Some of these children did make great gains with other methods, highlighting the need for a more flexible, data-driven approach to treatment.

Studies which directly compare specific behavioral treatment methods are rare and difficult to conduct due to differences in assessment procedures and populations served. Additionally, parents are hesitant to allow their children to be randomly assigned to a specific treatment method at such a critical stage in development. Therefore, no one program can claim to be more effective than another, nor are we able to predict efficacy of individual treatment methods for specific children (Feinberg & Vacca, 2000; Lord *et al.*, 2006). Variability in treatment effects suggests that other variables are determining outcome. In fact, the debate about which treatment is superior is ultimately of little help since no one treatment is best for all children. In the best behaviorally oriented programs, techniques are borrowed from many types of program, such as discrete trial, pivotal response training, fluency training, and peer modeling, using a combination of individual and group learning, and a combination of extrinsic (e.g. food) and natural reinforcers. A good program not only individualizes the program for the child, but frequently monitors progress and changes parameters as dictated by the child's development (e.g. moving from individual to group settings, reducing extrinsic reinforcers).

Available evidence suggests that 15 to 20 hours per week of individualized, well-planned interventions that target language, social, emotional, and pre-academic development significantly increase development for children with autism compared with no or minimal treatment (Bryson *et al.*, 2003; National Research Council, 2001). A recent study (Sallows & Graupner, 2005) documented successful mainstreaming following a four-year intensive behavioral program in about half of the children. However, community programs typically report using a variety of treatment methods (Stahmer, Collings & Palinkas, 2005).

When making recommendations for individual children, it is therefore important to determine what standard practices are currently employed in community and school settings and the rationale behind these practices (Akshoomoff & Stahmer, 2006). While treatment models derived from research studies may need to be modified before they can be implemented within individual community settings, these modifications need to be limited so as to not compromise the effectiveness, reliability, and validity demonstrated in controlled studies.

Future directions

Autism is a complex neurobiological disorder whose etiology is largely unknown. In addition to basic research on genetics and underlying neurobiological mechanisms, an important clinical area for future research concerns the validity of the current classification system used in diagnosing ASDs. Despite the DSM-IV categorical system for diagnosing autism spectrum disorders, individuals on the spectrum do not always demonstrate characteristics that fall neatly into any one of the diagnostic categories. Attempts at developing measures to capture the different ASDs have failed, suggesting a continuum of presentations rather than distinct subtypes (Lord *et al.*, 2005). Research is therefore necessary to substantiate the validity of, or improve upon, the current diagnostic system.

While a number of good screening tools and diagnostic instruments are now available for detecting and diagnosing autism, an important area of continued research is the development of methods for improving the early detection of children with autism. Children in the United States are not routinely screened for problems in development, and therefore unless a child's pediatrician is well informed about the early signs of autism spectrum disorders, that child may go unidentified until entering the school system, at which point the greatest potential for success of intervention has passed. Similarly, some evidence suggests that children from ethnic minority backgrounds are not identified as early as children from the majority culture (Croen, Grether & Selvin, 2002). A challenge for researchers, clinicians, and policy makers is to ensure that all children across demographic groups are identified as early as possible, and to ensure that early intervention services are available to all children.

Finally, continued research is needed to provide empirical support for interventions used in the treatment of autism, and to develop new empirically validated interventions. While a number of intervention approaches are commonly used in the treatment of autism, as outlined in the previous section, only behavioral methods have received substantial empirical support, and therefore research is needed to assess the validity of other intervention approaches, and to further develop behavioral methods. In particular, while social skills are

a primary target area for intervention among children with autism spectrum disorders, there are no social skills interventions designed for the autism population that have received widely replicated empirical validation, and this is therefore an essential area for further research. Finally, research needs to compare different intervention approaches with different types of children, to identify the components of various interventions that are most effective, and to develop new treatments that combine the most effective components of currently existing interventions.

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10

Diagnosing and treating right hemisphere disorders

Bonny Forrest

Our understanding of cognitive and behavioral disorders, especially disorders in childhood, must begin by leaving behind the once common assumption that the left hemisphere is the home for language, and the right hemisphere is the home for a confusing, clinically useless category of ''everything else,'' including emotions, body awareness, visuospatial abilities and social functions. Although scholars no longer view the right hemisphere as the seat of ''madness,'' it was not until the 1950s that interest in understanding the ''other'' hemisphere revived (Luys, 1879). Even now, if you pick up any book on brain functions, you are likely still to be reading about the dominance of the left hemisphere. Certainly, it is well established that the left hemisphere dominates for language. In as much as our primary means of communication is verbal language, then we may still think of the left hemisphere as dominant or most essential. But that dichotomy breaks down in two ways.

First, if we reflect on many of the most important moments in our lives — the look of pride in our parents'' faces when we are young, or the gaze of someone who loves us — then the relative importance of speech seems quite small compared with ''everything else.'' When you read that last sentence, it was likely that the images and emotions you experienced were summoned up and it was those emotions and images not the actual words, which gave the sentence meaning for you. It is those forms of meaning that are the realm of the right hemisphere.

Secondly, even if one hemisphere is dominant for some functions, it is now clear that most functions of the brain are more bilaterally based. The evolution of our understanding of the brain allows us to theorize an intricate brain structure where most functions, with all their complexity, involve both hemispheres. Through the growth of cognitive science, we have progressed from believing that the two hemispheres are simply two organs operating independently, performing separate and perhaps competing functions, to recognizing that the two hemispheres operate through parallel distributed processing mechanisms and a complex array of architectures (such as motor neurons), which allow the two hemispheres to contribute to any one function.

New technologies continue to tell us that many functions are bilateral when viewed more ecologically, in the context of daily life. For example, we have learned how important both hemispheres are for the production of ''complete'' language, not just ''pure'' content strung together without affect, tone, or prosody — that is, a form of language that would create misunderstanding rather than communication (Jackson, 1958).

Unfortunately, despite recent advances in understanding the function and importance of the right hemisphere, we still lack sophisticated and precise definitions of disorders that emanate from the right hemisphere; have few instruments to assess the development of social or spatial skills; and have even fewer empirically validated treatments available. So far, many of the supposed right-hemisphere disorders defy categorical classifications, and are fraught with unresolved controversies concerning diagnostic criteria. This lack of understanding is perhaps most evident from one fact: for right-hemisphere disorders, we are still left without diagnostic counterparts to verbal language disorders of the left. We have milestones for verbal development, but only a rudimentary understanding of the markers for visual, social, and emotional development.

Not surprisingly, therefore, right-hemisphere disorders — which include graphomotor, visual-spatial, and emotional problems — are rarely included under formal definitions of learning disabilities and have often been described as overlapping with autistic spectrum disorders. These definitional difficulties likely stem from the lack of tests to assess the fine differences that exist in children and the lack of terminology to describe social and emotional experiences or difficulties. If you do not know how to define or assess a disorder, it is impossible to treat it. So, because of the fundamental difficulties with definitions and assessment in right-hemisphere disorders, the focus for intervention most often becomes the most notable symptom, a focus which may, or may not, lead to improved daily function in the classroom for any particular child.

As a result of these definitional difficulties, the literature about the right hemisphere consists of studies that have used inconsistent criteria for including participants, and studies that resulted in the most formal definitions of right-hemisphere disorders have typically relied on instruments or measures that are no longer commonly used. To attempt to correct for this set of concerns, this chapter includes references to current literature whenever possible, with additional historical references also provided.

This chapter therefore will provide an overview of currently identified disorders of the right hemisphere. It will first review the prevailing definitions and their associated neuropsychological manifestations. Next, the challenges in finding instruments that assess developing right-hemisphere functions will be described. New technologies will be discussed, along with difficulties that are frequently

encountered in specific skill areas, with possible interventions outlined. Finally, future research directions will be explored.

Hemispheric organization

A number of theories about the neuroanatomical differences between the two hemispheres and their development support the differentiation of behaviors, across the hemispheres, as is observed in the literature. Additionally, a number of factors that affect development (e.g. hormones) appear to affect the two hemispheres differently and therefore must be taken into account when attempting to understand any right-hemisphere disorder.

Goldberg and Costa (1981) postulated that the two hemispheres have distinct process modes. The right hemisphere is comprised of a greater number of association areas and is therefore more aptly suited for intermodal integration (e.g. motor or visual-spatial). The left hemisphere processes across specific modality areas and integrates between those areas that are specialized for a particular function (e.g. various aspects of speech). This description of the brain's architecture supports the notion that the left hemisphere communicates within modality while the right hemisphere tries to integrate across modalities.

Additionally, Thatcher (1994) has postulated a model of hemispheric development based on neuroanatomical differences and their development that is consistent with Goldberg and Costa's (1981) theory of processing differentiations between the hemispheres. Thatcher proposes two related growth models based on EEG activity: (1) for each level of skill development, a growth cycle in network connectivity; and (2) for each tier (that is, cluster of skill levels) a growth cycle in location and extent of EEG activity, which is presumably related to connectivity changes. At each skill level, the growth cycle involves three increases in connectivity: (1) first in the right hemisphere, (2) then in the left hemisphere, and (3) finally, across both hemispheres, in parallel. Then the cycle repeats. In general, in the right hemispheres, connectivity contracts during a cycle, moving from distant connections to close ones (i.e. integration to differentiation). In the left hemisphere, connectivity expands, moving from close connections to distant ones (i.e. differentiation to integration).

Thatcher (1994) also proposes tiers of lobe development. Each tier involves systematic movements in the extent and location of connectivity, denoted as ''spurts'' in growth. The border between tiers is marked by a frontal ''spurts,'' followed by spurts moving from front to back, with clusters of ''spurts'' as well. These tiers are related to patterns of cognitive development previously identified in children. In this model, a powerful role for the evolution of the frontal lobes

and development of executive function can be postulated. The executive system acts as the integrator of all interconnected activities through growth spurts at the end of each tier of development. For example, at about the age of nine years an abstract tier begins, precipitated by a strong frontal growth spurt which may act to coordinate or direct the integration of activities for which the two hemispheres are specialized.

In addition to the neuroanatomical and developmental differences between the hemispheres postulated by Goldberg and Costa (1981) and Thatcher (1994), a number of additional differences between the hemispheres appear to be related to neuroanatomical architecture and development. For example, electrical activity in the frontal lobes shows early differentiation for positive and negative emotions (Thatcher, 1994). Greater frontal activity in the left hemisphere relates to positive or approach affect and greater frontal right activity relates to negative or avoidance affect. Additionally, in determining lateralized functions, hemispheric specialization is also influenced by other variables (e.g. gender and age). Males have stronger lateralization for verbal stimuli and females have stronger lateralization for nonverbal stimuli (Devinsky & D''Esposito, 2004). The role of testosterone on the growth of the left hemisphere, and more generally its possible link with some right-hemisphere disorders characterized by pragmatic speech difficulties, may prove to be an interesting line of future research. How these differences affect specialization, hormones or aging are related to the architectural and developmental differentiations remains unclear. However, assessment of any right-hemisphere disorder must necessarily address the impact of these differences on presentation in any particular child (Semrud-Clikeman Hynd, 1990).

Finally, it is important to describe one more model of development and specialization. It has been postulated that the hemispheres may once have been equally specialized for activities now thought of as primarily right-hemisphere specific. In this model, with the evolution of language, the non-linguistic functions were crowded out of the left hemisphere and now reside predominantly in the right, because the left hemisphere became more specialized for language (Nass & Koch, 1991). It may also be relevant that, when there is damage during early development, the left hemisphere is more resilient, while right-hemisphere functions seem to be more affected by insults such as prophylactic treatment or prematurity. Whether this difference represents the ''preservation of language at all evolutionary costs,'' the difficulty of measuring damage to ''right hemisphere-like'' functions that in fact take place in both hemispheres, or the increased vulnerability of the right hemisphere, given the relatively more distant connections across the hemisphere, remains a question to be explored.

Definitions and neuropsychological manifestations

One purpose of this chapter is to review the diagnostic classifications of right-hemisphere disorders. If one were to include only those categories delineated by more formal classification systems, this section would be very short. However, within clinical practice, many more diagnostic labels exist and guide the delivery of services, despite their lack of empirical validation in the literature. Many of these labels are tied to the specialty of the clinician making the diagnosis and, as a result, the disorders to which they are applied often appear to overlap. The next section will attempt to review comprehensively the common clinical labels applied to right-hemisphere disorders (and many that are misunderstood to be right-hemisphere based). Some of these classifications have fallen into disuse; still others persist within specific disciplines and reflect the emphases of those disciplines (Geller, 2005).

Semantic pragmatic disorder

Children with Semantic Pragmatic Disorder (SPD) or pragmatic language impairment have difficulties with conversational interactions. (Volden, 2004). As is the case with most right-hemisphere disorders, the definition of SPD remains surrounded by uncertainty, as does the differential diagnosis of SPD from autism and other forms of developmental language impairment (communication disorders: expressive language disorder, mixed receptive-expressive language disorder, and phonological processing). Neither of the two recognized sets of diagnostic criteria for mental disorders (Diagnostic and Statistical Manual of Mental Disorders [DSM-IV-TR] and International Statistical Classification of Diseases and Related Health Problems-Tenth Revision [ICD]) recognizes the existence of SPD. Speech and language therapists and some clinical and school psychologists continue, however, to identify the disorder in children because of its clinical utility in assisting with interventions.

Developmental right parietal lobe and right hemisphere syndromes

Weinberg and McLean (1986) identified two types of learning difficulties in children who also had difficulties with arithmetic and social-emotional function. The first type is marked by hyperprosody and over-emotionality. These children also misperceive social situations. The second type is marked by hyperprosody and lack of emotionality, with profound deficits in affect expression.

Similarly, Voeller (1986) described 15 children who displayed inappropriate affect and an inability to decipher the emotional states of others. The children also displayed stronger verbal and reading skills, motor impersistence, and greater rates of attention deficit hyperactivity disorder — inattentive type associated

symptoms. Later, Voeller (1991) described these children as exhibiting social-emotional learning disabilities, and the term social-emotional processing disorder has also been used in the literature to describe children exhibiting similar difficulties. Both of these classification systems appear to have fallen into clinical disuse as of late.

Left hemisyndrome

Denckla (1978) described a group of children with deficits in arithmetic, visual-spatial and social perception skills. These children also present with significant motor weaknesses. Neuropsychological deficits included mild delays in speech and reading. Denckla located the source of these difficulties in the right hemisphere. Unfortunately, similar sets of children have not been described with any consistency in the literature, leaving the reliability of this construct open to further investigation.

Hyperlexia

Although the predominant reading models now focus on disruptions in sound blending or phonological processing as the major cause of commonly identified reading disorders, a small thread in the literature continues to refer to the contributions of the right hemisphere to word recognition and the development of select reading disorders. In particular, Silberberg and Silberberg (1967) described hyperlexia as one potential disorder in linguistic processing that may stem from right - hemisphere disruption. They defined hyperlexia as a superior ability for reading accuracy without similar ability for reading comprehension. Clinically, ''hyperlexia'' is frequently used to describe superior single-word reading skills seen in children who have other developmental disorders, but the term has not been used with any consistency in the literature. At least one more recent study (Richman & Wood, 2002) suggested that some of hyperlexic children may show evidence of Nonverbal Learning Disability Syndrome (NVLD) (see below).

Inattention

Because it has been hypothesized in the literature that the right hemisphere is dominant for attention, it is important to include inattention in the discussion of right-hemisphere disorders (Heilman & Van Den Abell, 1980). Discussions of potential right-hemisphere based syndromes have in fact included in attention among the possible symptoms that can present with such disorders. More recent studies of attention appear to differentiate between hyperactivity and inattention as exhibiting different neuropsychological profiles, and there is some speculation that the Diagnostic and Statistical Manual for Mental Disorders (DSM) will treat these two symptom presentations as distinct diagnostic entities in the near future (Manly *et al.*, 2005; Sandson, Bachna & Morin, 2000).

Nonverbal disorders of learning

When Johnson and Myklebust (1967) first posited the existence of "non-verbal disorders of learning," they identified several distinct disorders within the overall category: disturbances in learning to tell the time; following directions; in body orientation; understanding the meaning of the behavior of others; in playing music and following rhythm; and in understanding meaning as conveyed in art. In addition, they described a separate subgroup of children who had deficiencies in social perception. According to Johnson and Myklebust (1967), children with difficulties in social perception typically have average or above average abilities in language but have difficulty using their language skills to convey ideas and interest. These children were also described as showing twenty- to thirty-point discrepancies between their psychometrically assesed verbal and performance abilities.

In recent years, the majority of research into NVLD has been conducted by Rourke (1987) and his colleagues, with a focus on the total constellation of neuropsychological assets and deficits that he hypothesized to result in poor social relatedness.

Children with NVLD are a heterogeneous group who are currently conceptualized as exhibiting problems in visual-spatial-organizational, tactile–perceptual, psychomotor and nonverbal problem solving skills. According to Rourke (1995), these deficits coexist with strengths in rote verbal learning, phoneme-grapheme matching, amount of verbal output and verbal classification. In school, these children are identified by their severe difficulties in mathematics, poor performance in athletic activities, difficulties with pragmatic language and relatively advanced skills in phonemic spelling and word recognition. Rourke hypothesizes that children with NVLD exhibit social deficits that are the result of both their poor visual–spatial abilities and their tendency to alienate peers with superior language characteristics.

The research to date, however, leaves many unanswered questions about the relationship between cognitive abilities and social skills of all children, including those with NVLD. Clinical observations and the literature have indicated that the constellation of assets and deficits identified by Rourke does not necessarily help to understand significant differences among children with nonverbal disorders of learning (Johnson & Myklebust, 1967; Badian, 1983; Semrud-Clikeman & Hynd, 1990; Pennington, 1991). For example, it has been found that some children with the social deficits characteristic of NVLD do not exhibit poor mathematics abilities. Conversely, a number of children exhibit all the other clinical features of NVLD (e.g. motor clumsiness, visual-spatial deficits) but do not have social difficulties. Additionally, studies examining the relationship among executive functions, spatial abilities and social skills have found

contradictory results (Edgin & Pennington, 2005; Gunter, Ghaziuddin & Ellis, 2002). Finally, some recent studies have not found support for the presence of NVLD symptoms in some disorders in which NVLD has been hypothesized to exist (McDonough-Ryan *et al.*, 2002; Weber Byars *et al.*, 2001). To further complicate the situation, current classifications that rely on Verbal and Performance IQ index differences (Drummond, Ahmad & Rourke, 2005) may be limited in their applicability because those indices have been abandoned when tests like the Wechsler Scales (i.e. the Wechsler Intelligence Scale for Children, Fourth Edition, or WISC-IV) are updated psychometrically.

Other syndromes or disorders with right hemisphere implications

Arithmetic

Arithmetic skills have been traditionally associated with left-hemisphere function. However, during development, the acquisition of numerical concepts may be based on spatial capacity for understanding relationships between or among groups. Thus, some authors have postulated that some aspects of mathematical operations are also reliant on the right hemisphere (Weintraub & Mesulam, 1983).

Pervasive development disorders

A comprehensive review of Pervasive Developmental Disorders (PDD) is beyond the scope of this chapter, and the reader is referred to other chapters in this volume and other specialized texts. It would be remiss, however, not to at least mention the overlap of PDD and the clinical labels described in this review. PDDs include autism, Asperger's Syndrome, Rett's, and Childhood Disintegrative Disorder. These broad categories do not provide clinicians with classifications specific enough to describe children who are in need of a diagnosis to obtain services, and the classifications that have sprung up to fill the gap are often used inconsistently or imprecisely. For example, a child with an intelligence quotient of 130 and a child with an intelligence quotient of 60 can both be diagnosed with autism, but many clinicians have instead used the term "high-functioning autism" to more aptly describe the child with the higher intelligence scores. This differentiation gives service providers and schools guidance as to the appropriate levels of and place for intervention. Since the term "high-functioning autism" is not described uniformly, however, its use may lead to confusion among families, service providers, schools and clinicians.

The difficulties clinicians face in diagnosis result not only from the broadness of the PDD categories, but also from two other factors. First, the "not otherwise specified classification" includes children with impairments in reciprocal social skills or communication skills, or who present with stereotyped behaviors,

but who do not meet full criteria for autism or Asperger disorder. This is the most common category in the recognized diagnostic schemes in which children are placed who need services primarily as a result of social impairments. Second, the relationships between NVLD and other diagnoses are not clear. For example, there is some speculation that all children with Asperger's syndrome exhibit the NVLD (Rourke, 1995). If the definition of the syndrome is confined to a specific neuropsychological profile as identified on specific tests, it may be the case that children with Asperger's syndrome frequently exhibit the syndrome. However, given the lack of large-scale subtyping studies documenting intelligence or neuropsychological differentials in children with Asperger's syndrome, it is far from settled that all children with Asperger's syndrome display NVLD. Moreover, the Asperger's syndrome criteria currently exclude children with clinically significant language delay. If you observe the group who are most frequently included in the "high-functioning autism" classifications, many would have neuropsychological profiles which are consistent with those observed by Rourke and his colleagues, but frequently they lack some of the more behaviorally focused symptoms first described by Johnson and Myklebust (1967).

Developmental Gerstmann syndrome

Some investigators have noted similarities between children with right-hemisphere learning disabilities and those identified as experiencing Developmental Gerstmann Syndrome (GSD; Semrud-Clikeman & Hynd, 1990). However, the syndrome as described (dyscalculia, dysgraphia, right-left confusion, and finger agnosia) is controversial. More recent electrical stimulation studies leave little doubt that GSD, when truly present, is most likely to be associated with left-sided posterior inferior parietal lesions (Miller & Hynd, 2004).

Minimal brain dysfunction or neurological soft signs

Neurological soft signs include poor motor coordination, sensory perceptual difficulties, and difficulties in sequencing of complex motor tasks. This constellation of difficulties has not been localized to a specific brain structure and the term "soft" indicates that the person shows no other signs of specific neurological impairment. A body of literature links these soft signs, or minimal brain dysfunctions, to a number of psychiatric disorders associated with right-hemisphere neuropsychological impairments (Pine *et al.*, 1997).

Epidemiology/prevalence/incidence and developmental course

The difficulties in defining right-hemisphere disorders have made large scale or epidemiological studies all but impossible. Accordingly, prevalence or incidence

estimates of right-hemisphere disorders are necessarily misleading, but some put numbers between 0.1 to 1.0% (Forrest, 2004). Case reports and small samples predominate and add to confusion in terminology. Similarly, given the lack of research in these disorders, there is little understanding of their developmental courses.

Assessment of right-hemisphere disorders

As stated previously, the assessment of right-hemisphere functions has significantly lagged behind the assessment of language disorders. For example, since we do not have visual-spatial milestones, our ability to assess visual-spatial development is rudimentary. In addition, clinicians have very few tests to assess pragmatic language issues; for example, the Comprehensive Assessment of Spoken Language – Non-literal Language and Pragmatic Judgement subtests (Carrow-Woolfolk, 1999) represent the most ecologically valid assessments available at this time. Even fewer tests exist to assess social-emotional development. Recent releases of measures which assess social skills – such as the Autism Diagnostic Observation Scale (Lord *et al.*, 2002), the Social Communication Questionnaire (Rutter, Bailey & Lord, 2004), and the Pervasive Development Disorders Behavior Inventory (Cohen & Sudhalter, 2005) – represent leaps forward in terms of quantitatively assessing social abilities. However, these instruments often do not allow differentiation among diagnostic disorders for children functioning at either extreme of abilities. Nevertheless, because they focus on the assessment of social abilities they help with the thorough assessment of right-hemisphere functions, and performance on these scales may form the basis for both targeted and comprehensive interventions.

New technologies

New radiological technologies such as functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) hold particular promise in furthering our understanding of the right hemisphere (see Bigler, this volume). fMRI observes functioning in the brain by detecting changes in blood flow. DTI images the fibrous structures of the brain using the diffusivity of water. In spite of these technological advances which allow us to track functions and pathways within the brain, few studies have used them to study right-hemisphere disorders, probably because of the lack of concrete classification systems on which to base criteria for including participants in a study. The few studies that exist have provided us with a glimpse of the neuroanatomical structure and function

relationships of right-hemisphere disorders. For example, in one study where six participants were included based on VIQ/PIQ differences, the subjects with NVLD displayed less activation in limbic areas responsible for processing emotion in the normal population (Vallabha, 2003). The participants with NVLD also exhibited greater activity than controls in language areas including the orbital gyrus, inferior, middle and superior frontal gyri, fusiform and superior temporal gyri, insula, striatum and inferior and superior parietal lobules. The study concluded that it is likely that this population relies on their linguistic strengths to compensate for their nonverbal weaknesses. Additionally, the persons with NVLD showed more active responses for low-intensity emotions in comparison with controls because of an impaired capacity for attention to and discrimination of visual details. Similarly, a DTI study examining individuals with velocardiofacial syndrome (who have been identified as exhibiting the NVLD profile) found bilateral involvement of white matter but, more particularly, left hemisphere involvement (Barnea-Goraly & Krasnow, 2003).

Common areas of intervention

Due to the controversy surrounding the disorders described in this chapter, most are not formally recognized as learning disabilities, nor recognized by many school districts as justifying interventions. The most common diagnostic label applied to right-hemisphere disorders is Learning Disorder - Not Otherwise Specified (LD-NOS). Given the vagueness of that label, parents frequently describe difficulties in having right-hemisphere disorders addressed in the classroom; most do not form the basis for a formal Individual Education Plan (IEP) unless the autism spectrum or Pervasive Development Disorder classification is used. This creates an often unfortunate dilemma for the clinician, who is faced by the very real circumstance of the ''label'' affecting the diagnostic process. When accommodations are provided, the common areas for intervention include pragmatic language, social skills, and visual–spatial aspects of learning.

Generally, interventions need to be targeted at the strengths or weaknesses of a particular child, and to use a child''s strengths to improve the specific areas in need of development. As a result, interventions need to be viewed dynamically. As a child reaches a new developmental stage, old interventions will not necessarily work, and new strategies will need to be employed (Foss, 1991).

Pragmatic language

Pragmatic language interventions require multi-step, multi-level assessments and treatments. Areas that children with pragmatic language difficulties may need

to work on include receptive language skills, perspective taking, awareness of nonverbal/body language, adjusting language to audience (e.g. teacher or peers), adjusting to setting (e.g. classroom or home), recognizing peers'' lack of interest in a topic and other nonverbal cues, recognizing a sarcastic response or use of non-literal language, and thinking before speaking (controlling impulses). The focus will need to be on breaking down everyday social interactions into component parts and teaching the child many of the things that the rest of us take for granted in our daily interactions. These skills will need to be taught like any other subject (e.g. mathematics or science). After direct instruction in the component skills, emphasis turns to working on real-life conversations.

Role playing with a child having pragmatic language difficulties is essential. It is also important that someone in the school setting is available for guidance during social interactions. As skills become more automatic and flexible, the child should start making note of others'' use of pragmatic language and should be able to fine-tune his or her interactions with less direct input from adults or peer role models. As children become more adept at basic skills, they will need to advance to issues such as turn-taking, introducing a new topic, shifting a topic, interrupting, joining an established conversation, seeing another's view point, and small talk (Volden, 2004).

Social skills

Two recent studies have explored the effects of social-competence intervention programs, designed specifically to address the needs of children with social perception deficits (Guli, 2005; Glass, Guli & Semrud-Clikeman, 2000). Children completed exercises adapted from creative drama and theatre classes in order to practice processes involving perception of emotions, interpretation, and response. Evidence from these studies suggests that the children participating developed some self-awareness of their feelings and behaviors and that this self-awareness led to improvements in social interactions. More specifically, the treatment group was observed to have significantly fewer solitary behaviors and significantly more positive interactions than the clinical control group.

Visual–spatial abilities

Students struggling with mathematics or science might improve their performance by receiving extra coaching, but they could also develop the visual–spatial skills which make it easier to learn those subjects. Therefore, the specific goals included in an Individualized Education Plan (IEP) should relate to compensating in the classroom for visual–spatial weakness with regard to the specific academic area affected and to specific curriculum requirements, especially as they relate to vocational planning (Telzrow & Koch, 2003). Generally, few products exist aimed

at improving basic cognitive visual–spatial skills, and most interventions are aimed at accommodating the academic weakness. At least one study has found improvement in visual abilities using computer-assisted technology (Filippopoulos, 2005).

One promising venture is the Cognitive Abilities Educational Software Project at Lexia Learning Systems, Inc. (2006) a three-year federally funded project to develop computer programs which improve fundamental cognitive abilities. This software is focused on developing the underlying cognitive abilities which enable efficient learning. For some students, the software is designed to enhance an already solid foundation. For others, it is intended as a remedial measure to help develop missing abilities.

In general, children with visual–spatial difficulties should be taught using verbally based strategies and self-monitoring techniques to assist in the processing and comprehension of social information, visual stimuli, and spatial relationships. These remediation approaches to develop, challenge and exercise nonverbal skills need to be implemented incrementally, so as not to result in increased frustration.

Future research directions

Diagnosing and treating right-hemisphere disorders is plagued by uncertainty. In order for the field to move forward, a number of foundations need to be set. Firstly, epidemiological studies of naturally occurring learning styles and differences within classrooms need to take place. Secondly, large scale, multi-site investigations of right hemisphere disorders need to be organized and funded. Thirdly, a greater nexus between study design and clinical symptoms needs to occur. Current funding priorities emphasize research design over ecological validity; however, studying face processing (for example) in isolation from other social skills yields very little useful clinical information for families of children suffering with social disorders, or for schools trying to provide services. More pediatric neuropsychologists need to be involved in research design and methodology to increase the ecological validity of our current research protocols. Finally, new instruments that assess the development of right-hemisphere abilities need to be developed.

Clinically, we need to rethink the criteria used to differentiate children with right-hemisphere difficulties. Clinicians need to make important distinctions which can then become the focus of targeted interventions and treatment. For example, the term ''nonverbal learning disability'' could be reserved to describe a broader profile of assets and deficits experienced by most

children with right-hemisphere disorders while the term ''visual–spatial disability'' could be created for children with specific visual–spatial deficits that are so severe as to affect academic performance in subjects such as mathematics. A different diagnostic category (e.g. social processing disorder) could then be created for children whose social skills deficits are primary and impair daily life functions. Both groups may have difficulties with other cognitive abilities such as executive functions, but the emphasis for purposes of diagnosis, treatment, and intervention would be on the area of greatest functional impairment for the child. At present, because the social deficit in children with NVLD is thought to always occur as the result of the NVLD neuropsycholgical profile, children who do not have social deficits, but who exhibit visual–spatial deficits, are left in an uncertain clinical diagnostic territory. Some of these children are labeled as PDD–not otherwise specified, but that label does little to aid clinical intervention and treatment.

At present, DSM-IV (American Psychiatric Association, 2000) includes mathematics and language disorders but no visual–perceptual categories. Although children with visual–spatial deficits may have difficulties with the manner in which math is taught to them, they may not have deficits in their abilities to perform fundamental math calculations when their visual–spatial deficits are accommodated (e.g. through the use of graph paper for place alignment). Therefore, they would not qualify for a diagnosis of math disability, leaving Learning Disorder - Not Otherwise Specified as the only category available for diagnostic purposes. Similar to the pervasive development disorder, the LD-NOS category does little to aid in the provision of services or treatment.

Also, the current DSM does not recognize social difficulties as meriting a disorder status. A social-processing disorder category would lend diagnostic support to the importance of social interactions in the lives of children and allow us to differentiate among higher functioning children who are currently serviced through a high-functioning autism, Asperger''s or NVLD diagnosis. Although a difficulty in interacting with peers is at the root of most right-hemisphere disorders, we have very few diagnostic categories for social difficulties that interfere with academic or personal success. This lack of diagnostic specificity may result from the assessment and definitional difficulties noted earlier in this chapter.

As we evolve in our understanding of brain function, we may attempt to describe and capture the unique contributions of the right hemisphere to crucial aspects of our lives. The need or drive to connect with other humans was absent both from the instincts which Freud considered fundamental to all humans, and from the work of Charles Darwin, who heavily influenced Freud's concept of instincts. Despite the fact that Darwin's last major publication was *The expression*

of the emotions in man and animals (1985), neither major theorist, both critical to the development of psychology, gave a place in their theories to the desire of the self to connect with others. The omission of a social drive from the work of Freud and others, and the emphasis on scientific method in psychology, may have led us to omit social relatedness as a construct from our diagnostic tool box because it is simply too difficult to define, measure and assess. Yet this desire for social connection seems present in the humblest of species and appears integral to human existence. When it is absent, or social relatedness is impaired, the results can be devastating. For example, in children with NVLD, the inability to connect socially with their peers is believed to result in higher rates of suicide (Ozols & Rourke, 1985). If social interaction is in fact integral to our daily sense of self, we should aspire to diagnose the inability (or lack of desire) to engage in social interaction, and the development of spatial abilities that underpin social development, in ways that allow specific treatments and evidence-based interventions to be developed (Forrest, 2002).

Because social interaction appears to be integral to human existence, the notion that a neural network within the brain, separate from other networks but interacting with them, might mediate social abilities would seem plausible (Forrest, 2002). If the need to connect with other humans is fundamental, it would seem reasonable to hypothesize that within the brain evolution has provided a developmental progression and functional network specialized for social relatedness. Cognitive abilities may have developed or evolved to support more complex social interactions across greater distances. Facial recognition, the most frequent focus of studies examining social processing, is only one component of any such system. Other specific neuropsychological assets and deficits, as observed in studies and reported in the literature more generally, give us clues as to the cognitive skills and abilities that are integral to the entire process or system. A social processing network would involve integrated cerebral systems that synthesize the perception of objects in space as mediated by the parietal lobe and more specifically the right hemisphere; mental flexibility, reflection and feedback involving the frontal lobes; and expression of affect as regulated by subcortical areas such as the amygdala. The delineation of that social network, and the cognitive abilities that develop to support it, remains a realm to be explored and documented in all children.

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11

Genetic syndromes associated with intellectual disability

Bonita P. Klein-Tasman, Kristin D. Phillips, and Jill K. Kelderman

A central role of pediatric neuropsychologists is to apply an understanding of neurocognitive disorders to the assessment of a child's pattern of strengths and weaknesses, and to point families in the direction of appropriate interventions (Baron, 2003; Bernstein, 2000). In recent years, with advances in molecular and clinical genetics, there has been a surge in research examining the phenotypes associated with a broad range of genetically based neurodevelopmental disorders, in the search for a better understanding of genotype–phenotype relations (Denckla, 2000; Fisch, 2000). This knowledge is invaluable to neuropsychologists who can inform their assessments based on these investigations. In addition, knowledge about etiology has the potential to inform intervention suggestions, including recommendations to support transition to adulthood, once a body of knowledge about the impact of such interventions exists.

In this chapter, we discuss the importance of consideration of etiology in intervention planning for children with mental retardation syndromes. First, the potential strengths of an etiological approach, in contrast to one that focuses primarily on the level of functioning of the child, are described. Secondly, an outline of the assessment targets that are typically addressed with children with mental retardation is presented. Thirdly, the cognitive and behavioral phenotypes characteristic of a number of genetic syndromes with associated intellectual disability are presented, with a focus on available literature about appropriate interventions targeted to particular genetic disorders. Finally, we present a discussion of the limitations to our current knowledge about interventions for children with genetic syndromes associated with intellectual disability as well as directions for future research.

An etiologically based approach to intellectual disability

The most traditional approach to characterization of the needs of children with intellectual disabilities places strong emphasis on the child's level of intellectual

and adaptive functioning. The American Psychiatric Association''s DSM-IV-TR (APA, 2000) and the tenth edition of the American Association on Mental Retardation''s volume on definition, classification and systems of support for mental retardation (AAMR, 2002) both take this level of functioning approach, defining mental retardation as below average intellectual abilities coupled with adaptive deficits present before the age of 18. A number of complementary approaches to the dimensional nature of mental retardation are offered. One approach is to emphasize the cognitive level and adaptive functioning level of the person with mental retardation. A second approach, favored by the AAMR, is to consider intellectual functioning together with an emphasis on the level of support that the individual appears to need in daily life, as predictive of their level of functioning. As adaptive functioning and needs for support are likely to be overlapping constructs, these approaches provide largely convergent information about the general level of functioning of the child, emphasizing level of functioning as critical to understanding the support and intervention needs of the person with mental retardation (Dykens & Hodapp, 1997; Baumeister & Baumeister, 2000; Pennington, 2002).

In contrast to the level of functioning approaches, Hodapp and colleagues have advocated the use of an etiologically-based approach to improving our understanding of mental retardation. They contend that, when the underlying cause is known, an etiological approach has the potential to be a powerful tool in the determination of the needs of people with mental retardation (Hodapp & Dykens, 2001; Zigler & Hodapp, 1991). However, Hodapp and colleagues (Dykens & Hodapp, 1997; Hodapp & Fidler, 1999) also mention a number of caveats regarding the use of an etiologically based approach to understanding children with genetically based neurodevelopmental disorders. First and foremost, although research indicates that there are characteristic patterns of strength and weakness, and behavior problems for some syndromes, not every person with a given syndrome will show a ''characteristic'' pattern. Relatedly, not every genetic syndrome will be associated with a characteristic pattern with corresponding sensitivity and specificity. Secondly, there are many influences on behavior other than the genetic etiology of a developmental disability, such that the pattern of deficits seen in a given child is not fully attributable to the genetic disorder in question. Thirdly, developmental changes in phenotypes of neurocognitive disorders are present. Finally, the level of functioning of the child may indeed play a significant role in regard to intervention, regardless of etiology (e.g. talk-based counseling is unlikely to prove beneficial to a child with severe intellectual disability).

Despite these caveats, given the focus of neuropsychologists on information processing styles and patterns of individual strength and weakness, the

etiologically based approach appears to be consistent with a neuropsychological approach to assessment and intervention. Mental retardation has been broadly related to slower processing speed and cognitive efficiency (Baumeister & Baumeister, 2000). Knowledge of the etiology of mental retardation, however, can add greater detail to the portrait of the child with a cognitive disability by providing initial hypotheses about the patterns of strengths and weaknesses that are likely to be present. Expectations about the nature of these strengths and weaknesses can assist neuropsychologists in choosing appropriate assessment tools to sample the areas of functioning most likely to be relevant to the child at hand. The main message of this chapter is that these phenotypic patterns can also point toward potentially useful intervention targets or strategies.

Typical assessment targets and methods

There are several main targets in the neuropsychological assessment of a child with a genetic syndrome associated with intellectual disability. These are described in the following sections.

Assessment for "Mental Retardation" diagnosis

A critical task is to assess for the presence and degree of mental retardation or intellectual disability based on the relevant diagnostic criteria. Diagnostic criteria for mental retardation include intellectual impairment and deficits in adaptive behavior (AAMR, 2002; APA, 2000). Intellectual impairment is generally established through the administration of a norm-referenced measure of intellectual abilities (e.g. Differential Abilities Scales – II(Elliott) or Stanford-Binet–Five (Roid, 2003). Adaptive behavior is typically assessed by the administration of a parent- or significant adult-report measure of adaptive behavior (e.g. Vineland Adaptive Behavior Scale (Sparrow, Cicchetti, & Balla, 2005)), as well as measures of academic achievement.

Description of unique cognitive strengths and weaknesses

Although the child's overall level of functioning may provide an indication of the kinds of supports that may be needed, more tailored identification of the child's unique "peaks and valleys" in abilities is critical to intervention. Such a focus can enable the adults in the child's world to capitalize on strengths and help support or remediate areas of relative weakness.

Assessment of behavioral or emotional functioning

Assessment of emotional and behavioral functioning is needed, as concomitant behavioral or emotional issues can be a significant factor in child adjustment.

Individuals with mental retardation are at high risk for the development of internalizing and externalizing psychological disorders (Reiss, 1994). The presence of psychiatric difficulties in individuals with mental retardation is referred to as "dual diagnosis" (Matson & Sevin, 1994; Nezu, Nezu & Gill-Weiss, 1992; Reiss, 1994; Sturmey, 1995; Sovner, 1986). Estimated prevalence rates of psychiatric diagnosis in individuals with mental retardation range from 10% to as high as 80% (Borthwick-Duffy, 1994; Nezu, Nezu & Gill-Weiss, 1992). Numerous researchers (Rush *et al.*, 2004; Sovner, 1986; Sovner & Hurley, 1983) suggest that individuals with developmental disorders have psychiatric difficulties which are conceptually similar to DSM disorders, but they are less likely to be diagnosed than are typically developing individuals. Emotional and behavioral difficulties may be overlooked in the individuals with a syndrome associated with mental retardation due to a lack of understanding of the relationship between developmental disability and psychopathology (Cooper, Melville & Einfeld, 2003) and perhaps also to a misconception that they would not respond to traditional treatment modalities. The presence of intellectual disability together with psychiatric and behavioral problems presents unique treatment challenges (Fletcher, 2000). Children with these comorbid difficulties are especially likely to have difficulties at home and at school and to be vulnerable to unfavorable long-term outcomes.

Assessment of school and family context

Finally, the assessment of family functioning and identification of school resources as a context for the implementation of intervention suggestions is important. Families are likely to be concerned about decisions regarding placement and level of support, level of services needed, and the fit of areas of difficulty with the assets of the special education system. Issues related to acceptance of a mental retardation diagnosis, as well as the role of any typically developing siblings in the family may also be important targets for assessment and intervention. It may be particularly important to assess for appropriate parental and school expectations of the child's level of functioning.

Genetic syndromes associated with intellectual disability

Phenotypes and suggested interventions

In the following section, the phenotypes of a number of genetic syndromes associated with varying degrees of intellectual impairment are described. Pertinent intervention literature, consisting primarily of case reports and suggested interventions, is presented for each syndrome. Although this is not an exhaustive list, syndromes that have received a great deal of attention in the literature

are included, as well as some syndromes that are not as well known. Descriptions are provided for the following disorders: Fragile-X syndrome, Down syndrome, Angelman syndrome, Prader-Willi syndrome, Inverted duplication 15 (Idic-15), Neurofibromatosis-1, 22q Deletion syndrome (VCFS), 5p- (cri-du-chat syndrome), and Williams syndrome.

Fragile-X syndrome

Fragile-X syndrome is a single gene disorder in which the fragile mental retardation 1 gene (FMR1) becomes inactivated it contains a large number of repeats, and therefore does not effectively produce a critical FMR1 protein (DeBoulle *et al.*, 10 T; Tassone *et al.*, 10 9). As the X chromosome is

present and affect speech (Abbeduto & Hagerman, 1997). Other noted difficulties include poor math and abstract reasoning skills, and difficulty with planning. A relative strength in early reading and spelling skills is seen (Hagerman, Kemper & Hudson, 1985; Kemper, Hagerman & Altshul-Stark, 1988). Declines in IQ scores with chronological age are typical (Fisch *et al.*, 1996), although this is more characteristic of males with the disorder than females (Fisch *et al.*, 1999).

In terms of adaptive and behavioral functioning, daily living skills are an area of relative strength while socialization skills are an area of relative weakness (Zigler & Hodapp, 1991). Attention difficulties have been noted (Friefeld *et al.*, 1993). Higher than normal levels of hyperactivity have also been reported (Hagerman & Sobesky, 1989). In boys with Fragile-X syndrome, very high prevalence rates of comorbid Attention Deficit/Hyperactivity Disorder (ADHD) have been found (72% by Backes *et al.*, 2000; 90% by Bregman, Leckman & Ort, 1988). Social anxiety and gaze aversion are also often described (Einfeld, Tonge & Florio, 1997; Dykens & Hodapp, 1997). Emotional and social difficulties in girls with Fragile-X include social anxiety, loneliness, and proneness to depression (Hagerman & Sobesky, 1989).

Interventions for persons with Fragile-X

Suggested interventions for children with Fragile-X syndrome have targeted both cognitive abilities and behavior change. Notable, however, is the lack of strong empirical support for specific interventions for children with this disorder. For example, it has been suggested that sign language may be appropriate for some individuals with language delays; however, the fine motor deficits in individuals with Fragile-X may impede the use of this strategy. This observation provides an example of the need to consider a broader representation of the phenotype in intervention planning (Hodapp & Dykens, 1991). Similarly, given the degree of distractibility and shyness associated with Fragile-X syndrome, appropriate intervention may include minimization of visual and auditory distraction in the classroom or workplace, and the implementation of interventions focused on the individual rather than a group. This suggests that interventions appropriate for the child with ADHD may translate to children with co-occurring attentional concerns and Fragile-X. Again, however, this has not been well studied empirically. Although not yet examined empirically, biofeedback and relaxation techniques, skillbuilding, and behaviorally oriented supportive psychotherapy may be appropriate treatments for anxiety and psychosocial development; these have been considered on a case-by-case basis to date. Improvement in attention span and reduction of hyperactivity has been noted for children treated with medications, specifically the stimulants (Hagerman, Murphy & Wittenberger, 1988). Notably, the only group-based intervention

study in Fragile-X syndrome provided evidence that a number of sleep-related difficulties were considerably reduced using a variety of behavioral techniques including introduction of a bedtime routine, reinforcement of positive bedtime behaviors, clear parental instructions, and ignoring of challenging bedtime behavior (Weiskop, Richfield & Matthews, 2005).

Down syndrome

Down syndrome is the most common genetic etiology of mental retardation, with an incidence of approximately 1 in 800 live births. In the majority of cases, Down syndrome results from an extra copy of chromosome 21, but mosaicism is also apparent. Physical features of Down syndrome include characteristic facial dysmorphologies and congenital heart abnormalities. Neuroimaging studies have indicated smaller whole brain volumes (Frangou *et al.*, 1997; White, Alkire & Haier, 2003). Some investigations have found larger ventricles, smaller planum temporale (Frangou *et al.*, 1997), and reduced temporal, left medial frontal, and cerebellar volumes (White, Alkire & Haier, 2003; Wang *et al.*, 1992). Notably, there is an increased risk of early onset Alzheimer's disease in Down syndrome (Epstein, 1989).

In terms of cognitive functioning, intellectual functioning is typically in the range of moderate mental retardation, with some variability observed (Klein & Mervis, 1999; Pennington *et al.*, 2003). Some individuals with Down syndrome have intellectual abilities in the broadly average range (Epstein, 1989); these individuals typically have a mosaic genetic presentation. Individuals with Down syndrome generally show a particular weakness with grammatical aspects of language and a relative strength on spatial tasks (Abbeduto *et al.*, 2001; Klein & Mervis, 1999). Verbal short-term memory is typically more impaired than is visual (Wang, 1996), and there is general evidence of memory deficits (Pennington *et al.*, 2003). In terms of adaptive functioning, individuals with Down syndrome typically show a relative strength in their social skills and a relative weakness in daily living skills (Zigler & Hodapp, 1991).

A number of studies have indicated that parents report lower levels of behavior problems in children with Down syndrome than are reported for children with other developmental disabilities (e.g. Myers & Pueshel, 1991; Dykens & Kasari, 1997), and that children with Down syndrome generally have an "upbeat" personality (Hodapp & Desjardin, 2002). Dykens and Kasari (1997) also found an increase with age in internalizing symptoms, including anxiety, depression, and withdrawal. ADHD is not as commonly reported for individuals with Down syndrome, with Myers and Pueschel (1991) showing a rate of only 6.1% in children and adolescents with Down syndrome, based on psychiatric and psychological evaluations.

Interventions with persons with Down syndrome

Both broad intervention and case studies have found that individuals with Down syndrome with severe language problems benefit from learning sign language, particularly when combined with speech learning (Kouri, 1989; Miller, 1992). Hodapp and Desjardin (2002) advocate a visually-based, recognition-oriented intervention strategy for teaching, reading, and vocabulary building to individuals with Down syndrome, such as using flashcards rather than employing a phonetic reading approach. Additional research has demonstrated the effectiveness of emphasizing the development of phonological awareness to improve reading (Cupples & Iacono, 2002) and rehearsal training to advance memory skills (Conners, Rosenquist & Taylor, 2001).

Several interventions have been suggested to be partially effective in addressing motor difficulties in persons with Down syndrome; these include sensory integration therapy, "vestibular stimulation," and "neurodevelopmental therapy," all of which include techniques for muscle strengthening and target both gross and fine motor skills (Uyanik, Bumin & Kayihan, 2003; but see Tupper, this volume, for further information regarding the success of these techniques in general). Uyanik *et al.* (2003) advocated using these therapies together, rather than separately, when designing interventions for children with Down syndrome. They examined pre- and post-intervention performance on several measures of motor functioning, but did not compare performance to an appropriate control group. As such, these findings remain speculative.

Hines and Bennett (1996) have reported the advantages of early intervention in children with Down syndrome. Functional assessments, conducted to identify problematic behaviors in youngsters with Down syndrome, and to serve as guides to intervention, have demonstrated effectiveness (Anderson & Long, 2002; Brooks *et al.*, 2003). Additionally, parent training procedures, involving teaching parents to utilize increased structure and planning in daily activities, may be effective in addressing behavior concerns in children with Down syndrome (Huynen *et al.*, 1996). Awareness of the risk for early onset Alzheimer's disease in this population is also critical, as it may influence aspects of long-term planning.

Angelman syndrome

Angelman syndrome is a genetic disorder usually resulting from a hemizygous microdeletion on chromosome 15 of maternal origin, including the UBE3A gene (Kishino, Lalande & Wagstaff, 1997; Matsuura *et al.*, 1997; see Clayton-Smith & Laan, 2003 and Williams, 2005 for a more complete discussion of the multiple possible genetic mechanisms for this disorder). Physical features of Angelman

syndrome include the presence of ataxia and hypotonia as well as seizure disorder. There have been few neuroimaging studies of Angelman syndrome. Leonard *et al.* (1993) reported that anomalous Sylvian fissures were common.

The cognitive functioning of individuals with Angelman syndrome typically falls in the severe to profound range of mental retardation (Cassidy, Dykens & Williams, 2000). Phenotypic studies have indicated especially poor motor functioning and expressive language, with relative strengths in nonverbal communication (Clarke & Marston, 2000; Penner *et al.*, 1993; Williams *et al.*, 1995). Echolalia occurs to a lesser degree than in individuals with Down syndrome or Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS; Duker, van Driel & van de Bercken, 2002), as well as other developmental disabilities of mixed etiologies (Didden *et al.*, 2004). This finding is consistent with observations regarding impairment in verbal abilities in persons with Angelman syndrome, and their generally sparse efforts to communicate verbally. Hand-flapping and attention difficulties have been noted in both case studies and parent report (Summers *et al.*, 1995; Williams *et al.*, 1995). In terms of behavioral functioning, a "happy disposition" characterized by frequent smiling and laughter is often described (Clayton-Smith, 1993).

Dykens and colleagues (2000) reviewed studies of behavioral difficulties in Angelman syndrome, commenting that the findings are fairly consistent. In comparison with an age- and ability-matched sample of individuals with developmental disabilities of mixed etiologies, parents of children with Angelman syndrome rated them significantly lower in irritability and lethargic behavior, based on a parent report checklist (Summers & Feldman, 1999). The most common behavioral findings from case reports include speech difficulties and laughter, with hyperactivity and feeding concerns occurring to a lesser extent (Summers *et al.*, 1995). Attention and sleep difficulties have been confirmed by parents reports as well (Clarke & Marston, 2000; Summers *et al.*, 1995). In particular, difficulties affecting most aspects of sleep (initiation, duration, tendency to be awoken, and disorientation when woken up) have been observed (Walz, Beebe & Byars, 2005). In an examination of the developmental trajectory of the behavioral phenotype of Angelman syndrome, Clayton-Smith (2001) found that attention difficulties were reduced with age, and the happy temperament observed in these individuals remained across development. In addition, there is some evidence that the presence of smiling and laughter occurs most often during social interactions (Oliver, Demetriades & Hall, 2002).

Intervention with persons with Angelman syndrome

Few intervention studies exist that address the treatment of behavioral difficulties in Angelman syndrome and most of those that are available are case reports.

One case study indicated that behavioral and pharmacological treatment was effective in addressing sleep difficulties (Summers *et al.*, 1992). A parent training model to increase the use of gestures in children with Angelman syndrome has also been described as effective (Calculator, 2002). Behavioral training procedures to improve daily living skills such as toileting have been demonstrated as effective as well (Didden *et al.*, 2001).

Prader-Willi syndrome

Prader-Willi syndrome (PWS) is a genetic disorder resulting from a hemizygous deletion on the paternal chromosome 15. Physical features of PWS include short stature (Cassidy, 1984; Hudgins, McKillop & Cassidy, 1991), as well as hypotonia and hypogonadism; the latter is identifiable even in newborns with PWS (Aughton & Cassidy, 1990). Neuroimaging studies have indicated alterations in GABA(A) receptor composition (Lucignani *et al.*, 2004), and evidence of mild abnormalities on MRI includes slight cortical atrophy and a small brain stem (Hashimoto *et al.*, 1998).

The cognitive functioning of individuals with PWS typically falls within the borderline to moderate mental retardation range. A predominant phenotypic feature of PWS is a strong interest in food and a lack of sensitivity to physiological sensations of satiety. Studies have indicated a relative strength in simultaneous processing and a relative weakness in sequential processing (Hodapp & Desjardin, 2002). An examination of language functioning indicated that poor articulation and oral motor problems are the most commonly seen difficulties in children and adults with PWS (Lewis *et al.*, 2002). There is some indication that "differential outcomes training," which involves pairing a unique reinforcer with a particular discriminative stimulus, can be used for learning and improvement in memory among individuals with PWS (Hochhalter & Joseph, 2001).

Prader-Willi syndrome is associated with a number of behavioral concerns, including obsessive-compulsive behaviors (particularly related to food), higher levels of stubbornness, emotional lability, and impulsivity, as well as a risk for anxiety, withdrawal, low self-esteem, and depression (Dykens & Cassidy, 1999). Parent-reports of behavior problems indicate that difficulties tend to increase with age (Steinhausen *et al.*, 2004) and Wigren and Hansen (2003) found that, unlike typically developing children, the rate of compulsions in PWS did not decrease from childhood to adolescence. Using parent ratings of social competence, one study found that individuals with PWS received significantly lower scores in the "behavior with others" domain than did participants with either Down syndrome or Williams syndrome (Rosner *et al.*, 2004). In addition, Koenig, Klin and Schultz (2004) found that individuals with PWS performed worse on a task assessing the ability to make social attributions than did

IQ-matched controls, and the PWS group were not significantly different from a group with PDD-NOS. A longitudinal examination of 53 adolescents and adults with PWS found that eight were diagnosed with psychiatric disorders, four with psychosis and four with bipolar disorder (Descheemaeker *et al.*, 2002). The remaining sample ($n = 45$) did not have diagnosable psychiatric problems.

Interventions for persons with Prader-Willi syndrome

Suggestions for behavioral interventions in PWS often revolve around issues related to food, and obesity tends to be a primary concern (Dykens & Cassidy, 1996; Dykens & Hodapp, 1997). There is evidence that PWS-related obesity can be treated through such behavioral methods as self-monitoring (Altman, Bondy & Hirsch, 1978; Heiman, 1978). In addition, there is some indication that food can be utilized for reinforcement. One study found that preferred foods could be used to increase activity level in adolescents and young adults with PWS (Caldwell, Taylor & Bloom, 1986). Dykens and Cassidy (1996) suggested that social skills training and interventions emphasizing peer relations may be effective in ameliorating affective difficulties in individuals with Prader-Willi syndrome. Given that obsessions and compulsions are also commonly reported, Dykens *et al.* (2000) suggest using obsessive topics as motivation for completing tasks; that is, offering discussion of these topics as a reinforcer for completing work.

Inverted duplication (Idic) 15

Idic-15 is a genetic disorder resulting from a marker chromosome of material from chromosome 15. Physical features include hypotonia and a high incidence of seizures (Borgatti *et al.*, 2001). There are very few phenotypic studies of inverted duplication 15 beyond case descriptions and no current neuroanatomical studies. However, based on available research studies, it appears that motor functions and language abilities are delayed and autism spectrum disorder symptoms are commonly seen (Baker *et al.*, 1994; Flejter *et al.*, 1996; Gillberg *et al.*, 1991; Leana-Cox *et al.*, 1994; Maraschio *et al.*, 1981; 1988; Martinsson *et al.*, 1996; Mignon *et al.*, 1996; Schroer *et al.*, 1998; Webb, 1994; Wolpert *et al.*, 2000). Recommendations for managing the effects of Idic-15 typically include speech therapy, occupational and physical therapy. Given the overlap in symptoms with the autism spectrum (Rineer, Finucane & Simon, 1998), interventions typically used for children with autism spectrum disorders are also likely to be beneficial (see Wolf, Fein & Akshoomoff, in this volume). There have been no intervention studies conducted to date.

Neurofibromatosis-1

Neurofibromatosis-1 (NF-1) is an autosomal dominant disorder resulting from a mutation on chromosome 17 that has the potential to affect multiple organ systems (NIH NF-1 Consensus Development Conference held in 1988; Kayl & Moore, 2000). A wide variety of clinical manifestations have been documented, ranging from severe cosmetic disfigurement and brain tumors to café-au-lait spots and freckles (Kayl & Moore, 2000). Morphological studies have indicated overall larger brain volumes and the existence of unidentified hyperintensities, generally located in subcortical and hindbrain regions (Cutting *et al.*, 2004). Research on the impact that these abnormalities have on cognitive functioning has been inconsistent, with earlier studies finding no association (Dunn & Roos, 1989; Duffner *et al.*, 1989), and more recent studies suggesting a link between the two (Goh *et al.*, 2004).

The cognitive profile of NF-1 is generally associated with low average to average intellectual ability, although the rate of mental retardation is about twice that of the general population (North, 2000). There is also a high risk for learning disabilities and attentional difficulties in this population, with prevalence rates ranging from 30 to 65% (Johnson, Wiggs & Stores, 2005; North, 2000). Studies on the neurocognitive profile of NF-1 have found a variable pattern of abilities, but results generally indicate predominant weaknesses in the development of visuospatial skills, fine motor skills, and executive functioning (North, 2000). Although these individuals show deficits when attempting complex motor tasks, average range performance on more basic motor tasks, such as finger tapping, has been documented (Johnson, Wiggs & Stores, 2005). Less consistent findings have been found in the area of language (see Moore & Denckla, 2000 for a review). However, a few studies have highlighted difficulties with receptive and expressive language, phonological awareness, nonsense word decoding, single-word reading, and associated linguistic memory (Billingsley *et al.*, 2003). Based on these patterns of difficulty, suggested interventions include reading assistance that focuses on phonemic awareness, as well as speech and language therapy, and guidance in executive functioning (Johnson, Wiggs & Stores, 2005); notably however, very few studies have been conducted looking at remediation of learning and attentional concerns in children with NF-1. The sensitivity and specificity of the cognitive pattern of strengths and weaknesses in NF-1 have not been demonstrated. It appears that there is considerable variability in the phenotype (Kayl & Moore, 2000; North, Hyman & Barton, 2002).

The behavioral phenotype in neurofibromatosis includes an elevated risk for Attention Deficit/Hyperactivity Disorder, with 30–50% meeting ADHD criteria (Mautner *et al.*, 2002). Additional concerns include social problems, anxiety, depression, withdrawal, and obsessive-compulsive behavior

(Dilts *et al.*, 1996; Johnson, Wiggs & Stores, 2005). Parents reports of children and adolescents with NF-1 included higher ratings of social difficulties as well as internalizing and externalizing problems, in comparison with national norms on the CBCL (Johnson *et al.*, 1999).

Interventions for persons with NF-1

Since there has been little research addressing how to best support learning disabilities in NF-1, it has been suggested that approaches similar to those used in the typically developing population be employed (Cutting *et al.*, 2004). Recommendations for addressing attention concerns include a multimodal approach which incorporates stimulant medication with social skills training that targets specific deficits (Barton & North, 2004). Stimulant medication has been found to have beneficial effects in treating attention difficulties in neurofibromatosis (Mautner *et al.*, 2002). Johnson *et al.* (1999) proposed several interventions for addressing social and emotional difficulties in NF-1, including informing families of the heightened risk for these difficulties, conducting thorough evaluations for other areas of functioning which may impact the appearance of these difficulties, regular administrations of measures to assess behavior, and treatment for psychosocial difficulties.

22q11 Deletion syndrome (22q11 DS)

This syndrome, also referred to as velocardial-facial syndrome, results from a microdeletion on chromosome 22q11 (Driscoll *et al.*, 1993). Physical features include congenital malformations such as short stature, scoliosis, cardiac abnormalities, and cleft palate. Neuroimaging studies have indicated overall smaller brain volumes with particular reductions in white matter, relatively enlarged frontal lobe, lack of symmetry in parietal lobe tissue with reductions in grey matter in the left hemisphere (Eliez *et al.*, 2000; Kates *et al.*, 2001), differential symmetry of the head of the caudate (Sugama *et al.*, 2000), and increased cerebral spinal fluid in the temporal and posterior brain regions (Bearden *et al.*, 2004).

Cognitive abilities range from average to moderately impaired, with mean IQ falling in the borderline range (Sobin *et al.*, 2005; Swillen *et al.*, 2000). The pattern of skill development in 22q11 DS includes a relative strength in language with impairment in visuospatial abilities, nonverbal reasoning (Sobin *et al.*, 2005; Swillen *et al.*, 2000), and abstract reasoning (Golding-Kushner, Weller & Shprintzen, 1985). These deficits, combined with findings that reading and spelling are relatively stronger than math scores, has led some researchers to suggest a pattern consistent with the cognitive features of Nonverbal Learning Disability (Moss *et al.*, 1999). Generally, receptive language abilities

are superior to expressive skills; this is likely to be attributable to severe articulation difficulties found among individuals with 22q11 DS, as evidenced by improvement in expressive language abilities following surgery and speech therapy (Shprintzen, 2000).

The behavioral phenotype in 22q11 DS generally includes a pattern of withdrawal, shyness, and impulsivity (Dykens, Hodapp & Finucane, 2000; Shprintzen, 2000; Swillen *et al.*, 1997), as well as social difficulties (Swillen *et al.*, 1999). Psychopathology concerns include separation anxiety disorder, phobias, and obsessive-compulsive disorder (Shprintzen, 2000). In addition, Papolos *et al.* (1996) found high rates of symptoms suggestive of bipolar disorder and ADHD. Reports of psychosis, including schizophrenia, and personality disorders have also been cited (Pulver *et al.*, 1994).

Interventions for persons with 22q11 Deletion syndrome

Little empirical investigation has been undertaken with regard to interventions with this population. Recommended interventions include computer assistance for class instruction (Kok & Solman, 1995), as well as occupational and physical therapy to address motor delays, although no outcome research exists to date on the effectiveness of these interventions in individuals with 22q11 DS (Shprintzen, 2000). There is some indication that psychopharmacological treatment with methylphenidate for attention difficulties in this syndrome may lead to a manic state (Papolos *et al.*, 1996), suggesting that further study as to appropriate medication management is warranted.

5p- syndrome

Cri du chat syndrome, or 5p- syndrome as it is now more often called, results from a partial deletion on the short arm of chromosome 5 (Niebuhr, 1978). Neuroimaging and radiological studies are sparse, but appear to indicate atrophy of the brainstem at the pontine level and cerebellar abnormalities (Kjaer & Niebuhr, 1999; Tamraz *et al.*, 1993). The cognitive profile in 5p- syndrome includes abilities generally falling in the profound mental retardation range, in addition to substantial delays in language ability (Carlin, 1990). Speech intervention and use of sign language have been recommended for individuals with 5p- syndrome. One study found that these interventions led to some speech development in 50% of a sample of 62 individuals with 5p- syndrome, with 75% utilizing sign language as a primary communication modality (Carlin, 1990). Increased language development has also resulted in a reduction in behavioral problems.

The behavioral phenotype in 5p- syndrome includes problems with attention, concentration, and impulsivity, as well as aggressive, self-injurious, and

stereotyped behaviors (Dykens *et al.*, 2000). Examination of play behavior in young children with 5p- syndrome found that over half the time was spent engaging in nonproductive and non-play behaviors, which lends credence to the hypothesis of excessive activity in this population (Sarimski, 2003). One study examining parent-reported behaviors in a sample of 66 families with 5p- syndrome found that 82% of affected children reportedly engaged in stereotyped behavior, with aggressive behavior occurring in 88% of study participants (Collins & Cornish, 2002). Additionally, self-injurious behaviors were reported for 92% of children.

Interventions for persons with 5p- syndrome

Cornish and Bramble (2002) recommend using nonverbal strategies in behavioral intervention to avoid reliance on verbal skills, given that they are a primary weakness in children with 5p- syndrome. Results from a case study indicated that teaching a two-and-a-half-year-old child daily living skills, including eating and rolling a ball, led to a decrease in self-stimulating and self-injurious behavior (Denny *et al.*, 2001). Few other intervention studies exist for this population and more systematic studies of intervention approaches are strongly warranted.

Williams syndrome

Williams syndrome is a neurodevelopmental disorder resulting from a hemizygous microdeletion of at least 20 genes on chromosome 7q11.23 (Hillier *et al.*, 2003). Physical features of Williams syndrome include dysmorphic facial features, stunted growth, and musculoskeletal problems, as well as connective tissue abnormalities including congenital heart abnormalities (Morris & Mervis, 1999). Results of a recent neuroimaging investigation (Reiss *et al.*, 2004) indicate that, in comparison with healthy controls, adults with Williams syndrome show overall reduction in brain size, and significant reductions in cerebral and brainstem volumes, with no differences in cerebellar volume. After controlling for cerebral cortical reduction, Reiss and colleagues found significant reductions in occipital cortex and thalamic gray matter in the Williams syndrome group; these are areas known to play a role in visual–spatial processing. Also identified were significantly larger amygdala, superior temporal gyrus, orbital prefrontal cortex, and dorsal anterior cingulate. A recent fMRI (functional magnetic resonance imaging) investigation found consistent hypoactivation of an area of the parietal cortex commonly associated with visuospatial construction tasks for individuals with Williams syndrome compared with well-matched controls (Meyer-Lindenberg *et al.*, 2004). Meyer-Lindenberg and colleagues (Meyer-Lindenberg *et al.*, 2005) also found significantly diminished amygdala activity in response to viewing

threatening faces and, conversely, increased activity while viewing threatening scenes, relative to age, sex, and IQ matched controls.

Although Williams syndrome is a rare disorder (i.e. it is reported at an incidence of 1 in 7500; Stromme, Bjornstad & Ramstad, 2002), the cognitive and behavioral phenotypes are increasingly well defined (see Mervis & Klein-Tasman, 2000 for a review). Research about the cognitive abilities of individuals with Williams syndrome has identified a characteristic pattern of strengths and weaknesses (Mervis *et al.*, 2000), which has been described as the Williams Syndrome Cognitive Profile. This profile appears to be characterized, across development, by a relative strength in auditory short term memory, as measured by digit span tasks; language abilities at or above general cognitive ability levels; and a significant weakness in visuospatial constructive skills and fine motor dexterity. Fluid linguistic abilities are usually present, although delays in early language acquisition are the norm rather than the exception (Mervis & Robinson, 2000). This profile has been observed in non-English-speaking populations as well (Vicari *et al.*, 2004). In terms of adaptive functioning, personal care and domestic responsibility, skills appear to be areas of relative weakness, possibly due to visuospatial constructive and motor difficulties (Mervis, Klein-Tasman & Mastin, 2001).

Individuals with Williams syndrome tend to be highly sociable, while at the same time anxious and tense (Klein-Tasman & Mervis, 2003). Persons with Williams syndrome typically show a strong interest in social interaction which is observable even in infancy (Mervis *et al.*, 2003). However, they are ultimately unsuccessful at establishing sustained friendships with peers (Davies, Howlin & Udwin, 1997; Davies, Udwin & Howlin, 1998) and social–communicative deficits have been reported (Laws & Bishop, 2004). Elevated levels of anxiety, fear, and worry as well as a high rate of attention problems have been observed (Dykens, 2003; Leyfer *et al.*, 2006). Although elevated levels of depression have not been reported in the literature, Dykens and her colleagues (2000) caution against overlooking possible depressive symptoms, given the generally happy presentation of individuals with Williams syndrome. Additionally, high levels of sound sensitivity have been observed, with accompanying problem behaviors in response to this sensory sensitivity (Levitin *et al.*, 2005).

Interventions for persons with Williams syndrome

To support cognitive development, linguistically based interventions such as rhyming games, songs, and a phonetic approach to reading have been suggested, to take advantage of strengths in auditory skill and memory (Hodapp & Desjardin, 2002). As early language development is typically delayed, most people with Williams syndrome receive speech therapy. Occupational therapy to address

visuomotor construction difficulties is also recommended. In addition, given the genetic basis for the difficulties with visuospatial construction, it is often recommended that motor skills and written tasks be accommodated and modified, with an emphasis placed instead on the use of computers for written work and greater emphasis on verbalization for problem solving (Dykens & Hodapp, 1997). Most people with Williams syndrome receive occupational therapy. However, no empirical studies have been undertaken to validate these interventions.

Regarding psychosocial functioning, several authors have recommended a variety of behavioral interventions for persons with Williams syndrome, based on syndrome-specific characteristics (Dykens & Hodapp, 1997; Dykens *et al.*, 2000; Semel & Rosner, 2003). These suggestions have targeted attention difficulties, hyperacusis, obsessive thinking, anxiety, depression, and social skills difficulties (Dykens *et al.*, 2000; Semel & Rosner, 2003), as well as impulsivity, adaptability, and low tolerance for frustration (Semel & Rosner, 2003). Dykens and Hodapp (1997) have discussed using an individual's strengths as a guide for determining particular interventions, including capitalizing on linguistic strengths and the interest in others, through the use of talk and group therapies; and incorporating music into intervention approaches. Dykens and colleagues have suggested that people with Williams syndrome may benefit from minimization of distractions and other interventions typically used with children with ADHD, as well. With regard to sensory sensitivity, they suggest helping to provide children with a sense of control over exposure to loud noises by giving notice that a loud sound will occur, and one case study found that earplugs were useful. Discussion of obsessive interests has also been recommended as a motivator for task completion. Brief reassurance and distraction are recommended strategies for addressing fears. There is also generally a need for social skills training to support development of friendships as well as appropriate stranger-wariness. Semel and Rosner (2003) emphasized the use of reinforcement, distraction, and clear instructions, in addition to capitalizing on verbal strengths, when working with persons with Williams syndrome. There are no studies evaluating the efficacy of these suggested treatment approaches for the behavioral difficulties seen in Williams syndrome; as such, the efficacy and validity of these recommendations is uncertain at best.

Transition to adult independence: an area of particular neglect

As is evident from the review above, several intervention modalities typically emerge for individuals with genetic syndromes associated with intellectual disability. These include speech therapy, occupational therapy, and physical therapy, and interventions to address psychosocial or behavioral issues. Given that the

ultimate goal is to provide psychoeducational and behavioral supports in childhood that maximize independence in adulthood in the community, it is particularly surprising that there is so little mention of recommendations or research regarding successful transition planning for people with genetic syndromes.

Transitions can be considered points of relative vulnerability for children with special needs (Bernstein, 2000). The transition between secondary school and young adulthood poses unique challenges. Milestones such as securing employment, obtaining post-secondary education, and learning to live independently may be particularly daunting for students with special needs. Young adults with disabilities are at higher risk for high school drop-out and experience poor employment success (Hasazi *et al.*, 1989), and fewer than 8% of young adults with disabilities are either fully employed or enrolled in further education, living active social lives, and living independently in their communities (Wagner, 1995).

The Individuals with Disabilities Education Act (IDEA) specifies that transition planning should be based on the outcome, incorporating employment and adult living objectives as well as community experiences, with services to be based on the student's interests and preferences (see Maedgen and Semrud-Clikeman, this volume). Specific components to successful transition plans have been identified in the literature. Students with disabilities fare better in regard to post graduation employment success when they have experienced employment experiences and vocational training as part of their curriculum (Sax & Thoma, 2002; Hasazi, Gordon & Roe, 1985). Training in specific skills such as completing job applications, interviewing, working, and adapting skills to meet work-site demands should be provided for students with disabilities (Burdick, Pond & Yamamoto, 1994). Hands-on participation in work experiences and curriculum targeting vocational skills during secondary school are associated with higher levels of post-secondary school employment (Colley & Jamison, 1998). Teaching such skills in the context of an instructional strategy emphasizing problem solving skills and considering decisions as related to future consequences should be implemented as a way to enhance self-determination. Relevant Individual Education Plan goals include reducing the level of input from others in decision-making, and increasing the degree of risk in situations where the student is allowed to make choices (Leggett & Bates, 1996).

Given the comprehensive nature of their evaluations and considerations, pediatric neuropsychologists are uniquely positioned to identify cognitive and behavioral strengths, advocate for the student, provide psychoeducational and consultative services to family and school personnel, and support realistic expectations. Transition planning at earlier developmental periods includes similar themes of optimally supporting development and developing appropriate parental expectations (Rosenkoetter, Hains & Fowler, 1994). Consideration of the etiology

of intellectual disability, including the developmental trajectory and challenges present for that particular etiology of mental retardation, as well as literature regarding effective interventions, should be central to the assessment and recommendation process (Bernstein, 2000). Little if any empirical work has been conducted concerning individual variables in transition planning, and there are no empirical publications about transition plans for particular genetic syndromes.

Future directions for intervention research

As is evident from the review above, there is very little available empirical research about the types and effectiveness of interventions for children with genetic syndromes associated with intellectual disability. With few exceptions, the intervention research currently published consists of case reports, some small group studies, and a preponderance of clinical impressions and informed speculation. Intervention studies that do exist generally do not include contrast groups or even wait-list controls, and as a result, specificity is uncertain.

Given the rarity of the disorders discussed in this chapter, the preponderance of case study investigations and recommendations based on clinical impressions is to be expected. A single case-based approach has a clear set of associated strengths and is valid for considering possible forms of support and intervention (see Morgan & Morgan, 2003). However, a downside to this individualized approach for more subtle cognitive, behavioral, and emotional difficulties is that those practitioners conducting interventions with children with intellectual disabilities are forced to recreate the wheel for each client seen, when they might benefit from broader experiences when treating common problems.

Although not reviewed in this chapter, there is a lack of empirically based literature about effective interventions for children with intellectual disabilities more generally. At the same time, children with less than average intellectual abilities are often excluded from evaluations of treatment efficacy in the empirically supported intervention literature (e.g. Kendall, 1994; Pfiffner & McBurnett, 1997; TADS Team, 2004). Children with intellectual abilities falling in the mildly delayed or borderline range are particularly neglected in the treatment literature. Many children with the genetic disorders associated with intellectual disabilities reviewed in this chapter fall in this range, which represents a particular chasm in the literature.

It is possible, even likely, that client variables such as etiology may moderate successful treatment, and particular etiologies of intellectual disability may be associated with particular intervention needs. The rarity of the disorders reviewed here provides a particular challenge to researchers to be creative in their research endeavors. As such, it may be helpful to take a cue from the empirically

supported interventions approach present in regard to more general psychopathology (see Chambless *et al.*, 1998; Chambless & Ollendick, 2001; King & Ollendick, 1998), by developing protocols (see Kerwin, 1999; Mindell, 1999) to manage common clusters of problems which are present for people with particular genetically based neurodevelopmental disorders. Experts with knowledge of a particular etiology of intellectual disability could then collaborate with colleagues who conduct treatment research with typically developing populations, to develop promising treatment protocols based on the profiles of strengths, weaknesses, problematic behavior, and emotional experiences that present. Use of protocols for typically developing children will likely require modification for use with children with cognitive impairments and their families.

Although development of promising protocols is one critical step, dissemination of the protocols is also challenging. A given practitioner is unlikely to see more than one or two children with a particular disorder. It would be helpful if the protocols developed could be shared with community practitioners and other professionals, with encouragement to collect local data about the feasibility and effectiveness of the suggested interventions (see Addis, 1997 and Herbert, 2003 for discussions of treatment dissemination). With the use of the internet, it is possible to design web portals for practitioners to report about their successes and failures, to more effectively hone treatments. In this way, better advantage of individual creativity and innovation can be taken, while at the same time contributing to over research-based knowledge.

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12

Remediating specific learning disabilities

Karen E. Wills

Neuropsychologists have collaborated with neurologists, educational and school psychologists, and other educators, in studying the nature and treatment of specific learning disabilities (SLD) (e.g. Lyon *et al.*, 2006; Semrud-Clikeman, Fine & Harder, 2005; Moats, 2004). For many years, neuropsychologists have focused their efforts on identifying cognitive correlates of SLD, working from the perspective that children with SLD had qualitatively different learning styles or information processing abilities when compared with other children. However, except for well-replicated difficulties with phonological processing and naming speed among young children at risk of reading problems, consistent correlates or predictors of these differences in learning have not been found. Furthermore, while research on the etiology of SLD, including isolation of chromosomal anomalies in some families with reading disabilities (Plomin & Kovas, 2005), has clarified a biological basis for some SLDs, it has not directly contributed to enhancing either identification or remediation.

Concurrent research in neuropsychology, behavioral genetics, and developmental neuroscience has led to a reconceptualization of the developing brain as "plastic," and influenced by its milieu throughout the lifespan. For example, functional neuroimaging research has documented brain plasticity in response to reading interventions, buttressing studies showing that specific interventions can improve reading skills in people with dyslexia (Shaywitz *et al.*, 2004). Recent studies have confirmed structural and functional brain differences between good and poor readers. Effective reading instruction changes the pattern of brain activation among beginning readers, whether they are learning to read at a typical pace, struggling with their reading, or learning to read after years of dyslexia. In particular, studies have demonstrated that there is increased activation of left temporal lobe language processing systems during reading, as readers become more proficient. As struggling or dyslexic readers learn to read, the pattern of brain activation shifts towards that seen in normally fluent readers (Aylward *et al.*, 2003; Papanicolaou *et al.*, 2003; Sarkari *et al.*, 2002; Shaywitz *et al.*, 2004; Simos *et al.*, 2002; 2005).

At one time, it was presumed that any brain-based problem such as SLD was permanent, life-long, and intractable. Many of the laws governing special education placement and programming reflected this view. Indeed, the intractable nature of SLD has been assumed, based upon the fact that 70% of children in special education placement for third grade are still diagnosed with SLD at high school graduation (Shaywitz *et al.*, 1999). However, research on brain activation during reading, as well as research on reading behavior, has led to a reconceptualization of reading problems (e.g. dyslexia). Reading disorders are conceptualized as (a) brain-based, (b) increasingly difficult to remediate with increasing age, but (c) amenable to ''normalization'' given intensive, well-designed treatment provided as early as possible (Lyon *et al.*, 2006). While there may be some children whose reading disabilities are indeed intractable, such cases are perhaps fewer than has been assumed.

Existing, hard-won, civil rights protections remain critically important for those children with intractable SLD; however, there is increased emphasis on truly remediating rather than merely accommodating the disability whenever possible. Although there is less evidence of effective remediation for math and writing disabilities, these also are presumed to be amenable to treatment if the right treatment strategies can be identified through well-designed empirical research. The first step in doing such research is to define and identify which children have SLD.

Defining specific learning disabilities

Efforts to define SLD have a long, complex, and sometimes contentious history woven of educational trends, scientific knowledge, political agendas, and cultural values. That history is well documented elsewhere (Hallahan & Mock, 2003; Lyon *et al.*, 2006). Of particular importance, however, in the context of this book's focus on remediation, is the change in the United States' 2004 special education law, which now strongly emphasizes children's response to intervention (RTI) as a determinant of SLD status (Donovan & Cross, 2002; President's Commission on Excellence in Special Education, 2002; see Maedgen & Semrud-Clikeman, this volume). This change is anticipated to have a broad impact on how, at least in the US, learning disabilities are defined, identified, and addressed. Changing the definition and identification process also significantly impacts research on the epidemiology, etiology, and remediation of SLD. Research over the past 20 years or so, including that conducted by neuropsychologists such as Reid Lyon and Jack Fletcher, has substantially informed the legal reconceptualization of SLD (Fletcher *et al.*, 2004). In turn, new education laws, if adequately funded, should promote an increased amount and quality of educational intervention research

which could further refine SLD definitional criteria and assessment procedures. Therefore, the US federal definitions of SLD will be used as a convenient starting point for discussing effective SLD interventions.

From 1975 through 2004, although specific rules varied from state to state, legal definitions of SLD in the US typically required the identification of a severe ability-achievement discrepancy. Ability has usually been operationalized as an IQ score on tests such as the Wechsler or Stanford-Binet Intelligence Scales, while achievement has been represented by a standardized composite reading, math, or writing score on a test such as the Woodcock-Johnson Tests of Achievement or Wechsler Individual Achievement Test. This "discrepancy criterion" was supposed to separate the "learning disabled," whose average to better intellectual ability should enable them to respond well to individualized instruction in specific subject areas, from "slow learners," who were expected to lag persistently behind same-age peers despite remedial academic interventions.

The discrepancy criterion has not served its intended purpose, however. Educational and psychological research has shown no consistent, meaningful differences in the nature and severity of learning disabilities or in the rate of gain in response to intervention, between children with and without an ability−achievement discrepancy (Francis *et al.*, 2005). The discrepancy criterion provides no information about the nature or severity of the child's specific learning problems, so it does not help educators to tailor interventions to the needs of the individual child. Often intervention is postponed until children fall "far enough behind their ability" on achievement tests (often, not until second or third grade, or later). At that later age, it is significantly harder for children to "catch up" with their peers' academic skills (Torgesen *et al.*, 2001). Children struggling with early learning skills, particularly those with language difficulties, may obtain low scores on IQ tests as well as on achievement measures, exhibiting no discrepancy and therefore failing to qualify for special education help. Groups defined as "SLD" by a discrepancy criterion are not stable over time (Francis *et al.*, 2005); as maturation, instruction, changes in the nature of tested skills, and test score variability affect the magnitude of ability−achievement differences.

The 2004 reauthorization of the US Federal Individuals with Disabilities Education Act (IDEA-2004, signed into law in December 2004 and effective July 1, 2005) explicitly removed the "discrepancy criterion" as a required basis for determining a child's eligibility for SLD support services, a substantive change from the 1997 and earlier versions of IDEA. In coming years, individual states will be developing their own specific procedures for interpreting and applying IDEA-2004, but as of July, 2005, "a local educational agency shall not be required to take into consideration whether a child has a severe discrepancy between achievement and intellectual ability" (P.L. 108−446, Statute 2658, Section 614,

Part 6A). IDEA-2004 provides a broad definition of SLD, with inclusion and exclusion criteria specified:

(A) IN GENERAL.—The term ''specific learning disability'' means a disorder in 1 or more of the basic psychological processes involved in understanding or in using language, spoken or written, which disorder may manifest itself in the imperfect ability to listen, think, speak, read, write, spell, or do mathematical calculations.
(B) DISORDERS INCLUDED.—Such term includes such conditions as perceptual disabilities, brain injury, minimal brain dysfunction, dyslexia, and developmental aphasia.
(C) DISORDERS NOT INCLUDED.—Such term does not include a learning problem that is primarily the result of visual, hearing, or motor disabilities, of mental retardation, of emotional disturbance, or of environmental, cultural, or economic disadvantage. (P.L. 108−446, Section 602(30))

Assessment of SLD

The 2004 IDEA states that an evaluation to determine whether a child has a disability warranting special education must ''use a variety of assessment tools and strategies to gather relevant functional, developmental, and academic information'' and ''use technically sound instruments that may assess the relative contribution of cognitive and behavioral factors, in addition to physical or developmental factors'' [(Section 614(b)(2)]. Provisions are added stating that assessment tools

(i) are selected and administered so as not to be discriminatory on a racial or cultural basis; (ii) are provided and administered in the language and form most likely to yield accurate information on what the child knows and can do academically, developmentally, and functionally, unless it is not feasible to so provide or administer; (iii) are used for purposes for which the assessments or measures are valid and reliable; (iv) are administered by trained and knowledgeable personnel; and (v) are administered in accordance with any instructions provided by the producer of such assessments. (P.L. 108−446, Statute 2658, Section 614(b))

The child is to be assessed in all areas of suspected disability, and ''assessment tools and strategies that provide relevant information that directly assists persons in determining the educational needs of the child'' are to be utilized (IDEA, 2004). The child cannot be determined to have an SLD if academic deficiency is due to lack of English proficiency, lack of instruction in math, or lack of ''appropriate instruction in reading, including the essential components of reading.'' Those essential components of reading as specified in the 2001 revision of the Elementary and Secondary Education Act, which has been called ''No Child Left Behind,'' (ESEA-2001), include: ''(A) phonemic awareness; (B) phonics; (C) vocabulary development; (D) reading fluency, including oral reading skills; and (E) reading comprehension strategies.'' [P.L. 107−110, Section 1208(3)].

P. L. 107–110 further defines "reading" as involving motivation to read, and possession of sufficient background information and vocabulary for reading comprehension, in addition to these 5 essential component skills.

Finally, IDEA-2004 specifies that "[i]n determining whether a child has a specific learning disability, a local educational agency may use a process that determines if the child responds to scientific, research-based intervention as a part of the evaluation procedures" [P.L. 108–446, Statute 2658, Section 614 (b)(6)(B)]. Criteria for scientifically based reading research are precisely defined, with respect to reading in P.L. 107–110, Section 1208(6), as objective, peer-reviewed, data-based, well-designed empirical studies. Thus, IDEA-2004 places strong emphasis on assessment of specific competencies and needs, goal setting and specific outcome measures, and assessment of the quality and validity of the intervention procedures as well as of individual variability in children's response to intervention (RTI) (Donovan & Cross, 2002; Lyon *et al.*, 2001; President's Commission on Excellence in Special Education, 2002; Steubing *et al.*, 2002).

The traditional psychometric or "test, place, and program" model for SLD determination, now falling out of favor, included 3 steps: (a) a child struggling academically is referred by teacher or parent for psychological testing; (b) tests of intelligence, academic achievement, and sometimes other relevant cognitive abilities (phonological awareness, naming speed, etc.) are administered; and (c) if the child meets state-mandated criteria on some combination of IQ, achievement, and information-processing tests, some type of individual or small group instruction is provided, generally in a pull-out special education room by a specialized instructor. The RTI or "prevent, program, test, and reprogram" model, recommended in the proposed regulations under IDEA-2004, includes several steps which differ in terms of the teacher–student ratio, the amount of time spent on individual versus larger group instruction, and the extent to which the instructional content is specifically responsive to the academic needs of an individual student. Steps included in an RTI model include:

(a) In schools or classrooms where a high percentage of children are known to be at risk of academic delay, additional teacher training in effective instructional methods is provided; this "enhanced whole-class instruction" is the "primary prevention" measure;
(b) All students are screened using measures of phonological awareness and naming speed to identify those whose difficulties predict delay in learning to read (since these scores predict reading difficulty, which is associated with writing and math difficulties);
(c) All students are monitored to assess response to whole-class instruction, and those making poorest progress are assigned to more intensive small-group

instruction (e.g. 30 minutes per day in a group of 5 or 6 students using a structured curriculum); this would be a ''secondary prevention'' strategy;

(d) Students who still fail to progress adequately would be assigned to a highly individualized curriculum, with content specifically tailored to their academic needs, and more intensive support (e.g. 2 hours per day in a group of 1 to 3 students).

While some have argued for the abolition of any formal testing, other than measures of specific academic skill mastery, many psychologists and neuropsychologists would advocate a less radical approach. For example, Fletcher *et al.* (2005) advocate use of low achievement, combined with RTI, and assessment of comorbid disorders as a model for assessment and identification of SLD. In addition to assessments that specify which academic skills the child has mastered, and which are lacking, other tests, interviews, and questionnaire measures can be used to identify factors likely to impede or facilitate the child's participation in the treatment process. Relevant comorbid factors include, for example, problems with attention, memory, and executive function; communication disorders; social, emotional, and behavioral difficulties; and family and community stressors. Conversely, factors that might facilitate response to treatment include family and community resources, advanced language skills and mature adaptive, social-emotional, and self-advocacy skills. Research to identify such ''moderator'' variables is an essential enhancement of the RTI model.

A major drawback of the traditional model is its ''snapshot'' or ''one shot'' approach to assessment, which lacks continuous monitoring of treatment progress or outcome. To monitor progress in children identified by the RTI model as ''at risk'' or as having SLD, Lyon *et al.* (2006) discuss strategies and advantages of curriculum-based measurement (CBM). CBM can be utilized by teachers to set goals, monitor progress towards the goal, and systematically raise goals or adapt instruction when student progress exceeds expectations (Fuchs, Fuchs & Hamlett, 1989). Just as with traditional assessment, CBM per se, even with repeated measurement, does not improve outcomes for SLD students; but when teachers use CBM systematically to raise the bar as students succeed, or provide extra help when students fall short of goals, educational outcomes are improved.

Remediating SLD in reading

Reading decoding

Current research and public policy emphasizes prevention of SLD, first and foremost, to reduce remedial demand and costs. Despite methodological limitations of many studies, there is strong data to indicate that early intervention can reduce the number of students who have significant reading difficulty to less

than 10% of the class. This is accomplished by providing small group, phonics-based instruction to kindergarten to first grade students who fall in the bottom quartile on group-administered reading tests or teacher ratings of reading prowess. Some studies have yielded positive results for all but 2% of "at risk" beginning readers (Denton & Mathes, 2003; Lyon *et al.*, 2006; Torgeson, 2000). According to a recent comprehensive review by Lyon and colleagues (2006), gains appear to be greatest for comprehensive, integrated reading programs that include explicit instruction in phonics (the "alphabetic principle"), reading comprehension (deriving meaning from text), and fluency (providing opportunities for practice). Moreover, gains appear to be lasting for children who respond well to interventions during kindergarten and first grade (e.g. once a child's reading improves, s/he does not "drop back" to being a poor reader).

The National Center for Education Statistics (2003) reported that 37% of fourth-grade children (60% of those living in poverty) could not read at the most basic level required to meet grade-level educational standards. So, the "first tier" of reading intervention under the Elementary and Secondary Education Act of 2001 is [P.L. 107–110, Section 1208] to improve teacher education and early reading instruction for all children in the preschool to first-grade levels. This could be considered a "primary prevention" approach to minimizing the emergence of reading problems.

Proposed regulations based on IDEA-2004 suggest that all children struggling to comprehend or produce grade-level work, despite good reading instruction, should be given empirically validated remedial teaching, the earlier the better. Those who respond by "catching on and catching up" would not be considered to have a "specific learning disability." This "secondary prevention" approach has proven effective in research studies on children at high risk of developing reading disabilities, including children whose parents' reading disabilities contribute both genetic and shared environmental risk factors for reading problems (Wadsworth *et al.*, 2000) and children living in poverty, who tend to have more limited verbal interaction and literacy exposure from parents, compared to more affluent children (McLelland, Kessenich & Morrison, 2003; Tunmer, Chapman & Prochnow, 2003). Such programs (reviewed in detail by Lyon *et al.*, 2006; Kamps & Greenwood, 2005) provide frequent, structured, small group work on explicit, phonics-based reading instruction.

Children who show limited progress even with this "second tier" intervention would be categorized as "SLD" and provided with yet more intensive "third tier" intervention, such as daily individual or very small group (3 to 5 students) remedial tutoring, for longer time periods with increased individual explanation and feedback. In published studies, it appears that the content of instruction does not change appreciably from the "second tier" interventions, but the format shifts

closer towards one-to-one tutoring. Small group instruction (3 students per teacher) has been shown to work as well as one-to-one; larger groups (10 to one) are less effective (Lyon *et al.*, 2006). According to Lyon *et al.* (2006), Torgeson's (2004) PASP (phonological awareness plus synthetic phonics) program, and other programs emphasizing phonological awareness and phonemic decoding skills (Blachman, 1997; Vellutino, Scanlon & Jaccard 2003) have yielded significant improvement in reading abilities of at-risk early readers. ''Reading Recovery'' (Shanahan & Barr, 1995) has been shown to be significantly more effective when modified to include explicit instruction in phonological awareness and phonics (Tunmer *et al.*, 2003). Programs that emphasize phonological awareness only, without explicitly tying word-segmentation and word-blending skill to printed letters and text, do not appear to effectively improve children's reading—decoding skills (e.g. Pokorni, Worthington & Jamison, 2004).

Tutoring every struggling child would be prohibitively expensive, and therefore, a major emphasis of recent studies has been to demonstrate effectiveness of whole class or small group interventions. These have proven effective for a majority of students. On the other hand, some students (around 5 to 10% across published studies) fail to progress given enhanced teacher preparation and small group, moderately intensive instruction. These are the students who clearly need more one-to-one help. Models for a ''layered'' approach (Lyon *et al.*, 2006) show that pull-out tutoring in very small groups (no more than 1 teacher to 3 students) conveyed a clear advantage, over enhanced teacher-training in classroom reading instruction, for students who were struggling most during kindergarten and first grade. These studies did not take a sequenced approach; rather, they assigned students to different levels of instructional intensity based on the severity of initial lags. Therefore they do not provide a clear model of what might happen in the sequenced RTI model currently being advocated.

Models for the ''sequenced'' approach, in which children who initially do not respond to focused classroom teaching are subsequently pulled out for small group or individual tutoring, also have been studied. Coyne *et al.* (2004) showed that some ''at risk'' students responded well to kindergarten interventions and needed no further tutoring during first grade. Those who did not respond well in kindergarten needed continued intervention, with the poorest kindergarten responders requiring the most intensive first grade help. McMaster, Fuchs, Fuchs and Compton (cited in Lyon *et al.*, 2006) studied children's responses to a whole class intervention, the Process Assessment of the Learner (PALS) program, implemented over seven weeks. As found in previous studies, reading improved substantially with PALS, more so than with standard instructional practice, in both high-poverty and middle-class schools. Students whose reading did not

improve given the PALS program did better, subsequently, with one-to-one adult tutoring than with continued whole-class PALS.

O'Connor *et al.* (2005*a*), in a four-year, sequenced, multi-tier study of reading remediation, provide an example of how this approach to assessment and intervention might work from kindergarten to third grades. Students at risk for SLD in reading were identified based on kindergarten tests of phonological awareness and naming speed, and provided with either standard classroom instruction, or one or two layers of intervention. They found very substantial benefit to the whole class of kindergarten through third grade children from professional development for teachers (their "Layer 1" intervention), with enhanced integration of general education and special education teachers. Individual pull-out for special education was the Layer 2 intervention (small groups, three times per week), reserved for children who did not benefit sufficiently from Layer 1 teaching enhancement, alone. Importantly, "Layer 2" was "fluid" over the years, because children varied in the ease with which they mastered different aspects of the reading process; one child might need extra help with letter–sound pairings, another with blending, yet another with fluency. Very few students consistently scored below expectations at every testing cycle, and few scored low in every component of the reading process. These findings again support the notion of focused intervention rather than more global labeling, and of tailoring intervention to the child's specific needs rather than using a "one size fits all" approach. Layer 3 added daily 1:1 or 1:2 instruction and further aided the most severely struggling children (O'Connor, Harty & Fulmer, 2005*b*).

Some students who "caught up" to average reading levels continue to require Level 2 interventions in order to maintain their average standing; some others fail to respond even to the most intensive intervention. O'Connor and colleagues have suggested that those students who fail to benefit significantly from even the Layer 2 interventions are severely challenged by the increasing demand for competent reading as they move up into third grade, particularly when faced with new content vocabulary and increasingly complex language, e.g. in social studies and science texts. There are few studies that address the needs of students with severe, persisting reading disability. Clearly there remains a need to predict and explain these individual differences in response to instruction; that, perhaps, will be a key future role of psychological and neuropsychological assessment, in conjunction with neuroimaging and behavioral genetics.

Results of reading interventions are less encouraging for students identified at older ages (Torgeson *et al.*, 2001), but with specifically targeted, intensive, sustained intervention by well-trained teachers, significant gains can be seen even in children who are diagnosed with reading problems after third grade. Word recognition skills show most improvement, with smaller gains in reading

comprehension, and still smaller improvement in fluency. Limited fluency diminishes the child's reading comprehension for longer connected text, and reduces pleasure in reading, thereby limiting reading practice for most children. Not surprisingly, the extent of improvement in all areas is associated with students' age and with the severity of the delay, older and more severely impaired students showing smaller treatment gains even with intensive one-to-one intervention. Among older children, moreover, treatment gains appear less likely to be sustained over time without continued maintenance interventions.

A variety of specific remedial programs have been tested, with good results, but efficacy seems to depend upon certain common critical elements rather than any one published or experimental curriculum (Lyon *et al.*, 2006). These include commercially available tutoring programs such as Orton-Gillingham approaches, Lindamood Phoneme Sequencing Program (Lindamood & Lindamood, 1998), and Phono-Grafix (McGuiness, McGuiness & McGuiness, 1996), as well as experimental programs (e.g. Manset-Williams & Nelson, 2005) that present instruction in phonological awareness, sound-symbol association, syllables, morphemes, syntax, and semantics via direct, systematic, sequenced instruction and continuous individual monitoring of student needs. Intervention using Maureen Lovett's "PHAST Track" (phonological and strategy training) programs have yielded significant gains for severely delayed older readers, and studies are ongoing of PHAST PACES, a program for high school students with reading disabilities (Lovett, Barrett & Benson, 2003).

Some components of popular reading programs may be nonessential, for example, the multisensory component (i.e. having students see, hear, say, trace, and write letters to recruit auditory, visual, tactile and kinesthetic sensation), used with Orton–Gillingham tutoring, and the "phonological awareness" component of Lindamood tutoring (i.e. teaching children to segment words, clapping hands or placing blocks to mark each phoneme). Multisensory components may be helpful insofar as they are explicitly tied to learning letters and letter-groups. However, these instructional components have not been shown to facilitate improvement in reading skills over text-focused phonics instruction (Lyon *et al.*, 2006).

In summary, the most effective "learning to read" programs are those which include early identification of "at risk" and struggling readers, who can be identified on the basis of impairment in phonological awareness and rapid recognition of symbols, including letters or numerals), and that provide explicit, comprehensive, intensive instruction, including:

1. Explicit and systematic instruction in phonemic decoding (the alphabetic principle) at the level of syllables, morphemes, and words;
2. Explicit and systematic instruction in reading comprehension (deriving meaning from text), including instruction in vocabulary and word recognition;

3. Sufficient assisted practice to improve reading fluency or efficiency (speed of accurate decoding), such as assisted oral reading (Kuhn & Stahl, 2003), repeated oral reading of sight-words (Levy, 2001) and connected text (Stahl, 2004), and increased familiarity with recognizing linking orthographic patterns to word meanings (Wolf & Katzer-Cohen, 2001; Wolf, Miller & Donnelly, 2002);
4. Teaching to mastery (with continuous progress monitoring of individuals);
5. Providing emotional support and gradually incremented challenges (scaffolding);
6. Greater intensity (hours per week) and length (total duration) of instruction;
7. Teacher training and support, with monitoring to ensure that programs are implemented in the community schools as they were developed and validated in educational "labs";
8. Multiple "layers," both simultaneous (so that more severely disabled readers receive more time, smaller student–teacher ratio, closer individual monitoring, and more highly trained teachers) and sequential (so that students who do not make good progress in a whole class intervention are moved to a more intensive level of intervention).

Reading comprehension

Reading comprehension problems can occur in people who do not have problems with single-word decoding or fluency, though this is relatively rare. This pattern of SLD tends to be identified in the later elementary grades (Leach, Scarborough & Rescorla, 2003). Underlying these difficulties are problems with vocabulary knowledge, listening comprehension, and working memory, that can contribute to poor reading comprehension in older students, with or without decoding and fluency problems.

Interventions for reading comprehension difficulties have emphasized teaching text-analysis skills (i.e. vocabulary building, finding facts, identifying themes) and metacognitive strategies, such as predicting, justifying, and confirming meaning in the text and relationships between text concepts and prior knowledge. Additional strategies have included activating background knowledge; comprehension monitoring; and the use of graphic organizers (see Bos & Anders, 1990; Clark & Uhry, 1995). Instructional methods that incorporate both skills and strategies seem to produce optimal improvement in reading comprehension, better than teaching either alone.

Optimal instruction is explicit (not dependent on contextual or incidental learning), well supported and guided (not left to the student in isolation), adjusted to the individual learner via continuous progress monitoring, and includes programmed generalization across different sorts of text (Lyon *et al.*, 2006;

Vaughn & Klinger, 2004). The Kansas University Learning Strategies Curriculum (Schumaker, Deshler & McKnight, 2002) is an example of such a program shown to improve reading comprehension strategies and, more broadly, organizational and study skills, among students with and without SLD.

Remediating SLD in written expression

Berninger (2004) has identified several levels at which writing SLD can occur, namely, (a) handwriting legibility or automaticity; (b) spelling; and (c) compositional fluency or quality. Writing is viewed as involving multiple essential components including motor and sensory-motor skills (visual, kinesthetic, proprioceptive, vestibular); language skills (orthographic, phonological, and morphological knowledge, as well as vocabulary, sentence, and discourse formulation); concept-formation; attention and executive function; memory; affect; and motivation. Consistent with the variability that underlies writing difficulties, the brain systems that contribute to writing change with maturation, practice, and/or attained skill level. Initially, brain areas associated with motor learning are presumed to be most important (e.g. the primary motor areas, cerebellum, and frontal areas), whereas in skilled writing performance, association areas and neural networks that support the fine-tuning of motor control processes are presumed to play a more important role (e.g. the motor association cortex, basal ganglia, and parietal areas). As such, there are a number of potential sources of complication, in the development of written expression (Berninger *et al.*, 2006; Graham *et al.*, 2006).

Writing involves motor processes at the ''gross'' level (e.g. sitting balance, position, and posture); specific sequenced muscle programs (e.g. drawing lines, angles, curves) that involve primary motor cortex; and more abstract plans for producing letter shapes which are ''good enough'' approximations to be legible. Children typically begin by ''drawing'' the letters, along with pictures and sometimes invented letter-like forms, until repeated practice yields ''automatic'' retrieval and production of letters. There is often a normal, transient deterioration in the appearance of printed letters and words as children move from drawing each one, to more automatic printing (often during first or second grade, in US schools) but before legible printing is fully automatized. Traditional intervention has consisted of copying ''drills''; however, more recently, studies have shown that impaired letter formation among beginning first-grade writers improved more given visual cues to assist with letter formation, combined with practice in writing letters from memory, than in response to either of these strategies alone, or to repeatedly copying letters (see studies reviewed in Berninger & Amtmann, 2003).

Sensory systems involved in handwriting include vision and visual perception, which are likely important in early non-automatic writing, or

"copying and drawing," of letters. Studies show little association between visual perception and writing beyond the very early stages where letters are "drawn and copied." Skilled writing may depend more upon kinesthetic and proprioceptive cues than upon visual feedback, though clearly both are important. The importance of proprioceptive cues may explain why awkward, slow "finger sequencing" (i.e. touching each fingertip, in turn, to the thumb) among young children is a good predictor of later hand writing problems. Other studies have shown that finger sequencing and finger gnosis (i.e. naming which fingers are lightly touched, when the hand is hidden from view) are associated with problems of "number sense" and counting (Noel, 2005). Neither of these tests is highly reliable in five- to six-year old children, however, and perhaps both tests are serving as markers of impairment in prefrontally mediated behaviors. Design copying seems to be a skill quite separate from handwriting in normally developing beginning writers; specifically, poor design copying is not associated with poor handwriting, or vice versa, in young children. Among older children, however, there is a strong association between quality of design copying and of handwriting (Berninger, 2004). Poor handwriting in older children may be reflecting subtle impairment of sensory and motor control systems that also will affect other graphomotor work (such as drawing or copying). Relevant sensory systems include the kinesthetic (sense of touch and pressure from pen, paper, or keyboard), the proprioceptive (senses muscle and joint position, direction, and speed of movement), and vestibular (senses head position, posture, balance, and helps to coordinate smooth gaze and hand movement).

In order for the letter- and word-printing process to become automatic in a meaningful way, children need to automatize the associations between letter names or sounds, their mental image (visual and/or proprioceptive), and their printed representations. The association between letter names ("bee"), letter sounds or phonemes (/b/), and letter forms or graphemes ("b" or "B") is arbitrary, and must be memorized. Difficulty with memorizing and retrieving the name-to-grapheme or sound-to-grapheme association forms the basis for many writing disabilities, and mirrors the difficulty of readers with dyslexia in establishing automatic, effortless recognition of print-to-sound (grapheme-to-phoneme) associations (Berninger, 2004; Berninger *et al.*, 2006). Indeed, the inaccuracy, inconsistency, and slow or variable speed of making such associations seem to underlie the frequent comorbidity of dyslexia and dysgraphia. Excepting rare cases of children with autism and hyperlexia, the child cannot spell a word that s/he cannot read, nor can s/he compose written sentences or narrative beyond the level of textual complexity that s/he can comprehend.

A number of writing/reading programs for young children attempt to make the phoneme-grapheme relationship more familiar, meaningful, and recognizable,

by linking the letter shapes and sounds to images and vocabulary familiar to young children. An example is ''*L*etterland,'' in which 'B' or 'b' is represented as 'a bouncy brown bunny.'' Rhymes (providing verbally mediated memory cues) help the child recall how to move in order to form the letter correctly: ''Brush DOWN Ben's big long ears, go UP round his head so his face appears for lower-case ''b'' (www.letterland.com).''

Spelling single words involves phonological awareness for word segmentation (for example, realizing that CHART has three sounds,/ch/,/ar/,/t/), as well as increasingly complex phoneme–grapheme knowledge (i.e. printing the right letter or letter-group to match each word sound. In this case, realizing that /ch/is represented by a two-letter diphthong, /ar/ includes an r-controlled ''A'' so again requires two letters; and the /t/ which is almost silent when saying the word must be included when spelling it). With practice and experience, morpheme knowledge emerges (''Let's see, you said he CLIMBED the tree yesterday, so I have to add ''ed''.'') Although poor readers very rarely can spell well, many good readers also have poor spelling (Moats, 2004). Improvement in spelling does not occur from writing per se, but from explicit teaching of sound-and-letter patterns (orthography), with opportunities to practice correct written spelling (Berninger *et al.*, 2002; 2006; Graham, Harris & Chorzempa, 2002).

Assistive technology for writing problems, such as keyboarding, voice dictation, and use of word prediction software is popularly prescribed (Freeman, MacKinnon & Miller, 2004; MacArthur, 1996) but as yet has little empirically validated efficacy for students with writing disabilities (Berninger & Amtmann, 2003), other than as aids for students with major motor impairment such as cerebral palsy, spina bifida, or paraplegias. In a single-subject, ABAB-design study of three students with writing disabilities, Hetzroni and Shrieber (2004) found improvement in spelling errors, reading errors, organization and structure, but no difference in length (word count), when students used a word processor instead of handwriting. Handley-Moore and colleagues (2003), in a similar study, reported improvement in two of three students for spelling and legibility, but again no difference in total length of written work. ''Low tech'' devices, such as rubber pencil grips, weighted pencils, or slant-boards, also have not been subjected to systematic empirical study. This is an area for fruitful research, perhaps through collaborative occupational therapy and neuropsychology studies. Lenker and colleagues (Lenker *et al.*, 2005) have described limitations of existing assistive technology outcome research, and provide a framework for conceptualizing and conducting studies that may provide clearer guidance about how and when to recommend assistive technology for students with SLDs.

Written expression involves not only the motor act of handwriting, and the phonological and memory skills involved in spelling, but also the translation of

concepts into well-formed, organized narratives. Language, attention, memory, and reading abilities are all essential to good writing. Effective intervention strategies include use of explicit coaching in discourse structure (e.g. the Direct Instruction program, "Expressive Writing;" Walker *et al.*, 2005), as well as organizational strategies such as Self-Regulated Strategy Development (SRSD; Graham & Harris, 2003; Troia & Graham, 2002). The latter involves the student in developing an organized writing plan, thinking about the basic parts of their composition, word choice, and self-regulation including setting goals, monitoring their own progress, and crediting success to use of organizational strategies. Second-grade students, as well as high schoolers in the Self-Regulated Strategy Development program wrote "longer and stronger" stories and essays than students in a typical, unstructured "Writers' Workshop" comparison group (Lyon *et al.*, 2006), showing that even young students with SLD in writing can improve significantly. Having peers help with monitoring progress made an even greater difference. However, Troia and Graham (2002) showed that successful instruction in story-writing did not transfer to improved essay writing, suggesting that generalization of writing strategies across genre must be planned, not assumed.

Remediating SLD in mathematics

Research on the neuropsychology of mathematical learning and learning disabilities is extensive, although less comprehensive than for reading (Deloche & Seron, 1987; Donlan, 1998; Geary, 1995; Keller & Sutton, 1991; Shalev, 2004). The prevalence of SLD in math is estimated at roughly 6% of elementary school children (Barbaresi *et al.*, 2005; Rourke & Conway, 1997). Shalev, Manor and Gross-Tsur (2005), in a study of Israeli fifth- through eleventh-grade students, showed that at older age levels, math disabilities are very persistent and tend to get worse over time. Similarly, Dennis and Barnes (2002) found that math disabilities in children with spina bifida and hydrocephalus not only persisted into adulthood, but were associated with lower functional independence. Moreover, the authors have suggested that functional numeracy is more closely associated with independent living skills in adulthood than is functional literacy.

Children with math disabilities tend to make errors that are similar to those of younger, normally developing children, as opposed to ones that are qualitatively atypical. This suggests that for some children, math disabilities may be associated with a "maturational lag" (Barnes *et al.*, 2002; Desoete & Roeyers, 2005). Although children with math specific disabilities can be meaningfully differentiated from those who have "math + reading" disabilities (Fletcher, 2005), finer distinctions are needed when designing remediation; the lack of clear evidence for such finer distinctions within the math disability subtype of SLD has likely hampered efforts

at both diagnosis and remediation. While cross-sectional analyses have revealed that there is more than one subtype of math disability (Desoete & Roeyers, 2005), there is, as yet, no clear subtype by intervention type articulated for the math disabilities. Moreover, it is not known whether an individual child's subtype of math disability remains stable, or changes, with maturation, instruction, or changes in academic demands.

Geary (1995) has described the different competencies required to do math as including: (a) basic number sense or "numeracy;" (b) the semantics of number and rapid automatic retrieval of number meanings; (c) procedural knowledge; (d) visuospatial abilities, including an understanding of the spatial representation of numbers, appreciation of the "number line," and the ability to align and keep track of digits within a multicolumn computation; (e) mathematical problem solving; and (f) conceptual knowledge, i.e. understanding basic principles underlying mathematical procedures, relationships among different procedures, different ways to solve the same problem, etc. (for example, understanding that subtraction is the inverse of addition, or that multiplying "times n" means replicating a quantity "n times"). Research on the development of mathematical abilities suggests that children are born with "number sense" and show an appreciation of numeracy as toddlers and preschoolers, well before they learn to count in sequence, or associate number names with quantities (Butterworth, 2005). Certain concepts of quantity, sequence, pattern, physical categories or similarities and differences are developed very early, without formal teaching, and draw upon innate cognitive capabilities (Butterworth, 2005; Geary, 1995). For some children, problems with understanding basic number concepts appear to underlie "dyscalculia" or a primary disability in mathematical thinking, but such cases seem to be in the minority among those who have difficulty with math learning (Geary, 1995; Fletcher, 2005).

For others, "semantic" problems with math may be associated with the same neuropsychological impairment that produces SLD in reading (dyslexia). A child with dyslexia may have difficulty automatizing symbol-sound-concept associations that include numerals, just as they do with letters. These children may have trouble memorizing and rapidly retrieving number names, and associating a quantity value with a printed numeral, just as they have trouble rapidly associating sounds with printed letters. As with decoding skill, it appears that "drill and practice" (i.e. explicit instruction about these associations, with guided practice in recognizing them) may be an effective intervention, particularly for very young children (e.g. before the second grade). There is very limited research on math learning interventions of this type, however. Older children show improvement with drill and practice, but this may not persist once the drill stops (Geary, 1995). Therefore, older children who still show problems with automatically recalling

number names and facts may benefit from using formulas or algorithms; visual strategies such as a "mental abacus;" or concrete aids such as a "multiplication facts chart," while working on complex math procedures.

To remediate procedural, visuospatial, and conceptual problem solving deficits, it may be possible to "layer" or "sequence" math interventions. As with reading interventions, the first level of math intervention often involves professional development for teachers. In fact, teaching teachers in greater detail about children's mathematical development improves their ability to present mathematical concepts more clearly and effectively (Lyon *et al.*, 2006).

Geary (1995) has outlined several suggestions for improving whole-class math instruction, including: (a) offering a clear statement of both the immediate goal ("find the answer for X") and the long-term, real life goal for math problem-solving (e.g. "This math procedure is used to figure out sports averages or voting records ..."); (b) providing explicit instruction in math procedures, including distributed practice, over an extended time period; (c) include practice on a mixed set of problem types, until the procedure is automatized – this should be followed by cumulative review; (d) for children with visuospatial difficulties, provide cues and labels to clarify spatially presented information, e.g. label the "ones" and "tens" columns in a multicolumn problem; (e) provide explicit instruction in math concepts, presented in child friendly contexts, e.g. using sports or school stories, rather than stories about salaries or "miles per gallon"; (f) have children generate different ways to solve a problem, or to apply procedures, and discuss the merits of these different strategies; and (g) analyze errors to clarify misunderstandings, while explicating and summarizing concepts, in order to assist children in understanding why some solutions work but others do not.

A second-tier intervention involves increased time for individualized instruction and guided practice. Fuchs and associates (e.g. Fuchs *et al.*, 1991) have experimentally demonstrated effective instruction for both high-achieving and low-achieving students, as well as remediation for students with SLD in basic arithmetic skills, including rapid retrieval of math facts and accurate computation. Their approach utilizes an explicit, step-by-step explanation of procedures and concepts; pictorial or concrete representations ("math manipulatives"); verbal rehearsal ("self-talk") of the problem-solving steps, with gradual fading of overt self-talk; timed practice on mixed problem sets, including systematic, cumulative review of previously mastered problem types. Teaching self-regulation strategies was also shown to further improve the efficacy of this approach.

Fuchs *et al.* (2003) have also developed a program to teach math problem solving skills for solving "word problems." They initially studied third-graders with varying math achievement levels. In their program, the teacher demonstrates and explicates examples of particular problem types; this is followed by the use

of a ''backward chaining'' approach, in which the student solves the last step, then several final steps, before finally learning how to set up the problem. At each step, students are asked to explain their work and they receive corrective feedback, with periodic cumulative review. Importantly, Fuchs *et al.* (2003; 2004) demonstrated gains in these higher-level math problem-solving skills even among students whose basic math computation skills were weak. This finding argues against the traditional tenet that children must master computation facts before they can learn more complex math problem-solving.

There has been some clinical speculation, but with no published evidence, that recent changes in math instruction may be increasing the number of children who are struggling with memorization of math facts (math fluency) and with mastery of basic computation procedures. Current proposed standards offered by the National Council of Teachers of Mathematics have been sharply criticized for their focus on a child-centered learning philosophy over direct instruction in mathematics facts and procedures. As an example, the ''Everyday Math'' curriculum, developed at the University of Chicago, has been widely adopted as an alternative to traditional math curricula that emphasize repeated practice with basic arithmetic equations. ''Everyday Math'' is instead a ''spiraling'' curriculum, with an emphasis on applied problem-solving. It is intended to teach math concepts by connecting mathematical activities to children's real world experience, as opposed to teaching just a series of ''formulaic'' procedures that are rote and formulaic. However, the ''Everyday Math'' curriculum is challenging for children who have difficulties with language development and reading comprehension difficulties, in comparison with traditional cumulative equation-based math instruction (e.g. the ''Saxon Math'' and similar curricula). This serves as one example of the way in which both the format and content of the math curriculum may alter the prevalence of math disabilities among children. Outcomes of both regular classroom math teaching and remedial math instruction methods clearly require further empirical research.

Comorbidities with SLD

The need for relatively homogeneous groups in research studies often limits generalizability of remediation research to real world populations. Nonetheless, comorbidity with the SLD is the rule, rather than the exception. A large percentage of children struggle with both reading and math (Fletcher, 2005) or show both the presence of reading disabilities and specific language impairment (Eisenmajer, Ross & Pratt, 2005). Children with more than one disability generally present as more impaired on academic measures and have been found to respond less well to intervention than children with a single disability (Fuchs, Fuchs & Prentice, 2004).

Neuropsychological assessment of students with SLD is most useful when it can identify and address treatment across the constellation of individual factors that seem likely to facilitate or impede a particular student's progress.

Attention problems, including Attention Deficit Hyperactivity Disorder (ADHD), clearly interfere with academic progress. Rabiner *et al.* (2004) studied response to reading tutoring in children with attention problems but no reading problems; children with reading problems who had normal attention; and children with both reading and attention problems. The inattentive children who had normal reading skills benefited somewhat from tutoring, while the inattentive children who were poor early readers failed to benefit from tutoring. Those who were poor readers but had normal attention benefited substantially from tutoring. This suggests that factors underlying the comorbidity of reading and ADHD require greater explication, in order to understand how to more effectively remediate reading concerns. ADHD also is associated with writing and math problems, presumably because problems with working memory and impulsivity interfere with the precise sequencing of letters, words, or arithmetic computation steps (Hooper *et al.*, 2002). Stimulant medication (Lerer, Lerer & Artner, 1977), as well as increased structure and guidance during the writing process (Berninger, 2004) and coaching in self-regulation strategies (Graham & Harris, 1996) have been shown to be particularly important for children with ADHD who have comorbid SLD's.

Language problems in kindergarten are predictive of reading and writing disabilities in later grades, and language improvement during the early grades is associated with better reading outcomes (Catts *et al.*, 2002). Children who have both language and reading disabilities respond less well to reading interventions, than those with pure reading deficits whose language is otherwise normally developing (Eisenmajer, Ross & Pratt, 2005). Thus, assessment and intervention for language impairments that may underlie, or be comorbid with, academic difficulties is important.

SLD in reading and writing, as well as language disorders, have been suggested to be more prevalent among children with disruptive behavior disorders (DBD) than in the general population. On the other hand, Svensson, Lundberg and Jacobson (2001), in a study of 163 Swedish boys with DBD, found that while over 70% of their sample had reading and spelling problems, only 11% showed severe difficulties; this is about the same proportion as in the general population. Moreover, problems with literacy were associated with restricted socioeconomic and educational opportunities, rather than any increased prevalence of dyslexia.

Findings are inconsistent regarding the relative risks of social-emotional problems given different types of SLD''s. Rourke and his associates have argued that pure reading disorders are not necessarily associated with any increased risk

of behavioral disturbance, whereas math or nonverbal LD, and mixed "math + reading" LD, are associated with increased social–emotional difficulties (Rourke, Van der Vlugt & Rourke, 2002, pp. 218–20). Other studies report increased social–emotional difficulties among all subtypes of children with SLD, including those with reading disorders, though children with multiple types of SLD seem to fare least well, across studies (Semrud-Clikeman *et al.*, 2005). The relationship between social-emotional problems and SLD's is reciprocal. Academic difficulties are associated with diminished self-esteem, increased anxiety and depression, and even with increased risk of suicidal behavior (Hendin, 2005; Martinez & Semrud-Clikeman, 2004). Conversely, children with clinically significant psychopathology may struggle with schoolwork, and be too preoccupied with worry or overwhelmed with negative affect to be accessible to instruction without special intervention.

"Math anxiety" (Hembree, 1990) is specific apprehension about mathematical endeavors (homework, test-taking, sitting through math classes, etc.), associated with but distinguishable from generalized anxiety. Math anxiety is associated with avoidance of mathematical homework and classes, and with increased emotional arousal which interferes with optimal concentration and accuracy while problem-solving. Students with high math anxiety are more likely to rush to complete work, make errors, apply less creative or flexible problem-solving strategies, and become distracted more easily by noise, movement, or by their own intrusive and self-disparaging thoughts (Ashcraft & Faust, 1994; Geary, 1995, p. 275). Effective treatment has focused on decreasing anxious arousal via systematic desensitization with relaxation training, combined with decreasing worry and self-disparaging thoughts via cognitive–behavioral therapy techniques, while increasing math knowledge and skills (Geary, 1995, p. 277). While there does not seem to be much literature about reading anxiety or writing anxiety, certainly both of these phenomena are seen clinically and, presumably, might respond to similar sorts of intervention.

Conclusions and directions for future research

Behavioral and brain-imaging research suggests a biopsychosocial or diathesis-stress conceptualization of SLD. Even when a child has genetically determined brain differences (i.e. the diathesis) that make learning harder to achieve, the degree of observed SLD will depend upon environmental demands (stress) and support. Thus, SLD in reading may be preventable, even in an older child, when intensive remediation is made available. This suggests that, at least with regard to reading disability, that an SLD is neither wholly permanent, nor wholly malleable, but both lifelong and, to some extent, remediable. Research suggests that

individual differences in children's ease of acquiring new skills represent an ability continuum, rather than a categorical or qualitative difference in learning capability. Just as SLD itself appears to be graded, rather than categorical, remediation strategies also need to be graded, rather than "one size fits all."

Studies also suggest that learning disabilities can be modular rather than global, and therefore remediation strategies also need to address specific modules or component skills. For example, one child struggles to decode text, but comprehends well, while another decodes fluently but fails to discern the meaning. Mastery of foundational skills may or may not facilitate mastery of higher level skills; children can learn math problem-solving strategies, for example, without having mastered automatic retrieval of basic facts. Perhaps because of this modularity, direct treatment of cognitive indicators or precursors of academic problems generally does not translate to improved achievement. For example, even though deficient phonological awareness and slow naming speed serve as robust predictors of early reading difficulty, direct training in phonological awareness or rapid naming has not yielded significant gains in reading ability (De Jong & Vrielink, 2004).

Lyon, Fletcher, Fuchs & Chhabra (2006) have stated that "the cornerstone of effective practice" for students with SLD is "an instructional approach that is explicit, well-organized, and that routinely provides opportunity for cumulative review of previously mastered content ... whether teachers are addressing foundational skills or higher-order processes." Self-regulation strategies and peer mediation add value to teacher-directed instruction. Academic gains are content-specific; for example, instruction in decoding does not necessarily yield improvement in fluency or comprehension, and therefore, effective programs must comprehensively address all the essential components of each academic ability, in an integrated way. Progress monitoring must be frequent and used to inform intervention. Research, and (subsequently) research-based practice, needs to account for heterogeneity among students with SLD, particularly for comorbidity of SLD in math and literacy, and comorbidity with ADHD. General education should be geared towards primary and secondary prevention of SLD's so that special education can focus on tertiary prevention that is, the intensive specialized treatment of small numbers of students who have not responded to research-based educational practice.

A key question remains, as always, how can we predict, or identify as soon as possible, which children will require tertiary prevention? At present, neither IQ alone; IQ-achievement discrepancies or other aspects of a neurocognitive profile; socioeconomic status; or initial level of difficulty in phonological awareness, naming speed, decoding, and fluency can reliably predict RTI (O'Connor *et al.*, 2005a). Predictive assessments may need to involve measurement of change over

time, in addition to measurement of severity of academic delays or deficiencies at any given point in time (Fletcher *et al.*, 2004). This raises new questions: How much change, over how much time, on what specific abilities or skills, constitutes adequate or expected gains? An ideal measure might assess RTI over, say, one month, to predict future progress, rather than wait a full school year to determine who needs additional help. For example, Compton *et al.* (2005) identified several measures of individual children's responses to instruction in word-decoding that predicted their gains in other aspects of reading (e.g. sight-word identification, text reading fluency, accuracy, and comprehension). How long must struggling students be monitored? O'Connor and colleagues (2004) found that some children needed ongoing intervention through third grade, when their study ended; presumably, some might need lifelong help. Even if a child shows adequate gains in one skill (e.g. decoding), he or she might need help with a different skill (e.g. fluency). O'Connor's study implies a need for continuous academic screening, including children who had no early intervention as well as those who recovered, as children grow up to face increasingly complex academic demands.

SLD remediation strategies impact classroom structure both socially and economically. Adopting an RTI model may increase inclusion of mildly delayed young children, who could be served in small groups in the classroom, while increasing pull-out one-to-one time for older, severely delayed children, particularly those with multiple SLD's and comorbid conditions. One argument for inclusion has been that regular classroom placement supports the child's self-esteem and peer group identity. If full inclusion implies persistent academic failure, however, that in itself may stigmatize the youngster (Martinez & Semrud-Clikeman, 2004). Remediation research should incorporate a range of outcome variables, encompassing not only the child's academic abilities, but also his or her social and emotional adaptation.

Even well-validated interventions, well-trained teachers, and well-written policies and laws, cannot succeed without adequate funding for implementation, which will be likely to require ongoing social and political advocacy. Public support for funding education initiatives might be easier to obtain when there is clear documentation of successful outcomes, and clear benefits to general education as well as to special education children, of the enhanced teacher training and individualized interventions included in proposed regulations for IDEA-2004.

As effective primary and secondary prevention is provided for increasing numbers of ''at risk'' children, there will inevitably be increased opportunity to identify individual differences that may contribute to persisting SLD. Remediation studies to date have not clearly considered gender differences in the prevalence of reading versus math disabilities, or whether there might be any gender-specific considerations in remediating these problems. For example, math anxiety seems

more frequent in girls, perhaps associated with a stereotype that ''Girls can''t do math'' (e.g. Keller & Dauenheimer, 2003). Some large-scale epidemiologic studies have found a significantly greater incidence of both reading and math SLD in boys than in girls (Barbaresi *et al.*, 2005; Katusic *et al.*, 2001) whereas others have found no significant gender difference (Shaywitz *et al.*, 1990). In the population-based Rochester, Minnesota sample collected by Colligan, Katusic and colleagues (Katusic *et al.*, 2001), which reported about twice as many boys as girls among children with SLD, further analyses showed that reading disability was strongly associated with biomedical risk (low birth weight) in girls, but not in boys (St. Sauver *et al.*, 2001). Whether etiological risk factors would affect responsiveness to treatment remains to be studied.

An important RTI moderator may be self-regulation, which itself appears to be both a trainable skill and an heritable individual difference (Posner, 2005). Successful SLD remediation for older children emphasizes self-regulation strategies, in addition to basic skills training. As yet, however, few studies consider whether initial individual differences in self-regulatory processes mediates success in learning and applying task-specific self-regulation strategies. As noted earlier, the role attention, executive function, memory, language, motivation, and parental support may play in RTI has been explored very little in remediation research (although see Rabiner *et al.*, 2004). Research is needed to understand how such factors may moderate or mediate the relationship between instructional strategies and learning outcomes. Understanding interrelationships among problems of learning across subjects, socialization, adaptive functioning, attention and self-regulation, communication, family and community influences, will also help inform individual clinical neuropsychological assessment of children with learning disabilities.

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13

Managing attentional disorders

Donna R. Palumbo and Joshua Diehl

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental syndromes, with recent data suggesting prevalence rates in school-aged children between 8–10% (American Academy of Pediatrics & Subcommittee on Attention-Deficit/Hyperactivity Disorder, 2001; Barbaresi *et al.*, 2002; Katusic *et al.*, 2002; Leibson *et al.*, 2001). Symptom onset is by the age of seven, with symptoms often evident between the ages of three to five years. The accurate diagnosis and effective treatment of ADHD in children can be critical to their academic, social, and interpersonal functioning. However, this is complicated by high rates of comorbid disorders in children with ADHD, including learning disabilities. The role of behavioral and neuropsychological assessment in diagnosis and treatment planning and effective treatment interventions will be discussed in this chapter. Furthermore, cognitive theories of ADHD and neuropsychological research, along with implications for clinical practice and future research will also be discussed.

The diagnosis of ADHD

ADHD is primarily characterized by two groups of core symptoms: (1) inattention and (2) hyperactive and impulsive behaviors. Currently, the DSM-IV-TR (APA, 2000) categorizes ADHD into three major subtypes: (1) Predominantly Inattentive Type (ADHD-I); (2) Predominantly Hyperactive/Impulsive Type (ADHD-H/I); and (3) Combined Type (ADHD-C), with the latter being the most common. Symptoms include short attention span, distractibility, forgetfulness, disorganization, restlessness, hyperactivity, impulsive responding and talkativeness. Overall, the male-to-female ratio for diagnosis is approximately 2:1 in community surveys (Cohen *et al.*, 1999; Fergusson *et al.*, 1993; Szatmari, Offord & Boyle, 1989). Estimates vary widely, but persistence of symptoms into adolescence ranges from 40–70%, with residual symptoms into adulthood in about 50% of affected individuals (Barkley, 2005; Gittelman *et al.*, 1985;

Mannuzza *et al.*, 1991). In addition to meeting symptom-specific criteria, children must also meet impairment criteria for ADHD to be a valid diagnosis. This requires that the symptoms be developmentally inappropriate and impair functioning across a range of settings, including academic (or occupational), social, family and interpersonal interactions.

The diagnosis of ADHD is made based upon history, observation, and medical and psychological evaluation. Tools that are useful in obtaining observational data include teacher and parent rating scales of childhood behaviors. Most commonly used for ADHD are the Conners Parent (CPRS-R) and Teacher (CTRS-R) Rating Scales (Conners, 1997). These scales are easily completed and have excellent normative data (Goyette, Conners Ulrich, 1978). Results can be indicative of ADHD symptoms at home and school. In addition, they provide an objective measure of treatment response when used as a repeated measure. Other behavioral rating scales typically used include: ADHD Symptom Checklist-4 (ADHD SC4; Gadow & Sprafkin); the Brown Attention Deficit Disorder Scales (Brown, 1996, 2001); ADD-H Comprehensive Teacher's Rating Scale (Ullmann, Sleator & Sprague, 1991) and the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2005).

While behavior rating scales may be helpful in making the clinical diagnosis of ADHD, there is no neuropsychological or physiological test or imaging study that can definitively "diagnose" this condition. Neuropsychological tests can be useful in identifying attention, memory, learning, and other cognitive problems which may be present in a child with ADHD, but test outcomes alone are not diagnostically sufficient. Inattention and impulsivity are not symptoms specific to ADHD and differential diagnosis must always be considered. These symptoms may be caused by other neurological or psychiatric conditions. For example, pervasive developmental disorders, obsessive-compulsive disorder, depression, anxiety, seizures, lead toxicity, medication side effects, mental retardation, head injury, Tourette Syndrome, in-utero exposure to toxic substances (e.g. alcohol) and psychosocial adversity all can present with attentional and behavioral concerns that may "mimic" ADHD (Palumbo, Maughan & Kurlan, 1997). Thus, it is important to obtain a thorough history and perform a careful evaluation prior to making the diagnosis of ADHD. Neuropsychological test data should be used in conjunction with behavioral, medical, and historical data when making a diagnosis.

ADHD and related medical and psychiatric concerns

It is atypical to identify ADHD without also observing comorbid psychiatric or behavioral disorders (Kadesjo & Gillberg, 2001). ADHD is commonly comorbid

with affective disorders (Angold, Costello & Erkanli, 1999), anxiety disorders (Angold *et al.*, 1999), tic disorders (Comings & Comings, 1985; see Hunter, this volume) conduct disorder (MTA Cooperative Group, 1999), and other dysregulatory disorders (Nigg & Casey, 2005). It is thought that this overlap, especially with dysregulatory disorders, represents shared cognitive and affective mechanisms (Nigg & Casey, 2005). Moreover, common systems between disorders might promote neuropsychological rather than behavioral definitions of subtypes in ADHD (Coghill *et al.*, 2005).

While health factors are not as central to ADHD as they are to some other disorders, there are significant health risks that are secondary to the behavioral characteristics and medical treatment of the disorder. Children with ADHD are more likely to have major injuries that lead to both inpatient and outpatient emergency department admissions (Leibson *et al.*, 2001). They have a higher rate of burns, poisoning, head injury, and fractures in particular, than children with other psychiatric disorders, even controlling for psychosocial risk factors (Rowe *et al.*, 2004). Driving accidents are a particular area of concern. Individuals with ADHD are at high risk for driving offenses (e.g. tickets, suspended licenses) and accidents that result in bodily injury more than people with other psychiatric disorders (Barkley, Guevremont & Anastopoulos, 1993). However, stimulant medications have proven to be effective at tempering the effects of ADHD on driving (Cox *et al.*, 2004). A related behavioral risk for individuals with ADHD is contracting a sexually transmitted disease (STD). The rate of STDs is four times higher in individuals with ADHD than would be expected in the general population (Fischer *et al.*, 1993). Those diagnosed with ADHD have sex earlier, have more sexual partners, and are less likely to use contraception, all of which lead to higher rates of teen pregnancy and STDs (Barkley, 2005). Due to the many factors described above, health care costs for children and adolescents with ADHD are double that of children without the disorder (Leibson *et al.*, 2001).

The neurobiology of ADHD

The complete pathophysiology of ADHD remains unclear. To date, most anatomic studies have utilized small sample sizes and results have been confounded by factors such as methodology, gender differences, and development. In addition, the majority of research has focused on ADHD, combined subtype (ADHD-C), which is the most common subtype. However, tentative findings support theories suggesting that hypoactivity of the right prefrontal and subcortical brain regions, most notably the caudate nucleus and globus pallidus, are involved in the expression of ADHD symptoms (Castellanos, 2001*a*).

Several lines of evidence point to dysfunction of prefrontal cortex (PFC) in ADHD. The PFC has outputs to many other cortical regions including the striatum, amygdala, locus coeruleus and subthalamic nucleus (Castellanos, 2001*b*). Given this extensive circuitry, there are many functions presumed to be subsumed by the PFC, including several pertinent to ADHD. Among these are working memory, planning and organization of behavior, filtering out irrelevant stimuli, and inhibiting inappropriate behavioral responses (Robbins, 1996). These functions provide for effective guidance of behavior. Lesions of PFC can lead to inattention, distractibility, impulsivity, and hyperactivity (Alexander & Stuss, 2000; Stefanatos & Wasserstein, 2001). The PFC receives subcortical inputs from both dopaminergic and noradrenergic systems, and depletion of catecholamine inputs to PFC in non-human primates can mimic the effects of PFC lesions (Brozoski *et al.*, 1979). Since the most effective medications for treating ADHD impact dopaminergic and noradrenergic neurotransmission, there has been great interest in the role of catecholamines in PFC function. It appears that manipulating these neurotransmitter systems can ameliorate many ADHD symptoms in the majority of patients. Experimental neurophysiology and neuropharmacology studies have shown that medications used to treat ADHD have direct and specific effects on PFC neurons (Grace, 2001).

There is also evidence that basal ganglia circuits may play an important role in the manifestations of ADHD. Certain lesions in the basal ganglia have been associated with inattention, impulsivity, and behavioral disinhibition (DeLong, 2002; Max *et al.*, 2002). The frontal cortex and basal ganglia are highly interconnected and it is generally agreed that these interconnections underlie important functional interactions (Alexander, DeLong & Strick, 1986; Palumbo *et al.*, 1997). Thus, it may be most appropriate to think of ADHD as a disorder of cortical–basal ganglia circuits rather than simply a disorder of PFC function.

Since ADHD is not a fatal disorder, material for clinicopathological studies is rarely available. Fortunately, advances in quantitative anatomical neuroimaging have provided some insights into possible structural brain abnormalities in ADHD. A consistent finding has been slightly reduced frontal lobe volumes in individuals with ADHD compared to controls (Faraone & Biederman, 1998). Some studies have shown reduced volumes of frontal cortex and basal ganglia structures in the right hemisphere compared to the left (Dickstein *et al.*, 2005; Faraone & Biederman, 1998; Overmeyer & Taylor, 1999); however, bilateral abnormalities have also been described (Lipkin *et al.*, 2005). Using a regional subparcellation method, it has been demonstrated that both prefrontal and premotor areas are smaller in ADHD subjects and that the volume reduction is present in both gray and white matter (Lipkin *et al.*, 2005).

Together, these findings support the idea that frontal lobe and basal ganglia circuits are abnormal in ADHD. They are also consistent with the notion that there is lateralization of the abnormality, with possibly greater right hemisphere involvement.

Abnormal cerebral volume does not necessarily imply abnormal structure or function. Thus, physiologic measures are important for establishing the underlying dysfunction of the frontal lobe and basal ganglia in ADHD. Studies have pointed to abnormal function of the dorsolateral PFC in ADHD, with most studies showing decreased PFC perfusion (Rubia *et al.*, 1999). However, there has been little consensus as to the specific abnormality (Faraone & Biederman, 1998). In a SPECT study of resting regional cerebral blood flow (rCBF) in drug-naïve children with ADHD, there was decreased left dorsolateral PFC perfusion compared to the right (Spalletta *et al.*, 2001). The magnitude of the asymmetry correlated with both symptom severity and a neuropsychological measure of attention. Another SPECT study showed reversal of the normally asymmetric right > left dorsolateral PFC rCBF pattern during a response inhibition task (Langleben *et al.*, 2001). The most severely hyperactive individuals had the greatest left > right asymmetry. A study examining response inhibition in children with ADHD found consistent decrements on response inhibitions tasks when compared to normal controls (Casey *et al.*, 1997). Furthermore, performance on these tasks was correlated with anatomical measures in the region of the prefrontal cortex, caudate and globus pallidus, predominantly in the right hemisphere. These results suggest that the right PFC plays a role in response inhibition while it is theorized that the basal ganglia may be involved in executing responses. Despite these compelling data, differences in subject age, presence of comorbid symptoms, task employed, and exposure to medication have limited the ability to compare studies and draw definitive conclusions. Regardless of these limitations, the most consistent finding arising from functional imaging studies has been the suggestion of abnormal PFC perfusion.

Another line of functional imaging research has focused on pharmacological measures in ADHD. One study of children with ADHD showed increased ^{18}FDOPA uptake in the midbrain that correlated with symptom severity (Ernst *et al.*, 1999). In adults with ADHD, there was decreased uptake in the PFC (Ernst *et al.*, 1998). These studies point to abnormalities in catecholamine regulation of PFC circuits. Taken together, these studies indicate that subcortical frontal structures and disruption of catecholaminergic transmission are most likely involved in the pathophysiology of ADHD. Therefore, studies of executive functioning (EF) have become a prominent focus of neuropsychological investigation in ADHD.

Cognitive functions

Over the past decade, there has been a wealth of research examining neuropsychological functioning in ADHD. Although there is no specific diagnostic test for ADHD, neuropsychological testing has proven to be a useful tool in discovering patterns of cognitive functioning associated with the disorder (Nigg, 2005). However, this area of research has been limited regarding generalization of findings since the vast majority of studies have included almost exclusively elementary school-age males (Paule *et al.*, 2000); thus females and adolescents have not been adequately studied, affecting generalizability of findings regarding cognitive profiles in ADHD. Additionally, the impact of comorbid disorders on outcomes has not been fully appreciated. Thus, while neuropsychological testing can be quite helpful for planning academic and behavioral interventions and gauging therapeutic change over time, caution must be taken when interpreting clinical findings and comparing individual results to research findings (Barkley, 2005; Nigg, 2005).

Several cognitive theories have been posited about the core deficit of the disorder, including the domains of attention, state regulation and motivation, processing of temporal information, and executive functions (Nigg, 2005). Likewise, Tannock and colleagues have identified three domains of interest in empirical studies designed to isolate specific cognitive functions that may underlie ADHD: (1) visual-spatial orienting; (2) state activation; and (3) higher-order cognitive functions, known as executive functions (Paule *et al.*, 2000). Basic sensory, perceptual and short- and long-term memory functions are presumed to be intact (Barkley, 1997*b*; Douglas, 1983).

Executive functions (EF), including response inhibition, working memory, cognitive flexibility, planning, and fluency have all been studied, to some extent, as to their relationship to ADHD (Pennington & Ozonoff, 1996; see also Mahone and Slomine, this volume). Barkley (1997*a*) proposed a ''unifying theory'' of ADHD, suggesting that a primary deficit in behavioral inhibition underlies the problems seen with both self-regulation and secondary features such as hyperactivity, inattention, and other executive functions. Thus, the fundamental problem underlying ADHD is hypothesized to be a core deficit in delaying or inhibiting a behavioral response. Barkley also posits the presence of developmental effects, such that the hyperactivity symptoms decline with age, while inattention and impulsivity remain present. In Barkley's model, young children exhibit a greater level of ADHD/HI-related symptoms. As academic and social demands increase, ADHD-C becomes the more apparent presentation, with greater cognitive symptoms characteristic of ADHD-I as affected individuals enter into adulthood. This theory has generated much consequent research, including attempts

to understand the hierarchy of EF (Sonuga-Barke *et al.*, 2002). Others have attempted to explain ADHD through models with multiple neurodevelopmental pathways to account for the heterogeneity of the disorder (Nigg, 2006; Sonuga-Barke, 2005).

The neurocognitive heterogeneity of ADHD is problematic for determining core deficits; it is unlikely that a unitary profile of functioning will characterize all individuals with the disorder (Doyle *et al.*, 2005). Some research indicates different cognitive profiles between ADHD-H/I, ADHD-C and ADHD-I, with memory retrieval and executive functions more significantly impaired in children without hyperactivity (Denney & Rapport, 2001), and reward systems more deficient in ADHD-C (Coghill *et al.*, 2005). Others have suggested that ADHD-I and ADHD-C are in actuality distinct disorders (Milich, Balentine & Lynam, 2001). These differences are also suggestive of the presence of impairments in multiple neural circuits (Coghill *et al.*, 2005).

It is becoming more evident that any unifying theory for ADHD must account for different and dynamic developmental trajectories, and most likely multiple neural pathways, to explain the heterogeneity of the disorder (Nigg, 2006; Nigg & Casey, 2005). Neuropsychological research is promising in that it has shown consistent deficits that span across several neural systems, and may serve as a more parsimonious characterization of ADHD subtypes than the current behavioral diagnostic criteria (Nigg, 2005).

Neuropsychological outcomes

The emergence of these various hypotheses regarding the etiology of ADHD has generated considerable discussion and consequent investigation, with a particular focus on some aspect of EF deficits. As a result, several neuropsychological tests have received increased research attention, both as outcome variables for theoretically-driven research and also in an effort to evaluate their clinical usefulness (see Table 13.1). Areas of interest have included measures of inhibition (Continuous Performance Tasks, Go/NoGo, Stop, Stroop Color-Word), planning (Tower of London, Tower of Hanoi; Shallice, 1982; Simon, 1975), set-shifting (Wisconsin Card Sorting Task; Grant & Berg, 1948), organization (Rey Osterreith Complex Figure), working memory (Serial Addition Tests, Digit Span Forward/Backward), visual–spatial memory (Bedard, Martinussen, Ickowicz & Tannock, 2004), and verbal fluency (COWA, FAS).

Continuous performance tasks (CPTs), which measure sustained attention and inhibition, have received significant research and clinical attention. CPTs are widely used, can be easily administered and scored by computer, and take relatively little time to yield multiple variables of attention, reaction time

Table 13.1. Review of commonly used neuropsychological measures in ADHD

Neuropsychological test	Author, date of publication	Cognitive functions tested	Reliability/validity information	Cited references
Conners CPT	Conners, 1995	Inhibition, attention, vigilance	Reliability = adequate to good, has a negative practice effect Validity = low to moderate validity, cognitive processes tested are unclear, excellent sensitivity but low specificity for ADHD Best normative dataset of all of the CPTs.	Epstein *et al.*, 2003; McGee *et al.*, 2004; McGee, Clark & Symons, 2000
Test of Variables of Attention	Greenberg & Dupay, 1993	Inhibition, attention, vigilance	Reliability = good, has a negative practice effect Validity = low to moderate validity, good sensitivity, and questionable specificity for ADHD	Preston, Fennell & Bussing, 2005; Shatz, Ballantyne & Trauner, 2001
Gordon Diagnostic System	Gordon, 1991	Inhibition, attention, vigilance	Reliability = adequate Validity = low to moderate validity, cognitive processes tested are unclear, low discriminant validity for ADHD	Forbes, 1998; Mayes, Calhoun & Crowell, 2001; Reilly *et al.*, 1999;
Wisconsin Card Sorting Test	Grant & Berg, 1948; Heaton *et al.*, 1993	Set-shifting, cognitive flexibility,	Reliability = variable, from poor to excellent	Klorman *et al.*, 1999; Ozonoff & Jensen, 1999

Table 13.1. (*cont.*)

Neuropsychological test	Author, date of publication	Cognitive functions tested	Reliability/validity information	Cited references
		abstract concept formation	between studies, higher in clinical samples, often depends on experience level of examiner Validity = Good validity in adults, but constructs/ factors very general, good sensitivity and poor specificity Poor discriminative validity for ADHD	
Tower of London	Culbertson & Zillmer, 1999; Shallice, 1982	Planning, implicit memory	Reliability = low, particularly between manualized and computerized versions, but little known about its reliability Validity = unclear, questionable for planning, other potential theoretical explanations	Riccio *et al.*, Romine, Davis & Sullivan, 2004; Sonuga-Barke *et al.*, 2002
Tower of Hanoi	Davis, Bajszar & Squire, 1994; Simon, 1975; Welsh & Huizinga, 2001	Planning, implicit memory	Reliability = low, but little known about its reliability, recently revised to improve reliability	Klorman *et al.*, 1999; Kopecky *et al.*, 2005; Ozonoff & Jensen, 1999

Table 13.1. (*cont.*) Review of commonly used neuropsychological measures in ADHD

Neuropsychological test	Author, date of publication	Cognitive functions tested	Reliability/validity information	Cited references
			Validity = unclear, questionable for planning, other potential explanations	
Rey Osterreith Complex Figure Test	Meyers & Meyers, 1995; Rey, 1958; Osterreith, 1944	Planning, visuospatial organization, visual memory	Reliability = variable, ranges from poor to excellent Validity = construct and discriminant are good. Poor discriminative validity for ADHD.	Shin *et al.*, 2003
Stroop Color-Word	Golden, 1978; Stroop, 1935	Inhibition	Reliability = good, but significant practice effects and few alternate forms Validity = good for some constructs, poor discriminative validity for ADHD	Homack & Riccio, 2004; Ozonoff & Jensen, 1999
Trail making tests	Reitan & Wolfson, 1985; Russell & Starkley, 1993	Attention, sequencing, mental flexibility, visual search, motor functioning	Reliability = good, but subject to practice effects Validity = good, better discriminant validity in Trails B	Houghton *et al.*, 1999
Verbal fluency	Benton & Hamsher, 1978; Korkman, Kirk & Kemp, 1998	Verbal fluency		Brocki & Bohlin, 2004; Geurts *et al.*, 2004; Hurks *et al.*, 2004; Mahone *et al.*, 2001

and impulsivity. Several versions are available to clinicians, including the Conners' CPT (Conners, 1995), which is the most commonly used version. The Conners' CPT is utilized in many The National Institutes of Health-funded and industry-sponsored ADHD clinical trials and treatment studies. Other commonly used CPTs include the Gordon Diagnostic System (Gordon, 1991) and the Test of Variables of Attention (TOVA; Greenberg & Dupay, 1993). The different systems are comparable in their diagnostic accuracy (Mayes, Calhoun & Crowell, 2001). In general, on the CPTs, children with ADHD have shown slower reaction times, more omission/commission errors, and an absence of performance decrement over time when compared to typical peers (Losier, McGrath & Klein 1996; Riccio & Reynolds, 2001). There are differences in these patterns of performance between the different subtypes of the disorder (Collings, 2003) and questions remain about the domain specificity of various CPT subtests (Epstein *et al.*, 2003). Similarly, questions about specificity exist. CPT's do not seem to be reliable at differentiating ADHD from other psychiatric conditions (Forbes, 1998; McGee, Clark & Symons, 2000; Preston, Fennell & Bussing 2005; Schatz, Ballantyne & Trauner, 2001). Despite having high sensitivity (72–88%), CPTs have shown very low specificity (20–37%) for identifying ADHD (Rielly *et al.*, 1999).

As discussed above, it is likely that disruptions in central nervous system functioning have an effect on attention, thus affecting CPT scores across diagnostic entities (Riccio & Reynolds, 2001). Despite this, CPTs are often used as the sole diagnostic tool for confirming the presence of ADHD, even when the manual (Conners, 1995) and research findings recommend that it be used in conjunction with a battery of additional tests. Therefore, while the CPT paradigm alone is not ideal for diagnosis, it has become, and ultimately remains a widely considered tool for documenting the impact of ADHD symptoms on attention specifically, and cognitive functioning more broadly. It has also been found to be particularly useful to assess change over time, especially when looking at treatment response (Conners & Barkley, 1985).

Other EF tasks have produced mixed or limited results. The Tower of Hanoi/London (TOH/TOL; Shallice, 1982; Simon, 1975) and the Wisconsin Card Sort Test (WCST; Grant & Berg, 1948) distinguish between ADHD Combined Type and other ADHD subtypes, with the combined group performing worse (Klorman *et al.*, 1999; Kopecky *et al.*, 2005). However, a recent TOL study of 106 children between the ages of 7–15, with ADHD and a comorbid diagnosis (e.g. anxiety, mood, or oppositional/defiant disorder), failed to incrementally differentiate between comorbid conditions, and age and gender were more predictive of performance on the TOL than diagnostic categorization (Sarkis *et al.*, 2005).

Similarly, tasks measuring verbal fluency indicate impaired performance in ADHD on letter-generated (e.g. FAS) fluency, but intact performance on semantic category (e.g. animal) fluency, when children with ADHD are compared to children with other psychopathology or typical development (Hurks *et al.*, 2004; Mahone *et al.*, 2001). Tannock, Martinussen and Frijters (2000) reported deficits in color naming in children with ADHD, which improved with methylphenidate treatment. The Stroop Color-Word test and the Rey Complex Figure Test both appear to distinguish ADHD from typical controls, but have not consistently been found to discriminate ADHD from among other clinical groups (Homack & Riccio, 2004; Shin & Kim, 2003).

Several studies have attempted to examine specific profiles of functioning between disorders that exhibit deficits in EF. These studies are especially relevant given a recent meta-analysis that showed children with ADHD had the strongest and most consistent deficits in several areas, including processing speed (i.e. performance on Trails B), planning (i.e. performance on Tower Tests), organization (i.e. performance on the Rey Osterreith), set-shifting (i.e. performance on the WCST), continuous performance test omissions and commissions, and working memory (Martinussen *et al.*, 2005). Studies comparing ADHD to autism have helped elucidate profiles of EF deficits across disorders. For example, children with ADHD have shown relative deficits in tasks that measure inhibition and verbal fluency, while individuals with autism show specific difficulty with planning and cognitive flexibility (Geurts *et al.*, 2004; Ozonoff & Jensen, 1999).

Despite the advances in theoretically-driven research concerning neuropsychological deficits in ADHD, there are important gaps in the current literature that must be addressed. Many studies do not clarify which subtypes are being tested or whether subjects are being combined across multiple subtypes. Researchers must also identify whether the target group has comorbid disorders that could affect outcome measures. Carefully defined research samples are needed to make valid comparisons between studies. Other psychiatric disorders are needed as controls to address the specificity of putative deficits. Finally, performance on tests can change as a child ages (Brocki & Bohlin, 2004), so longitudinal study is needed to better understand the neurodevelopmental course of the disorder. Overall, the neuropsychological heterogeneity of ADHD must be taken into consideration if EF deficits are to be used as endophenotypes in ADHD research (Doyle *et al.*, 2005).

Many of the findings described above, while interesting theoretically, highlight the absence of an objective diagnostic assessment for ADHD and lack of precision in terms of the sensitivity and specificity of the measures used for diagnosis. The lack of a ''gold standard diagnostic instrument'' only reinforces the use

of multiple subjective and objective tools. Therefore, due to their high sensitivity but low specificity, neuropsychological tests are currently more appropriate as an adjunctive set of measures, rather than a set of diagnostic tools when evaluating for ADHD.

Motor functions

ADHD was once known as "Hyperkinetic Syndrome of Childhood," implicating a dysregulation of motor activity as the core feature. Currently, two of the three ADHD types are characterized by hyperactivity. Children with ADHD exhibit significantly greater activity level than both typical controls and individuals with non-ADHD psychiatric conditions (Halperin *et al.*, 1992), even in their sleep (Corkum, Tannock & Moldofsky, 1998; Konofal *et al.*, 2001). Coordination can also be significantly impaired in ADHD. Although excess motility is a descriptive characteristic of the disorder, individuals with ADHD show reduced physical strength, dexterity, visual–motor coordination, and are at increased risk for poor fitness (Harvey & Reid, 2003). Children with ADHD are often described as clumsy and struggle with motor activities ranging from tying shoes to playing sports (Karatekin, Markiewicz & Siegel, 2003). In fact, there is considerable overlap between ADHD and developmental coordination disorder (Kadesjo & Gillberg, 1998; also see Tupper, this volume).

Motor and phonic tics commonly co-occur in ADHD, and rates of tics in children with ADHD are reported to be around 10% independent of treatment (MTA Cooperative Group, 1999). The natural history of co-occurring tic disorders is such that ADHD symptoms tend to emerge prior to tics, so ADHD is typically diagnosed first. Epidemiologic studies of Tourette syndrome (TS) reveal estimates of 50–75% of children with TS will have comorbid ADHD (Comings & Comings, 1985; Kurlan *et al.*, 2002; also see Hunter, this volume). Often, the ADHD is most impairing in these patients and requires treatment, while tics may not. Previous observational data suggested that methylphenidate (MPH) could permanently exacerbate or induce tics, but empirical studies have not supported this finding (Palumbo *et al.*, 2004; Tourette's Syndrome Study Group, 2000). The high rate of comorbidity between ADHD and TS is hypothesized to involve shared pathophysiology of basal ganglia circuitry (Mink, 2001; Palumbo *et al.*, 1997; Sheppard *et al.*, 1999; for further discussion, see Hunter, this volume).

Another area of interest with regard to motor functioning in ADHD is motor response/execution. Interestingly, one of the cognitive theories described in the previous section, behavioral inhibition (Barkley, 1997*a*) relates directly to motor functioning since it involves the inhibition of a proponent motor response.

It should be noted, however, that putative motor response/execution deficits may be in addition to and not necessarily purely a result of cognitive deficits (Toplak & Tannock, 2005). This question merits further research, as it addresses the issue of core deficits, and may have implications for understanding the endophenotypes of the ADHD subtypes.

Interventions for ADHD

Medications: Stimulants

Stimulants (i.e. methylphenidate; Ritalin; Concerta; Metadate; Focalin; Dexedrine; and Adderall) are the most commonly prescribed and best studied psychotropic medications for children in the United States (Biederman, Newcorn & Sprich, 1991; Safer, Zito & Fine, 1996); Solanto, Arnsten & Castellanos, 2001). Stimulant medications are considered to be first-line treatment for ADHD by the American Academy of Child and Adolescent Psychiatry (2001) and the American Academy of Pediatrics (AAP Subcommittee on Attention-Deficit/Hyperactivity Disorder, 2001). The most significant clinical advance in stimulant treatment is the development and use of effective, long-acting therapies, now widely prescribed. Long-acting stimulants reduce the need for multiple doses and eliminate the need for a midday school dose for the most children with ADHD, thus simplifying treatment.

Preclinical studies have demonstrated that the stimulants mainly block the reuptake of dopamine (DA) and, to a lesser extent, norepinephrine (NE) by presynaptic neurons and increase the release of these monoamines into the synapse (Volkow *et al.*, 1998). While the effects of stimulants in the brain vary, it appears that alteration in dopaminergic and noradrenergic function is necessary for clinical efficacy in treating ADHD. One hypothesis to explain the treatment effects of stimulants for ADHD is that stimulants lead to an enhancing of the inhibitory influence of the frontal cortex noradrenergic pathways on striatal structures that are involved with DA neurotransmission (Zametkin & Liotta, 1998). Stimulant treatment in ADHD has been shown to improve cognitive functions including visual-spatial memory (Bedard *et al.*, 2004); response speed and execution (Bedard *et al.*, 2003; Paule *et al.*, 2000); color naming speed (Tannock *et al.*, 2000); Stroop naming speed (Bedard, Ickowicz & Tannock, 2002); story retelling (i.e. working memory; Francis, Fine & Tannock, 2001); and attention/vigilance (Denney & Rapport, 2001).

Most adverse effects of stimulants tend to be mild and can usually be managed clinically. The most commonly reported side effects include insomnia, decreased appetite, weight loss, irritability, abdominal pain and headaches (Barkley, 2005;

Barkley, McMurray & Edelbrock, 1990). However, some of these purported side effects, such as insomnia and irritability, may be inherent symptoms of ADHD rather than results of treatment (Barkley, 2005). Toxic reactions, although rare, can occur with stimulants and are generally related to excessive dosages. Such toxic effects may include anxiety, agitation, autonomic instability, and psychosis (Biederman *et al.*, 1999).

Recent safety data are equivocal regarding a concern that stimulants might inhibit growth, although subtle reductions in height may be possible (Holtkamp *et al.*, 2002; Lisska & Rivkees, 2003; Poulton & Cowell, 2003; Wilens *et al.*, 2003*b*). A recent one-year study of 6–13-year-old children continuously treated with methylphenidate (MPH) found no significant height reduction over a 12-month period (Wilens *et al.*, 2003*b*). One study conducted with adolescents with ADHD found a delayed tempo of growth associated with ADHD independent of stimulant treatment, and concluded that temporary deficits in growth and height through mid-adolescence may normalize by late adolescence (Biederman *et al.*, 1999). A prospective, follow-up study in adults found no significant reduction of height attained with stimulant use, but side effects such as nausea and vomiting associated with higher dose levels of stimulants were associated with adult growth decrements (Carlson *et al.*, 2000). A study examining bone mineral density, associated with linear growth, found no significant differences in bone density between children treated with MPH for 1–2 years and a control group (Lahat *et al.*, 2000).

An important point to consider when weighing the risks and benefits of stimulant therapy is that the prognosis for untreated ADHD children is quite guarded (Barkley, 2005). The NIH Consensus Statement on ADHD (1998) indicated that children with ADHD who are untreated, or under-treated, have an increased risk for school failure, school drop-out, substance abuse, trouble with the law, and developing additional psychiatric disorders. Indeed, substance abuse may be significantly increased in untreated ADHD adolescents when compared to those who have been treated with a stimulant (Wilens *et al.*, 2003*a*). The persistence of ADHD symptoms, especially inattentive symptoms, in addition to oppositional-defiant behaviors and conduct disorder was predictive of substance abuse in a sample of adolescents referred for treatment (Molina & Pelham, 2003).

Modafanil, an atypical stimulant currently marketed to treat narcolepsy, is currently being studied for safety and efficacy in ADHD treatment. A large, multi-center study has been undertaken to address limited data regarding the efficacy of modafanil in ADHD. Rugino and Copley (2001) reported an open-label study of modafanil in 11 children with ADHD, administered over a four-week time period. Behavioral ratings showed modest improvement in ADHD symptoms, consistent with non-stimulant treatment effects.

However, while the safety and efficacy of stimulant treatment has been extensively studied, the vast majority of subjects studied have been school-aged males with ADHD-C. Studies with adolescents, adults, females and individuals with ADHD-I are less common, and as a general rule, are lacking in the literature. This is of particular concern, because studies have demonstrated that females with ADHD are at a higher risk for developing and demonstrating psychological impairment than males with ADHD (Rucklidge & Tannock, 2001). Important differences in ADHD symptomatology exist as a function of both comorbidity and gender (Newcorn *et al.*, 2001), that have yet to be fully addressed in the pharmacological literature. These findings have important implications for treatment outcomes and warrant further study.

Medications: non-stimulants

Non-stimulant medications have been less well studied than stimulants with regard to ADHD. Fewer studies, smaller sample sizes, and briefer lengths of treatment during studies when compared to stimulants currently limit our knowledge regarding efficacy and long-term safety of non-stimulant therapies. However, there are some neurobiological rationales to support the use of non-stimulants in ADHD treatment. Based on the hypothesis that ADHD is pathophysiologically related to overactivity of the central noradrenergic system (Zametkin & Rapoport, 1987), it has been proposed that the use of medications that act as agonists at presynaptic alpha-2 noradrenergic receptors may be effective. Activation of noradrenergic autoreceptors in the locus ceruleus results in decreased release of norepinephrine and reduced turnover of the neurotransmitter. This has contributed to the move to study noradrenergic agonists as a treatment modality.

Clonidine is a commonly prescribed treatment for ADHD, often in conjunction with a stimulant. Safety and efficacy data were lacking until the TACT study (Tourette's Syndrome Study Group, 2002) which was a multi-center, double-blind, placebo-controlled, 16-week clinical trial of clonidine, alone and in combination with MPH, to treat children with tic disorders and comorbid ADHD. The study demonstrated that clonidine was both safe and effective in reducing ADHD symptoms in children with tics. The combination of MPH and clondine was also found to be safe and the most highly effective in this sample. Clondine seemed to have complementary behavioral effects with MPH and was found to be superior for improving cognitive aspects of ADHD (e.g. inattention) while MPH reduced more of the hyperactivity and impulsivity. A recent study designed to replicate TACT but with a primary ADHD sample (no tics) also demonstrated safety and efficacy of clonidine, with and without MPH. Sedation with clonidine was the most common side effect in both studies. However, the

latter study did not achieve the same robust efficacy with clonidine as demonstrated in the TACT study (Palumbo *et al.*, 2005). Thus, there appear to be differential treatment effects which may be due to differences in the neurobiology of these two groups. Further research is planned to help clarify the differential treatment responses.

Over the past few years there has been increasing use of guanfacine, an alpha2-noradrenergic agonist with a longer half-life and a more favorable side effect profile (less sedating) than clonidine, in managing the symptoms of ADHD. Guanfacine also displays a more selective alpha2A receptor binding profile than clonidine, which is a nonselective agonist. As a result, guanfacine may have a more specific action on the neurotransmitter system important in ADHD; it may also be better tolerated as a result. Research with nonhuman primates concluded that norepinephrine can enhance cognitive functioning of the prefrontal cortex through actions at alpha2A adrenergic receptors and that this process may be important for ADHD (Arnsten, Steere & Hunt, 1996). Administration of guanfacine to monkeys was shown to improve performance on the delayed response task, which is linked to prefrontal cortical function (Leckman *et al.*, 1991).

Recent neuropsychological studies have found that in normal adults guanfacine and clonidine both improve performance on a paired associates learning task, but only guanfacine was associated with improved planning and working memory scores (Jakala *et al.*, 1999*b*). Clonidine (but not guanfacine) caused a worsening of performance on a delayed matching to sample visual short-term memory test (Jakala *et al.*, 1999*a*). These results suggest that the differing pharmacologic profiles of the drugs might result in differing cognitive effects relevant to ADHD and that guanfacine may be superior to clonidine. Concurrent with these studies, two open-label (Chappell *et al.*, 1995; Hunt, Arnsten & Asbel, 1995) and one small, controlled clinical trial (Scahill *et al.*, 2001) have presented evidence to support the efficacy of guanfacine for ADHD. Additionally, one study that compared guanfacine to dextroamphetamine in adults with ADHD found comparable efficacy between the medications on ADHD rating scales and neuropsychological test performance (Taylor & Russo, 2001).

Atomoxetine is a non-stimulant medication recently approved and marketed for the treatment of ADHD. A selective norepinephrine reuptake inhibitor (SNRI), its mechanism of action is believed to be through blockade of the presynaptic norepinephrine transporter. Clinical trials have established efficacy for ADHD, with a moderate treatment effect with low discontinuation effects (Biederman *et al.*, 1999; Michelson *et al.*, 2001). A two-year clinical study of children treated with atomoxetine showed only minimal effects on weight and height (Spencer *et al.*, 2005). Thus, atomoxetine appears to have a similar safety profile as seen with stimulants, with the exception of warnings regarding the

possibility of liver toxicity and suicidal thinking (FDA; 2005). Study results are consistent with anecdotal clinical use reports, indicating that atomoxetine is fairly well tolerated but does not appear to be as potent as stimulants in reducing the full range of ADHD symptoms.

Cholinesterase inhibitors used to treat dementia, such as donepezil, are being investigated for possible use in treating ADHD (Rugino & Copley, 2001), but their efficacy and tolerability have not yet been well established. Wilens and colleagues reported a study with five children in which donepezil was used as adjunctive treatment for ADHD, with demonstrated improvement in behavior and functioning (Wilens *et al.*, 2000). Interestingly, the potential cognitive-enhancing role of cholinergic agents suggests that they may have a treatment effect on EF rather than on the primary symptoms of ADHD. As such, they may play a role as adjunctive treatments for addressing the cognitive effects of ADHD that often prove most problematic for children and adolescents with the disorder.

Additional stimulant and non-stimulant treatments are currently being studied. As such, it is expected that future medication management of ADHD will involve additional, and perhaps adjunctive pharmacologic options. Therefore, while medication treatment may not totally normalize EF and other cognitive functions in ADHD, it is likely to be a critical component to the overall treatment plan.

Psychosocial treatments

The most effective treatment for ADHD is multimodal, and includes medication, academic accommodations, and behavioral interventions (MTA Cooperative Group, 1999). During the NIMH Multimodal Treatment for ADHD (MTA) trial, when psychosocial treatment was combined with medication management, children required lower dosages of stimulants to achieve normalization of behavior and a higher percentage of children achieved normalization when compared to use of either treatment alone. Notably, this finding is often not well reported in the popular press. More importantly, it strongly suggests that medication alone is not the model to follow when working with children and adolescents with ADHD.

Specific psychosocial techniques have been empirically demonstrated as effective in reducing core behavioral difficulties in children with ADHD. These are: (1) parent training (Pelham & Hoza, 1996); (2) classroom management (Pelham & Sams, 1992); (3) social skills training (Brune & Bordenstein, 2001); and (4) academic skills training (Evans, Pelham & Grudberg, 1995). Based on these findings, the National Institutes of Health Consensus Panel on

ADHD (1998) considered multimodal treatment to be the "gold standard" for ADHD therapy and provided practice recommendations that prominently include psychosocial therapies.

Parent training

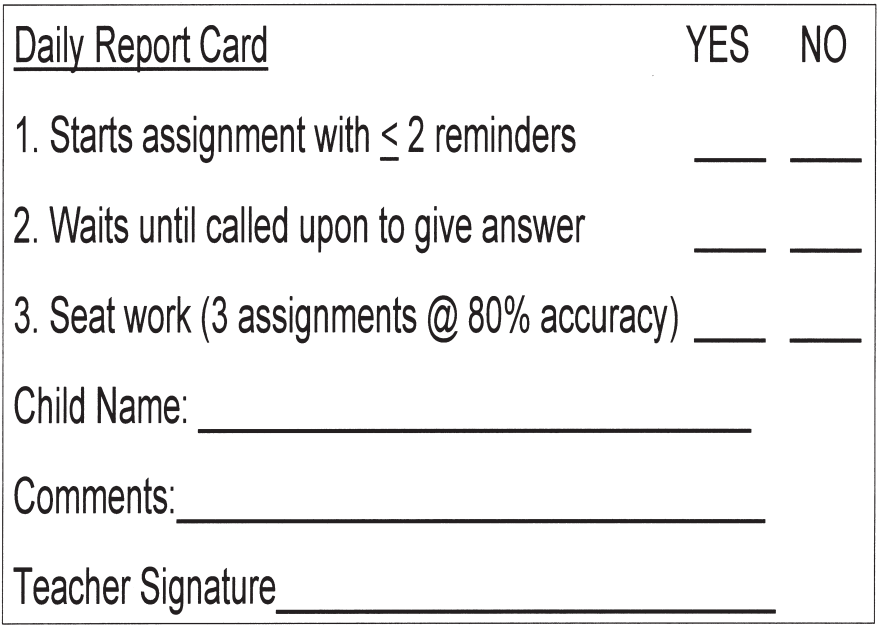
Parent training focuses on behavior within the family. Parents are taught to implement behavioral strategies to help manage their child's ADHD behaviors. Structured parent training programs, such as the COPE program (Cunningham, Benness & Siegel, 1988), have been empirically shown to reduce inappropriate behaviors. With programs such as COPE, parents attend weekly sessions with a therapist over an 8–16 week period. After the initial training period, support and contact with the therapist can be reduced, but continues as long as is deemed necessary for ensuring that effective behavioral management is taking place. Often, during major developmental transitions or life stressors, maintenance sessions and relapse prevention sessions are required. Concurrent classroom management involves collaboration between teachers and parents to target and reduce inappropriate behaviors. Classroom behaviors are identified and a "Daily Report Card" (DRC) is developed which serves to monitor and change identified behaviors (Pelham & Sams, 1992); an example of the DRC is included in Figure 13.1.

The DRC also serves as a means of communication between parents and teachers. Rewards are determined for acceptable behavior and consequences applied for unacceptable behavior. The rewards and consequences are applied both in school and at home so that there is consistent reinforcement for desired behaviors. If the correct rewards have been identified, this is a highly motivating and effective technique that is easily implemented.

Some studies have indicated a lack of incremental value for parent training over medication alone (Wells *et al.*, 2000). There is also evidence that not every family benefits from parent training, as some family attributes, such as high stress or poor communication, can interfere with treatment (Hartman, Stage & Webster-Stratton, 2003). As such, variables that influence the efficacy of parent training constitute a large gap in our knowledge. There is also little research on how parent training affects the generalization of a broader set of behavioral techniques, which is most likely the greatest area of influence for this intervention.

Social skills training

Social skills training occurs in a group setting, and teaches children to improve interactions with peers, resolve conflicts and manage anger appropriately.



Adapted from: Pelham, W.E., & Waschbusch, D. (1999). *Behavior therapy with ADHD children*. In H. Quay & A. Hogan (Eds.) *Handbook of disruptive behaviour disorders*, pp 225-78. New York: Plenum Press.

The Daily Report Card (DRC) should:

1. Identify behavioral goals
2. Select 3-5 target behaviors for DRC
3. Define goals in highly specific terms
4. Explain DRC to child
5. Link DRC with home-based rewards
6. Monitor / modify as needed
7. Troubleshoot with parents and teachers as necessary

Figure 13.1 Sample Daily Report Card

Studies show social skill deficits in individuals with ADHD lead to severe problems with peer relationships, including more conflict with friends and fewer dyadic friendships, which cause them to develop a bad reputation or to experience social rejection by peers (Gentschel & McLaughlin, 2000; Hoza *et al.*, 2005*b*). Social deficits can persist even after successful pharmacological, behavioral, and combined treatments have been undertaken (Hoza *et al.*, 2005*a*). The focus of social skills training is on developing social and behavioral competencies, decreasing aggression and building self-esteem. Initially, sessions occur weekly for anywhere from 8–16 weeks, with follow-up programs for generalization of

skills and relapse prevention. These are often integrated with parent and teacher interventions.

Interestingly, a series of studies looking at social skills intervention have shown no difference between the use of a multimodal approach that involves social skills training and parent training in combination with methylphenidate over methylphenidate alone (Abikoff & Hechtman, 2004*a*; 2004*b*; Hechtman & Abikoff, 2004). This suggests that social skills training may target similar behaviors to those impacted by psychopharmacological treatments, and social skills training may serve as an alternative for families who are reluctant to use medication. Nonetheless, there are few studies on the long-term efficacy and incremental value of social skills training for individuals with ADHD. While there is some evidence that social skills interventions improve assertion, cooperation, and decrease externalizing behaviors in the immediate term, improvement does not often last through follow-up (Antshel & Remer, 2003).

Additionally, future studies need to more thoroughly examine treatment response in subgroups of ADHD, especially since there is some evidence that individuals with ADHD-I respond better than those with ADHD-C to social skills training (Antshel & Remer, 2003). Additionally, many studies show positive effects of social skills training, but are limited by small sample sizes (as small as 4—10) and the absence of control groups. There is also a relative lack of consistency among outcome measures that makes comparisons among findings difficult.

Coaching

"Coaching" is another popular strategy for intervention when working with ADHD children, particularly those with identified executive dysfunction (Dawson & Guare, 2004; see also Mahone and Slomine, this volume). Coaching involves providing feedback to the recipient regarding future or past behavior, that keeps them focused on the task at hand while encouraging them to continue appropriate behaviors. The coaching process has two main steps: (1) setting goals and (2) holding regular, often daily coaching sessions. Goal setting basically helps the recipient select goals that he or she would like to work on, that are focused and attainable, taking into account the developmental level of the recipient. Potential obstacles should be identified, with the outlining of strategies to overcome them. The intervention plan should be in writing and reviewed periodically, allowing for shifting and changing of goals as needed. Daily coaching sessions basically involve a review of the previous day's plan and goal attainment, and developing the plan for the current day; as such, they often occur early in the day, to maximize organization and effect. Rewards for attainment of goals can be incorporated into the plan, which may be most helpful with younger children.

At this time, only minimal research has been provided concerning the use of coaching strategies, outside of educational settings.

Addressing learning disabilities and ADHD

Learning disabilities are estimated to co-occur in approximately 40% of children with ADHD (MTA Cooperative Group, 1999; see also Wills, this volume). For children who exhibit complex behavioral and cognitive problems, such as ADHD, neuropsychological testing is often the most effective means to examine for learning disabilities (LD). Depending upon the type and nature of the LD, specific interventions aimed at ameliorating or accommodating these problems should be implemented. Often, effective intervention will involve educators specially trained in LD, to maximize support and needed accommodation.

Academic skills training targets those abilities necessary for academic success and, in tandem with other ADHD specific supports, helps children improve organizational strategies and study habits. This can often be achieved through the school system, with use of a trained ''teacher's aide'' or resource teacher working with the student both within and separate from the classroom. The identification and implementation of appropriate accommodations and training in select academic strategies is often a necessity for children and adolescents with ADHD; there is evidence that this approach can significantly improve academic and functional outcomes, particularly when combined with other treatments (Barkley, 2005).

In our clinical experience, medication and behavioral treatments alone rarely suffice to address all the child's academic and cognitive limitations associated with ADHD, making school-based interventions a critical treatment component. Classroom accommodations, including preferential seating, extended time for tests and projects, testing modifications, reduced homework load and test-taking in a quiet, distraction-free environment are commonly implemented to aid the child with ADHD in school. In many cases, children with ADHD, especially if LD is present, will require formal classification by the school system. When this occurs, an individualized educational plan (IEP) or more commonly, a ''Section 504 plan'' is implemented, focusing on accommodating the child's particular cognitive and academic weaknesses. Depending upon the child's particular cognitive profile, he or she may receive speech/language services, occupational and/or physical therapy and academic assistance or tutoring in specific areas such as math and reading.

EF deficits in children with ADHD are often not assessed by traditional school testing methods. Therefore, if a child with ADHD has been assessed by the school and is deemed ineligible for services, he or she may require additional evaluation

to determine if EF deficits are significantly impeding school performance. In these cases, neuropsychological evaluation is extremely helpful in delineating the child's cognitive profile and making school-based recommendations for interventions based on those findings.

Future needs regarding ADHD intervention

Children with ADHD often experience compromised functioning in many areas, including behavioral, cognitive, academic, social and interpersonal difficulties. Comorbid psychiatric and learning difficulties are the norm, not the exception, in ADHD. Therefore, thorough medical and psychological evaluation is necessary to identify the full spectrum of the disorder and for effective treatment planning. Neuropsychological assessment, while not diagnostic in and of itself, can be a useful tool to aid diagnosis and treatment. Effective interventions are multimodal and can include medication management, behavioral therapies, social skills training, coaching and academic interventions. Currently, there are no well-controlled empirical studies of cognitive remediation in ADHD to support its use as an evidence-based treatment; as such, studies examining the impact of multimodal treatment and the use of structured interventions, both at home and in the classroom are strongly needed. This is particularly needed with groups less commonly studied, such as females, ethnic minorities, and children with ADHD-I.

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14

Managing dysexecutive disorders

E. Mark Mahone and Beth S. Slomine

Executive function (EF) is a term used to refer to self-regulatory behaviors necessary to select and sustain actions and guide behavior within the context of goals or rules. In essence, EF involves developing and implementing an approach to performing a task that is not habitually performed (Mahone *et al.*, 2002*a*). Initiation, planning, organization, shifting of thought or attention, inhibition of inappropriate thought or behavior, and efficiently sustained and sequenced behavior are all crucial elements of EF. As such, EF should be viewed as a multidimensional construct, comprised of sub-components that are separable from the specific cognitive (i.e. linguistic, visuospatial) domains in which they are assessed (Harris *et al.*, 1995).

Recently, an influential model argued that inhibitory control is the core (and developmentally fundamental) component of EF (Barkley, 2000). Other researchers, however, have proposed that inhibitory control develops in parallel with other more ''intentional'' skills including response preparation and working memory (Rapport *et al.*, 2001). The term ''intention'' is used in behavioral neurology to refer to four component processes: initiation, sustaining, inhibition, and shifting (Heilman, Watson & Valenstein, 1993). Whereas attention is considered to precede sensory detection/perception, intention is thought to occur between sensation/perception and action, and involves a state of preparedness to respond (Denckla, 1996*a*). Intention and working memory may be subsumed under the construct of executive function. Both are fundamental in the development of functional competence in children, and in mediating the severity of presentation of a variety of learning problems. Children with executive dysfunction may fail to adequately develop the requisite skills to interact productively and effectively with the environment, despite appropriate intelligence. Thus, interventions designed to ameliorate the impact of cognitive deficits in other domains (e.g. language, visuospatial skills, academic skill) should take into account not only the child's intellectual level and availability of external support, but on the integrity of these executive control skills (Mahone & Zabel, 2001).

Neurobiology of EF

Executive functions are supported by a distributed neural network with cortical and subcortical components including the frontal cortex and its striatal-thalamic-cerebellar connections (Durston, 2003; Royall *et al.*, 2002). Current neurological models of frontal lobe structure and function have their basis in a well-described series of five parallel frontal-subcortical circuits (Lichter & Cummings, 2001), of which two are related to motor function, originating in skeletomotor and oculomotor regions of the cortex; the other three, originating in dorsolateral prefrontal, anterior cingulate and orbitofrontal cortices, are thought to be crucial in cognitive (''executive'') and socioemotional control. Frontal projections to the basal ganglia and cerebellum form a series of frontal-striatal-thalamo-frontal and frontal-cerebello (dentato)-frontal circuits (Krause *et al.*, 2000). These circuits link specific regions of the frontal lobes to subcortical structures, supply modality-specific mechanisms for interaction with the environment, and provide the framework for understanding the neurobiological relationship among disorders (Castellanos, in press). In order to link these frontal-striatal circuits to behavior, Heilman and colleagues (Heilman, Voeller & Nadeau, 1991; Heilman, 1994) conceptualized the striatum as acting to gate sensation into two systems: ''how'' (organization and praxis) and ''when'' (response inhibition). This frontal-subcortical network thus supports these intentional ''how and when'' functions that range from the more elementary boredom tolerance to higher-order problem solving functions.

Childhood disorders with executive dysfunction

There are major periods of gain in skills supporting EF that that are thought to correspond to periods of myelination and maturation of the prefrontal cortex and frontal-striatal brain systems (Brocki & Bohlin, 2004). The frontal systems that support EF have a protracted period of development (Thompson *et al.*, 2005), and are vulnerable to disruption via a variety of etiologies. This is likely why so many children with acquired neurological or neurodevelopmental disorders present with concerns involving executive dysfunction. A variety of known neurological conditions are associated with executive dysfunction, including (but not limited to) traumatic brain injury (Slomine *et al.*, 2005), hydrocephalus (Burmeister *et al.*, 2005), early treated phenylketonuria (Gassio *et al.*, 2005), obstructive sleep apnea (Beebe *et al.*, 2004), some forms of epilepsy (Riva *et al.*, 2005), and late effects of chemotherapy and radiation (Anderson *et al.*, 1997). In addition, a number of behaviorally defined neurodevelopmental or neuropsychiatric disorders commonly present with executive dysfunction, including Attention Deficit Hyperactivity Disorder (ADHD; Willcutt *et al.*, 2005), dyslexia (Reiter, Tucha & Lange, 2005), Obsessive Compulsive Disorder (OCD; Evans, Lewis & Iobst, 2004),

and high functioning autism (Goldberg *et al.*, 2005). Children with Tourette syndrome tend to manifest executive dysfunction only when the disorder coexists with ADHD and/or OCD (Mahone *et al.*, 2001; Mahone *et al.*, 2002*a*). Similarly, children with mood and/or anxiety disorders may not manifest executive dysfunction unless they also have some other neurological disorder or ADHD.

There is emerging evidence that the subcomponents of executive dysfunction observed in children may be dissociable — especially with respect to inhibitory control and working memory. For example, children with high-functioning autism have been found to have impairments, relative to controls, on spatial working memory tasks (Goldberg *et al.*, 2005), yet perform similarly to controls on measures of inhibitory control (Nyden, Hjelmquist & Gillberg, 2000; Ozonoff & Jenssen, 1999). Conversely, children with ADHD commonly show deficits, compared to controls, on tasks of inhibitory control (Mahone *et al.*, 2001; 2005; Mostofsky, Newschaffer & Denckla, 2003), and working memory (Martinussen *et al.*, 2005). Children with spina bifida and hydrocephalus are rated by their parents as having significant problems with initiation and working memory, but have relatively spared skills in behavioral regulation and inhibitory control (Mahone *et al.*, 2002*c*). Thus, interventions must address the multidimensional nature of executive dysfunction, accounting for the unique patterns of impaired and preserved skills found in different disorders.

Development of executive functions in childhood

The natural history of the challenges and associated risks observed in children and adolescents with neurological disorders can be delineated from the developmental systems perspective. Young children with brain compromise are especially vulnerable to difficulties with regulation of behavior, attention, and stamina, all of which can impact functional independence. Developmental neuropsychologists need a framework for approaching childhood executive control deficits that includes an understanding how the child's nervous system interacts with his/her environment, and how these interactions change over time. In children there is often no focal lesion, but rather a disruption to normal overall brain development, typically affecting multiple neurobehavioral systems. These children are often "off developmental track" in comparison to their peers, and traditional developmental timelines, based on theories of normal development, may be less applicable (Mahone & Slomine, in press). Yet, expectations that exist in the academic setting are based on skills presumed to be "on line" at each major transition. Many children with executive dysfunction experience periods of stress and unexpected difficulty at ages when dramatic increases occur in expectations for independent functioning as well as rapid and efficient information processing (Holmes, 1987).

Preschool

Prefrontal brain systems undergo rapid changes during the preschool years, including pruning of synaptic connections and subcortical myelination (Thompson *et al.*, 2005). Correspondingly, there has been an increased interest in assessment of EF in preschool children over the past ten years (Espy *et al.*, 2001; Espy, 2004; Zelazo *et al.*, 2003). In preschoolers, these skills (particularly inhibitory control, rule use, working memory and motor persistence) play a significant role in the development of socialization and the readiness for academic learning. A variety of disorders have been associated with measurable, yet dissociable, evidence of executive dysfunction in the preschool years (Espy, 2004). For example, former preterm infants demonstrate more perseverative errors on visual search tasks than age-matched controls (Espy *et al.*, 2002). Children with autism also have increased perseverative behavior (McEvoy, Rogers & Pennington, 1993), but not deficits in planning or working memory (Griffith *et al.*, 1999). Preschoolers with lead exposure perform most poorly on tests of spatial working memory, set-shifting, and planning (Canfield, Gendle & Cory-Slechta, 2004), while preschoolers with ADHD have deficits in inhibition and sustained attention, but not consistently in working memory (Mahone *et al.*, 2005). Preschoolers with traumatic brain injury show deficits in both working memory and inhibitory control, but not on tasks requiring shifting of response set, and only in groups older than 36 months, suggesting that performance-based measures may not be sensitive to certain forms of executive dysfunction prior to age three (Ewing-Cobbs *et al.*, 2004). Indeed, neurological dysfunction in young children may not translate directly to behavioral deficits in preschool and early elementary school, due to the high level of structure provided in classroom settings (Bernstein & Waber, 1990), coupled with the relatively low demands for independent work completion, and the (expected) willingness of helping professionals to break complex tasks down into manageable parts. These children, nevertheless, often possess the biologic risk, and often "grow into" their executive dysfunction.

School-age years

In school-aged children, EF skills are central to successful acquisition and efficient use of academic skills, particularly in efforts to overcome learning problems of all kinds (Denckla, 1996*a*, *b*). By fourth grade, emphasis on individual skill acquisition (i.e. learning to read) gives way to a new expectation of independent skill utilization (i.e. "reading to learn"). As children with executive dysfunction are exposed to these new expectations, a core problem begins to emerge. While they have reasonable access to single skills, they may lack the ability to bring these skills together and use them efficiently for more integrated learning exercises. Academic and behavioral performance often begins to decline as the

step-by-step learning environment of the first and second grades is replaced by expectations of independent utilization of these "learning to learn" skills (Bernstein, 1996). Coupled with the increased volume of information to be learned comes the marked increase in demand for writing (requiring fast and efficient graphomotor skill) as the primary means of communicating knowledge, and a rapid increase in the demand for automaticity in accessing previously learned skills (Mahone & Zabel, 2001). Problems in motor or procedural learning (also dependent on basal ganglia and cerebellar function and a component of nearly all demonstrated academic skills) may be seen at this point. When such deficits exist, they lead to slow and inefficient behavioral output, and the requirement for deliberate, controlled (and likely cortically-based) mental effort to perform tasks that are expected to be overlearned or automatic by this age. When children must focus attention on these procedural aspects of work, they have less ability to focus that attention on the actual content areas being taught, and may begin to appear more "inattentive."

Adolescence

Middle school represents a major increase in the demand for organizational skills. As children and adolescents with executive dysfunction reach middle school, problems with inhibitory control may less noticeable, and issues with spontaneous use of skills, strategic initiation of tasks, and mental flexibility often become more salient. They are required to "remember to remember" to initiate and complete daily activities on a regular schedule, and must manage academic work that is increasingly integrative and longer in length. Thus, when working with adolescents with executive dysfunction, it is important to consider the concept of a "time-referenced symptom" (Rudel, 1981), which considers risk in response to the expected changes in demands in the environment at different stages of development (Bernstein, 2000). An apparently benign insult (with few immediate effects) can have more significant impact later, as the nervous system grows and the loss of function assumes greater consequence in a person's life (Mahone & Zabel, 2001).

Measurement of executive functions

The general approach to assessment of executive functions draws information from three primary sources; history, observations, and formal testing (Bernstein & Waber, 1990), but takes into account the unique life circumstances and the chronicity of illness seen in children. Despite the plethora of assessment methods available, parents often report to clinicians that their child is not well understood, and note that assessments often fail to "fit" with the child who they observe in the home. Neuropsychologists use four types of test procedures

to assess the EF construct: (1) individual tests designed to measure specific aspects of EF (e.g. Tower of London, Verbal Fluency); (2) parent/teacher rating scales (e.g. Behavior Rating Inventory of Executive Function – BRIEF; Gioia *et al.*, 2000); (3) ''process'' observations (e.g. percent set-loss errors on Verbal Fluency from the Delis-Kaplan Executive Function System – D-KEFS; Delis, Kaplan & Kramer, 2001); and (4) intra-individual contrasts within/between tests with presumed low and high demand for executive control (e.g. D-KEFS Trail Making Test Number–Letter Switching versus Visual Matching). While all four procedures are readily available to the clinician, there is limited support for the validity of the latter two methods in children and adolescents (Beebe, Ris & Dietrich, 2000; Wodka *et al.*, 2006*b*). Rating scales such as the Behavior Rating Inventory of Executive Function (BRIEF; Gioia *et al.*, 2000), which incorporate a wide range of sub-components of the EF construct and rate behaviors seen in daily life functioning, may enhance the ecological validity of clinic assessments, and potentially contribute to better prediction of patient outcomes. Indeed, the BRIEF has been shown to capture executive dysfunction in clinical groups when performance-based measures alone have not (Cummings *et al.*, 2002; Mahone *et al.*, 2002*a*).

The relationship between IQ and predictive validity of neuropsychological tests has also been the topic of some controversy (Jung *et al.*, 2000; Russell, 2001). Dodrill (1997; 1999) observed that while IQ scores below the average range are often correlated with a variety of neuropsychological measures, the same relationship does not hold true for individuals with above average IQ. In contrast to IQ tests, most neuropsychological tests (especially those assessing executive functions) were designed to measure deficits. Floor or ceiling effects of the neuropsychological measures may limit the correlation with IQ among individuals with either very low or well above average IQ (Russell, 2001). For example, children with ADHD are often described by parents as having impairments in ''real-world'' functioning, even when they have above average intelligence and are free from associated learning disorders (Mahone *et al.*, 2002*a*). These findings call into question the ecological validity of laboratory measures of EF, especially among children who are either bright or gifted, or for those functioning well below the average range, and suggest that performance-based measures of EF may be of limited utility in these groups (Mahone *et al.*, 2002*b*).

Evidence-based intervention for executive dysfunction

In the adult literature, there are a growing number of studies examining the efficacy of interventions to improve EF (for review, see Turner & Levine, 2004). In contrast, there are very few studies that have examined efficacy of intervention

techniques targeting EF in children. While there is a paucity of research on the efficacy of neuropsychological interventions to address executive dysfunction in children, there is an emerging literature describing the theoretical considerations and models for remediation of EF in children (Marlowe, 2000; Ylvisaker, Szekeres & Haarbauer-Krupa, 1998; Ylvisaker *et al.*, 2005). Because of this gap in the literature, the remainder of this chapter will focus on both general and specific principles of intervention for executive dysfunction. When possible, evidence-based treatment strategies will be provided. Table 14.1 includes a summary of relevant evidence-based studies of neuropsychological interventions for executive dysfunction. Additionally, there exists a growing research literature highlighting the efficacy of pharmacological intervention targeting EF in children. The pharmacological interventions are briefly summarized below, followed by a more detailed review of neuropsychological interventions.

Pharmacological interventions

Stimulant medications such as methylphenidate have been used extensively to treat executive dysfunction in children with ADHD. These medications have consistently been associated with improvement in executive function, including measures of verbal and visual working memory, motor planning, and response inhibition (i.e. Barnett *et al.*, 2001; O'Driscoll *et al.*, 2005; Vance, Maruff & Barnett, 2003). Methylphenidate has been used for treatment of EF deficits in children with other neurological disorders such as traumatic brain injury, epilepsy, brain tumors, leukemia, and encephalitis, although its effectiveness in these populations is less clear (Weber & Lutschg, 2002).

Other medications have also shown promise in minimizing EF dysfunction. For example, in children with traumatic brain injury and EF difficulties, amantadine hydrochloride, a dopamine agonist and psychostimulant, was associated with improved parent ratings of EF (Beers *et al.*, 2005). Similarly, an alpha-2a adrenergic agonist, guanfacine, was also found to improve parent ratings of EF in children with Tourette Syndrome (TS) and mild executive dysfunction (Cummings *et al.*, 2002).

General principles for neuropsychological interventions for executive dysfunction

A theme common in neuropsychological intervention techniques involves an in vivo, systematic approach to teaching problem solving during everyday activities. The few intervention studies that have been conducted (primarily in adults with traumatic and acquired brain injuries) support this approach

Table 14.1. Evidence-based studies of neuropsychological interventions for executive dysfunction

Study	Participants	Age range	Intervention	Study design	Main outcome measures/results	Generalization	Follow-up
MTA cooperative group, 1999	579 children with ADHD	7–9	Medication, behavioral treatment, combined, or standard community care for 14 months	Randomized controlled trial	All four groups showed reduction in symptoms with combined treatment; medication management superior to behavioral treatment and standard of care and parent and teacher ratings	Few differences on other measures between four groups	Not assessed
Pelham *et al.*, 2000	117 children with ADHD, 60 in the combined medication and behavior group, 57 in behavior only group	7–9	Combined medication and behavior versus behavior intervention only during summer treatment program	Randomized controlled trial	Children in combined group were better than behavior-only group on five measures, rule following, sportsmanship, peer negative nominations, and teacher post-ratings	No difference on 30 additional measures	Not assessed
Konrad *et al.*, 2000	94 children, 31 with ADHD,	8–12	Positive feedback for successful response	Controlled group study	Response inhibition improved to the level of controls	Not assessed	Not assessed

	37 with TBI, and 26 controls		inhibition on a computerized stop-signal task		in children with ADHD. Children with TBI improved, but not as much		
Wodka *et al.*, 2007	58 children with ADHD and 84 controls	7–16	Immediate visual reinforcement for correct responses; immediate response costs for errors	Controlled group study	Children with ADHD had significantly more errors than controls on go/no-go test, even when provided reinforcements and feedback; ADHD group performed worse when given feedback than when not given feedback	Not assessed	Not assessed
Klingberg *et al.*, 2005	53 children with ADHD, non-medicated, impaired working memory	7–12	Computerized, mass practice of working memory task	Randomized, controlled trial	Span board task improved	Parent ratings showed significant reduction in inattention and hyperactivity/impulsivity	3-month follow up, maintained improved spatial span and parent ratings
Michel *et al.*, 2005	40 children, 20 with ADHD and matched controls	7–12	Varying types of monetary reinforcement for	Controlled group study	Stop-signal reaction time improved in both groups, but	Not assessed	Not assessed

Table 14.1. (*cont.*) Evidence-based studies of neuropsychological interventions for executive dysfunction

Study	Participants	Age range	Intervention	Study design	Main outcome measures/results	Generalization	Follow-up
	with impaired behavioral inhibition		behavioral inhibition on a stop-signal computer game		controls reacted faster on go trials and children with ADHD improved ability to inhibit responding with both immediate and delayed reinforcement		
Slusarek *et al.*, 2001	33 children with ADHD, 33 with other psychiatric disorders, 33 controls	6–12	Varying types of reinforcement for behavioral inhibition on a stop-signal computer task	Controlled group study	The performance of children with ADHD improved with high vs. low incentive	Not assessed	Not assessed
Butler & Copeland, 2002	31 off-therapy cancer survivors with impaired attention	6–22	Three components: attention exercises, metacognitive strategies, cognitive behavioral strategies	Controlled group study	Conners CPT improved	Digit span and sentence memory improved, arithmetic did not	Not assessed
Klingberg *et al.*, 2002	14 children with ADHD	7–15	Computerized, mass practice of working memory task	Randomized, double blind, placebo controlled	Trained spatial working memory improved	Untrained spatial memory, visual reasoning improved; motor activity decreased	Not assessed

Yerys *et al.*, 2003	6 children with sickle cell disease with impaired memory	11–15	Academic tutoring vs. tutoring and specific learning/ memory strategies	Controlled group study	Word list and digit span improved in the strategy group relative to tutored-only group	Not assessed	Not assessed
Suzman *et al.*, 1997	5 children with ABI with impaired problem solving	6–11	Four components: problem solving training	Case study	Computer game improved	Improved ROCF, word fluency, antecdotal report of improved real life tasks	Not assessed
Gureasko-Moore *et al.*, 2006	3 boys with ADHD; with impaired organization of materials; all taking methylphenidate	12	Self-management training and monitoring	Case study	Teacher ratings of classroom preparation skills improved	Not assessed	Maintained several days after treatment faded
Snyder & Bambara, 1995	3 boys with LD with impaired organization of material	14	Self-management training and monitoring	Case study	Teacher ratings of classroom preparation skills improved	Not assessed	Maintained treatment effect during once per week follow up
Feeny & Ylvisaker, 2003	2 children with TBI with impaired behavioral regulation and organization	6–7	Cognitive and behavioral support, executive function routine	Case study	Decreased frequency of aggression and disinhibited behavior	Antecdotal report of improved real life tasks	8 year follow up showed continued low rate of disruptive behavior

Table 14.1. (*cont.*) Evidence-based studies of neuropsychological interventions for executive dysfunction

Study	Participants	Age range	Intervention	Study design	Main outcome measures/results	Generalization	Follow-up
Zabel *et al.*, 2004	1 girl with spina bifida with impaired initiation	13	Use of programmable assistive device	Case study	Improved parent satisfaction with child's initiation of self-catherization	Not assessed	Not assessed
Crowley & Miles, 1991	1 boy with TBI with impaired self-monitoring	16	40 one-hour sessions to address deficits in mathematical calculations, mostly related to poor self-monitoring, sequencing, and perseveration	Case study	Test performance improved from 48% to 59%; improved completeness and performance on mathematical calculation		Dropped below goal level when cues were removed

(Cicerone *et al.*, 2005). The most common methods of intervention strategies for improving performance of functional life skills among children with executive dysfunction are described below. Firstly, the best context for intervention is through everyday functional activities. Teaching cognitive processes in a wholly decontextualized manner is of questionable value, as intervention devoid of context rarely leads to generalization to the real world (Ylvisaker *et al.*, 2005). Based on this view, it is imperative to teach and support executive control skills in the context of every day routines. Specifically, as the child learns to complete a multistep task by following a set sequence of steps (with multiple opportunities to practice the routine), the task becomes less novel and the child is able to improve functional activities with less reliance on higher level (effortful) executive control skills. Moreover, these executive control skills emerge and develop from employing a process of slowly introducing EF demands into routines, such as expecting the child to initiate each step independently, or alternate the sequence of steps to achieve a goal more efficiently.

Secondly, individuals with executive dysfunction should be taught the general problem-solving strategy of systematic thinking (Marlowe, 2000; Ylvisaker *et al.*, 2005). Because executive dysfunction involves a discrepancy between ''knowing and doing'' (Denckla, 1996*a*), teaching skills is not sufficient. Interventions must also be rehearsed, coached, and practiced (in order to support overlearning or automaticity) in the environment in which they will be needed, explicitly supporting the ''how and when'' skills associated with the child's unique areas of problem behavior. These skills should be taught in a developmentally sensitive manner, involving the careful consideration of the child's cognitive development and his/her developmental needs and challenges (Holmbeck, Greenley & Franks, 2003).

Thirdly, the development of *metacognitive skills* is essential in promoting functional competence and independence (Marlowe, 2000; Mateer, Kerns & Eso, 1996). Metacognition is the knowledge about the nature and content (including strengths and weaknesses) of one's own cognitive skills. It involves the ability to reflect and act on the knowledge of one's own cognition in order to modify those processes and strategies (Dennis *et al.*, 1996). Metacognition includes active regulation, self-monitoring, and self-evaluation of cognitive processes, in which the child gradually takes conscious control of the learning. For example, a child using metacognitive strategies recognizes that he/she is a slower writer and asks for extra time on a class assignment. Children have been observed to improve functional life skills when they are taught explicitly to identify causes of success and failure, and when they are provided direct feedback about their performance. Specifically, developing these metacognitive skills have proven to be successful in improving functional skills in children with ADHD

(Gureasko-Moore, DuPaul & White, 2006), learning disorder (Snyder & Bambara, 1997) and brain injury (Crowley & Miles, 1991).

A fourth principle used to promote functional life skills in children involves structuring the child's environment by establishing simplified, consistent routines for daily tasks. Children exist in multiple contexts (most notably, home and school) that include a variety of supports or risk factors that must be modified or fostered to enhance treatment outcomes (Mash, 1998). Treatments are best implemented in each setting by those people with whom the child has the most daily contact (e.g. parents, teachers, coaches) in order to bring about maximum benefit. These "everyday people" (Ylvisaker *et al.*, 1998) are often readily available to implement routines and provide the most immediate feedback, enhancing functional skills and contributing to the development of metacognitive strategies. Initially, the feedback is external to the child. Its effectiveness depends on the immediacy and consistency with which it can be given, and thus made part of the child's routine. Immediacy and consistency of external feedback also support the establishment of routines, which allow for tasks of daily living to become more automatized and habitual, thus allowing the child to focus attention more directly on new learning. As tasks become more automatized and habitual, supports can be faded out.

Below are descriptions of interventions geared toward ameliorating the functional impact of executive dysfunction manifest in the "intention" skill deficits of preparing to respond (i.e. initiation, planning/organization) and inhibitory control, as well as those that focus more on supporting working memory dysfunction. While interventions have been separated below to address these specific subcomponents of EF, it should be noted that there is significant overlap. Dysfunction in one area (e.g. initiation) may impact skill development in another area (e.g. planning); conversely, intervention in one area may positively impact dysfunction in another. In addition, it is recognized that interventions necessarily change depending on the age and functional level of the individual, and should be modified at known developmental transitions. For example, treatments for preschool children must include feedback that is tangible, immediate, and frequent. In contrast, treatments for adolescents recognize the increased organizational demands of middle school, along with the emergent desire for autonomy (Chronis *et al.*, 2001). A list of general strategies for EF intervention (considering the age of the child) is provided in Table 14.2.

Interventions for initiation

There is scant literature describing intervention strategies for children with deficits in initiation, although interventions to support initiation emphasize

Table 14.2. Intervention strategies for executive functions

Problem	Age	Strategies
Initiation	Preschool	• Place a variety of age-appropriate toys within reach • Model play with toys • Prompt the child to engage in playing • Reinforce attempts at self-play
	School-age	• Develop a list of tasks • Prompt child before each step of multi-step tasks • Establish a system of verbal or nonverbal signals to cue • Reinforce self-initiating of tasks
	Adolescence	• Develop predetermined schedule with start times • Use a prompting system (checklists, post-its, pager) • Reinforce for developing and using a task list and starting independently
Planning and organizing	Preschool	• Establish and employ routines • Encourage use of narrative language to promote organization • Use photos or symbols to guide the child through multi-step tasks
	School-age	• Teach mnemonic strategies and categorization (e.g. graphic organizers) • Teach strategies to identify goals and plan steps to attain goal • Discuss with teachers how much time should be spent on homework • Emphasize the planning process repeatedly
	Adolescence	• Create time lines for long-term projects • Set aside a 'study time' each day for planning and prioritizing assignments • Carry a written log of activities, schedules, assignments, due dates • Monitor effectiveness of the organizational systems
Problem	Age	Interventions
Inhibitory control	Preschool	• Keep unnecessary objects out of reach • Provide clear expectations and rules • Use short directions and visual presentation of rules (e.g. stop signs) • Give child immediate and frequent feedback about behavior • Frequently change and rotate salient reinforcers

Table 14.2. (*cont.*) Intervention strategies for executive functions

Problem	Age	Strategies
	School-age	• Remove unnecessary distractions • Teach skills that promote emotional control (i.e. counting to 10) • Use a reinforcement system to promote compliance
	Adolescence	• Create contracts with clear consequences • Teach internal verbalizations to stop and think before responding • Teach strategies to check work for careless mistakes • Reinforce careful behavior
Working memory	Preschool	• Simplify and repeat directions as necessary • Slow rate or presentation • Alert child when essential information is presented • Establish and employ routines for most daily activities • Use photos or symbols to guide child through multistep tasks
	School-age	• List tasks to be completed – refer to list regularly • Written directions for multistep tasks • System of verbal or nonverbal signals to cue the child • Check in regularly on extended tasks • Reinforce the child for checking and following the list of tasks/instructions
	Adolescence	• Implement organizing devices (calendar, PDAs) • Rehearsal and pre-teaching of new material • Daily use and review information in storage devices • Encourage active listening (ask questions regularly)

cueing the "how" and "when" aspects of task approach skills have been examined in adults with deficits in initiation (e.g. O'Connell, Mateer & Kerns, 2003). For children with initiation deficits, cues can be generated directly by caregivers (teachers, parents, siblings), by strategically placed signs or notes (e.g. a note on a bathroom door or on a desk in the class), or through technical assistance (e.g. timers, alarms, watches, pagers). Caregivers can help a child by establishing a set schedule for when tasks are to be completed, then cueing the child if the task is not initiated at the designated time. The child can decide how to be cued, and can use verbal or nonverbal signals from the caregiver, alarm clocks, or cues temporally related to a naturally occurring event (e.g. immediately after lunch; Dawson & Guare, 2004). Pagers can also be used to help remind individuals

to start a self-care activity that has been otherwise taught and mastered. Using a paging system, reminders and other messages can be sent at pre-designated times. While paging systems have been useful for adults with executive dysfunction (Wilson *et al.*, 2001), few studies have examined the use of paging systems with children. In one case report, a paging system with a displayed message (i.e. ''time to catheterize'') was useful in increasing parent satisfaction with independent initiation of a self-care task in an adolescent with spina bifida (Zabel *et al.*, 2004).

The process of cueing to promote spontaneous initiation is supported with a number of discrete steps. First, it is crucial that the child is familiar and proficient with the task to be completed; otherwise, poor initiation may be due to anxiety or lack of knowledge. For example, before a child with paraplegia can spontaneously initiate needed weight shifting in the wheelchair (to avoid pressure sores), he/she must first practice and master the task under supervised conditions. During practice, the child is explicitly guided through the correct physical movements to complete the task. Secondly, self-talk strategies (e.g. ''the alarm is going off, so I need to shift my weight'') can be used to minimize confounding working memory dysfunction, and to increase the child's motivation for independent behavior. Self-talk strategies also can be helpful to assist the child in re-starting or providing concrete transitions when work stops for any reason. Thirdly, it is often helpful to have a written plan/schedule for when a task is to be completed (e.g. perform a weight shift every 2 hours). Fourth, use multiple external cues (e.g. alarm, teacher reminder, sign on desk) for each task to be initiated. Finally, the same ''everyday people'' who provided cues can be available to help fade cues as the child becomes more independent with initiating the task.

Interventions for organization and planning

Several strategies for managing problems with organization and planning have been described in the literature (Marlowe, 2000; Ylvisaker *et al.*, 2005). These strategies recognize that it is important to engage children in familiar/organized routines and provide only as much external support as needed to complete the task. The effectiveness of a highly structured routine has been validated in school-aged children with significant executive dysfunction (Feeny & Ylvisaker, 2003). In addition to a structured routine, strategies that explicitly teach the child the process of learning and delineating how information is organized promotes organized problem solving. For example, teaching an organizational strategy to learning list of words was found more efficacious than general academic tutoring in improving word list recall (Yerys *et al.*, 2003) in adolescents with executive dysfunction.

Marlowe (2000) emphasized that children with executive dysfunction can be taught steps to problem-solving, including identifying a goal to be accomplished, identifying potential strategies to accomplish goal, selecting best strategy, developing a sequential series of steps to accomplish plan, identifying and collect materials to complete task, beginning task according to plan, monitoring for accuracy, modifying as necessary throughout the task, and cleaning up. The efficacy of a problem-solving training program, which employed many of these components, was examined in a small group of children following brain injury. Results revealed that this type of training technique improved performance on a computer-based problem-solving task (Suzman *et al.*, 1997). Moreover, participants, parents, and teaching staff reported generalization of the training program.

Language development plays a critical role in enhancing a child's ability to plan and organize plan (Marlowe, 2000; Vygotsky, 1962). Ylvisaker and colleagues have emphasized the importance of helping the child to create a narrative about how to approach problems in an organized fashion (Ylvisaker *et al.*, 1998). A similar approach involving verbal labeling and highlighting the steps to a task has been outlined by Bernstein (1996). Throughout tasks, increasingly use language that highlights organizational components of the activity. The use of language is critical to the development of a plan. Explicit language is necessary to identify what steps are involved in completing a task, how long will each step take, what materials are needed, and what sequence of steps is necessary (Marlowe, 2000; Ylvisaker *et al.*, 1998). At the end of the task, plans and goals are reviewed in order to discuss what worked and what did not. This type of explicit training in verbal mediation strategies has been found to improve organizational skills in adolescents with ADHD (Gureasko-Moore *et al.*, 2006) and learning disabilities (Snyder & Bambara, 1997), and has shown positive effects on homework completion/accuracy among adolescents with ADHD (Habboushe *et al.*, 2001).

Providing external organizers in order to cue children to guide themselves through multistep activities can enhance performance, compared with simple verbal instruction. For young children, sequenced photos of child engaged in a routine can be used. These photos can be adapted to the specific demands of the routine. Written cues can be used for older children who are more proficient readers. Since many children with organization and planning problems can learn routines, but have more difficulty with novelty, it is essential to train all caregivers (''everyday people'') on routines in place. Feeney and Ylvisaker (2003) employed graphic organizers, specifically photograph cues, along with a structured daily routine and several additional cognitive and behavioral strategies to improve disruptive behavior in two children following TBI. Results indicated significant

reduction in the target behaviors following the implementation of external organizers combined with a daily routine and cognitive/behavioral supports.

Interventions for inhibitory control

Because deficits in inhibitory control often present as disruptive behavior or impaired socioemotional regulation, strategies that identify environmental antecedents that precede disinhibited behavior are important. Additionally, it is often necessary to set up and implement a system that reinforces appropriate behavior by providing clear expectations about how to behavior and what to expect (e.g. stickers, or points to earn a larger prize) following explicitly defined "good" behavior. Alternatively, consequences for unwanted behavior should also be made explicit and employed consistently. Controlled studies of intervention to improve behavioral inhibition reveal that children with ADHD can respond to reinforcement with improved inhibitory control (Michel, Kerns & Mateer, 2005); however, they may need a high incentive reinforcer in order to demonstrate improved inhibition (Slusarek *et al.*, 2001). Further, the presentation of reinforcers may change given the age of the child. In preschool children, for example, it is important to provide clear instructions for what to do, rather than what not to do, in order to reduce off task behavior. To illustrate, if a child is grabbing items on a table, instead of saying, "don't grab," it is preferable to tell the child to place his or her hands in his/her lap. Older children may benefit from cues to "stop and think," or strategies including taking a deep breath or counting to 10 before responding. Elementary and middle school children benefit from establishing an internal system of verbal or nonverbal signals to cue attention and self-control of disinhibited behavior (Suzman *et al.*, 1997; Crowley & Miles, 1991).

While these behavior management techniques are often helpful for children with inhibitory control difficulties, they usually do not ameliorate the problem entirely. Children with ADHD, for example, have increased disinhibition (relative to controls), even when provided immediate reinforcement for correct responses and response costs for errors (Wodka *et al.*, 2007). Similar findings were noted in a group of children with TBI (Konrad *et al.*, 2000). Therefore antecedent control (in addition to reinforcement programs) may be particularly salient in children with neurodevelopmental or acquired neurological disorders.

Some of the most compelling evidence for behavioral intervention to improve inhibitory control in children comes from intensive summer treatment programs (Pelham *et al.*, 2004). These 8-week outpatient programs typically include both parent training (i.e. token point systems, use of contingent reinforcement, effective commands, daily report card, time out) and direct skills (social, sports,

problem-solving) training with children (Chronis, Jones & Raggi, in press). In addition to documented improvements in behavioral control among children with ADHD when used alone, these programs have also demonstrated large effects when combined with pharmacotherapy (Pelham *et al.*, 2000), potentially allowing for reduced dosing of stimulant medication. Indeed, these intensive summer treatment programs served as the model for those employed in the NIH Multimodal Treatment of ADHD (MTA) studies. In these large-scale studies, the effects of this behavioral program alone were so large that incremental medication effects were only obtained on 5 of more than 80 outcome measures obtained (Chronis *et al.*, in press; MTA Cooperative Group, 1999).

Interventions for working memory

Interventions to support dysfunction in working memory emphasize both environmental control and direct instruction. Many of the strategies described above in the section on organization and planning deficits are also relevant for children with working memory difficulties. Previewing and reviewing the new content of tasks can also help students to establish the cognitive framework for more efficient comprehension during classroom instruction. When children are expected to complete multi-step tasks, multiple-steps can be provided in writing or visually as long as the instructions remain in view for the child to refer to following each step. Caregivers or teachers should check in regularly with the child to ensure that they remain on task and are using their written/visual instructions appropriately.

In addition to the compensatory strategies described above, direct practice of working memory skills has also been found to improve performance. While the utility of decontextualized massed practice has not been emphasized in this chapter, there are several recent studies demonstrating promising results. In one randomized controlled study computerized mass practice of spatial working memory improved performance in a span board task in a small sample of children with ADHD (Klingberg, Forssberg & Westerberg, 2002). A follow-up study with a larger sample of children with ADHD confirmed improved spatial working memory with computerized practice (Klingberg *et al.*, 2005). Moreover, exposure to massed practice was associated with a reduction of inattentive, hyperactive, and impulsive symptoms based on caregiver ratings and both the improved span board and caregiver ratings remained evident three months after the training. Similarly, another study examining massed practice of attention exercises in conjunction with metacognitive and cognitive and behavioral strategies revealed improved attention span and vigilance, but not mathematical

calculations in a sample of children with EF dysfunction following treatment for cancer (Butler & Copeland, 2002).

Summary and conclusions

Executive function is a multidimensional construct, comprised of interrelated components that develop throughout childhood in conjunction with known periods of brain development. Typically, developing children display significant gains in executive control skills during preschool and elementary school years that allow for successful acquisition and efficient use of academic skills. As children move into adolescence, functional expectations increase, as children are expected to display greater independence during everyday tasks. While there is a substantial literature describing the development of executive functions in typically developing children and executive dysfunction in populations of children with developmental and acquired neurological abnormalities, there is limited literature describing the efficacy of intervention strategies used to ameliorate executive dysfunction. Designing studies to examine efficacy of interventions for executive dysfunction is particularly difficult because of limitations in ecological validity of office-based assessment. The studies with the best experimental design use interventions that are easy to employ (i.e. medication) or either examine the impact of a specific neuropsychological intervention (i.e. massed practice) on individual components of EF, often with limited generalizability to the real world. In contrast, holistic approaches utilize a large amount of time and resources and therefore have only been implemented in case studies and thus provide important, but limited evidence for efficacy. Moreover, using these multicomponent designs, it is difficult to isolate the effective components of the intervention. Further research is encouraged to define and standardize intervention approaches, and employ them in controlled studies that examine generalizability and follow-up.

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15

Pediatric movement disorders

Scott J. Hunter

Movement disorders are seldom considered when discussing pediatric neuropsychological disorders, despite their common presentation in a number of childhood conditions. This lack of consideration is most likely due to the general awareness that the quintessential movement disorders are ones known to primarily affect aging individuals, i.e. Parkinson and Huntington disorders. Hence, it is often surprising to pediatric neuropsychologists in training, as well as to persons outside the field, that Huntington disorder can arise in children and adolescents. Similarly, it is often a novel consideration for non-physicians that a well discussed neuropsychiatric disorder such as Tourette syndrome (TS) is most appropriately classified as a movement disorder, in response to its neurological etiology and attendant symptoms. Thus, there is a fairly wide "hole" in the neuropsychological literature in terms of understanding pediatric movement disorders and how they can be distinguished from disorders of motor control and executive functioning (see chapters in this volume by Tupper and by Mahone and Slomine). This is an interesting observation, given an increased interest in the pediatric movement disorders and advances in identification and treatment. It is the goal of this chapter to broaden the understanding of pediatric neuropsychologists and other child clinical specialists about the movement disorders, and to encourage further consideration of co-occurring disorders, such as Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive-Compulsive Disorder (OCD), that often complicate the diagnosis and treatment of movement disorders in children (Pliszka, Carlson & Swanson, 1999).

Identification and classification of the pediatric movement disorders

Movement disorders are classified as disturbances in central motor control that manifest as disruptions in body posture and gross and fine motor skill (Delgado, Albright & Leland, 2003; Dewey, Tupper & Bottos, 2004; Pranzatelli, 1995; 2003). Muscle tone and response are most often affected. There is some difficulty in terms

of classification, given the overlap with disorders of motor control (see Tupper, this volume). It is believed that involuntary movement disorders can be differentiated from motor control disorders (i.e. cerebral palsy) and other disorders that affect movement (i.e. seizures) by examining underlying pathophysiology, using appropriate observation (including neuroimaging and electroencephalography or EEG), and evaluation (Delgado *et al.*, 2003; Lennox, 2003). Similarly, involuntary, developmentally related movement difficulties such as jitteriness, excessive blinking associated with rapid eye movements in sleep myoclonus, and ritualistic behaviors, such as rocking, are separated from the pediatric movement disorders, by their etiology and physical demonstration (Delgado *et al.*, 2003; Dewey *et al.*, 2004; Pranzatelli, 1995).

There is a broad spectrum of movement disorders that arise secondary to neurological insult; spasticity, dystonia, athetosis, tremor, chorea, and ataxia are often seen in response to such developmental disorders as cerebral palsy, stroke, or severe traumatic brain injury. These difficulties will be discussed briefly in this chapter and Tupper considers them more directly in his chapter in this volume. Similarly, hyperkinesis observed in ADHD is also considered to represent a form of secondary movement disruption (cf. chorieform syndrome described in relationship with minimal brain dysfunction in the 1960s; see Palumbo, Maughan & Kurlan, 1997 and Palumbo and Diehl's chapter in this volume for further discussion). The focus of this chapter, however, is on the putative primary disorders of movement, which are believed to have associated neuropsychological difficulties accompanying their expression, specifically ones that are inherently tied to their diagnosis.

Extrapyramidal aspects of the movement disorders are frequently tied to basal ganglia region pathology (Dewey *et al.*, 2004; Kurlan, 1994; Palumbo *et al.*, 1997). Difficulties in movement are classified as dyskinesias (abnormal movement) and include hypokinesia or bradykinesia (a decreased or slowed level of movement), hyperkinesia (excessive movement), and akinesia (absence of movement). Commonly observed motor difficulties include athetosis (a twisting movement of the limb, trunk, or face), chorea (continuous involuntary movements varying between jerks and fluidity), and ballismus (rotary or flinging movements of the limbs). Each of these patterns of movement disruption can be seen in association with underlying subcortical and cerebellar disturbance. Myoclonus, a sudden rapid muscular jerk, and tremor, a rhythmic, oscillating movement of the limb, are also observed. Likewise, tics constitute another category of frequently observed motor disturbance. Tics are most often associated with Tourette Syndrome, a disorder that includes the presence of motor and vocal tics, both of which are characterized by an urge to perform the movement or vocalization, followed by a significant feeling of relief. Tics can also occur in

isolation. They are highly ritualized, stereotyped, rapid, and repetitive movements that have no other purpose. They may be simple, such as eye blinking or head jerks, or more complex, involving a combination of movements, such as reaching down and touching the ground while walking. Each of these movement difficulties contributes to a pattern of frustration for individuals experiencing them; they may inhibit engagement, mobility, or interaction with the environment, and can lead to emotional distress (Dewey *et al.*, 2004; Leckman & Cohen, 1999).

Pathophysiology

Various researchers in the movement disorders, such as Kurlan (1994; Palumbo *et al.*, 1997) and Pranzatelli (1995; 2003) have commented that the "clinical hallmark of dysfunction of the basal ganglia and extrapyramidal motor system is the appearance of involuntary movements" (Palumbo *et al.*, 1997, p. 475). Consistent with this, neurological disruption associated with the primary pediatric movement disorders is believed to reflect a disturbance in frontal-subcortical circuits that are principally mediated through the basal ganglia (Dewey *et al.*, 2004; Palumbo *et al.*, 1997; Stahl, 1988; Stern *et al.*, 2000). For example, Stern and colleagues, using event-related positron emission tomography (PET) techniques to study TS, showed that the primary aberrant regions of the brain most involved in the expression of vocal and motor tics include interrelated sensorimotor, executive, and limbic-subcortical circuits. As such, disturbance to one of the basal ganglia mediated circuits appears to influence a wide ranging, yet still specific cascade of events, including the expression of various motor difficulties (Stern *et al.*, 2000).

Stahl (1988) has identified a triadic model of basal ganglia circuitry that is believed to be most relevant to understanding the underlying pathophysiology of the movement disorders. Specifically, caudate, putamen, and globus pallidus originating circuits are proposed to underlie the initiation, execution, and redirection of movement. Concurrently, dorsolateral prefrontal circuitry, through which projections to the subcortical structures contribute to the engagement and maintenance of thought and behavior, is proposed to underlie the expression of neuropsychological dysfunction; specifically the dysexecutive syndrome, that accompanies some movement disorders over time. The putamen, which in tandem with the caudate forms the striatum, has been implicated in the onset and ongoing disturbance of motor planning and execution associated with the movement disorders. Difficulties associated with Huntington disorder, for example, including the classic presentation of choreiform movements appear to reflect a predominant disruption of the striatum, with gross pathological changes seen across the striatum and its circuits (Dewey *et al.*, 2004).

Similarly, motor tics have been found noted to involve disturbances in the putamen and its associated circuitry (Castellanos, 1997; Stern *et al.*, 2000).

Varying neuropsychological profiles are associated with the movement disorders; while this will be discussed in greater detail in the sections associated with juvenile-onset Huntington disorder and Tourette syndrome to follow, some basic discussion of broader pathophysiological underpinnings is warranted. Kurlan (1997), following Stahl (1988), proposed that disturbances in the subcortical components of the dorsolateral and orbitofrontal-based circuits contribute to the pattern of cognitive disruption commonly seen in conjunction with the movement disorders. As mentioned previously, dysexecutive deficits, including difficulties with problem solving, fluency of movement and thought, maintenance and shifting of cognitive set, and the ability to effectively organize and then retrieve information, are often seen in tandem with the more pervasive movement disorders like Huntington and Parkinson in adults. These are also seen with many of the involuntary movement disorders in children (Dewey *et al.*, 2004), and similar disturbances in the frontal-striatal circuitry are proposed to underlie some of the executive concerns seen with ADHD-Combined Type (Barkley, 2005; Castellanos, 1997). This combination may, in fact, underlie the susceptibility to the comorbid presentation of ADHD and the pediatric movement disorders (Palumbo *et al.*, 1997; Pliszka *et al.*, 1999). Disinhibition, irritability, and emotional difficulties are observed as a result of lateral orbitofrontal and ventromedial-anterior cingulate circuit disruption, which also involves the ventromedial caudate and dorsomedial globus pallidus (Stahl, 1988). Disturbances within this circuit, that also involve projections through the ventromedial striatum and the dorsomedial thalamus, lead to negative symptoms including apathy, reduced initiative and motivation, and akinetic mutism, which comprise the emotion-related disturbances often seen in Huntington disorder (Palumbo *et al.*, 1997).

Defining the predominant pediatric movement disorders

Apart from the neurodevelopmental disorders which are commonly associated with motor control disturbances, such as cerebral palsy, there is a series of neurodevelopmental disorders that are presumed to reflect subcortical disturbance, and which can be characterized as pediatric movement disorders (Palumbo *et al.*, 1997) or involuntary motor disorders (Dewey *et al.*, 2004). These include Tourette Syndrome (TS) as a principal representative of a ''Developmental Basal Ganglia'' Syndrome [DBGS] (Kurlan, 1994; Palumbo *et al.*, 1997), but may also include a series of neuropsychiatric disorders, including Obsessive-Compulsive Disorder, Aggression, Stuttering, and ADHD, that are often seen to occur in tandem with

TS and/or with each other. Whether the movement disorder is primary or secondary, there is strong association seen between the onset of these disorders and their underlying pathophysiology, suggesting that they may share common aspects of etiology (Bradshaw, 2001; Castellanos, 1997; Palumbo *et al.*, 1997). This chapter will focus predominantly on Tourette Syndrome, and will refer to it as a principal representative of the neurodevelopmental movement disorders.

A less commonly known movement disorder, with associations with the proposed disorders defining the DBGS, is Opsoclonus-Myoclonus Syndrome (OMS). A presumed autoimmune disorder that involves both ocular and somatic dyskinesias, that is believed to be associated with Sydenham's chorea and chorea seen with CNS-lupus, OMS can be found to occur in tandem with paraneoplastic disorders or following viral infection. OMS is thought to involve a neurodegenerative process that typically remits with intensive chemotherapies, although ongoing neurodevelopmental features present in many cases. Underlying pathophysiology is complex; cerebellar, brainstem, and subcortical circuits are implicated (Pranzatelli, 1992; 1995; 1996; 2003). It is frequently accompanied by difficulties with attention, behavioral regulation, obsessive compulsive disorder symptoms, and many youngsters develop difficulties consistent with a comorbid diagnosis of ADHD (Pranzatelli, 1996).

As noted in the introduction, the classic example of a movement disorder is believed to be Huntington Disorder, a neurodegenerative disorder. While pediatric-onset Huntington disorder is quite rare, its presentation in children and adolescents is frequently quite virulent. It is a striking example of how a disorder that slowly impacts functioning in adults can have a rapid, and often more deleterious impact when it presents in childhood.

The sections that follow address in more detail both juvenile-onset Huntington disorder and Tourette Syndrome, as examples of the pediatric movement disorders. Discussion will be provided regarding Sydenham's chorea, and PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection; Swedo *et al.*, 1998), as additional examples of more commonly considered pediatric movement disorders. Emphasis is particularly placed on current empirical knowledge, specifically regarding intervention. Less emphasis is placed on concrete approaches to neuropsychological assessment; instead, discussion is centered on the patterns of symptoms encountered, and how they are best understood and remediated.

Juvenile-onset Huntington disorder

Huntington Disorder (HD) is a complex, inherited progressive movement disorder, characterized by a pattern of select motor control, mood, and ultimately

personality changes. Cognitive decline is a hallmark feature of HD. HD is associated with a genetic defect of the first exon of the IT-15 gene on the short arm of chromosome 4, which leads to an expanded CAG segment; this segment becomes progressively more unstable as it is increased. Spermatogenesis contributes to further expansions in the gene segment. Most adults who develop HD have greater than 40 CAG repeats; likelihood of expression is related to the number of repeats an individual has, with greater numbers leading to increased vulnerability. An important observation with regard to the onset of HD in childhood and adolescence is the relationship between the number of CAG repeats and earlier disease onset (Gambardella *et al.*, 2001). Individuals with early onset HD show greater than 60 CAG repeats, with the majority of individuals showing trinucleotide expansions between 80 and 100. Similarly, there is significant relationship between the number of repeats an individual presents and the presence of an affected father. Telenius *et al.* (1993) showed that most early affected individuals have an affected father. Essentially, the level of severity and the level of vulnerability to developing HD at an early age increases in successive generations of an affected family, due to the amplification of trinucleotide repeats that takes place (Gambardella *et al.*, 2001).

Pathophysiologically, HD involves the progressive degeneration and ultimate atrophy of the striatum, specifically the caudate nucleus. Atrophy of the striatopallidal and striatonigral fiber bundles is responsible for the presence of progressive movement abnormalities. Early changes in the disease process are limited to the subcortical structures, most specifically the basal ganglia and its associated circuits with frontal and motor regions. However, with disease progression, cortical degeneration has been identified both on magnetic resonance imaging (MRI) and with autopsy.

Juvenile-onset HD occurs in approximately 10% of affected individuals and onset is typically well before age twenty (Vargas *et al.*, 2003). It is contrasted with adult onset in its presentation; children who develop HD often show intentional tremors, spasticity, rigidity, and substantial intellectual decline, indicative of a rapidly progressive course (Gomez-Tortosa *et al.*, 1998). Adults typically present with initial onset of psychiatric concerns, specifically anxiety and depression, followed by the development of chorea.

The clinical course of juvenile-onset HD is typically a negative one, with progression to early dementia observed. Descriptions of cases often highlight early evidence of dysarthria, loss of fine and then gross motor control, evidence of progressive dystonia, and over time, increased spasticity and rigidity. Neuropsychological profiles, often associated with single case studies, have described observations of symptoms consistent with severe ADHD, including hyperactivity, impulsivity, and significant distractibility, coupled with decreased

cognitive efficiency and flexibility. Memory deterioration often accompanies the changes in engagement and language skill. Notably, psychiatric symptoms appear to increase with progressive intellectual decline. Similarly, many youngsters develop seizure disorders, which further challenge cognitive growth (Nance & Myers, 2001).

Empirically-supported interventions for juvenile-onset Huntington disorder

Discussions regarding disease progression in children have highlighted the need for early implementation of special educational supports for children with early onset HD (Nance, 2001; Nance & Myers, 2001). Because executive controls are frequently quite impaired, substantial structure and support are recommended. Ultimately, as the disease progresses, regression occurs and full-time medical and adaptive care is required. There are few longitudinal studies of this disorder, most likely in response to its rare presentation and frequent negative outcome (Dewey *et al.*, 2004). Similarly, few descriptions of more than single case studies have been presented with regard to intervention (Dewey *et al.*, 2004; Nance, 2001). Palliative care is often the most efficacious approach; management of seizures and the motor control difficulties, coupled with the development of appropriate supportive educational interventions, is typically prescribed. Family-based supportive interventions, regarding preparation for disease progression, ultimate dementia and death of the affected individual, are also recommended.

Sydenham's chorea

One of the first pediatric movement disorders to be described, Sydenham's chorea (also called St Vitus dance) was originally identified in 1686 by Thomas Sydenham, to classify a group of children demonstrating a "sudden onset of rapid involuntary and purposeless limb movements . . . accompanied by alteration[s] in behavior and emotion" (Dale, 2003, p. 183). Following this initial classification of the disorder, a relationship was identified between the development of the choreic movement disorder and rheumatic fever. With the onset of the twentieth century, streptococcal infection was isolated as a cause of rheumatic fever and ultimately, as a contributing factor to the development of Sydenham's chorea. Over time, further understanding of the underlying etiology for the choreic motor disorder has emerged. The development of antistreptococcal antibodies forming in reaction to the presence of the Group A beta-hemolytic streptococcus (GABHS) bacterium appears to impact neurological functioning at some point during the illness (Dale, 2003). Through molecular mimicry, these antibodies are believed to "cross-react with basal ganglia brain antigens" to produce the symptoms observed (Kurlan, 2004, p. 371; Dewey *et al.*, 2004;

Swedo, 1994). Work to date has in fact shown not only a very strong relationship between rheumatic fever and the development of this characteristic neuropsychiatric disorder, that includes chorea, attentional and executive difficulties, and emotional sequelae including anxiety and depression, but also possible onset of a broader pattern of movement difficulties, including tics (Dale, 2003; Swedo, 1994). Obsessive-compulsive disorder is also believed to be a common co-occurring difficulty (Asbahr *et al.*, 1998; Dale, 2003; Walker, Lawrenson & Whilmshurst, 2005); this pattern of broader phenotypic expression is in fact suggested to also underlie PANDAS, coined by Swedo and her associates to describe the variety of possible neurodevelopmental concerns that arise in response to streptococcal infection (Swedo *et al.*, 1998).

Sydenham's chorea typically presents as a short-duration disorder. Its course is in fact generally no more than one year's duration in most affected individuals. It most often affects children between the ages of 5 and 15, with its greatest prevalence during the early elementary grades (Dewey *et al.*, 2004). Chorea is not the only presenting motor disturbance; individuals with Sydenham's can show fasciculations of the tongue, ballimus, facial grimaces, decreased muscle tone, and disruptions in gait and movement (Swedo, 1994). Changes in speech are also described. Unilateral and bilateral disruption in motor skill can be observed (Dewey *et al.*, 2004). Distinguishing some of the symptoms of Sydenham's chorea from complex motor tics and other forms of motor impairment is often difficult; hence, it is typically necessary to make use of appropriate disease-related titres to evaluate for Sydenham's following actual and presumed infection.

Sydenham's chorea is believed to represent striatal region inflammation that dissipates across time. Some neuroimaging studies have shown localized changes to the basal ganglia following streptococcal infection (Dale, 2003), but most studies using conventional computerized tomography (CT) or magnetic resonance imaging (MRI) have failed to demonstrate evidence of ongoing striatal region changes. Studies conducted during the acute phase of Sydenham's, using volumetric analyses, have shown enlargement of the caudate and putamen (Giedd *et al.*, 1995; 2000). There has been suggestion that, for some children, striatal changes may persist for an extended period of time or become permanent (Dale, 2003). Similarly, there have been studies that have identified the presence of higher levels of antineuronal antibodies in children with Sydenham's, as well as in some children with OCD and Tourette syndrome (see Dale, 2003; Dewey *et al.*, 2004). A common serologic marker has been described (D8/17 B lymphocyte antigen), that is found at an increased level in some patients with these disorders (Dale, 2003). This has led to speculation that there may be a shared or even inherited marker for the development of these disorders (Dale, 2003; Dewey *et al.*, 2004). This genetic vulnerability may lead to the development, over time,

of a more significant pattern of motor and psychiatric concerns in some children with a history of Sydenham's; this is an area of active research at this time (Walker *et al.*, 2005).

Empirically-supported interventions for Sydenham's chorea

Treatment for Sydenham's chorea remains variable, and is predominantly medical in its approach (Walker *et al.*, 2005). Most children who develop the disorder are treated with a course of antibiotics, specifically a ten-day course of oral penicillin, and bed rest (Garvey & Swedo, 1997). Development of a more significant symptom presentation can prove quite disruptive to daily life for affected children; this may necessitate the addition of other pharmacological agents, to address the behavioral, emotional, and movement difficulties. One recent study, described by Dewey *et al.* (2004) appeared to show efficacy for the use of valproic acid for patients with more severe presentations. Similarly, Walker and associates suggest that haloperidol, pimozide, and clonidine can also be helpful, although they also highlight the lack of controlled studies with these medications in this population (Walker *et al.*, 2005). In cases where ongoing difficulties like tics and OCD emerge, use of intravenous immunoglobulin has been suggested as a possible treatment (Walker *et al.*, 2005). Management of OCD symptoms often involves administration of selective serotonin reuptake inhibitors.

Interestingly, no specific neuropsychological profile has been identified in conjunction with Sydenham's chorea, even during the acute phase of the disorder. It is believed by some neurologists that the neurobehavioral disruption seen with Sydenham's chorea is secondary to the movement disturbance that develops in response to inflammation of the subcortical region. Management of short-term difficulties in cognition and behavior is an area needing further elaboration.

Tourette syndrome

Tourette Syndrome (TS) is a complex neuropsychiatric disorder which is defined by the presence of vocal and motor tics, involuntary actions that can involve a "psychic pressure" for their activation, followed by a sense of release after their completion. Diagnosis of TS, as defined by the DSM-IV (APA, 2000), requires the presence of multiple motor tics, and the presence of at least one vocal tic, occurring over the course of the day, for at least one year. Its onset is typically during childhood; in order to be diagnosed as TS, symptoms must be present prior to age 18. It is noted in the literature that the tics characterizing TS typically wax and wane (Leckman & Cohen, 1999); the number, frequency, complexity and severity of tics change over the course of the disorder (Bradshaw, 2001; Brown & Ievers, 1999; Leckman, 2002). TS and its spectrum of related concerns, the chronic

and transient tic disorders, appear to differ from other movement disorders, like chorea and dystonia, due to the stereotyped nature of tics (Leckman, 2002). TS frequently is accompanied by a number of psychosocial and neurobehavioral concerns (Kurlan, 1997; Leckman, 2002; Palumbo *et al.*, 1997); children and adolescents with the disorder are at significant risk for demonstrating a number of co-occurring psychiatric disorders, including ADHD, Obsessive-Compulsive Disorder (OCD), Conduct Disturbances (CD), and Learning Disabilities (LD). As a result of the frequent comorbidities, it is often difficult to tease apart the concerns that are described by youngsters coping with this disorder; social rejection, anxiety, dysphoria, variable rates of learning success, and low self-efficacy are commonly reported (Leckman & Cohen, 1999; Palumbo *et al.*, 1997; Pliszka *et al.*, 1999). Similarly, the degree of co-occurring difficulties seen in youngsters and adolescents with TS has contributed to difficulties in fully elucidating the underlying neuropathology and pathophysiology of the disorder (Palumbo *et al.*, 1997; Voelker, 2004).

Etiologically, TS is proposed to be "a disorder of neurochemical regulation with complex genetic and environmental determinants, the latter acting at critical developmental stages" (Bradshaw, 2001, p. 55). TS is presumed to exist within a spectrum of related tic and motor control disorders defined within DSM-IV (APA, 2000), including Transient Tic Disorder of Childhood, a frequently "self-limiting disorder" that involves the presentation of a single or multiple motor or vocal tics over the course of one to eleven months; and Chronic Motor or Vocal Tic Disorder, involving the observation of either a motor or vocal tic, on an intermittent basis, for more than one year's duration. Notably, all tics, whether vocal or motor in demonstration, are defined by their repetitive, stereotyped presentation, over a limited duration of time. It is suggested that tics exist along a continuum of ritualistic and stereotyped habit behaviors, and research to date has suggested a strong relationship with the compulsive behaviors seen in OCD (Leckman & Cohen, 1999). While typically involuntary, tics can be suppressed; in fact, many children learn to monitor and suppress their expression over the course of a school day. This is often followed by a "burst" of tics later in the day (Leckman, 2002; Leckman & Cohen, 1999).

The defining feature of tics, for most individuals experiencing them, is their being preceded by a sensation of tension, which is then followed by a transient feeling of relief after their expression. Specifically, in persons presenting with tic disorders, the feeling of tension precedes the performance of almost 90% of tics experienced; this differs with the other movement disorders, where few individuals report experiencing a premonitory sensation or consequent sense of relief (Leckman & Cohen, 1999; Verdellen *et al.*, 2004). Tics can be quite complex in their presentation. Most observed tics, whether vocal or motor, are simple,

discrete and fairly defined; jerks, shrugs, twitches, grunts, and utterances are common examples (Leckman, 2002; Leckman & Cohen, 1999). Tics often occur in ''paroxysmal bouts'' (Bradshaw, 2001, p. 56), with most tics lasting only a second in duration. At times, however, tics can be quite forceful, and as a result, prove injurious to the person experiencing them; for example, rapid myoclonic-like jerks of the arm can lead to shoulder dislocation. Early bouts of tics often occur without the child's clear awareness. As time progresses, there arises a cycle of premonitory urge and a subsequent feeling of relief. Notably, tics characteristically wax and wane in their expression. Children can experience exacerbations in their frequency when under psychological stress or in response to decreased environmental engagement, and a diminishment in frequency can be seen during times of high activity, reduced stress, and attentional engagement. Many children attempt to ''mask'' their tics, either through efforts at suppression, or alternatively, by trying to ''incorporate them into strategically appropriate points or breaks in voluntary activity'' (Bradshaw, 2001, p. 57; Leckman & Cohen, 1999). This typically reflects awareness that others perceive tics as ''weird'' or ''strange events.'' Children with TS express experiencing embarrassment at having tics, which can lead to fears of rejection and isolation.

Prevalence and incidence of Tourette syndrome

The prevalence of Tourette syndrome is reported as falling between 1-3% in children and adolescents (Leckman & Cohen, 1999; Robertson, 2006). Transitory tic disorders are more common in childhood; 4-5% of children may demonstrate periods of motor or vocal tics at any given point during development. In fact, transient vocal and motor tics are believed to be quite frequent among the general population (Leckman, 2002; Leckman & Cohen, 1999). Males are more frequently affected; Leckman and Cohen have suggested prevalence in boys of between 1 and 8 out of 1000, while only 0.1 and 4 girls per 1000 meet diagnostic criteria for TS (Leckman & Cohen, 1999). TS is a chronic condition, with onset typically during the early years of childhood. Most cases develop between the ages of 5 and 10 years. Peak incidence is seen by 11 years of age. Tics often worsen with the onset of puberty, although there is typically an accompanying diminishment with adulthood (Bradshaw, 2001).

Tourette Syndrome is very often diagnosed in tandem with other significant neuropsychological disorders. It is frequently comorbid with OCD and ADHD. An estimate of comorbid prevalence of these disorders with TS is almost 50% (Leckman & Cohen, 1999; Palumbo *et al.*, 1997; Yeates & Bornstein, 1996). Similarly, a significant number of individuals show such learning disabilities as dyslexia, arithmetic disorders, and disorders of written expression in tandem with TS (Dewey *et al.*, 2004; Leckman, 2002). Yeates and Bornstein (1996) found

that arithmetic difficulties were more prevalent in children with TS without other disorders. Anxiety and depressive disorders are also strongly associated with TS, with a greater degree of generalized and social anxiety difficulties reported (Palumbo *et al.*, 1997). Not surprisingly, these co-occurring difficulties with behavioral control, mood regulation, and learning often serve to exacerbate the symptoms of TS for many children. While rare, it is not unusual for someone to present solely with TS, or tics alone. Notably, when that pattern is observed, there are seldom associated neuropsychological concerns (de Groot *et al.*, 1997; Yeates & Bornstein, 1996). Instead, deficiencies in neuropsychological functioning, including learning disabilities, attentional difficulties, and behavioral control difficulties are most often associated with psychiatric comorbidity (Hunter *et al.*, 1999; Yeates & Bornstein, 1996).

ADHD is the most common co-occurring neuropsychiatric disorder seen with TS. It is comorbidly diagnosed at a prevalence rate of 40% in youngsters with TS (Bradshaw, 2001; Leckman & Cohen, 1999), and in fact, may often precede the onset of TS symptoms. It is uncertain whether children with TS are predisposed to developing ADHD symptoms; the DBGS model highlights the strong relationship between the two disorders at the pathophysiological level, given the overlapping involvement of frontal-subcortical circuits proposed to underlie both TS and ADHD (Palumbo *et al.*, 1997). Similarly, the two disorders appear to share genetic variation patterns: both TS and ADHD are believed to represent multifactorial genetic determinants. Leckman and Cohen (1999) have proposed that TS represents an autosomal dominant inheritance pattern, with strong, but "incomplete penetrance and variable expression" (Bradshaw, 2001, p. 61). Concordance rates for TS in monozygotic twins exceed 50%, while much lower concordances are seen with dizygotic twins and first-degree family members. These concordance patterns are actually quite similar to ones proposed for ADHD (Mazei-Robison *et al.*, 2005; Stein *et al.*, 2005). Notably, both disorders are believed to involve, in part, genes related to dopamine regulation and transport (Cuker *et al.*, 2003; Voelker, 2004).

Comorbidity between TS and OCD is observed to emerge over time, and to in fact surpass that of ADHD in terms of prevalence and incidence (Bradshaw, 2001; Palumbo *et al.*, 1997). Some researchers have proposed that OCD "is possibly an alternative manifestation of a common gene causative for TS and OCD" (Bradshaw, 2001, p. 59). When OCD emerges in individuals with TS, it is not infrequently observed to be of a more severe pattern behaviorally and cognitively; Bradshaw comments that OCD in persons with TS tends to "be more violent, sexual, and aggressive and to involve more symmetrising behaviors [i.e. a need to achieve a feeling of body symmetry]" (p. 59). Approximately 50% of individuals with TS present with comorbid OCD symptoms (Leckman & Cohen, 1999;

Palumbo *et al.*, 1997; Stern *et al.*, 2000; Woods *et al.*, 2000). Of particular interest with regard to genetic and pathophysiological modeling, 30% of individuals diagnosed with OCD have co-occurring tics, while approximately 45% have a reported family history of tic disorders (Leckman & Cohen, 1999).

Tics and compulsions share a common behavioral presentation, namely the pressure felt to perform an action until the underlying sense of tension is relieved. This has contributed to a degree of uncertainty in the literature regarding the underlying nature of complex tics versus compulsions; they are often quite difficult to distinguish at the behavioral and descriptive level (Woods *et al.*, 2000). Similarly, that they are often seen to co-occur suggests that there may be, at the neurological level, a broad phenotype that underlies the pathophysiology of habit disorders, including tics, TS, some forms of anxiety, and OCD.

A group of children have been identified who have shown onset of tics and co-occurring OCD symptoms following streptococcal infection. These youngsters were first described by Swedo and her associates (Swedo *et al.*, 1997; 1998), and were identified as presenting with the development of PANDAS, or pediatric autoimmune neuropsychiatric disorders after streptococcal infections. Similar to the etiological process described previously for Sydenham's chorea, children with PANDAS show the onset of tic disorders and other associated emotion regulation and behavioral difficulties following streptococcal-infection. Despite ongoing investigations (Dale, 2003; Kurlan, 2004), controversy has developed about the hypotheses behind PANDAS and its relationship with both Sydenham's chorea and Tourette syndrome (Kurlan, 2004). Swedo and her associates, as well as others like Dale, have shown that there may be a distinct autoimmune related disorder, that is very similar in its presentation to Tourette syndrome, and that may in fact share many of the comorbidities that are common with TS. However, such etiological aspects as GABHS infection and later onset of motor and vocal tics have not been firmly established; Kurlan (2004) has suggested that until ''carefully controlled, prospective studies'' have taken place, the temporal link between a common infectious agent like GABHS and the clinical presentation of a tic disorder remains uncertain. Similarly, attempts to show that autoantibodies, proposed as inducing the disease process, are present at differential levels in the brain and nervous system in persons with PANDAS and other neuropsychiatric movement disorders remains equivocal. Recently, Singer and associates (Singer *et al.*, 2004) showed no difference between individuals with PANDAS and normal controls when Enzyme-linked immunosorbent assay (ELISA), a biochemical technique used to detect the presense of specific antibodies measurements were used to identify autoimmune antibodies in the CSF. At this time, much remains speculative with regard to the possible autoimmune aspects behind TS and related infection-specific tic disorders (Church *et al.*, 2003; Kurlan, 2004).

Empirically-supported interventions for Tourette syndrome

Pharmacological approaches

Treatment for TS is often tied to the level of distress described and to the degree to which tics impact daily functioning. Historically, pharmacological management has been the foremost approach to addressing tics. Dopamine antagonists have, in the past, been the first-line approach; medications like haloperidol and pimozide have been noted to have a positive effect in ameliorating both vocal and motor tics (Bradshaw, 2001; Jankovic, 2001; Leckman & Cohen, 1999). Unfortunately, they have also demonstrated a disruptive negative side effect profile, including sedation, cognitive slowing, and extrapyramidal symptoms, which has seriously limited their acceptability to both parents and patients with TS (Leckman & Cohen, 1999; Nicolson *et al.*, 2005; Sandor, 2003). More recently, placebo-controlled, double-blind studies examining the impact of newer atypical dopamine antagonist medications, like risperidone and olanzapine, have shown efficacy (Gaffney *et al.*, 2002; Sandor, 2003), both in children and adults; but again, negative side effects like sedation and weight gain have been described and have limited their use by patients. Similarly, because many of the newer medications have been investigated only in adults, it is uncertain whether the impact on TS severity is actually replicated when treating children. Dosing concerns are also at issue, given the different metabolic rates and developmental levels children present. These issues, in particular, have impacted parental willingness to have their children take neuroleptics, or to participate in newer medication research protocols.

Nicolson *et al.* (2005), in an effort to consider alternative dopamine antagonists for the treatment of TS, investigated the efficacy of metoclopramide, a D2 receptor antagonist that is comparable to haloperidol in action, particularly within the striatum. Of interest with this medication is its observed selectivity in terms of basal ganglia circuit impact, and its demonstrated lack of antipsychotic effects: it has been thought to be less prone to lead to negative cognitive side effects when used for the treatment of tics. In a double-blind, placebo-controlled investigation of metoclopramide, following a series of successful case reports and open-label investigations (Acosta & Castellanos, 2004), Nicolson and colleagues reported a significant (38.7%) decrease in scores on the Yale Global Tic Severity Scale (YGTSS) after an eight week trial; this contrasted with a small reduction (12.6%) observed in patients treated with placebo. 64% of the children treated with metoclopramide were identified as positive responders in contrast with those given placebo (i.e. reporting both decreased number of tics and less severity of those tics experienced). Side effect reports, including sedation and appetite increase/weight gain were minimal. One participant in the study, not included

in the final report, experienced an intensification of dysphoric affect that abated when the medication was discontinued. Nicolson *et al.* (2005) reported these results as being favorable with regard to intervention tolerability and outcome.

Efficacy for the use of selective serotonin reuptake inhibitors in TS is equivocal. There are few studies suggesting serotonergic involvement in the initiation and maintenance of tics (Bradshaw, 2001; Jimenez-Jimenez & Garcia-Ruiz, 2001). Similarly, there is a literature suggesting that selective serotonin reuptake inhibitors, which positively address OCD symptoms, may exacerbate tics (Como & Kurlan, 1991; but see Scahill *et al.*, 1997 for a contradictory view). This has consequently limited their consideration in the treatment of TS alone, but not with regard to TS with comorbid OCD (Kossoff & Singer, 2001).

Noradrenergic involvement has been presumed, however, to be of etiological interest, given its role in the engagement of striatal circuits. Clonidine, a noradrenergic receptor agonist, has been demonstrated to impact tic severity (Leckman & Cohen, 1999; Sandor, 2003). Similarly, it has been identified as having a positive impact on some symptoms, including impulsivity and motor activity, in ADHD (Bradshaw, 2001). Similarly, Guanfacine, an adrenergic agonist like Clonidine, has been investigated for treatment of behavioral concerns associated with TS. Several reasonably controlled studies have been conducted and have shown some benefit for this pharmacologic agent (Cummings *et al.*, 2002; Kossoff & Singer, 2001). Interestingly, Cummings and associates included assessment of neuropsychological functioning as an outcome measure in their investigation; this is quite striking, since few controlled drug studies in TS have included cognitive functioning measures. Included were pre-treatment and post-treatment parental completion of the Behavior Rating Inventory of Executive Function (BRIEF); ADHD-related rating scales (ADHD Rating Scale IV and Connors Parent Rating Scale, Revised); and completion of a series of attentional and executive tests, including Digit Span, Self-Ordered Pointing Test, Letter-Word Fluency Test, Tower of London, and the Test of Variables of Attention (TOVA). Guanfacine was only associated with changes on the Metacognitive Index of the BRIEF; no improvement was reported on any of the performance based measures of executive and attentional capacity. Some performances on measures were seen to decrease with Guanfacine administration this may have reflected dosage levels and their impact on engagement and sedation. Clonidine and Guanfacine are described as being reasonably tolerated. Sedation, headaches, and rebound effects, particularly an exacerbation in tics, have been seen as common side effects. Monitoring of potential hypertension following withdrawal is also recommended (Kossoff & Singer, 2001).

Use of stimulant medications to treat co-occurring ADHD symptoms has been a fairly controversial area of practice with regard to TS (Leckman & Cohen, 1999).

Because stimulants are dopamine agonists, they have been felt to be potentially risky in the treatment of comorbid ADHD and tic disorders, given the propensity to increase and intensify tics (Bradshaw, 2001; Robertson, 2006). Similarly, there has been a long-held worry among clinical practitioners and parents of children with ADHD that the use of stimulant medications increases the likelihood of tics emerging. However, Kurlan has suggested that the emergence of tics with the implementation of stimulant medication may more likely reflect the underlying comorbidity of tic disorders with ADHD (Kurlan, 2001; Palumbo *et al.*, 1997; The Tourette Syndrome Study Group, 2002). Similarly, a decade of definitive research by Biederman and his colleagues (Spencer *et al.*, 1999; 2001) has shown that while there is evidence of tic emergence and then decline following initiation of stimulants, there is no contraindication to the use of stimulants for the effective management of ADHD and comorbid TS (also see Castellanos, 1997; 1999; Kurlan, 2003; Palumbo, Spencer, Lynch, Co-Chien & Faraone, 2004). Given the shared pathophysiology of these disorders, and their shared genetic linkage, it is likely that a dynamic process underlies their co-occurrence following implementation of stimulants, such as methylphenidate (Palumbo *et al.*, 2004; Robertson, 2006).

Atomoxetine has also been recently investigated as an alternative approach to managing comorbid ADHD and TS. A selective noradrenaline reuptake inhibitor, it has been studied predominantly in individuals without tics, across both open-label and double-blind trials (Kelsey *et al.*, 2004). While only brief case reports have been offered regarding its efficacy, including the description of initial tic exacerbation in some cases, additional recent studies have suggested that the majority of individuals do not experience an exacerbation in their tics (Robertson, 2006). Atomoxetine may prove to be a useful intervention for children with a propensity toward tic increase when their ADHD symptoms are being treated with stimulants.

Alternative pharmacologic approaches to the treatment of tics have been described, although studies have been quite limited (Jimenez-Jimenez & Garcia-Ruiz, 2001). Clonazepam, a benzodiazepine, has been suggested to have a positive effect on tic expression, but no controlled studies have been undertaken. Similarly, use of botulinum toxin has been suggested for tic management, given its efficacy in the treatment of dystonia and spasticity (Jimenez-Jimenez & Garcia-Ruiz, 2001; Kossoff & Singer, 2001). Encouraging findings were obtained during a pilot study of 10 patients, with use being considered for both motor tics and suppression of vocal tics. To date, however, no controlled trials have taken place. Similarly, use of both transdermal and oral nicotine has been investigated for the management of tics. This area of investigation has been controversial, particularly with children, and few significant trials have been undertaken (Kossoff & Singer, 2001).

Behavioral approaches

Behavioral treatment of TS is a less commonly considered avenue of intervention within the extant literature; this may be because the typical presentation of youngsters with TS is to physicians, rather than psychologists and neuropsychologists. However, in line with the history of success of behavioral interventions for habit disorders and OCD, it has been well presumed that habit reversal (HR) interventions may be one of the more efficacious methods for addressing tic maintenance. In a review of the HR model and its historical application to TS, Verdellen and colleagues (2004) identified that tics have often been considered, psychologically, as operationally-conditioned responses to premonitory sensations. Specifically, by relying on learning theories, hypotheses have been put forward that tics are maintained "through a process of operant conditioning, i.e., negative reinforcement, the sequence of unpleasant premonitory sensations followed by tics that relieve these sensations may account for the maintenance of tics" (p. 502). Consequently, behavior therapists have suggested that tics are conditioned responses that arise whenever novel or previously experienced negative sensations are experienced. The association of these sensations with environmental contingencies (i.e. thoughts, emotional experiences, or stressors) serves to classically condition tics with the sensory experience.

Given the background conditioning underlying tic maintenance, the implementation of habit reversal interventions, including awareness training around tic emergence, application of alternative and incompatible responses to break the conditioned chain, and the addition of stress reduction and reinforcement supports, has been identified as a successful option (Azrin & Peterson, 1990; Verdellen *et al.*, 2004). Azrin's group, as well as a recent review edited by Woods (2005), have both suggested that the use of habit reversal interventions can foster a reduction of tics at between 55% and 95% success. Notably, this wide range of "successful effects" has to be taken with some skepticism, since few controlled studies, let alone ones using appropriately large samples, have ever been engaged.

A more recent avenue of intervention for tics, and co-occurring obsessions, compulsions, and aggressive behaviors has emerged from the cognitive-behavioral literature addressing intervention for OCD. Because it has been observed that tics and compulsions resemble one another, it has been suggested that implementation of a response prevention paradigm may be an efficacious means of intervening behaviorally with tic disorders. In a small study, which tested the hypothesis that response habituation can decrease tics, Hoogduin and colleagues (Hoogduin, Verdellen & Cath, 1997) exposed four patients with tic disorders to the premonitory sensory sensations while having them suppress tics. They found that

three of the four individuals with TS whom they treated could habituate within the training session (i.e. participants were taught to habituate and suppress tics over ten sessions). Reported improvements ranged from a 68% to 83% reduction in tics (Hoogduin *et al.*, 1997). This group has since attempted to both replicate and extend these behavioral intervention findings, using a manualized treatment approach for response prevention and habit reduction, in order to examine the efficacy and individual response rates for each of these interventions. Verdellen *et al.* (2004) reported that, in a fairly well controlled sample of young adults with TS, who were not depressed or showing the presence of other neuropsychiatric disorders, both forms of behavioral intervention were efficacious in reducing severity and frequency of tics. Their results demonstrated that both habit reversal and response prevention led to a decrease in tics; using learning theory to explain their results, the authors proposed that both methods of intervention might interrupt the stimulus-response sequence seen in the performance of tics (e.g. the engagement of the tic to bring relief from the premonitory sensations). The authors additionally suggest that habituation may be one of the important mechanisms supporting both habit reduction and response prevention; through the use of a competing response to address the discomfort felt, exposure to the premonitory stimulus may be taking place. As such, each of these methods may be achieving a similar goal, increasing the likelihood that an individual can tolerate the premonitory sensation without engaging in the diversionary tic behavior.

Despite several methodological concerns with the above described study, which are well addressed by the authors (pp. 509–10), these results, when coupled with the available small sample and single-case studies regarding behavioral intervention for tics (see Woods, 2005), suggest that implementation of non-pharmacological intervention should be considered. In fact, the results indicate that this is a reasonably supported approach to addressing TS. This is particularly informative given the discomfort many individuals with TS experience with the use of medications.

Cognitive approaches

An alternate psychotherapy-based approach, which is surprisingly not well researched but is believed promising in its application, is the use of more directly cognitive interventions for supporting alteration and reduction in discomfort with TS. Because children with TS often demonstrate reduced self-efficacy and lower self-esteem (Leckman & Cohen, 1999), further research is needed in regards to the implementation of thought-based, evaluative interventions, that effectively teach better problem-solving skills and greater tolerance of tics, themselves. Using this approach in combination with efficacious behavioral interventions,

and supportive accommodations both at home and school for comorbid concerns, may prove to be a more sustainable pattern of intervention.

Future directions in the treatment of the pediatric movement disorders

Like many medically based neurodevelopmental disorders that impact children, initial emphasis is most often on pharmacological intervention. However, given the difficulties present with regard to establishing efficacy and comfort with use, due to the complex side effect profiles seen, as well as concerns about dosing and metabolism, the development of behavioral and cognitive approaches to intervention with the movement disorders remains a wide open area. Work done to date with TS, addressing the vocal and motor tics and their expression, as well as the common comorbidities seen with TS, have highlighted the usefulness of behavioral intervention. Further controlled studies are strongly warranted, particularly in light of findings regarding combined success for medication management and behavioral intervention over the long term in ADHD (see ongoing analyses related to the Multimodal Treatment Study of Children with ADHO (MTA) project, MTA Cooperative Group, 1999).

Disorders like OMS, mentioned at the beginning of the chapter, and Sydenham's chorea have had relatively little consideration to date within the neuropsychological community. This may reflect the fact that these youngsters, like children presenting with juvenile-onset HD, often get managed first and foremost by physicians. In the case of Sydenham's chorea, the disorder is most often time-limited, as well; this may lead to treating clinicians focusing on the "full-blown" stages of the disorder, and dealing less with potential ongoing issues after recovery. With regard to OMS, several studies have strongly indicated a need for neuropsychological management; this author is in fact currently conducting a series of case studies looking at possible ongoing cognitive and behavioral changes and their response to immune-system interventions. Clearly, clinical trials and sustained emphasis on neurocognitive and behavioral changes in these disorders is warranted, to best direct ongoing intervention considerations.

Further investigation is warranted concerning the comorbid development of difficulties children with the pediatric movement disorders present with, and how they can best be disentangled. Because children with TS show significant vulnerability to co-occurring OCD, ADHD, and emotion regulation concerns, multicomponential studies are warranted, to better identify and then address the combinations of difficulties these youngsters present. Funding however is often limited for such large investigations; perhaps this is where multicenter approaches can be most helpful, as has been observed with the MTA studies addressing ADHD.

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16

Management of children with disorders of motor control and coordination

David E. Tupper

Clumsy or impaired performance of motor skills can result from a number of neurodevelopmental disorders, either as a primary or secondary consequence of the condition (Dewey & Tupper, 2004) (see Table 16.1). Altered motor control and coordination stem from a variety of causes, manifest at different levels of severity, affect functioning in other neuropsychological domains, and take various forms. Problems in controlling one's actions represent visible physical characteristics that often cause significant disability for children, and may continue to impact persons into adulthood unless managed effectively (Farmer & Deidrick, 2006; Keogh, Bernheimer & Guthrie, 2004; Mudrick, 2002).

This chapter will review the identification and assessment of pediatric motor disorders from a developmental neuropsychological perspective, with a focus on disorders that affect primary aspects of motor control and coordination, rather than as secondary symptoms or manifestations of the developmental condition. After a discussion of motor control theory and assessment issues, two major neurodevelopmental conditions will be presented, and current management methods for amelioration of the motor impairments associated with those conditions will be discussed. Reviewed in turn will be two common types of cerebral palsy and representative treatment methods, and the neuropsychological entity known as developmental coordination disorder, which is yet to be clearly defined and may not represent a homogeneous condition. These disorders were chosen to represent several of the common neuromotor impairments seen in pediatric neuropsychology practice and will provide examples of conditions where controversial treatment methods have been used in the past, but where current scientific understanding is likely to lead to more efficacious intervention methods in the future.

Table 16.1. Common neuropsychological conditions associated with motor impairment in children (not mutually exclusive)

Acquired brain injury	Hydrocephalus
Apraxia/dyspraxia	Mental deficiency
Atrophy/dislocation of the extremities	Muscular dystrophies
Autistic spectrum disorders	Orthopedic injuries
Cerebral palsy (diplegia, hemiplegia)	Peripheral neuropathies
Chromosomal abnormalities (e.g. Down syndrome)	Prematurity/low birth weight
Developmental coordination disorder	Sydenham's chorea
Juvenile Huntington's disease	Tourette syndrome

Motor control: a developmental neuropsychological perspective

Early theories relating to motor control and motor development were often based on the biological/maturational hypotheses of Gesell and McGraw, among others, and primarily provided descriptive information about the acquisition of motor milestones. As a result of advanced research into motor skill acquisition and development in the mid-twentieth century, which emphasized the interaction of perceptual and learning factors in motor skill, developmental maturational hypotheses decreased in popularity and theories were developed that took into account the interaction of various components of the motor system with other cognitive processes and the environment. Among the most prominent of the theories are the information-processing approach and dynamic systems theory. In general, motor control and development theories have shifted from having a sole focus on understanding of biological processes to incorporating organismic interactions with the environment (Tupper & Sondell, 2004).

The dynamic systems approach posits that the acquisition and performance of motor skills is determined by the interaction of many factors, including stimulus or environmental factors, perceptual and learning factors, and muscle and body development. Unlike the information processing approach, which assumes a brain-based command center that initiates relatively invariant movement sequences, the dynamic systems approach suggests that movements emerge from the dynamic interaction of bodily constraints (i.e. biomechanics, cognitive and emotional factors, strength), environmental characteristics (i.e. gravity, objects in space), and task requirements and constraints (i.e. tools, implements, rules). The nervous system is thought to constrain and control the various required components of an action through coordinative synergies which are self-organized and dependent on perception–action coupling (Geuze, 2004). Thus, dynamic systems theory contributes more of

a biological–ecological analogy to movement than the cybernetic analogy, represented by the information-processing approach. Each of these theories can be applied to the understanding of both normal and disordered movement and their underlying motor skills, although neither theory has directly led to the development of motor skills assessment instruments. The theories have also been quite slow in informing clinical neuropsychology practice (Denckla & Roeltgen, 1992; Deuel, 2002; Rosenbaum, 2005).

Aside from a dynamic systems perspective, a comprehensive developmental neuropsychological model of motor control and coordination has yet to be developed. There are presently few neuropsychological theories that address the normal development of motor control and learning, and which provide a better understanding of children with motor impairments and their correlated cognitive deficits. In fact, clinical neuropsychological practice has relatively limited assessment measures available in this area and often, neuropsychologists use only simple measures of discrete motor skills in their evaluations. The development and assessment of praxis, for example, is incompletely understood (Georgopoulos, 2004; Roy, Elliott, Dewey & Square-Storer, 1990). As will be seen later in the chapter, more refined classifications of children with motor impairments are sorely needed and neuropsychologists, who are uniquely trained in identifying both nervous system integrity and behavioral capacities, are positioned to use their multifaceted knowledge to develop a more integrated assessment and treatment approach.

Assessment of motor control

The objective assessment of motor abilities and movement skills began with limited attempts, in the seventeenth and eighteenth centuries, to measure specific physical capacities or capabilities such as strength, speed, weight lifting, and carrying. An early dynamometer used to measure grip strength was developed in the seventeenth century (see Burton & Miller, 1998). In the eighteenth century, physicians began incorporating motor testing into their neurological examinations, and neurologists such as Gowers and Duchenne used dynamometers as well as performance-based testing with objective pencil-and-paper tests to examine motor skills for abnormalities. Rudimentary motor assessments were developed by physical educators to standardize assessment of athletic prowess, and initial attempts at assessment of physical-motor efficiency for vocational applications were made. By the early twentieth century, psychologists such as Pillsbury and Woodworth, who had interests in the relationship between cognition and movement, had started investigating specific motor skills with more reliable and objective performance-based tasks.

Despite the increasing interest in the concept of motor ability in the early twentieth century, no standardized test of motor ability for clinical or physical educational purposes had been published. Nikolai Oseretsky, a Russian psychiatrist, published the first assessment instrument to measure motor behavior in children in 1925 (Ozeretskii, 1925). Using a developmental perspective, Oseretsky established tasks that spanned different motor skill categories with varying levels of difficulty, such as static and dynamic coordination, motor speed, simultaneous movements, and which could be differentiated based on age (Oseretzky, 1931). This scale was the first comprehensive attempt at developmental motor assessment, and has had significant influence on the development of objective motor assessment since then. Oseretsky's scale was quickly adopted worldwide and translated into many languages over the next 50 years (see Bruininks, 1978; Doll, 1946; Sloan, 1955). At about the same time, Brace (1927), an American physical educator, also proposed a scale of motor ability tests measuring a person's "native" performance of 20 physical stunts (walking, jumping and clapping, standing on each foot, etc.), to be used for determining one's achievement in physical education as well as for diagnosing special performance disabilities.

Over the past 40 to 50 years, assessment of motor ability and movement characteristics has become a prime activity of a variety of professions, and numerous test batteries and specific motor instruments have been developed (Burton & Miller, 1998; Lezak, Howieson & Loring, 2004) (see Table 16.2). Typically, valid, reliable, and objective measurement of various motor capacities is desired, and many purposes can be served by such measures, including: categorization or identification of a motor disability in a child (i.e. diagnosis); planning of treatment or instructional needs for children with motor proficiency limitations; evaluating effectiveness of treatment or developmental change in motor abilities over time; providing performance-based feedback information for healthcare, clinical, or reimbursement needs; or finally, predicting neurodevelopmental outcome at a later age. Motor proficiency assessment is often conducted when information is required concerning a child's developmental motor status (Buckley, 1983).

Roy *et al.* (2004) have described the variety of approaches used in clinical practice and research to study motor control and coordination. The first approach to examining the motor functions of the nervous system is the traditional neurological model. This method involves the use of a sign- or symptom-oriented approach to provide information about the functional integrity of the nervous system. The identification of pathology is the prime goal of this method, and the focus is on identifying neuromotor deficits linked to damage to brain regions arising from known pathological conditions. Similarly, the second approach, neuropsychological assessment, also makes inferences about neural correlates of

Table 16.2. Motor assessment methods in children

Test	Author(s)
Batteries:	
Bruininks–Oseretsky Test of Motor Proficiency (2nd edn.)	Bruininks & Bruininks, 2005
Dean–Woodcock Sensory-Motor Battery	Dean & Woodcock, 2003
Movement Assessment Battery for Children	Henderson & Sugden, 1992
NEPSY, Sensorimotor Domain	Korkman, Kirk & Kemp, 1998
Peabody Developmental Motor Scales (2nd edn.)	Folio & Fewell, 2000
Test of Gross Motor Development (2nd edn.)	Ulrich, 2000
Test of Handwriting Skills	Gardner, 1998
Test of Written Language (3rd edn.)	Hammill & Larsen, 1996
Timed Motor Examination	Denckla, 1973; 1974; 1985
Toddler and Infant Motor Evaluation	Miller & Roid, 1994
Wide Range Assessment of Visual Motor Abilities	Adams & Sheslow, 1995
Individual tests:	
Beery–Buktenica Developmental Test of Visual-Motor Integration (5th edn.)	Beery, Buktenica & Beery, 2004
Finger Tapping Test	PAR Staff, 1992; Various; see Baron, 2004; Spreen & Strauss, 1998
Grip Strength/Dynamometer	Various; see Baron, 2004; Spreen & Strauss, 1998
Grooved Pegboard	Various; see Mitrushina *et al.*, 2005
Purdue Pegboard	Tiffin, 1948/1968; Various; see Gardner, 1979
Repeated Patterns Test	Waber & Bernstein, 1994

neuromotor functioning, but they are based on objective tests that assess the child's motor status. Both approaches typically emphasize the measurement of the end product of a motor skill rather than how a motor skill is performed, which is the focus of the third approach, a kinetic analysis of deficits in the process of movements. This latter approach analyzes the spatial and temporal characteristics of normal and abnormal movements and helps reveal how movement is controlled by identifying disruptions in processing stages (e.g. reaction time, movement time and accuracy, variability, etc.) during a movement. Ultimately, a more complete understanding of motor control and

coordination impairments in children will be dependent upon the use of these three interdependent strategies to provide both a broadband diagnosis of the disorder and a more fine-grained analysis of the potential neurobehavioral processes that are affected. With this type of detailed assessment information, more effective intervention methods for addressing motor difficulties can be derived.

Motor disorders and their treatment

Cerebral palsy

Cerebral palsy is an umbrella term used to refer to a group of non-progressive syndromes of posture and motor impairment that result from an insult to the developing central nervous system (Koman, Smith & Shilt, 2004). Although definitions differ, it is considered a well recognized ''static encephalopathy'' beginning in early childhood and persisting throughout the lifespan, but the manifestations can differ at various developmental stages. Cerebral palsy was originally investigated (as ''cerebral paresis'') by William John Little in 1861, although it had been described clinically almost 50 years earlier. Cerebral palsy is the most common cause of physical disability in childhood (Koman, Smith & Shilt, 2004).

In many ways, cerebral palsy represents the prototypical neurodevelopmental disability, because of the wide continuum of comorbid symptoms associated with this condition (Blondis, 2004; Iannaccone, 1994). Cerebral palsy is actually a variety of conditions, dependent on individual factors such as the size, location, and timing of the brain lesion. While the defining features of cerebral palsy emphasize motor impairment, there are usually other associated limitations in orthopedic and muscular function, visual and perceptual capabilities, cognitive processing, and neurological and emotional function (Blondis, 1996; Capute & Accardo, 1996). Severity ranges from subtle motor impairment to involvement of the whole body (Shapiro, 2004).

Cerebral palsy is not a disease and does not imply a specific cause, although the impairments are usually secondary to malformations or lesions in the pyramidal or extrapyramidal tracts. The insult to the brain occurs during the early stages of development, either in the prenatal, perinatal, or early postnatal (up to age 2 years) periods. The exact worldwide prevalence and incidence of cerebral palsy are not known, but the overall prevalence is thought to be approximately 2–4 per 1000 children, or about 1 in 500 live births. Incidence of cerebral palsy in term infants differs from cerebral palsy in very premature babies, where the risk per baby is high; nevertheless, more than half of all

cerebral palsy cases occur in term or near term infants (Nelson, 1996; 2002). Risk factors for cerebral palsy include significant prematurity and/or low birth weight, potential asphyxiating birth complications, death of a co-twin or co-triplet in a multiple birth, or disorders of coagulation and intrauterine exposure to infection or inflammation (Nelson, 2002; Picard, Del Dotto & Breslau, 2000).

The variety of available classifications of cerebral palsy recognizes the heterogeneity of the disorders. According to Blondis (2004), cerebral palsy can be classified according to its clinical motor presentation, the cerebral pathophysiology involved, or topographically. A clinical classification of cerebral palsy typically identifies the extent of the tone, spasticity, and movement abnormalities demonstrated; common subtypes include spastic cerebral palsy (i.e. spastic diplegia, spastic quadriplegia, spastic hemiplegia), extrapyramidal cerebral palsy, hypotonic cerebral palsy, and ataxic cerebral palsy. Spastic cerebral palsy, which is the most common type and accounts for 66–82% of cases (Fennell & Dikel, 2001), results from dysfunction in the corticospinal tracts and leads to increased muscle tone, hyperreflexia, and the persistence of primitive reflexes. Pyramidal system involvement causes spastic forms of cerebral palsy while involvement of the basal ganglia results in involuntary movement abnormalities such as chorea and dystonia. Mixed forms are also possible. Common pathophysiological factors include periventricular leukomalacia, trauma, and hypoxic-ischemic injury. Finally, topographical classifications emphasize the body structures in which posture and/or movement are compromised; diplegia, hemiplegia, triplegia, and quadriplegia are common topographical variants.

Clinically, children with cerebral palsy demonstrate a variety of neuromotor and neuropsychological characteristics, only some of which may be apparent early in development. Common impairments seen with cerebral palsy, that result in functional disability, include abnormalities of muscle tone, muscle weakness, loss of selective movement, co-contraction of agonist and antagonist muscle pairs, altered patterns of muscle activation for postural control, musculoskeletal problems (especially contractures), and various degrees of sensory, perceptual, or cognitive impairment (Bracewell & Marlow, 2002; Mayston, 2001). The diagnosis of cerebral palsy is often made by a team of medical professionals based on a complete and developmentally-sensitive history, physical examination, and ancillary investigations. Neuromotor assessments become more important when the child is older, more subtle concerns are raised, or when treatment progress is to be measured.

Cerebral palsy cannot be cured, but treatment can often improve a child's functional capabilities (Goldstein, 2004; Mayston, 2005). Goals for the rehabilitation of a child with cerebral palsy must change with the child's age and must take into account the developmental potential of the child, and the interaction

Table 16.3. Techniques used in the management of the motor problems associated with cerebral palsy

Therapies
Physical therapy
Occupational therapy
Medications
Anti-epileptics
Anticholinergics
Baclofen
Benzodiazepines
Dantrolene
Dopamine and dopamine agonists
Neuroleptics
Clonidine
SSRIs
Botulinum and other toxins
Surgery
Orthopedic procedures
Dorsal (root) rhizotomy
Deep brain lesions/deep brain stimulation
Baclofen pump
Mechanical aids
Orthotic devices
Braces
Serial casting or peripheral splinting
Computers/communication devices
Theoretical methods or approaches
Neurodevelopmental therapy
Conductive education
Constraint-induced movement therapy
Early intervention (multidisciplinary)

of physiological recovery and normal developmental processes (Iannaccone, 1994). However, the main aim of therapy for the child with cerebral palsy should be to improve the quality of life for the person and their family, and to maintain their functioning throughout various developmental stages.

Intervention or management methods for children with cerebral palsy include a variety of medical, surgical, and rehabilitative strategies (Table 16.3). As with all pediatric interventions, a multidisciplinary treatment effort is often the best approach, although a number of specific treatment methods have been attempted for individual motor impairments. Although there is not conclusive evidence,

it is likely that plasticity mechanisms are significantly enhanced by the appropriate intervention method (Hadders-Algra & Gramsbergen, 2003). Thus, therapeutic attempts can not only improve strength or teach skills, but also may ultimately help the brain relearn and adapt to its injury. This is perhaps particularly true for children with motor disorders, since a child may be able to learn alternative strategies for movement that make use of their residual neurological and musculoskeletal function.

Some previous intervention methods, such as neurodevelopmental treatment (NDT), patterning, or conductive education, which proposed cures, have been controversial and proven ineffective (Butler & Darrah, 2001); several of these will also be discussed in a subsequent section. Presently, typical effective intervention methods for the motor impairments in cerebral palsy include medications to control seizures and muscle spasms, braces to compensate for muscle imbalance, mechanical aids to help overcome impairments, counseling for emotional and psychological needs, and physical and occupational therapy to improve the normal use of motor skills (Scrutton, Damiano & Mayston, 2004). There are, unfortunately, still only limited data from controlled studies available to support the use of various treatment approaches, but a number of new medical, surgical, and rehabilitative techniques are being utilized and researched (Goldstein, 2004). In general, continued research and refinement of new methods means that children with cerebral palsy can enjoy near-normal lives if their neuromotor and associated problems are properly managed.

Intervention for spastic diplegia

Attempts at intervention into the course of spastic diplegia can occur at several developmental timeframes, including early in infancy when motor difficulties are first suspected, and later in childhood, when cerebral palsy and its manifestations have been diagnosed and management of the consequences of the motor deficits is provided. These age-based intervention efforts will be discussed separately.

Early intervention

Motor and visuo-perceptual difficulties, including spastic cerebral palsy, are often suspected early in infancy with very low birth weight or premature births (Bracewell & Marlow, 2002; Fedrizzi *et al.*, 1993; 1996; Koeda & Takeshita, 1992). Infants at such high risk for developmental motor disorders now receive early intervention programs, consisting of multidisciplinary services from birth to age 5 years that attempt to minimize developmental delays, remediate disabilities, prevent functional deterioration, and promote adaptive functioning. Past studies on early intervention programs primarily addressed improvement

in motor skills, while the more recent focus has shifted to improving functional outcomes. Although research on the effectiveness of early intervention programs is difficult and often confounded, Blauw-Hospers and Hadders-Algra (2005) have provided a systematic review of the effects of early intervention programs on motor development and disorders in children.

These authors reviewed the growing literature on the effectiveness of early intervention programs on motor development in infants at very high risk for, or with, developmental motor disorders. They utilized a developmental approach, in that they paid particular attention to the timing of the interventions (applied, for example, in the intensive care unit [ICU], in clinics, or elsewhere) to try to find critical ages for beneficial treatment effects. They also tried to find methodologically sound studies that monitored follow-up at least to the preschool period. They found great heterogeneity in the early intervention studies, including the sample sizes, ages, and intervention methods used; a meta-analysis therefore could not be performed. Intervention methods used in the intensive care units varied from formal programs to general stimulation efforts, while post-ICU interventions often used neurodevelopmental treatment, conductive education, or infant stimulation. Preterm infants seemed to benefit most from interventions that mimicked the intrauterine environment; these had at least a temporary beneficial effect. For term infants, the review noted that intervention programs such as NDT in the first postnatal years do not have a beneficial effect on motor development in children at high risk for cerebral palsy, but there was substantial evidence suggesting that locomotor training or general developmental programs in which parents learn how to promote infant development and active motor behavior can produce a positive effect on motor development. Blauw-Hospers and Hadders-Algra (2005) concluded that interventions in children at risk for developmental motor disorders should be adapted to the child's age.

Management of spasticity

Spasticity is considered an abnormal increase in muscle tone, although technically it is a velocity-dependent increase in resistance to passive movement of a limb, and does not necessarily interfere with voluntary movement (Tilton, 2003). Nevertheless, children with spastic cerebral palsy show spasticity as one symptom of an upper motor neuron syndrome that affects movement (Ivanhoe & Reistetter, 2004). Impairment in voluntary movement is caused by symptoms associated with spasticity or the upper motor neuron syndrome such as weakness, dystonia, or ataxia, rather than the spasticity itself. Spasticity can have a devastating effect on functioning and comfort of a child with cerebral palsy, and may lead to musculoskeletal complications such as contractures. Spasticity does not always

require treatment, but when it does, there is now a range of treatments available (see Table 16.3).

The variety of interventions for spasticity include traditional therapies such as physical or occupational therapy, medications, new surgical procedures, mechanical aids and devices, and theoretically mediated therapeutic approaches. It should be noted that none of these methods reverses the neuronal injury in spastic cerebral palsy, but they can help manage the motor complications well enough to allow the child more normalized movement. Although there are anecdotal reports of the benefit of home-based and alternative therapies (i.e. chiropractic, homeopathy, or hyperbaric oxygen), they are generally considered of dubious value and typically have not been empirically validated (Koman, Smith & Shilt, 2004).

Therapies such as physical and occupational therapy are the cornerstone of cerebral palsy treatment. Physical and/or occupational therapy usually begins at a young age, and is essential in order to stretch the muscles, improve range of motion, prevent atrophy, maintain strength, maintain mobility about the joints, and reduce the potential for joint freezing or contracture development (Brunstrom, 2001). Sometimes orthotic devices such as braces, splints, or serial casting are used along with therapeutic exercises to help prevent contractures by stretching spastic muscles. Serial casting is a non-surgical method that increases musculotendinous length, while splinting is used to maintain muscle length, and braces (e.g. ankle-foot orthoses) help stabilize joints and maintain resting muscle length. Notably, scientific support to validate the use of most of these methods or their effect on spastic cerebral palsy is limited; however, most children with cerebral palsy receive therapy of some type, and successful medical and surgical interventions generally depend on the addition of physical and occupational therapy for maximum benefit. As Brunstrom (2001) states, it is particularly beneficial for children with cerebral palsy to "get them moving," so therapy is believed essential to maintain as much motor activity as possible.

A great variety of medications to reduce spasticity are available. Medications operate by different mechanisms, some of which involve receptors in the spinal cord, while others involve receptors in the brain. Orally administered medications used to treat spasticity include GABA agonists, α2-adrenergic agonists, muscle relaxants, and anti-seizure medications. Baclofen, Dantrolene (a muscle relaxant that interferes with contraction), and Diazepam (Valium) are commonly used medications, although anticholinergics, dopamine agonists, clonidine, and neuroleptics are sometimes used for various motor disorders. Baclofen is frequently used. It is an activator of the inhibitory GABA type B receptors, which modulate the stretch reflex in the spinal cord, thus blocking muscle contraction. Still, these oral medications reduce spasticity for only short times

and can trigger significant side effects, so other routes for delivering such medications are being explored. A prominent alternative method for delivering Baclofen is through an intrathecal baclofen pump, which is surgically implanted in the space surrounding the spinal cord and used to deliver medication continuously. Because this is such an invasive procedure, and is associated with a number of complications, it is typically used only for cases where spasticity is severe and debilitating; nevertheless, in those situations it is typically very effective (Brunstrom, 2001; Goldstein, 2004; Krach *et al.*, 2005; Tilton, 2003).

If spasticity becomes severe and causes significant contractures, stiff muscles, curvature of the spine, or uneven leg growth, then more invasive techniques may be needed. These techniques include surgical procedures such as dorsal rhizotomy, surgical muscle or tendon lengthening, contracture release, or even experimental surgeries such as deep brain lesions or deep brain stimulation (Chambers, 1997). Other non-surgical, but still invasive, options include chemodenervation with botulinum toxin (botox), or alcohol or phenol "washes" (injections into the muscle, used to reduce spasticity prior to the need for surgery). Dorsal root rhizotomy and botox treatments will be discussed briefly, as they represent more refined and current intervention methods for severe spasticity in cerebral palsy, and have been studied more extensively.

In a selective dorsal root rhizotomy, surgeons attempt to locate through electrical stimulation, and then cut, the overactivated dorsal root fibers which are the basis for the abnormal stretch reflex. The operation appears to permanently reduce spasticity in the legs and does not cause numbness or weakness. Although there is some controversy about how selective the technique actually is, research suggests that it can reduce spasticity in spastic diplegia and perhaps ultimately increase functionality (Mittal *et al.*, 2001).

Finally, a fairly recent intervention method for spasticity involves the use of botulinum toxin A, a synthetic form of the toxin produced by the bacterium *Clostridium botulinum*, which normally causes food poisoning in improperly canned foods (Pidcock, 2004). When a small amount of the purified toxin is injected directly into a muscle, the targeted muscle becomes weak, with the botox acting as a chemodenervation agent. Botox has proven to be a very successful treatment for muscle stiffness in children with spastic cerebral palsy, and has led to a revolution in effective treatment. There are no known side effects to botox treatment, but it is necessary to repeat the treatment every 3–8 months as the effects are only temporary. With use of physical therapy and other management methods, the effectiveness of botox can be extended into functional gains in motor outcome (Boyd & Hays, 2001; Boyd, Morris & Graham, 2001; Russman, Tilton & Gormley, 1997; Speth *et al.*, 2005).

Hemiplegic cerebral palsy

A great deal of progress has been made in the understanding and treatment of hemiplegic cerebral palsy in recent years (Goodman, 2002; Scrutton, Damiano & Mayston, 2004). Hemiplegic cerebral palsy (also called congenital hemiplegia) is the most common type of cerebral palsy among children born at term, and only second to diplegia among preterm infants (Neville & Goodman, 2000). It is a unilateral, static, non-progressive motor impairment of early onset that is cerebral in origin. Present-day knowledge strongly supports the notion that the brain lesion involved has an intrauterine origin, and an excess of prenatal adverse events has been recorded among children with congenital hemiplegia (Hagberg & Hagberg, 2000). Congenital hemiplegia differs from acquired hemiplegia in its age of onset; acquired hemiplegia typically occurs in childhood to adolescence, while congenital hemiplegia is recognized in infancy (Oskoui & Shevell, 2005).

A child with hemiplegic cerebral palsy has varying degrees of involvement in the ipsilateral upper and lower extremities, including impairments such as inadequate muscle recruitment, impaired sensation, and stereotypic posturing (Charles, Lavinder & Gordon, 2001). The involved upper extremity in these children tends to be used less frequently because it is less efficient due to insufficient force generation and control of affected muscle groups (Duff & Gordon, 2003; Smits-Engelsman, Rameckers & Duysens, 2004). Clinically, the motor and sensory deficits of children with hemiplegia particularly affect manipulative abilities and coordination of reaching and grasping; notable difficulties in tasks with bilateral manipulation are also often seen. Few studies have been published concerning the disability arising from impaired hand function in children with hemiplegia, and only a recent follow-up study documents the natural history of the impaired motor function in early adolescence (Fedrizzi *et al.*, 2003). As these children develop they tend to acquire increasing skill with the unaffected hand and increasingly neglect the impaired hand. This may be due to the presence of neuropsychological deficits related to cortical and sensorimotor damage, to nonuse, or simply to the capability of the unimpaired hand to learn motor skills (see Fedrizzi *et al.*, 2003; Fennell & Dikel, 2001).

Constraint-induced movement therapy

A number of investigators, most notably Edward Taub and his associates at the University of Alabama–Birmingham (Taub & Crago, 1995; Taub & Uswatte, 2000; Uswatte & Taub, 1999), have proposed that in hemiplegia (after various CNS lesions), disuse of the involved upper extremity may be a result of "learned nonuse" because it is more convenient to use the noninvolved upper extremity.

Based on early work with deafferented monkeys, Taub and his associates have developed a protocol for increasing the use of the involved (''impaired'') extremity, and the intervention is referred to as constraint-induced movement therapy (Taub, Uswatte & Pidikiti, 1999). This intervention is thought to increase the use and function of the involved upper extremity of individuals with hemiplegia by the restraint of the noninvolved upper extremity along with training of the involved extremity. Unlike adults with acquired hemiplegia, who have had functional use of their arms before their CNS lesion, children with hemiplegic cerebral palsy have not used the involved arm from early life. Thus, it has been suggested that constraint-induced movement therapy may be an intervention which could promote increased use of the upper extremity in children with hemiplegic cerebral palsy (Karman *et al.*, 2003; Taub *et al.*, 2004; Taub, Uswatte & Elbert, 2002).

Several early studies of constraint-induced movement therapy in children with cerebral palsy have been reported (Charles, Lavinder & Gordon, 2001; Crocker, MacKay-Lyons & McDonnell, 1997; Willis *et al.*, 2002), and they all noted improvement in hand function in the involved extremity following a program of ''forced use.'' The results of these small-sample studies suggested that nonuse may be a factor in the motor deficits demonstrated by children with hemiplegic cerebral palsy and that constraint-induced movement therapy could be an effective intervention for improving upper extremity function.

More recently, additional research involving larger sample sizes has demonstrated further support of constraint-induced movement therapy for treating children with asymmetric motor impairment. Taub *et al.* (2004) reported a randomized, controlled clinical trial of 18 children (ages 7 months—8 years) with hemiplegic cerebral palsy, in which either pediatric constraint-induced movement therapy (CIMT) or conventional treatment was provided. The CIMT involved promoting increased use of the affected arm and hand by intensive training coupled with bivalved casting of the less-affected upper extremity for the same period. Children receiving CIMT, compared to the controls, were found to have acquired more new motor skills, and showed improved quality of and frequency of unprompted use of the more affected arm, with functional gains maintained for 6 months. The authors concluded that pediatric CIMT produced major and sustained improvements in motoric function in young hemiparetic children.

Further extensions of CIMT in children with hemiplegic cerebral palsy have been provided by Eliasson *et al.* (2005) using a restraint glove; Gordon, Charles and Wolf (2005) using a sling as a restraint; and Naylor and Bower (2005) with gentle restraint of the unaffected arm and verbal instruction. Each of these ''child friendly'' restraints provided similar positive effects in post-treatment

upper extremity skills as the more invasive restraints used in early studies. CIMT is a solid example of the development and application of a neuroscientific approach to clinical practice in pediatric neuropsychology.

Developmental coordination disorder

Developmentally based motor problems have been discussed and investigated for almost 100 years (Smyth, 1992). Throughout the twentieth century, children with mild unexpected motor difficulties have been studied by professionals from a variety of disciplines, and investigators have provided a variety of definitions and classifications, as well as varied theoretical perspectives on possible etiologies (see Hadders-Algra & Gramsbergen, 2003; Tupper & Sondell, 2004). Terms such as developmental apraxia, dyspraxia, congenital maladroitness, clumsy child, mild cerebral palsy, developmental motor learning disability, movement learning disability, specific developmental disorder of motor function, and minimal brain dysfunction have all been used to describe this group of children (Chu, 1998*a*;1998*b*; Gubbay, 1975; Keogh, 1982; Roy *et al.*, 1990).

The current terminology comes from the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; APA, 1994), which describes children with developmental coordination disorder (DCD) as showing performance in motor activities substantially below that expected given the child's chronological age and measured intelligence. The motor disturbance necessarily interferes with academic achievement or activities of daily living, and cannot be due to cerebral palsy, other neuromuscular or medical conditions, or a pervasive developmental disorder. The diagnosis can be applied to individuals with mental retardation only if the motor difficulties are in excess of those expected for other individuals with intellectual deficiency. The DSM-IV indicates that the prevalence of DCD is 6% in the 5- to 11-year-old age range, and the developmental course often continues throughout childhood and adolescence, and possibly into adulthood, although good prevalence estimates in adults are not available. Individuals with DCD are often handicapped throughout their life in many aspects of daily living by their motor difficulties, including handwriting, sports, academics, social activities, self-care, and vocational performances (Cousins & Smyth, 2003; Larkin & Summers, 2004; LeNormand *et al.*, 2000).

The study of motor proficiency in children and adolescents with DCD has involved a wide range of sensory, motor, intersensory, and functional tasks. Most studies suggest that children with DCD exhibit poorer performance on all of these tasks than peers, especially tasks that involve accurate timing of responses and precise force control (Smits-Engelsman, Niemeijer & van Galen, 2001; Wilson & McKenzie, 1998). Although only limited research is

available on motor control characteristics of children and adolescents with DCD, and is often confounded by heterogeneous samples and unclear diagnostic criteria, several findings have consistently emerged (Williams, 2002).

Motor deficits frequently observed in children and adolescents with DCD include slower reaction, movement, and response times; difficulty with timing and force control of movements; increased variability of performance on various motor tasks; inability to adapt to changing movement demands; poor intersensory integration; and inconsistency in the use of motor control strategies in bimanual or multilimb coordination. The motor deficiencies have been found to persist with age, which suggests that children do not outgrow the motor problems, so they may be related directly to a central nervous system dysfunction rather than a developmental delay. Etiology is unclear. Unfortunately, there is considerable heterogeneity in the motor characteristics of children with DCD, and individual children with DCD may demonstrate unique patterns of motor control impairments on various test batteries (Geuze *et al.*, 2001).

Because a heterogeneous group of children with minor motor difficulties are often grouped together as showing DCD, treatment approaches have been multifaceted (Gordon & McKinlay, 1980). Formal reviews of the effectiveness of interventions for DCD have been provided by Pless & Carlsson (2000) and Polatajko *et al.* (2004). The following discussion will provide only a brief summary of the variety of approaches attempted in this heterogeneous group; as necessary, specific conditions researched will be identified. Main categories of intervention have been described as process or performance oriented by Sugden and Wright (1998), and their general categorization will be used here (see Table 16.4).

Table 16.4. A classification of the treatment approaches used in developmental coordination disorder (based on Polatajko *et al.*, 2004)

Process Approaches:
Neurodevelopmental Treatment
Sensory Integrative Therapy
Performance-based Approaches:
Conductive Education
Cognitive Approaches:
Cognitive Orientation to Daily Occupational Performance
Compensatory Approaches
Exercise Therapy
Neuromotor Task Training

Process-oriented approaches

Process-oriented approaches to the management of children with DCD have generally been rather controversial, as they often imply fixing or curing the underlying disorders. Process-oriented approaches are those that emphasize the role of the components of the motor performance, and usually focus on reinstituting a developmental hierarchy to alleviate the dysfunctional motor components. The two most notable process-oriented approaches include neuro-developmental treatment (NDT) and sensory integrative (SI) therapy.

''Neuro-developmental treatment'' is an approach initially developed over 40 years ago by Dr. Karel Bobath and his wife Berta Bobath, a physical therapist (summarized in Bobath & Bobath, 1984). The Bobaths initially began to develop a treatment method out of their clinical observations of children with cerebral palsy and, subsequently, NDT has been applied by other therapists to children with a variety of different motor difficulties. The underlying dysfunction was presumed to be the interference in normal postural control and motor development by the motor dysfunction of cerebral palsy (later, other motor disorders). The goal of NDT was the establishment of normal motor development by focusing on the sensorimotor components of muscle tone, reflexes, and other capabilities, with various handling techniques that controlled sensory stimuli. The child was thus a passive recipient of NDT treatment, and the ''normal'' developmental sequence was advocated as the means for placing children in ''reflex-inhibiting'' postures. NDT is considered a hands-on approach which uses inhibition, facilitation, and specific sensory stimulation to modify abnormal patterns of posture and movement, and to facilitate more normal patterns.

Although NDT is commonly used in treating various motor disorders, there is relatively little research published on its efficacy. A number of studies have been reported that show no significant effect of NDT (summarized in Polatajko *et al.*, 2004) and the American Academy of Cerebral Palsy and Developmental Medicine concluded in an evidence report (Butler & Darrah, 2001) that the preponderance of evidence did not confer any advantage to NDT over the various alternative treatments to which it was compared. There was no consistent evidence that NDT changed abnormal motoric responses, slowed or prevented contractures, or that it facilitated more normal motor development or functional motor activities. Such a passive treatment method is typically not advocated today.

Sensory integrative (SI) therapy was also first proposed about 40 years ago, based on the work of Dr. A. Jean Ayres, an influential occupational therapist with interests in learning and motor/sensory disabilities (Ayres, 1972). She noted that children with motor disabilities, some who would qualify as DCD today, appeared to have difficulty organizing sensory input in order to make an adaptive motor response (Ayres, 1985). She proposed that dysfunction in sensory

integration reflects problems organizing sensory input, which can lead to delayed motor development and learning. Ayres developed SI therapy to provide planned and controlled sensory input, which she argued allows the nervous system to effectively use such information for functional activities (Ayres, 1972).

SI therapy is usually administered by trained occupational therapists in a child-centered or individual situation. The child chooses among various sensory and movement activities (typically with some equipment involved) and the therapist modulates the activities to challenge but not overwhelm the child's sensory processing capabilities. Unlike NDT, the child is considered an active participant in the treatment program and is encouraged toward optimal activities by the therapist.

Empirical evidence for the effectiveness of SI therapy is also lacking. Although anecdotal reports of SI's effectiveness are described by occupational therapists, there has been no significant effect found for SI when compared to other methods of intervention in DCD (Polatajko *et al.*, 2004). According to Pless & Carlsson's (2000) meta-analysis, the least effective treatment approach for the motor disorders seen in DCD was SI therapy, when compared to a specific skills training or general abilities training approach.

Performance-oriented approaches

Approaches to DCD that emphasize adaptive learning, performance outcomes, and skill development are classified as performance-oriented approaches (Sugden & Wright, 1998). These approaches include conductive education, cognitive interventions, compensatory methods, exercise therapy, and neuromotor task training. The goals are typically to encourage and assist children with motor disorders to perform functional activities most effectively.

Conductive education is a learning-based methodology that is said to encourage delayed developmental processes to normalize, by both considering the child an active participant in treatment and attempting to maintain high levels of motivation and determination without the use of adaptive devices. The child is thought to be motivated to stimulate developmental motor processes through education, often in group activities. Key elements of conductive education include guidance and structured programs provided by the conductor (teacher, therapist, etc.) and use of a specific learning method called rhythmical intention, which involves verbalization of the intention to move and subsequent movement in tandem with specific rhythms, such as counting aloud. Daily or adaptive tasks are used, and task analysis and verbal regulation are the main components of task performance. Polatajko *et al.* (2004) note that only two empirical studies have been completed addressing conductive education, using only children with

cerebral palsy, and no support was found for any unique effects of conductive education compared to other methods.

Cognitive approaches to treatment are common for many other neurocognitive or learning disabilities. Cognitive approaches to managing developmental motor disorders are limited, but they focus on use of behavioral reinforcement and learning techniques to teach the child to consistently exhibit appropriate motor responses. One cognitive approach that has been investigated in children with DCD is called cognitive orientation to daily occupational performance (CO-OP). CO-OP is client-centered and is based on use of global, domain-specific and guided strategies to help children enhance their strategies to perform everyday tasks of childhood. Although administered by therapists, parents are encouraged to be involved in treatment sessions to help foster generalization of acquired strategies to home situations. Several pilot studies (Miller *et al.*, 2001; Polatajko *et al.*, 1995) have found improved skill acquisition and transfer, as well as higher levels of satisfaction with CO-OP, suggesting promise as an effective intervention in DCD (see also Polatajko *et al.*, 2001; 2004).

Compensatory interventions for motor disorders support or assist one's performance of a task with the primary goal of enabling independent task completion (see also Kurtz, 2003). Physical and occupational therapists often utilize specialized devices (braces, orthotics, splints, casts, crutches, computer keyboards, etc.) to make children as functionally independent as possible. For instance, current computer technology may be used for the compensation of written language skills (Deuel, 1995; Lie, O'Hare & Denwood, 2000). However, while some children may find that writing on a computer (''keyboarding'') is easier than writing with pencil and paper, for others the additional task of mastering the keyboarding technology, given motor impairments, is overwhelming. In one of the few relevant studies in this area, O'Hare, Lie and Denwood (1998) found a large proportion of their students with ''motor dysgraphia'' felt a keyboard was helpful, and their motor problems were not found to preclude successful keyboard use. The authors suggested that this form of accommodation should be considered in any child with a significant writing handicap secondary to motor dysgraphia. Berninger and Amtmann (2003) also recommend that keyboard instruction should occur early but should not replace handwriting instruction for beginning writers. To date, with the exception of teaching keyboarding skills to children with dysgraphia, no empirical data support the use of these compensatory devices for children with DCD.

Similarly, exercise therapy (a physical therapy technique) is primarily used for strength training of weak muscle groups. Weak muscles are strengthened through a range of active, isometric and resistive exercises, and benefits are greatest with already functional muscles. Some general effects of physical

exercises and activities on stress reduction or relaxation are also noted. Exercise therapy has been well studied in the physical therapy literature, and notable gains are noted for such treatment in children with defined neurodevelopmental conditions such as cerebral palsy and muscular dystrophy (Dodd, Taylor & Damiano, 2002). The effectiveness of exercise therapy in children with DCD has not been investigated (Mayston, 2005).

An additional performance-oriented intervention technique called neuromotor task training has recently been proposed for addressing motor dysfunctions in DCD. Neuromotor task training (NTT) is described as a "top-down" task-oriented treatment approach based on principles of motor control and learning research (Schoemaker *et al.*, 2003). In NTT, therapists use a taxonomy of task-specific or skill-based motor activities and focus on direct teaching of the tasks to be learned. The choice of tasks depends on the individual needs of the child as well as their capabilities, motivation and parental support. Strengths and weaknesses of functional performances are analyzed and therapists design the functional treatment exercises in such a way that they can analyze and adapt motor control processes required. Several initial studies (Niemeijer *et al.*, 2003; Schoemaker *et al.*, 2003) have suggested that children with DCD who are treated with a task-oriented learning program such as NTT can demonstrate improvements in motor skills and handwriting. Further research will be necessary to investigate whether these improvements can be maintained, and whether NTT is different from CO-OP or other performance-based approaches in its effectiveness.

Future directions

A great deal of progress has been made in the past twenty years in the management of children with disorders in motor control and coordination. Initially, a number of therapeutic interventions were proposed that have been found to be of little clinical or empirical benefit, such as neurodevelopmental treatment, sensory integrative therapy, or conductive education. More recently, new therapeutic endeavors have been developed that stem from solid scientific foundations and that promise further improvement of the functional status and quality of life of children with developmental motor disorders. Constraint-induced movement therapy as applied to children with hemiplegic cerebral palsy, and less-researched, but promising, performance-based techniques such as neuromotor task training for children with developmental coordination disorder are examples of the newer approaches which have shown empirical results.

One clear theme in the intervention effectiveness research discussed in this chapter is that the most beneficial treatment methods for children with disorders of motor control and coordination are methods that involve the child and family

as active participants and agents of change in their motor skills. As a dynamic systems perspective might predict, a child's motor development is dependent on both internal and external factors and stimulation for optimal performance and maturation. Therapists would do well to recognize the importance of learned behaviors in normal motor task performances and provide methods that encourage continued use of adaptive movements (see Mayston, 2005).

More clinical research is clearly needed. Neuropsychologists are in a unique position in working with children with developmental motor disorders, in that neuropsychology can provide a basis for a more complete neuroscientific and cognitive–behavioral understanding of the assessment and treatment techniques for children with motor problems. A neuropsychological model of both normal and disordered motor development in children is needed, as is a more comprehensive assessment methodology that addresses not only what movements are produced, but how they are produced, and how disordered movements affect one's functional status. Multidisciplinary research efforts ultimately will provide the needed interventions to impact the functional status of a child with a disorder of motor control or coordination, and neuropsychologists can use their expertise to provide unique contributions.

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Section III

Medical, rehabilitative & experimental interventions

17

Pharmacological interventions for neurodevelopmental disorders: using the autism spectrum disorders as a model

Thomas Owley

The neurodevelopmental disorders can be broadly defined as any central nervous system disease process that hinders the ability of a child to achieve age-appropriate developmental maturity as expected (Farmer, Donders & Warchausky, 2006; Hagerman, 1999). Such disorders may have a variety of etiological underpinnings, including ones that are primarily genetic or metabolic in their onset. Some examples of neurodevelopmental disorders include the Autism Spectrum Disorders (ASDs), mucopolysaccharidoses, Fragile X Syndrome, Down Syndrome, neurofibromatosis, velo-cardio-facial syndrome, Turner Syndrome, among others that are less commonly known (Hagerman, 1999; also see Klein-Tasman, Philips & Kelderman, this volume). Behavioral difficulties that can be the target of pharmacological intervention are common in these disorders. In this chapter, concepts relevant to the pharmacological treatment of neurodevelopmental disorders will be explored. The autism spectrum disorders will be used as a model, to look at how decisions are made with regard to pharmacological interventions for children with these disorders.

ASD as a model neurodevelopmental disorder

The Autism Spectrum Disorders (ASDs) are a group of debilitating neuro-developmental disorders characterized by (1) deficits in socialization; (2) deficits in language and communication; and (3) the presence of restricted, repetitive, and stereotyped patterns of behaviors, interests, and activities (American Psychiatric Association, 2000; see also Wolf, Fein & Akshoomoff, this volume). These disorders are best defined by the social difficulties that present in affected children. These difficulties include impairments in the use of nonverbal behaviors, such as using and interpreting facial expressions and body postures; poor eye contact; and a lower than typical use of gestures in social interaction.

There is a lack of spontaneous sharing of interests with others as well as deficits with seeking to share the interests or enjoyments of others. This failure in reciprocity can often make the child with ASD appear aloof or avoidant. The social interaction style of even the most socially able person with an ASD may appear odd or idiosyncratic. All of these difficulties can often lead to problems in navigating complex social situations and a failure to develop relationships with same-age peers.

The qualitative impairments in language and communication often include a delay or total lack of development of speech (Klin, Volkmar & Sparrow, 2000; see Wolf, Fein & Akshoomoff, this volume). Approximately half of individuals with an ASD never develop speech. The lack of speech is not accompanied by significant compensation through nonverbal behaviors like gesture or mime and the absence of nonverbal compensation helps differentiate children with autism from children with other language disorders. Sometimes the only speech present in children with ASD is imitative or echolalic. When speech is present, it is often idiosyncratic, stereotyped, or repetitive. A phrase or whole series of lines (''scripts'') may be repeated over and over in a noncommunicative manner. Idiosyncratic phrases may be used that signify needs or ideas, which are only intelligible to immediate family members. Speech may lack prosody. Pragmatic use of language is also impaired, and it is difficult for these individuals to initiate and maintain conversations. There are often problems deciphering metaphorical or other abstract aspects of language, and the literal interpretation of figures of speech, sarcasm, and ''kidding around'' often leads to confusion, anger, or embarrassment. It is important to note that receptive language skills may be surprisingly normal, even in some children without any expressive language, and not understanding this point, as we will see, can lead to trouble for the physician or other clinician seeing a youngster with ASD.

The third set of criteria that define the ASDs is the presence of restricted, repetitive, and stereotyped patterns of behavior, interests, and activities (American Psychiatric Association, 2000). Many of these individuals have preoccupations with particular themes (i.e., trains, a favorite television program, or the like). Others may have compulsive physical rituals to which they adhere with significant rigidity; such children will become quite upset and even physically aggressive when the need to finish a ritual is interfered with by a parent or other adult. Many children with ASD are adamant about adherence to routines, and small changes in a schedule, a usual practice, or the introduction of a novel situation will evoke anxiety and frustration. Some stereotyped movements (i.e., hand flapping, body rocking) occur at times of happiness or anxiety, and are indicators of excitement, or in other circumstances, may be an attempt to self-soothe.

Principles of using medication in neurodevelopmental disorders

While the model proposed in this chapter is specific to disorders encompassing the autism spectrum, the same principles apply to the use of medications when treating concerns in children with other neurodevelopmental disorders. Notably, it is very rare to find a pharmacological treatment that specifically and exclusively addresses a core symptom of any neurodevelopmental disorders. As such, the concept of identifying target symptoms, weighing risks and benefits, and using instruments to follow response is applicable across the family of disorders seen in children, which are described in this volume. Additionally, it is crucial to keep in mind that many of these disorders share a number of non-core symptoms that are typically the targets of medications (i.e., hyperactivity, anxiety, aggression, and/or depression).

Autism spectrum disorders

As has been mentioned in a previous chapter in this book, there is a place for the use of medication in ASD. It is in fact increasingly common to use medications to manage a number of core and comorbid symptoms seen with ASD (Owley, 2002). As an adjunct to social, environmental, and educational interventions, medications can often be quite useful (Findling, 2005). More importantly, there have been varying levels of efficacy established for their use. Nonetheless, it is important to remember that the use of medications should only follow a careful analysis of a specific child's behavior, preferably across all settings. As well, only after all other interventions have been explored, is it the case that medication should be considered. In fact, in many cases, carefully thought out and designed behavioral interventions will obviate the need for psychotropics. For example, consider a boy with attentional difficulties who cannot adequately focus in the classroom. While this situation may typically be considered an indication for the use of a medication, to increase the child's ability to focus, it is also the case that the use of an aide, assigned to the child, may more effectively serve the "same role," i.e. redirecting the child and helping him attend appropriately. Similarly, a young woman with ASD who is presenting with an insistence on sameness or behavioral rigidity may actually benefit enough from verbal cues and rewards to avoid the use of medication.

In this context, it is important that the psychopharmacologist working with a child with ASD, or other neuro-developmental disorders, is knowledgeable and conversant in the common behavioral interventions that are used for these disorders. Ideally, a child psychiatrist will work collaboratively with a neuropsychologist and/or behavioral psychologist, and obtain consultation from them

for complicated cases (Owley, Leventhal & Cook, 2006). More specifically, cognitive testing can often give vital information about the child's capability to benefit from various behavioral interventions, and which modes of learning are most useful. Similarly, neurocognitive testing often proves helpful in determining targets for intervention, both behaviorally and pharmacologically (Findling, 2005).

The pharmacologist's role in treating neurodevelopmental disorders

The concept of target symptoms

There are currently no medications available that specifically treat the social, communication, and language deficits in ASD. The concept of using particular target symptoms in making pharmacological decisions in ASD, as well as with regard to other neurodevelopmental disorders reflects this reality. We are not directly treating the ASD, but rather a constellation of symptoms that are interfering with the child's ability to function in various aspects of life (i.e., social, academic, vocational). Everyone significantly involved in the child's life (e.g. parents and other caretakers, teachers, healthcare providers, speech and other therapists) needs to be aware of what symptoms are being targeted by a particular medication, in as concrete, and ideally operationalized of terms as is possible. Vague questions about the child's general functioning are not reliable guides for treatment decisions, and should be replaced by direct inquiries about specific symptoms and how they affect functioning (Owley, Leventhal & Cook, 2006). This principle should both simplify and facilitate communication between those involved in the child's care, and help focus everyone working with a select child in concentrating on what has been identified as most important for change.

It is first necessary to identify target symptoms. This is not a task that is easy for the vast majority of parents, let alone professionals working with children with neurodevelopmental disorders. These individuals often know only a little information about what symptoms are amenable to available medications; although with the greater use of the internet, this is a fact that is changing all the time. Overwhelmed parents will often begin by simply stating that they do not know where to start when asked to provide their child's history, and in truth, parents often cannot be expected to present their chief complaints in the order of most to least distressing. The physician who leaves plenty of time for this first visit, and informs the parent that there is plenty of time (as well as having body language that reinforces this lack of time urgency) will find that parents relax and are able to give a better, fuller, more precise history. This fosters greater collaboration concerning the willingness to try medications and to evaluate their effectiveness.

Additionally, it is very important to recognize, and to share with families, that it is not unusual, due to the heterogeneity in response to medications in children with neurodevelopmental disorders, to have to try a number of medications before having some degree of success. This is often a worrisome aspect to pharmacological management that is best addressed through open communication.

Once there has been substantial discussion between the psychiatrist and the parents, the physician will often work to create a hierarchy of symptoms that reflect (1) what is most troublesome and (2) what is potentially amenable to medication. This may be complicated, since there may be many more factors influencing symptom presentation than is immediately obvious. For instance, what looks like unprovoked aggression, such as biting, may actually reflect the fact that someone in the child's environment is interfering with his or her compulsive behavior (Klin & Volkmar, 2000). In this case, it may prove best to conceptualize the situation as one in which the "compulsive behavior" is being directly treated, rather than the "biting." Collaboration between the physician and the psychologist, as well as the family members and teachers working with the child, is absolutely necessary when identifying and establishing a symptom hierarchy. Information from multiple settings allows the pharmacologist to better consider how behavior is both being displayed and what its antecedents may prove to be. This will foster a more effective determination about which medication to consider and why.

It is often difficult to determine what is causing a particular behavior. Hyperactivity is one such problem; it is a predominant concern in children with developmental disabilities and often contributes to significant morbidity. When the pharmacologist sees hyperactivity in a child with an ASD, several considerations are required: specifically, is the behavior evidence of (1) comorbid attention deficit hyperactivity disorder; (2) significant anxiety, which can also present with hyperactivity as a behavioral manifestation; (3) evidence of understimulation or behavioral oppositionality; or even (4) already prescribed drug side effects. Determining which of these etiologies is truly responsible for the presentation of hyperactivity will require that the pharmacologist take a number of factors and approaches into consideration, including obtaining detailed information about what parents, teachers, and therapists observe; learning more about the child's behavior as she or he is observed in the office or consulting room; and determining the response to particular medications that are being prescribed. Again, this argues for a significant level of collaboration between the psychopharmacologist and other professionals managing the child's care.

There will inevitably be symptoms described by both parents and teachers that are not, based on our current knowledge and experience, targets for any of the current medications available in our pharmacological armamentarium.

As such, when parents report symptoms that are not appropriate medication targets, it is necessary to specifically address this issue and not assume that this knowledge will be self-evident. If the physician does not do this, there is a risk that the parents will feel that they were not effectively heard, and as a result, they may become disillusioned with the approach being taken. It may be necessary to reiterate to the family and treatment team which target symptoms are being considered pharmacologically, and to redefine what will not or cannot be considered target symptoms as treatment collaboration continues, in order to ensure that all parties are working together.

In terms of prescribing medications for children with neurodevelopmental disorders, it is necessary to attend to the attribution processes that occur in both the parents and the clinician, specifically with regard to identifying whether changes taking place are due to medications being utilized, or whether they are more directly a byproduct of behavioral or maturational effects. Doing so, however, is very complicated. Using children with ASD again as a primary example, it is important to recognize that despite the presence of a significant disorder, affected children are maturing and achieving developmental goals. However, it is the rate at which these abilities and changes are achieved that is much less predictable. While the rate of change in most developmental areas is steady, even in the majority of cases of children with ASD (Klin *et al.*, 2000), it is certainly not uncommon to see a child suddenly make substantial improvements in social abilities or communication/language. In fact, this is particularly dramatic in areas that by their nature are often binary, such as when a child who never speaks suddenly begins to speak. It is only natural that those involved with the child will become excited, and begin to look for specific reasons for these observed changes.

When a psychiatrist or neuropsychologist treats many children with neurodevelopmental disorders, eventually and inevitably such a dramatic change will coincide with the starting of a new medication, or with a new dose of a medication that has been used over time. In such a situation, it is important that the physician explicitly state that the medication is unlikely to be the responsible factor for any direct improvements in either social or communication deficits. While there is the possibility in certain situations for indirect improvement — for instance, decreased social anxiety due to an SSRI, or improved attention, including social attention, due to the use of a stimulant a medication, it is rarely the case that the medication alone led to the change in social behavior. This must be made explicit because patients with ASD are often involved in behavioral programs that are aimed at improving social deficits or communication at the same time that medication trials are being attempted. These behavioral treatments are expensive, time-consuming, sometimes frustrating,

and usually bring about gradual change. However, these behavioral treatments are almost certainly responsible for the improvements in social or communication areas which are being observed; it is typically not the medication driving the change. If the physician makes the attribution that medication is responsible for the improvements (including by silently accepting the parents' own positive attribution about the medication and its effects), a great disservice may be done to the child with ASD and those actually responsible for the improvement. Instead, the physician has an opportunity to acknowledge that the efforts of all involved in this difficult behavioral work are yielding dividends.

Weighing benefits and risks

Helping parents look at risks and benefits of treatment is a necessary aspect of collaboration; the physician must help parents make a comfortable and informed decision about a prospective medication trial. As such, parents and the pharmacologist must assess possible treatment benefits (i.e. how alleviating symptoms can potentially improve quality of life) and then weigh them against the risks inherent in using that same medication. This process is more complex than may first appear, since it is often the case that benefit from response can be gradual and at times, even subtle. For example, a psychiatrist may be confronted with a patient with ASD who has tried many relatively benign medications in the past, under his or her previous physician's guidance. However, this patient has continued to have severe symptoms that are making it increasingly difficult for the family to manage from day to day. As a result, the family is now considering residential placement. As a result, the family may be willing to accept an increase in risk (i.e. the use of a neuroleptic medication that has potentially irreversible side effects, such as extrapyramidal symptoms) if there is a possibility that the patient will respond and subsequently be able to live at home. Such situations are complicated and demand the consideration of a number of factors, including whether this is a situation where residential placement may be a better option. In this instance, the risk/benefit ratio does not simply translate into whether the patient's potential improvement warrants a trial with a medication with an overall complicated side-effect profile, but instead involves consideration by the physician and the family of the entire case disposition. Conversely, a parent may not have even considered the use of medication for a child showing few externalizing difficulties but a significant level of internalizing concerns (i.e. social anxiety and some obsessionality), who is otherwise able to be conceptualized as doing well. In such an instance, a trial with an SSRI may be recommended, since the potential for benefit is greater than the risks that may be involved (e.g. decrease in obsessions, greater social engagement).

Monitoring change

As noted earlier, it is important to operationalize target symptoms as much as possible when working with patients with developmental disorders. As has been well delineated in the extant neuropsychological literature, one way to do this is through the use of parent and other significant adults' completion of rating scales (Aman *et al.*, 1985). These tools provide the physician with a framework from which to assess response to medication and a relatively easy, straightforward way to collect standard information about the patient's functioning in a variety of settings. The Aberrant Behavior Checklist, Community Version (ABC-CV; Aman *et al.*, 1985) is one scale in particular which captures many of the difficulties that children with ASD, let alone other neurodevelopmental disorders display. The ABC-CV is a 58-item questionnaire scored from "0" ("not at all a problem") to "3" ("problem is severe in degree"). It provides both an overall score and is also divided into five subscales; Irritability (which includes items such as crying or agitation); Lethargy (or social withdrawal); Stereotypy (such as recurring, repetitive movements); Hyperactivity (such things as unable to sit still, impulsive); and Inappropriate Speech (repetitive, excessive, or loud speech).

Since medications could also potentially worsen scores on these subscales, the test does not only reflect improvement but is also a measurement of potential drug-induced worsening in these areas. The ABC-CV was specifically developed to assess the effects of medication and other treatment interventions in individuals with developmental disorders. It has been shown to be sensitive to drug effects in previous clinical trials with children who have been diagnosed as having autistic disorder (King *et al.*, 2001; Owley *et al.*, 2005). Although rating scales cannot replace careful examination of the patient and interviews with parents and teachers, they may be particularly helpful with assessing which medication and dosages of medications are helpful, or deleterious in treatment planning.

Neurodevelopmental medications by class

Stimulants

For many years now, physicians have been prescribing stimulants and other medications traditionally used for ADHD at significant rates for patients with autism spectrum disorders. In a medication survey, Aman and colleagues (Aman, Lam & Van Bourgondien, 2005) found that stimulants were being prescribed for 12% of patients with autism. The rate of use may be positively correlated with the patient's level of functioning: in a higher functioning group of children with autistic spectrum disorders, 20.2% of children were receiving stimulants (Martin *et al.*, 1999). In another study of children with Asperger's disorder,

more than 75% had received stimulants at some point in their lives (Klin *et al.*, 1997). Community surveys suggest a steady rise in the use of these agents in children with Pervasive Developmental Disorders (PDDs; Aman, *et al.*, 2005).

Despite being used at a high rate, and despite the well-documented efficacy of stimulants in treating children with ADHD (MTA Cooperative Group, 2004), it has not been fully established that stimulants are effective in the treatment of hyperactivity and attentional concerns in children with autism. Traditionally, children with autism have been excluded from trials of ADHD precisely because it was not clear if hyperactivity symptoms of children with autism shared the same neurobiological substrate as those with ADHD. Early studies that suggested both a minimal therapeutic effect with dextro- and levo-amphetamine (Campbell *et al.*, 1972; 1976) as well as noting increases in stereotypies and irritability in patients, may have been responsible for the initial belief that stimulant medications are not helpful for children with ASD.

Subsequent reports of the effects of stimulants on autistic children have been published, but these have been primarily uncontrolled case reports, single-subject controlled studies, or uncontrolled group studies (Birmaher, Quintana & Greenhill, 1988; Realmuto, August & Garfinkel, 1989; Schmidt, 1982; Sporn & Pinsker, 1981; Strayhorn *et al.*, 1988; Vitriol & Farber, 1981; Volkmar, Stier & Cohen, 1985; Yuwiler *et al.*, 1981). While many of these uncontrolled studies reported some level of improvement, a number (especially the single case studies) noted significant adverse side effects, including increased activity level, worsening stereotypies, agitation, aggressiveness, and tics. In a recently published retrospective study of 195 children with autism treated with stimulants, these medications were poorly tolerated and often found to be ineffective (Stigler *et al.*, 2004).

However, there is much work yet to be done in this area. To date, there have been only three controlled studies of the use of stimulants in children with ASD. The first (Quintana *et al.*, 1995) was a double-blind, placebo-controlled study of ten subjects with autistic disorder, using 10 and 20 mg twice-a-day doses of methylphenidate (MPH). The authors found a statistically significant improvement for MPH compared to placebo, and no significant side effects were reported. A second study (Handen, Johnson & Lubetsky, 2000) was a double-blind, placebo-controlled study of MPH in thirteen children with autistic disorder. Participants were given placebo, 0.3 mg/kg MPH, or 0.6 mg/kg MPH. Eight subjects responded positively, based upon a 50% decrease on the Connors Hyperactivity Index. The authors did note significant side effects, primarily social withdrawal and irritability at the highest dose level. Interestingly, there was also

a high rate of reporting of side effects on placebo. Of note, there was a reported improvement in stereotypies when participants were on MPH in this study.

More recently, the Research Units on Pediatric Psychopharmacology Group (RUPP, 2005) undertook a double-blind, placebo-controlled crossover study of methylphenidate in 72 children with autism and hyperactivity. Using a teacher-rated Aberrant Behavior Checklist as a primary outcome measure, they found a 49% response rate (35/72) for children with ASD treated with MPH. Therefore, while they found that methylphenidate was often efficacious in the treatment of hyperactivity associated with autism, the magnitude of the response was less than that seen in typically developing children with ADHD, and adverse effects were more frequent (particularly irritability).

In summary, physicians treating children with autistic disorder and hyperactivity very commonly use stimulants, and controlled trials have thus far suggested only modest evidence for the usefulness of one stimulant (MPH) when treating this group of children. Considering how long stimulants have been in the psychopharmacological armamentarium, how often they are used in individuals with ASD, and the paucity of studies of stimulants suggesting their usefulness in this population, empirical data about the use of stimulant agents in this group is lagging far behind clinical trends. Of note, a very similar pattern exists for children with other neurodevelopmental disorders; specifically, use of stimulants appears to be broadly undertaken, but few well-controlled studies have been completed with regard to efficacy in developmental disabilities accompanied by inattention and hyperactivity (cf. neurofibromatosis; Mautner *et al.*, 2002).

Sympatholytics

Sympatholytics are medications that were originally developed for use in the treatment of hypertension, and have since been used in a number of areas of childhood pharmacology. The alpha$_2$-adrenergic receptor agonist clonidine has been shown to reduce irritability as well as hyperactivity and impulsivity in two double-blind, placebo-controlled trials (Fankhauser *et al.*, 1992; Jaselskis *et al.*, 1992). However, tolerance developed several months after initiation of the treatment in each child who was treated long term (Jaselskis *et al.*, 1992). Tolerance was not prevented by transdermal skin patch administration of the drug. If tolerance does develop, the dose should not be increased because tolerance to sedation does not occur, and sedation may lead to increased aggression due to decreased cognitive control of impulses. As the dose gets much higher, there are also concerns about side effects such as changes in blood pressure.

Adrenergic receptor antagonists, such as propranolol and naldolol, have not been tested in double-blind trials in children with autistic disorder, let alone in many of the other neurodevelopmental disorders. However, open trials have

reported the use of these medications in the treatment of aggression and impulsivity in persons within the spectrum of developmental disorders (Williams *et al.*, 1982) including autistic disorder (Ratey *et al.*, 1987). In a double-blind, placebo-controlled study of lofexidine, 12 children with autism and ADHD had positive outcomes on the ABC Hyperactivity subscale, and it was described as well tolerated (Niederhofer, Staffen & Mair, 2002). Finally, guanfacine use has been looked at retrospectively in 80 subjects with pervasive development disorders (PDDs) (Stigler *et al.*, 2004). There were some positive outcomes for hyperactivity and tics, and a tendency for higher functioning subjects to have a better outcome.

Neuroleptics

The term ''neuroleptics'' refers to medications that have traditionally been used for the treatment of schizophrenia and other psychotic disorders. They vary in their effects on the primary targets of dopaminergic and serotonergic neurons.

Typical neuroleptics

Because they were among the first developed psychopharmacological classes, typical neuroleptics have been among the most extensively studied drugs in the neurodevelopmental disorders, specifically autistic disorder. Trifluoperazine, haloperidol, and pimozide have been studied in double-blind, controlled trials lasting from 2 to 6 months. Reduction of fidgetiness, interpersonal withdrawal, speech deviance, and stereotypies has been documented in response to these treatments (Anderson *et al.*, 1984; Anderson *et al.*, 1989; Ernst *et al.*, 1992; Fish, Shapiro & Campbell, 1966; Naruse *et al.*, 1982). However, patients with autistic disorder are as vulnerable to potentially irreversible tardive dyskinesia as any other group of young patients (Campbell *et al.*, 1988; Wilmut *et al.*, 1997). Owing to the often earlier age at initiation of pharmacotherapy, patients with autistic disorder treated with typical neuroleptics may be at higher risk because of the potential increased lifetime exposure. Also, there are often difficulties with sedation in using these agents, as well as the possibility of rare but serious side effects such as Neuroleptic Malignant Syndrome (NMS). Overall, these side effects have made many clinicians cautious and prudent in the use of typical neuroleptics in this population.

Atypical neuroleptics

Particularly because of the positive response of many children with autistic disorder to typical neuroleptics, there was considerable interest in medications thought to have similar effects, but with reduced risk of extrapyramidal symptoms. In addition to treating the primary positive symptoms of psychotic

disorders (hallucinations and delusions), atypical neuroleptics have the additional effect of often effectively treating the negative symptoms of these disorders, which to some degree are similar to several of the social deficits seen in individuals with autistic disorder. Both risperidone and olanzapine have shown promise in open label trials in reducing hyperactivity, impulsivity, aggressiveness, and obsessive preoccupations (Barber *et al.*, 1998; Malone *et al.*, 2001; Masi *et al.*, 2001; McDougle *et al.*, 1997; Potenza *et al.*, 1999). One large double-blind, placebo-controlled study found risperidone to be more effective than placebo in the treatment of repetitive behavior, aggression, and irritability (McCracken *et al.*, 2002; McDougle *et al.*, 1998), and these gains appeared to hold up over time (Masi *et al.*, 2003). Weight gain has been a significant problem in longer term studies (Gagliano *et al.*, 2004; Masi *et al.*, 2003).

Open-label outcomes with olanzapine for similar target symptoms have been mixed, with positive results being found by some (Malone *et al.*, 2001; Potenza *et al.*, 1999), but not others (Kemner *et al.*, 2002). Weight gain was also a severe problem in these studies. The perceived effectiveness of these medications coupled with the problems with weight gain has led some pharmacologists to look at ziprasidone, which is not thought to cause weight gain, in the neurodevelopmental disorders population. In one study (Cohen *et al.*, 2004), a retrospective chart review was undertaken of adults who had been on a more commonly utilized atypical agent and were then switched to ziprasidone. Seven out of ten subjects reportedly did better than, or as well as with the previous medication while on ziprasidone, and there was a net weight loss. Another study with youths also found positive outcomes in six of twelve subjects with autism and also reported no weight gain. At one time, there were concerns about QTc prolongation (i.e., prolongation of a particular electrocardiogram interval that may be problematic) with ziprasidone, but recent studies have suggested that with careful monitoring, the atypical neuroleptics, including ziprasidone, are less likely than typical neuroleptic agents to be responsible for problems related to QTc prolongation.

Anticonvulsants

There is a high incidence of seizures in ASD, as well as with many of the other neurodevelopmental disorders. Because 25 to 33% of patients with autistic disorder have seizures, the psychopharmacological management of these patients must take into consideration any past or current history of epilepsy and the potential role anticonvulsants may have in the treatment of these youngsters (Volkmar & Nelson, 1990). Unfortunately, very few studies have been undertaken in this area.

In an open trial of divalproex, 10 of 14 patients responded favorably, including showing improvements in affective stability, impulsivity, and aggression (Hollander *et al.*, 2001). Valproate may have positive psychotropic effects, particularly when cyclical irritability, insomnia, and hyperactivity are present. Several children with autistic disorder were treated with valproic acid after electroencephalographic abnormalities were identified. These children had an improvement in behavioral symptoms associated with autistic disorder that appeared to coincide with valproate treatment (Plioplys, 1994).

In the only double-blind, placebo-controlled trial of valproate to date, Hellings and colleagues (Hellings *et al.*, 2005) tested 30 subjects with either placebo or valproate. Using the ABC-CV Irritability Subscale as a primary outcome measure, they found no difference between drug and placebo in the treatment of children and adolescents with autistic disorder. The medication was reasonably tolerated except for increased ammonia levels in two subjects (e.g. one with slurring of speech and cognitive slowing and one subject who experienced a skin rash). Of note, this study is difficult to view as either contradictory of use of valproate, or as even conclusive in its findings, due to a large placebo response on the part of the subjects included, as well as subject heterogeneity and the small size of the groups that were compared.

Surprisingly, considering how long it has been available and its use as an anticonvulsant, carbamazepine has not been well studied in either the ASD or more general neurodevelopmental disorders populations. Oxcarbazepine, a metabolite of carbamazepine, is also available as a treatment option. It may share positive psychotropic effects of carbamazepine, with less risk of agranulocytosis, but there is some concern about uncommon hyponatremia with this medication. This may temper its usefulness with children with neurodevelopmental disorders.

Levetiracetam has been looked at in one open-label study of ASD, in ten boys between the ages of 4 and 10 years (Rugino & Samsock, 2002). The researchers report improvements in hyperactivity, impulsivity, mood instability, and aggression in these children. Rash occurred in three subjects, but was transient in two, and thus only led to one subject stopping the medication. Further investigation is warranted.

The anticonvulsant class to be avoided, when possible, is the barbiturate class (e.g. phenobarbital). Because barbiturates have been associated with hyperactivity, depression, and cognitive impairment, persons placed on them should be changed to an alternative drug, depending on the seizure type (Brent *et al.*, 1987; Vining *et al.*, 1987). In addition, phenytoin (Dilantin) is sedating and causes hypertrophy of the gums and hirsutism, which may contribute to the social challenges for people with autistic disorder and other neurodevelopmental disorders.

Naltrexone

Naltrexone is an orally effective opiate antagonist, typically used in treating opiate- and alcohol-addicted individuals. Initial open-label trials of naltrexone in autistic disorder suggested that it may be useful as a treatment for the core symptoms of the disorder (Gillberg, 1995). However, double-blind trials have subsequently shown that naltrexone has little efficacy in treating either the core social or cognitive symptoms of autistic disorder (Campbell *et al.*, 1993). Still, it continues to be considered for the treatment of self-injurious behaviors (SIB) in persons with autism, despite the fact that controlled data are equivocal (Campbell *et al.*, 1993; Willemsen-Swinkels *et al.*, 1995).

For those who treat patients with autism everyday, better control of SIBs would be very welcome, since this behavioral concern is reported to lead to higher rates of institutionalization, social stigmatization, and decreased learning opportunities (Symons, Thompson & Rodriguez, 2004). Overall, a quantitative synthesis of all the trials with naltrexone in the treatment of SIB suggest that males are most likely to respond, but that more study is indicated for this medication for this particular set of symptoms (Symons, Thompson & Rodriguez, 2004). In terms of other symptoms, controlled trials have shown only a modest reduction in symptoms of hyperactivity and restlessness that are sometimes associated with autistic disorder (Campbell *et al.*, 1993; Feldman, Kolmen & Gonzaga, 1999). Potential side effects include nausea and vomiting. Controlled trials in persons with autistic disorder have not shown either an increase in liver dysfunction or other physical side effects. Notably, use of naltrexone may have an adverse effect on the behavioral and cognitive outcomes of persons with Rett Disorder, on the basis of a relatively large, randomized, double-blind, placebo-controlled trial (Percy *et al.*, 1994).

Lithium

Patients with autistic disorder often exhibit symptoms in a cyclic manner, and exhibit symptoms that are similar to some of those seen in the affective disorders. In particular, there is a high level of reported hyperactivity and restlessness, as well as sleep difficulties in this population. Additionally, youngsters with ASDs appear to be sensitive to medications, such as selective serotonin reuptake inhibitors (SSRIs), that modulate serotonin; such medications are capable of producing an impressive change in the clinical picture reminiscent of a bipolar mixed state, and this can occur at quite low doses in some individuals (Owley *et al.*, 2005). Consequently, there is much interest in how less responsive patients with autistic disorders might respond to agents typically used in the treatment of bipolar disorder, such as lithium. A single open trial of lithium revealed no significant improvement in symptoms in patients with autistic disorder without bipolar

disorder (Campbell, Fish, Korein *et al.*, 1972). Whether lithium would be helpful in a population with autism with symptoms similar to those seen in bipolar disorder remains unknown.

Anxiolytics

Benzodiazepines have not been studied systematically in children and adolescents with autistic disorder. However, their use to reduce anxiety in short-term treatment, such as before dental procedures, is similar to their use in management of anxiety in people without a PDD (Owley, 2004). There has been surprising little work done on the anxiolytic buspirone; one open-label study (Realmuto, August & Garfinkel, 1989) found improvement in the symptoms of hyperactivity in two out three children, while another open label trail found a decrease in anxiety and irritability in patients receiving buspirone (Buitelaar, Willemsen-Swinkels & Van Engeland, 1998). There are no other available reports in the literature, so efficacy remains unknown.

Glutamatergic antagonists

Interest in these agents has been sparked by the hypothesis that ASDs may be a disorder of hypoglutaminergic activity (Carlsson, 1998). In a double-blind, placebo-controlled study of the glutamatergic antagonist amantadine hydrochloride, there were substantial improvements in clinician-rated hyperactivity and irritability, although parental reports did not reach statistical significance (which may have been partially due to a strong placebo response; King *et al.*, 2001). In an open label study of memantine (another glutamanergic antagonist) by Owley, Leventhal and Cook (2006), in children with autism aged 3 to 12 years, there were significant improvements on a number of ABC subscales, including hyperactivity, lethargy, and irritability, as well as some evidence for improvements in memory functioning. Further study of these medications (particularly under controlled conditions) and consideration of the hypoglutaminergic hypothesis is warranted.

Acetylcholinesterase inhibitors

Interest in acetylcholinesterase inhibitors as a treatment began in earnest with the discovery that these medications could improve (e.g. slow the loss of) cognition, language, and overall functioning in patients with Alzheimer's disease. The proposed mechanism for improvement is increased availability of cerebral acetylcholine. In an open trial of donepezil, a cholinesterase inhibitor, Hardan and Handen (2002) found significant improvement in 4 out of 10 children and adolescents with ASD as measured by ABC-CV and CGI-S. Decreases were seen in particular in the hyperactivity and irritability subscales. The medication was

reportedly well tolerated. Chez *et al.* (2004) studied rivastigmine, another cholinesterase inhibitor, in 32 children with autism in a 12-week, open-label study. Testing suggested improvements in expressive speech and overall behavior at 6 and 12 weeks. Clearly, more testing under controlled conditions is indicated with these interesting agents.

Pyridoxine and dietary supplements

Pyridoxine, the water-soluble essential vitamin B6, has been used extensively as a pharmacological treatment in autistic disorder. In the doses used for autistic disorder, it is not being used as a cofactor for normally regulated enzyme function or as a vitamin; rather, it is used as a pharmacological agent to modulate the function of neurotransmitter enzymes, such as tryptophan hydroxylase and tyrosine hydroxylase. While Martineau *et al.* (1988) showed modest improvements in about 30% of children, recent reviews have concluded that there are little data to support the claim that vitamin B6 improves developmental course (Kleijnen & Knipschild, 1991; Pfeiffer *et al.*, 1995).

Fenfluramine

Although fenfluramine originally showed promise in the treatment of autistic disorder and associated cognitive dysfunction (Geller *et al.*, 1982), double-blind controlled trials did not confirm an improvement in cognitive function or a reduction in core autistic symptoms (Aman & Kern, 1989; Leventhal *et al.*, 1993). However, much like naltrexone, fenfluramine may reduce hyperactivity and impulsivity commonly present in autistic disorder and other developmental disorders (Aman *et al.*, 1991). The potential changes in neurochemical regulation after long-term administration (Leventhal *et al.*, 1993), which *may* represent neurotoxic effects (Schuster, Lewis & Seiden, 1986) and potential for acquired cardiac valvular disease when coadministered with phenteramine suggests that fenfluramine no longer be used in autistic disorder.

Secretin

A case series of three autistic patients that showed improvement in core symptoms after receiving the gastrointestinal hormone secretin (Horvath *et al.*, 1998) led to a series of studies on this substance as a possible treatment for ASD. The results have been disappointing, across all controlled studies done so far (Chez *et al.*, 2000; Coniglio *et al.*, 2001; Dunn-Geier *et al.*, 2000; Molloy *et al.*, 2002; Owley *et al.*, 2001; Roberts *et al.*, 2001; Sandler *et al.*, 1999; Unis *et al.*, 2002), showing the substance to be no more useful than placebo. These studies, along with the negative studies that followed initial excitement following open-label studies of naltrexone and fenfluramine, point to the necessity of performing

double-blind, placebo-controlled studies of any putative treatments to ensure safety and establish effectiveness.

Considerations for the future

There are certainly far fewer studies in any area of pediatric psychopharmacology than are actually needed. The numerous neurodevelopmental disorders have been particularly understudied in terms of pharmacological intervention, probably because of some of the problems unique to these disorders (i.e., lack of feedback from the subject directly, phenomenological heterogeneity). However, after a slow start, there is considerable progress being made in the study of the pharmacological treatment of all neurodevelopmental disorders. Much of this is possible as a result of better-defined groups made possible by improved diagnostic measures, as well as reliable outcome measures like the Aberrant Behavior Checklist. We now have considerable evidence for the effectiveness of certain treatments for particular symptoms, and reasonably good methods to operationalize symptoms in order to study new substances.

While this is progress, we are still without a medication that can improve the core symptoms of many of these disorders, particularly when it comes to improving cognition and intellectual functioning. Measuring change in cognition is complicated, and will be the source of continued work as new substances are tested for their ability to affect these primary difficulties. Although there are clearly strong genetic influences as the cause or creating susceptibility to many neurodevelopmental disorders, a more precise neurobiological substrate would allow for the development of medications that precisely target directly involved neuronal processes. Until such information is available, we are left with utilizing the information that we have in studying substances which we hypothesize could help. We can also, however, maximize the use of the medications that we do have available. One way to do this is through the use of pharmacogenetics to help us tailor medications for better individual responses. This work is also in its infancy, but holds tremendous promise for the future in helping children with debilitating neurodevelopmental disorders.

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18

Quantitative electroencephalography and neurofeedback

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Quantitative electroencephalography (qEEG) and neurofeedback have received substantial attention in recent years, as potential tools for the evaluation and treatment of neurodevelopmental disorders. Each technique relies on the premise that electroencephalographic (EEG) specificity can serve as a marker for a particular neurodevelopmental disorder or syndrome, or as a marker of specific cognitive deficits associated with neurological and neuropsychological disorders. This chapter presents a critical review of the relevant literature that applies qEEG and neurofeedback to pediatric disorders. Prior to a review of this literature, a brief discussion of the technology is in order.

Quantitative EEG

Quantitative EEG (qEEG) is a method of analyzing electrical activity of the brain and drawing comparisons between an individual and representative population. It involves the application of mathematical formulas and algorithms to traditional EEG, in order to derive quantitative patterns that correspond to diagnostic information and/or cognitive deficits. Patterns can be based on topographical organization (i.e. the location of specific patterns plotted on the surface of the scalp), amplitude, or spectral analysis (i.e. the presence of specific frequencies of EEG, either in isolation or in ratio to other frequencies). As these factors are influenced by the recording techniques utilized, some attention must be paid to basic electrophysiology and methods for acquiring information about cortical activity, in order to appreciate the issues inherent in qEEG research.

Information about the behavior of neural pathways can provide valuable insight into the functioning of an organism. Cortical activity has been identified as one means for gaining such insight. Cortical activity is ascertained from a variety of methods and techniques, each with inherent advantages and disadvantages. EEG has long been considered the gold standard for identification of cortically driven electrical activity (Nuwer, 1997). Most often, this method involves acquisition of

electrical activity through electrodes arranged on the surface of the scalp, though in some instances single electrodes are inserted directly into the cortex.

Several important aspects of EEG collection are worth mentioning at this point, as they shed light on some of the criticisms of EEG, and more specifically qEEG, and its use in diagnosis and treatment. The number of electrodes used in EEG varies depending on the goal of the study and region of interest. Greater spatial resolution is obtained with a larger number of electrodes used when collecting EEG. When establishing the parameters of a particular clinical or research study, the location of electrodes is predetermined, and careful attention must be paid to their arrangement on the scalp, in order to ensure that waveforms recorded from each electrode are representative of each associated region. Furthermore, the placement of electrodes must be consistent across individuals, a need that is complicated by the variability of head circumference, scalp thickness, and presence of such factors as hair. Standard methods of locating electrode arrays are employed to address such complications, such as the International 10–20 System (Homan, Herman & Purdy, 1987). Steps must also be taken to reduce impedance, the facilitative and resistant properties of the two entities involved in EEG collection, that yield some effect on net current flow between electrodes and the scalp (Duffy *et al.*, 1994).

EEG electrodes are quite sensitive and are capable of detecting electrical activity from sources well beyond the scalp. There is a plethora of confounding electrical sources, both intrinsic and extrinsic, which may be detected by these electrodes. Intrinsic artifacts are often produced by muscle movement, eye blinking, and cardiac activity. Extrinsic factors range from fluorescent bulbs to power lines in proximity to the electrodes. Thus, electrical activity from confounding sources must be limited, reduced, and at the very least accounted for, before EEG is rendered valid. Artifacts are addressed through the application of specific computer generated filters that maintain criteria for acceptance and rejection of characteristic components within electrical signals. These filters serve as a means to accept, attenuate, and reject specified frequencies of the electrical signal.

The electrical activity generated by cortical neurons is minute and attempting to record such activity at its true amplitude is not reasonable, particularly given the confounding impact of other, aforementioned factors. Thus, amplifiers are typically used in conjunction with the electrodes in order to increase the recording amplitude or voltage. Often multiple amplifiers are employed, which are capable of amplifying (intensifying) a predetermined range of signals through the specification of gain (the level of intensification). Because signals are a vacillating entity, amplifiers must be capable of adjusting their amplification of these signals in order to reduce distortion. Specifically, fluctuations in signal voltage can exceed voltages that the amplifier is set to accept, thereby resulting in signal distortion.

Following EEG acquisition, data must be processed, which typically first involves artifact reduction (i.e. removing overlapping waveforms generated by confounding factors). Following post hoc removal of artifact, electrical activity is averaged over a predetermined period, typically the time period surrounding the target event (such as an epileptic seizure or the presentation of a stimulus). Once waveforms have been processed, they may be analyzed through quantification of the properties of the waveform and comparison to representative populations.

EEG waveforms can be quantified according to their frequency, typically thought to represent the arousal of the brain, with higher frequencies indicative of increased arousal. There are five commonly accepted frequency bandwidths thought to represent distinct cognitive states of arousal. The *delta* frequency bandwidth ranges from 1 to 4Hz and is associated with sleep. *Theta* ranges from 4 to 8Hz and is associated with relaxation and other states of low arousal. The frequency bandwidth ranging from 8 to 12Hz is termed *alpha* and is associated with general wakefulness. *Beta* ranges from 13 to 21Hz and represents mental alertness or vigilance. *Gamma* is thought to be associated with learning tasks and ranges up to 42Hz. Coherence represents the similarity of waveform frequencies between two electrode sites. Waveforms are also considered in terms of their strength, or amplitude, which is measured in microvolts (mV).

Depending upon the purpose and goal, various methods of qEEG may be implemented. Mathematical formulas and algorithms can be computed to generate estimates of the location of specific electrical signals, their strength, and orientation (i.e. source analysis). For example, dipole analyses are often conducted in order to represent the strength, source, and direction of cortical activity. This analysis process involves the application of mathematical models that are based on references between multi-channel EEG recordings, taking into account core frequencies, amplitudes, and the shape and density of layers of skull and brain matter (Baumgartner, 1994; Cuffin, 1998; Michel *et al.*, 1992; Schimpf, Ramon & Haueisen, 2002; Stok, 1987; Wieringa, Peters & Lopes da Silva, 1993; Yvert *et al.*, 1997). Clinicians might also be interested in identifying and then comparing the ratio of one frequency range to another. Similarly, analyses directed at ascertaining coherence might also be completed "to obtain information about the temporal relationships of frequency components at different recording sites" (Nuwer, 1997).

Because the visual depiction of waveforms derived from EEG is a conglomeration of various individual component waveforms, analysis typically involves parsing these accumulated waveforms into individual frequency components. This procedure is known as spectral analysis or Fourier series analysis and yields the power of the various frequency sine waves of which the complex EEG

waveform is composed (Duffy *et al.*, 1994). Through spectral analysis, one can examine the frequency of individual waves and thus account for each component's contribution to the waveform.

Topographic mapping involves the visual depiction of the distribution of cortical activity (i.e. amplitude) through a color spectrum that is superimposed on a representation of the individual's head. Technological advances have allowed for the co-registration of the patient's magnetic resonance image (MRI) and the topographic color array (Kozinska, Tarnecki & Nowinski, 1998; Myslobodsky *et al.*, 1990). These topographic maps provide a more accurate anatomical reference for localization of EEG data, with electrode sites referenced to specific brain areas.

EEG power spectrum is a reasonably stable characteristic for healthy human subjects, with high specificity observed across the various frequencies examined for most individuals. Although it is believed to be reasonably sensitive to dysfunction (Hughes & John, 1999), changes in the concentration of neurotransmitters or in the underlying neuroanatomical structures secondary to disease process can disrupt homeostasis and thereby disrupt the normal pattern of EEG. With normal maturation, EEG frequencies increase as a function of age, with slow wave activity replaced by faster waveforms. The development of normal EEG is fairly linear in nature, changing in tandem with increasing age through childhood, with the rate of development being different for the various brain regions (Gasser *et al.*, 1988). In an analysis of EEG amplitudes and frequencies sampled from 158 normal 6–17-year-old children, Gasser and colleagues found a steady decrease in amplitude of slow frequencies bands (i.e. theta and delta) with a steady increase in amplitude of fast frequency bands (i.e. beta) across the age span (Gasser *et al.*, 1988). This pattern of normal developmental change is potentially useful in tracking growth of skills in clinical populations, but also strongly supports the need for control groups to assess for normal maturation.

Methodological considerations

Methodological problems are commonly inherent in neuropsychological and neurophysiological research. Krull and Adams (1996) have previously discussed some of these limitations in detail. Specific areas of concern include use of exploratory vs. confirmatory analyses, sample size and selection process, homogeneity of samples, control for important subject variables, consideration of moderating variables, reliability and validity of instruments, task administration procedures, statistical analysis process, specificity of results, and clinical significance of findings. This section addresses some of these problems as they are applied to EEG-related research, as well as their bearing on clinical applications.

Sample selection and sample sizes are often an issue in qEEG and neurofeedback research. Low base rates for many of the neuropsychiatric disorders, incomplete records for the patient population at question, and wide variation in the diagnostic processes or presentations of patients with the same diagnosis are some of the factors that influence suitable sample selection. Diagnostic processes employed range from brief rating scales (e.g. the Iowa Conners' ADHD Scale) to poor performance on continuous performance test (CPT). Rare is the study that employs structured diagnostic interviewing to obtain a diagnosis consistent with the Diagnostic and Statistical Manual (DSM) of mental disorders (APA, 1994; 2001). Matching on relevant demographic variables that are reasonable to control without changing clinical or demographic representativeness (e.g. parent educational level), and trying to subtype or find homogenous clusters within a given diagnosis, as well as the use of stringent DSM-IV criteria for patient selection by professional clinicians may help reduce some of these limitations in sample selection.

Another important consideration in sample selection is the mode of referral system that was in place for patient selection. Questionable selection and unrepresentative samples arise when the basis of patient selection is through self-referral or purposive sampling. This has been particularly problematic in the neurofeedback literature, where patient or parent self-selection of treatment options appears to be the rule rather than the exception (Monastra *et al.*, 2005). Proper selection of patient population (such as the selection of every consecutive patient identified) with random assignment into treatment groups is one way to minimize this error. Difficulties in sample selection can lead researchers to encounter situations where they are either left with a small sample size, which then fails to optimally represent the population of interest, or alternatively, with a large sample size where smaller group differences result in significant differences between the two groups. In either case, the results ultimately have very little clinical relevance and may not be applicable on an individual basis.

Group heterogeneity or within-group variability in symptom presentation can influence error variance and thereby influence intergroup differences. Heterogeneity can exist within the same diagnostic classification. For example, with Attention-Deficit/Hyperactivity Disorder (ADHD) it is important to not only consider different subtypes (ADHD-Combined type, ADHD-Predominantly Inattentive type, and ADHD-Predominantly Hyperactive-Impulsive type), but also common comorbidities, which are more often seen than not, and which frequently influence presentation. For example, ADHD often presents with comorbid emotional, behavioral, or learning problems (Decker *et al.*, 2001; Hechtman, 2000; Lalonde, Turgay & Hudson, 1998; Nolan, Gadow & Sprafkin, 2001; Pliszka, 1998, 2000; Schubiner *et al.*, 1995), which are likely to impact EEG patterns, as well as motivation and compliance with interventions. If children with

these common comorbid conditions are screened out, we are left with a sample that is not representative of the clinical population. Proper subgroup identification using standardized assessment techniques including the use of stringent independent diagnostic criteria and consistency in the selection of methods utilized for diagnosis and classification will increase group homogeneity and permit enhanced generalization to relevant clinical groups.

Another important variable that often fails to be accounted for in participant selection is medication. Most psychopharmacological medications contribute to short- and/or long-term effects on neurochemical and neurophysiological mechanisms, and to some extent may also lead to underlying neuroanatomical changes that alter associated cognitive abilities. Although the acute direct effects of the drug will be eliminated with an appropriate drug holiday, the learning, and thus neurophysiological changes, that have occurred due to the long-term drug treatment, will not necessarily be undone with the brief holiday. While obtaining drug-naïve patients may be extremely difficult for the researcher, it is considered the best option whenever possible. Alternatively, trying to control the type and dose of medication across groups, and subgrouping within particular patient groups may increase homogeneity and generalizability.

One of the most important methodological issues in any study is to have a proper experimental control. This is especially true when the study involves a clinical population and is making use of measures, like qEEG, that are vulnerable to many potentially confounding variables. Sociodemographic variables like gender, age, ethnicity, SES and education need to be adequately controlled.

When evaluating a treatment modality like neurofeedback or qEEG, which is ''machine operated'' (e.g. involves the assistance of a computerized program), the presence of a therapist is another factor that needs to be controlled; the person providing the intervention often contributes to a placebo effect, thus inflating the results. For example, the direct or indirect reinforcement of behaviors during the recording process has the potential to influence outcomes, regardless of whether the intervention of interest is effective. Thus, when using a medication or waitlist control, both of which do not include the regular presence of a therapist, one cannot separate the effect of the ''attention'' (e.g. praise) given by the therapist from the ''reinforcement'' given by the machine.

The selection of appropriate pre- and post-intervention assessment measures to quantify associated changes in the independent variable under consideration is a required aspect of causal inference. Assessment should be independent of intervention techniques and conducted in a manner that reduces experimenter bias (i.e. the use of blind raters or evaluators). By using an assessment tool that is too similar to the intervention procedure, ''practice effects'' cannot be separated from ''treatment effects.'' For example, using pre- and post-treatment administration

of a computerized continuous performance test (CPT) to demonstrate the efficacy of a computerized intervention that requires sustained effort merely demonstrates improved performance on computerized sustained attention tasks. As such, it should be no surprise that children who practice on one computerized task get better on a different computerized task. Improved clinical significance and generalizability is obtained by demonstrating efficacy in the child's natural environment on real-world tasks. For example, is the practice and feedback given during a computerized task followed by improved performance and behavior in the classroom during lectures or tests? This level of investigation is seldom considered, let alone pursued.

Clinical aspects of qEEG

Recent research using qEEG has provided some evidence of a relationship between EEG patterns and various disorders of childhood and adolescence. Electrophysiological subtyping based on qEEG has suggested the possibility of physiologically specifiable subtypes with these heterogeneous groups, including ADHD, mood disorders, autism, and learning disabilities (Chabot, di Michele & Prichep, 2005; Chabot, Merkin *et al.*, 1996; Gasser, Rousson & Schreiter Gasser, 2003; Johnstone, Gunkelman & Lunt, 2005; Tot *et al.*, 2002). Research has also suggested that these electrophysiological subtypes may have practical significance for evaluating the efficacy of psychopharmacological and other forms of treatment (Hirshberg, Chiu & Frazier, 2005).

There are a number of issues that have hindered the clinical application of qEEG. Studies directed at determining the psychometric properties of qEEG have varied greatly. Traditionally, the methodology used has been inconsistent and flawed (Nuwer, 1998). Moreover, results across studies sharing similar methodology have been quite variable and in some instances altogether contradictory (Nuwer, 1998). Exaggerated and/or misleading commercial marketing has not encouraged scientific acceptance (Boutros, Fraenkel & Feingold, 2005). Thus, the onus is clearly on the clinician and researcher to effectively assess the merits of existing research, in order to formulate any judgment on qEEG and its utility in the clinical setting.

Boutros and colleagues conducted a recent literature review to outline an approach for the development and evaluation of diagnostic tests applicable to psychiatry (Boutros, Fraenkel & Feingold, 2005). These authors identified a four-step approach to such a test development, which should be required prior to clinical use of a given technique. Step 1 involves the identification of a measure that reliably separates a deviant group from healthy controls. Step 2 involves the determination of the ability of the measure to differentiate the target group from

relevant clinical controls. Step 3 involves determination of sensitivity, specificity, and positive and negative predictive values of the measure. Step 4 involves the standardization of the measure in large and multi-center clinical trials. In the application of their four-step approach to the evaluation of the use of qEEG in ADHD, the authors concluded that the majority of studies met only the requirements for Step 1 (Boutros, Fraenkel & Feingold, 2005). A number of studies also met the requirements for Steps 2 and 3, though no studies were identified that met all four steps. Although the future impact of qEEG on clinical practice appears promising, current research and reviews suggest the need for further development prior to its use as a diagnostic tool.

Though EEG power is often described as being reflective of neurons discharging synchronously (Nuwer, 1997), it is tempting to assume that EEG power may also serve as an index of cortical information processing/cognitive processes. Within the different frequency bands of EEG, alpha and theta are the two that are often associated with cognitive changes (Klimesch, 1999). Alpha and theta waves are reported to respond in different and opposite ways during cognitive processing. When EEG power during a test condition is compared with a resting condition, alpha power often decreases (desynchronizes) and theta power increases (synchronizes) during task performance. On the other hand, increased alpha and decreased theta during resting EEG is often associated with better cognitive performance (Klimesch, 1999).

Previous studies have also shown the existence of different alpha bands (upper and lower bands) which often respond selectively, and at times in opposite ways, to different cognitive demands such as attention and memory (Klimesch, 1999; Petsche *et al.*, 1997). Within the theta band, the presence of wide frequency ranges and large power (4 to 7 Hz.) makes it difficult to detect associated cognitive changes. The large interindividual variability within theta makes it harder to estimate what might be considered ''normative'' theta power. Individual determination of frequency bands, with alpha frequency as a common point of reference, becomes very important. That is, since alpha frequencies are more readily identified and recognizable, the determination of where theta and beta begin should be based on where alpha ends (Klimesch, 1999). The implication is that an unbiased estimate of alpha and theta power can only be obtained if the traditional fixed band analyses are abandoned and the narrow frequency bands are adjusted to the individual alpha frequency of each subject (Klimesch, 1999).

Attention Deficit/Hyperactivity Disorder (ADHD)

qEEG has been applied to a number of clinical syndromes, as a tool for describing underlying deficits seen with the disorders. Attention-Deficit/Hyperactivity Disorder (ADHD) has received the most attention in qEEG studies. To review,

ADHD is a condition that occurs in 3–5% of the school age population (American Academy of Pediatrics Committee on Quality Improvement and Subcommittee on Attention-Deficit/Hyperactivity Disorder, 2000; see also Palumbo and Diehl, this volume), and is highly comorbid, often co-occurring with conduct disorder, oppositional defiant disorder, mood disorders, anxiety disorders and learning difficulties (Barry, Johnstone & Clarke, 2003). Two main clusters of symptoms have been identified: Inattention and Hyperactivity/Impulsivity (Lahey & Carlson, 1991). The typical treatment for ADHD is stimulant medication, with 70–80% of treated children responding favorably (Barkley, DuPaul & McMurray, 1990). To date, no treatment has been identified to provide long lasting improvement in ADHD in children. The benefits of medication are reported to be temporary, often with undesirable side-effects that may include decreased appetite, insomnia, anxiety, irritability and headaches occurring in approximately 20–50% of children treated with stimulant medication (Efron, Jarman & Barker, 1997; Levy, 1993). Additionally, long-term compliance is another obstacle to successive treatment outcome.

In a recent review of EEG studies of children with ADHD, it was concluded that between 30–60% of children showed abnormal EEG findings, including generalized and/or intermittent slowing (Chabot *et al.*, 2001). More specifically, an increase in activity in the delta and theta bands has been reported (Barry, Johnstone & Clarke, 2003). qEEG studies have reported higher average amplitude of delta, lower percentage time of in alpha, and higher amplitude of theta (Matsuura *et al.*, 1993). In addition, studies have reported increased absolute theta and alpha activity in frontal regions with reduced relative beta in posterior regions (Lazzaro *et al.* 1999; 1998), and intra-hemispheric and inter-hemispheric hypercoherence in frontal and central regions (Chabot *et al.*, 1996). However, despite these descriptions, actual EEG specificity for ADHD is not well supported. Chabot *et al.* (1996) noted that EEG differences between the hyperactive and inattentive types of ADHD likely suggest only a matter of degree of difference within the disorder, and do not specify the type of abnormality found across the disorder. They also reported that EEG measures obtained from individuals with the inattentive subtype of ADHD fall between those obtained from children meeting hyperactive type criteria and normal children.

Studies of qEEG in ADHD have led researchers to propose two possible models of neurophysiological patterns accompanying the disorder (Chabot *et al.*, 1999; Monastra *et al.*, 1999). The first model suggests there is underactivity over frontal, central and midline cortical regions in approximately 85–90% of patients with ADHD (Monastra *et al.*, 1999). The primary electrophysiological indicators of this underactivity include elevated theta power, reduced relative alpha and beta power, and elevated theta/beta power ratios predominantly over frontal and central

midline regions (Monastra, 2005). A second model of ADHD describes a pattern of excessive activity or "hyperarousal" over frontal regions. This pattern has also been reported to be particularly evident in those patients who have not responded optimally to stimulant medication trials (Chabot *et al.*, 1999). qEEG patterns in these groups of patients include increased relative beta power, decreased relative alpha power, and decreased theta/beta power ratios across all cortical recording sites in comparison to healthy participants (Monastra, 2005).

In a large scale study of children with ADHD aged 6-20 years, Monastra and associates attempted to demonstrate sensitivity, reliability, and validity of select qEEG techniques (Monastra, Lubar & Linden, 2001). In the first aspect of this investigation, 129 children were evaluated and diagnosed with appropriate subtypes of ADHD. Groups including both the Combined (ADHD-C) and the Predominantly Inattentive (ADHD-I) subtypes, as well as a control group, were identified using a semi-structured interview (i.e. Barkley's ADHD Clinic Parent Interview), parent rating scales (i.e. the Attention Deficit Disorders Evaluation Scale, or ADDES), and examination of performances on the Test of Variables of Attention (TOVA). qEEG data was collected from each group under four separate conditions: resting while eyes are fixated on a screen; silent reading; passive listening; and when drawing objects. Ratios of theta to beta frequencies were calculated for each task. Analysis of qEEG data revealed higher theta/beta ratios in both the ADHD-I and ADHD-C groups across all tasks. At first glance, this study appears to provide reasonable support for qEEG analysis. However, problems with the subject groups exist. In particular, although children were identified using standardized procedures, evaluation for comorbid conditions was not done. Although learning disabilities (LD) are common in ADHD, this sample was not screened and the occurrence of different LDs is thus unknown. Furthermore, although the control group used no medications, children in the ADHD groups were evaluated while on medication.

Despite these procedural problems, Monastra and colleagues proceeded to cross validate their findings with another group of 285 children (Monastra *et al.*, 2001). Again, children between the age of 6 and 20 years were evaluated, this time off medication, to obtain independent classification based on qEEG data. The authors reported an "83% classification agreement between diagnoses" based on qEEG and traditional structured interview methods. However, as all children were diagnosed with ADHD, test sensitivity and specificity could not be addressed. These results appear promising, though warrant further distinction between ADHD, comorbid conditions, and non-ADHD groups. Although these qEEG findings are apparently quite reliable, with test−retest reliabilities reported to be 0.96 in a subset of the sample, specificity for ADHD is questionable. Furthermore, as concluded by Loo and Barkley, as diagnostic accuracy of the qEEG is somewhat

less than traditional methods, it does not justify the added expense or time commitment over the structured clinical interview (Loo & Barkley, 2005).

Learning disabilities

A variety of EEG differences have been reported in individuals with learning disabilities (LD), including reduced EEG rhythm, low voltage background rhythms, and increased generalized slowing (Hughes & John, 1999). In qEEG studies of children with LD, a high incidence of excess theta or decreased alpha and/or beta has been reported (Hughes & John, 1999). Studies have also suggested that age and the presence of other comorbid diagnoses influence patterns observed; specifically, ADHD can influence the qEEG pattern seen among children with LD (Chabot *et al.*, 2005). For example, Lubar (1997) showed that children with LD and attention problems (without hyperactivity) demonstrate increased theta but low alpha power, whereas hyperactive children with LD have shown decreased alpha and beta power in comparison to normal controls (Dykman *et al.*, 1982). Problems common to all of these studies include the lack of defined LD subtypes and the tendency for over-inclusion of groups. ''Learning disorders'' are defined in a general sense and are not well characterized to specific learning disabilities subtypes; this significantly limits both specificity and generalizability.

Autism spectrum disorders

qEEG research with children with Autism has received relatively little attention. Early studies suggested a lack of hemispheric differences in EEG patterns in children with autism (Dawson *et al.*, 1989). One of the largest study to date that examined qEEG in children with autism has shown increased frontal/temporal and left temporal total power and decreased power asymmetry when compared with normal and handicapped children (Cantor *et al.*, 1986). However, more recent research indicates relatively high rates of epileptiform abnormalities and/or seizures in children with autism, which seriously impacts the demonstration of reliable qEEG differences (Ballaban-Gil & Tuchman, 2000; Hrdlicka *et al.*, 2004; Kim *et al.*, 2006; Rossi *et al.*, 1995). Further investigation is warranted, taking the issues of comorbidity and alterations in neurological status into account.

Other disorders of childhood

Several investigators have reported sensitivity data, though not specificity, for qEEG in a variety of clinical populations (Coutin-Churchman *et al.*, 2003; Gasser *et al.*, 2003; Ozge, Toros & Comelekoglu, 2004). In a comparison of 67 controls with a group of 340 patients with a variety of clinical diagnoses, Coutin-Churchman and colleagues reported reasonable sensitivity of qEEG power

for delta, theta, alpha, and beta spectra (Coutin-Churchman *et al.*, 2003). EEG was abnormal in 83% of patients though only 12% of normal subjects. The most common difference was reduced amplitude of theta frequencies, either alone or with increased beta or alpha. Reportedly, no normal subject displayed showed decreased theta. However, specificity of findings to clinical diagnoses was not demonstrated, as no measures distinguished any of the clinical groups from one another.

Gasser and colleagues compared a group of 158 children aged 6 to 16 years (Gasser *et al.*, 2003). Children were identified as mentally retarded ($n = 47$), learning-disabled ($n = 26$) or non-disabled ($n = 85$) based on traditional intelligence and academic testing. Using qEEG raters who were blind to diagnostic categories, significant differences in delta, theta, and alpha spectra correctly identify patients. However, again, no consistent pattern was identified that distinguished patient subgroups.

In a slightly better controlled study of stutterers, Ozge and colleagues also reported significant differences between patients and controls (Ozge, Toros & Comelekoglu, 2004). Comparing a group of 3−12-year-old children, 26 of whom presented with significant stuttering, with 21 matched controls, the proportion of delta activity over the frontal lobes, indicating decreased arousal, correctly separated groups. Although groups were well matched and comorbid conditions were screened for, clinical specificity requires the use of clinical control groups; no control was included in this study. These three studies illustrate that the current evidence for clinical use of qEEG is, at best, at the beginning phase of development. Based on the recommendations of Boutros and colleagues outlined above, the development of qEEG as a diagnostic tests in these populations is current at Step 1 and, thus, much more research is required prior to clinical application (Boutros, Fraenkel & Feingold, 2005).

Medication effect monitoring

The use of qEEG to monitor medication effects is a promising area of research. Changes in EEG patterning have been demonstrated to be sensitive to medication effects. Clarke and colleagues examined the EEG effects of stimulant medications in children with the combined subtype of ADHD (Clarke *et al.*, 2002). Following a 6-month trial on a stimulant medication, children with ADHD displayed significantly higher absolute amplitudes for theta, more relative theta, and less relative alpha than a control group. These authors concluded that the stimulants increased cortical arousal, thereby ''normalizing'' brain activity in the ADHD group. Although a reasonable first step, this study failed to include clinical controls or to randomize patients to treatment options.

In a more recent and better controlled study, Song and colleagues compared children with ADHD while on and off medication (Song *et al.*, 2005). Diagnoses were established based on DSM-IV criteria and comorbid conditions were considered. In addition, unlike many other studies, teacher ratings were employed to potentially address issues of generalizability. qEEG data was collected at rest and during the completion of a continuous performance task (CPT), both off medication and one hour following a single dose of methylphenidate (0.7 mg/kg). Results indicated increased alpha and beta over the frontal lobes and decreased theta over occipital and temporal areas, following medication. In addition, decreased theta/beta ratios were demonstrated at rest and increased ratios were demonstrated during performance on the CPT. Thus, probable drug and task specificity was observed. Although well controlled in terms of clinical sample and task design, this study failed to include a randomized drug trial and use of a blind placebo cross-over condition. Still, despite these concerns, results suggest that use of qEEG may show promise for better assessment and understanding of medication impact on aspects of psychopathology, particularly stimulant use for ADHD, and support the need for enhanced procedural controls which have been lacking in previous investigations.

In summary, results of recent qEEG investigations do suggest that a pattern of variability in the EEG spectrum reflects potential underlying differences between normal controls and clinical populations. There appears to be some sensitivity to the variety of clinical disorders seen by neuropsychologists and some sensitivity to drug effects. Specificity to clinical disorders is still far from apparent, however. None of the current studies available in the literature demonstrates qEEG patterns that are specific to different clinical conditions. Additionally, those studies that do examine specificity only report reliable differences when patient groups are broadly compared to control groups. Even more importantly, however, the degree of specificity shown by these studies does not appear to be any better than that available with traditional assessment and diagnostic methods, which do not require the added expense or time involved in qEEG. As such, recommendation for the use of qEEG in clinical diagnosis remains strongly tempered (Nuwer, 1997).

Neurofeedback

Neurofeedback involves the collection of qEEG data as a means of intervention, by using it to enhance an individual's self-control or cognition (Lubar, 1997). Feedback is provided to the individual using operant learning principles, with the assumption that the individual will learn to differentially control his or her EEG patterns. The procedure typically involves the individual watching or

monitoring a computer screen, which identifies qEEG patterns topographically. Through trial and error, or with the use of therapist-guided tasks, the individual learns to associate ''events'' (i.e. thoughts, concentration level, or ''mental control'') to changes in qEEG. By far, the majority of neurofeedback studies employing pediatric age ranges have focused on ADHD and control over attention processes.

Monastra and colleagues examined the added benefit of neurofeedback to traditional methods of intervention for children with ADHD. In this study, children aged 6–19 years were identified as having ADHD using traditional methods of semi-structured interview, as well as parent and teacher reports on the ADDES (Monastra, Monastra & George, 2002). However, they also used qEEG determined theta/beta ratios to screen patients into diagnostic categories. Twenty-four children were identified as having ADHD-I and 76 were identified as having ADHD-C, using this multi-method approach. All children were reported to be medication naïve and to have never been diagnosed with ADHD previously. Two treatment groups were developed. The first involved prescription of stimulant medication, parent coaching, and school consultation. The second treatment group included these same interventions, but also added neurofeedback. In both groups, medication was reportedly titrated based upon the children's performance on the TOVA, although specific medication levels were not reported for the groups as a whole. Neurofeedback involved qEEG ''to criterion,'' typically participation in over 40 sessions. Re-evaluation of ADHD symptoms was conducted roughly one year later, both on and off medication.

The authors presented results showing significantly better performance on parent and teacher ratings, as well as the TOVA for the group that received neurofeedback. While at first glance, this study might appear to provide support for the added component of neurofeedback, upon closer inspection, it raises significantly more questions than it answers. A number of substantial caveats to the findings are evident. For example, the groups were differentiated based upon the use of qEEG diagnostic indicators, but no evidence was given that the diagnosis was done blindly. Furthermore, multiple interventions were included, with no means described for determining the independent effects of intervention. Similarly, and quite surprisingly, no significant change in symptoms was reported for the group that did not receive neurofeedback. That is, in spite of numerous studies documenting the efficacy of stimulants and supportive therapy in the treatment of ADHD, children in this study were no better than when they were first diagnosed. This lack of stimulant efficacy strongly suggests a problem in the titration process and/or other aspects of the treatment; it may also suggest differential biases in reporting. It also suggests that a combination of factors present for one group may have been more inconsistently applied.

Clearly, a self-selection bias was present in this study. Parents were fully informed of the treatment choices and were permitted to pick which treatment their child engaged in. The neurofeedback condition undoubtedly incurred added cost, both in terms of time required and finances allocated; this raises the question of self-fulfilling expectations. In addition, positive change in performances on the TOVA is not unexpected following 40 sessions of practice on a sustained attention type task (i.e. the neurofeedback procedure).

However, these concerns do not fully negate a possible positive effect. While the results do not adequately explain the significant improvement reported for children's behavior by teachers, and the authors fail to control for information shared with teachers by parents, it is possible that this change may be related to the additional neurofeedback sessions. It is still uncertain as to whether the benefit arises for the feedback itself, from the added time with a therapist, or from the child's, parent's or teacher's expectations themselves. After all, placebo effects are well documented in the ADHD literature (Barkley, DuPaul & McMurray, 1990).

Fuchs and colleagues conducted a similar study with children with ADHD (Fuchs *et al.*, 2003). In this study, 34 newly diagnosed children with ADHD were treated with stimulant medication or neurofeedback without medication. Diagnosis was established through use of semi-structured interviews and poor performance on the TOVA. All participants reportedly showed evidence of average intellect. Twenty-two children were treated with neurofeedback, while 12 received traditional stimulant treatment. Neurofeedback involved training of sensorimotor rhythm over the right hemisphere, allegedly to decrease impulsivity; and training to increase beta over the left hemisphere, allegedly to improve attention. Both the neurofeedback group and the stimulant treatment group were reported to show significantly improved performance on the TOVA, and improvements were reported on parent and teacher rating scales. Since the neurofeedback group did not receive medication, these results were taken as support for equivalent efficacy of this method, when compared to stimulant treatment. However, significant procedural problems were present in the study that limits the validity of the results. Parents were permitted to self-select treatment options, giving rise to continued concern over self-justification and expectations, related to their investing in the more costly neurofeedback procedure. Furthermore, although this study certainly did control for a number of procedural factors, it still did not control for therapist exposure time or child expectations.

Similar results, and similar concerns, were raised in a recent study by Rossiter and colleagues (Rossiter, 2004). In this study, 62 participants, aged 7-55 years, were divided into combined (ADHD-C) and inattentive (ADHD-I) subtype groups. Self-selection of neurofeedback versus stimulant medication was utilized, and groups were compared on TOVA performance indices and parent or

self-ratings of attention and impulsivity. Following 40 sessions of neurofeedback, designed to increase beta in the left hemisphere for ADHD-I subtypes and increase alpha in the right hemisphere for ADHD-C subtypes, both groups reportedly demonstrated significant improvement. Again, however, concerns over self-selection and motivation limit the acceptability of the results.

In contrast to the above described studies, in a recent investigation designed to improve methodological controls, Egner and colleagues randomly assigned children to sensorimotor rhythm and beta training versus traditional treatment (Egner & Gruzelier, 2004). Notably, they found no significant group differences on the TOVA when comparing baseline to post-intervention follow-up.

Levesque and colleagues report one of the first studies to randomly assign children with ADHD to experimental versus control conditions (Levesque, Beauregard & Mensour, 2005). Fifteen children diagnosed with ADHD received neurofeedback to decrease resting theta and increase active theta and beta, while five children were assigned to a wait list control group. None of the children was reported to have comorbid diagnoses. Interestingly, functional magnetic resonance imaging (fMRI) was also employed, in an effort to examine activation in the anterior cingulate gyrus during an executive function task. In comparison with baseline measures, the children treated with neurofeedback were reported as showing significantly improved behavior on parent ratings scales and improved performance on the Integrated Visual and Auditory Continuous Performance Test (IVA). A similar change was not identified for the wait list control group. Furthermore, only the group that received neurofeedback was reported to demonstrate enhanced fMRI activation. Thus, although a wait list control group does not control for parent or child expectations or for therapist time, functional changes in cortical regions long associated with ADHD were described, and as a result, are intriguing and warrant replication with improved methodology.

Use with nonclinical populations

In addition to the application of neurofeedback to the treatment of clinical disorders, several investigators have examined its ability to alter cognitive functions in non-clinical samples. For example, Barnea and colleagues examined sensorimotor rhythm and theta feedback in a typically developing group of 10–12-year-old children (Barnea, Rassis, & Zaidel, 2005). After 20 neurofeedback sessions, children were reported as demonstrating improved performance on a recognition word task. Similarly, Hanslmayr and colleagues examined the effect of neurofeedback on performance of a mental rotation task in young adults (Hanslmayr *et al.*, 2005). Using an ABA design, individuals were assigned to one of three types of neurofeedback. Although no differences were present at baseline, after training the neurofeedback group reportedly showed improved performance

on the mental rotation task. However, several caveats exist; this study did not employ random assignment, but rather selected group membership based on the ability to change EEG during a baseline session. Furthermore, although the training tasks are somewhat different from the outcome measures, the study did not control for practice or time engaged in mental activation. This issue could be easily addressed by providing sham feedback across similar durations of time. In fact, this relatively straight-forward control technique is surprisingly absent from most neurofeedback investigations.

In summary, although the application of neurofeedback techniques to the treatment of pediatric disorders remains intriguing, investigations to date provide little clear support. The available studies are ripe with design flaws and/or experimental bias. As previously noted, common flaws include the use of multiple treatments within groups, no control group or inadequate control groups used, lack of a true placebo control (e.g. sham feedback with duration of sessions controlled), absence of blindness of evaluators and therapists, practice effects due to similarity of training and outcome measures, and lack of random assignment.

As has been recently stated by Loo and Barkley (2005) in their review of qEEG and neurofeedback in ADHD, the main issue to be addressed is whether EEG training, as opposed to some other factor inherent to the training sessions (e.g. reinforcement, examiner time, attention by the examiner) leads to the differential outcomes reported (Loo & Barkley, 2005). To date, none of the studies in the literature have successfully controlled for these concerns in a consistent manner. This substantially limits the acceptability of the results obtained and influences how this promising method is regarded by neuropsychologists and other practitioners. Improved methodological controls may more clearly allow for a demonstration of efficacy and specificity; however, as noted above about qEEG, attention should also be directed to both clinical practicality and the added benefit of neurofeedback to currently established diagnostic procedures and treatments. At this time, there is little evidence to suggest that this method adds to already available, and more efficacious interventions, at a minimal level of cost.

Conclusions and further recommendations

Currently, both qEEG and neurofeedback lack appropriate and significant empirical evidence to support their use with clinical populations. In fact, while techniques necessary to demonstrate evidenced-based interventions have been discussed in detail in the literature for a number of years, there continues to exist a dearth of well-controlled and appropriately conceptualized methodological studies of efficacy and specificity for either qEEG or neurofeedback. As such, this renders consideration of these methods as speculative at best.

At a time when empirical validation is expected, it is important to recognize that guidelines have been published that address how to investigate and establish the validity and appropriate applicability of intervention approaches. Assessment and intervention techniques can be classified as ''Well-established'' or ''Best-supported'', ''Probably efficacious'' and/or ''Promising.'' Similarly, interventions that lack empirical support can be identified and described, in order to guide decision making by clinicians (Kazdin & Bass, 1989). For an approach to qualify as empirically *Established*, the following criteria must be met:

- At least two good between group design experiments demonstrating efficacy in one or more of the following ways:
  - Superior to medication placebo, psychological placebo, or another treatment.
  - Equivalent to an already established treatment in experiments with adequate statistical power.

  OR
- A large series of single case design experiments ($n \geq 9$) demonstrating efficacy. These experiments must have:
  - Used good experimental designs
  - Compared the intervention to another treatment.

  In addition, the evidence must demonstrate
- Experiments that are conducted with treatment manuals.
- Characteristics of the client samples that are clearly specified.
- Effects must have been demonstrated by at least two different investigators or teams of investigators.

For an approach to qualify as *Probably Efficacious*, the following criteria must be met:

- Two experiments showing the treatment is (statistically significant) superior to a waiting-list control group.
- Manuals, specification of sample, and independent investigators are not required.

  OR
- One between group design experiment with clear specification of group, use of manuals, and demonstrating efficacy by either being:
  - Superior to pill placebo, psychological placebo, or another treatment.
  - Equivalent to an already established treatment in experiments with adequate statistical power.

  OR
- A small series of single case design experiments ($n \geq 3$) with clear specification of group, use of manuals, good experimental designs, and a comparison of the intervention to pill, or psychological placebo, or to another treatment.

At this point, it is important to note that both qEEG and neurofeedback meet criteria indicating that there is evidence supporting them as ''Promising'' or ''Probably efficacious'' techniques. As noted above, research to date on qEEG with ADHD populations suggests that there are reliable differences with regard to differential patterning of spectral bands, when compared with nonaffected, nonclinical samples; there is however no clear evidence of clinical specificity, particularly in light of numerous clinical comorbidities. Similarly, neurofeedback has been shown to have some potential impact on attentional performance; still, there has been no study to date that has shown generalizability, let alone clear evidence of specificity.

As reviewed above, although substantial improvements have been made over the years, the vast majority of research on both qEEG and neurofeedback techniques lacks scientific rigor, particularly in regard to random assignment and use of a true placebo control group. This indicates that research investigating these methodologies must fully respond to the criticisms that have been presented, now over a long period, and conform to clear guidelines offered within the scientific community if there is to be clear demonstration of a real effect, and a broader acceptance of their potential efficacy. This suggests that much work remains to be done by proponents of these methods, if validity is going to be considered ''well established''.

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19

Neuroimaging and its role in developing interventions

Erin D. Bigler

Neuroimaging is an essential diagnostic tool for many childhood and adolescent neurologic and neuropsychiatric disorders, conditions that often require neuropsychological assessment, consultation and/or treatment (Provencal & Bigler, 2005a; b). However, beyond diagnosis, there has been little systematic application of how to use neuroimaging information in the planning and implementation of treatment interventions in pediatric neuropsychology. In that sense, this chapter covers novel territory.

Whether it is data from the Center for Disease Control (CDC) or the World Health Organization (WHO), the most common neurological and neuropsychiatric disorders likely to be seen by pediatric neuropsychologists involve various acquired brain injuries (ABI) including birth related and traumatic brain injury (TBI), infection, stroke, various genetic disorders and a host of neuropsychiatric disorders including schizophrenia, Autism, Attention Deficit Hyperactivity Disorder (ADHD), and Learning Disabilities (LD) (Center for Disease Control, 2005a; b; Holm *et al.*, 2005; Langlois, Rutland-Brown & Thomas, 2005). The limitations of this chapter do not permit addressing these disorders in any in-depth fashion, nor numerous other pediatric conditions seen by neuropsychologists, but the significance of neuroimaging findings in some of these disorders will be discussed from the perspective that neuroimaging ''informs'' the clinician with unique information that assists the neuropsychological assessment process as well as planning and tracking treatment interventions. Clinically, the most is known about ABI, like childhood TBI, and, therefore, TBI will be used as an exemplar throughout the chapter. This chapter will not deal with specific genetic syndromes and various syndromes of mental retardation, which have been addressed elsewhere (Bigler *et al.*, 1999; Provencal & Bigler, 2005b) although some examples will be mentioned.

Diagnosis: the first step in treatment planning

From a diagnostic standpoint, there are several reasons for doing neuroimaging. First, for any acquired disorder, such as head injury, or any new onset symptom (i.e. paralysis), neuroimaging is critical in making the initial diagnosis by identifying observable pathological changes in the brain. In acquired, degenerative, and neoplastic disorders neuroimaging can identify changes over time and track the child neurodevelopmentally. The other main use of neuroimaging is in cases of developmental disorder, where often the imaging is not diagnostic of a condition, but is done to rule out a structural basis for the symptoms or disorder. Obviously, to plan proper interventions, accurate diagnostic conclusions first need to be made and neuroimaging findings inform the neuropsychological diagnostic process.

Types of neuroimaging

Neuroimaging is basically divided into structural and functional imaging. Computerized tomography (CT) and magnetic resonance imaging (MRI) are the prototype structural imaging techniques in contemporary use. Figure 19.1 shows a comparison between CT and MRI technologies and a post-mortem section. The traditional distinctions between CT and MRI have been that CT provides the best view of bone and can be rapidly obtained within seconds. This is important for life-threatening conditions like head injury, where a rapid image of the brain is important and CT has sufficient ability to detect gross abnormalities, such as a subdural hematoma and contusion. In contrast, MRI provides exquisite anatomical detail, with a variety of imaging sequences that have sensitivity to different types of pathologies (see Figure 19.2), but these MRI sequences take considerably more time than CT and are more susceptible to artifact and motion, and, therefore, cannot be done in some individuals (see Bigler, 2005). A recent MRI development is diffusion tensor imaging, which permits a determination of tissue integrity and even a method where white matter pathways can be displayed (Hermoye *et al.*, 2006; Lainhart *et al.*, 2005). Potential clinical applications of this method will be discussed later in the chapter.

In functional neuroimaging, some measure of blood flow, brain metabolic or physiological activity is obtained. Since in functional imaging the key objective is to show some type of activation or engagement of a particular brain region or area, image clarity for anatomic distinction is not always possible. The main methods of contemporary functional neuroimaging are positron emission tomography (PET), single photon emission computed tomogra-phy (SPECT), functional MRI (fMRI), magnetoencephalography (MEG), and quantitative

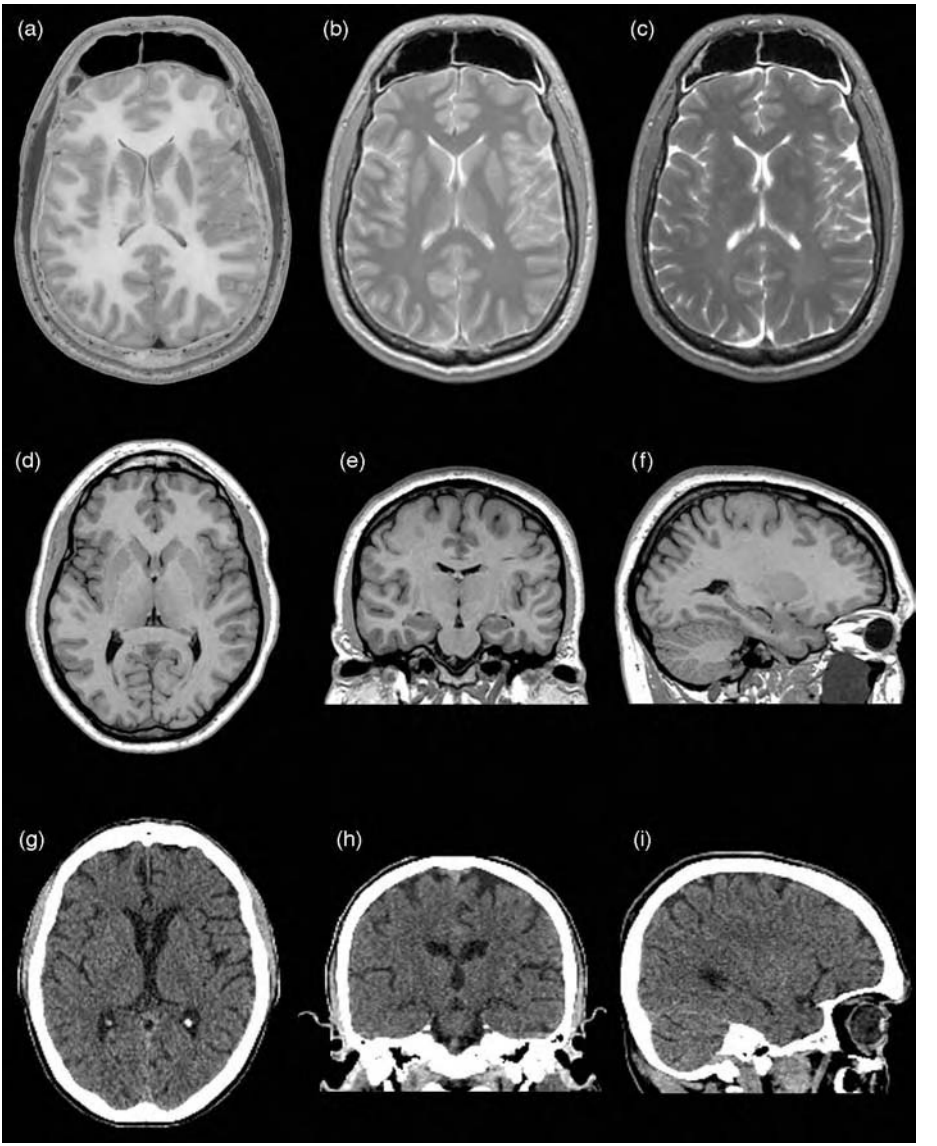

Figure 19.1 The top left axial cut (a) was performed at post-mortem, to compare to the pre-mortem imaging done at precisely the same level in (b) (a mixed weighted image) and (c) (a T2 weighted image). From a different individual, the middle row are all T1 weighted images in different planes: axial (d), coronal (e); and sagittal (f); Also, from a different individual, the bottom row depicts axial (g), coronal (h); and sagittal (i) images from CT scans. Note the differences in tissue differentiation between MRI and CT imaging, but that both provide good approximation of the actual brain as shown in (a). (A colour version of this figure is given in the Plate section.)

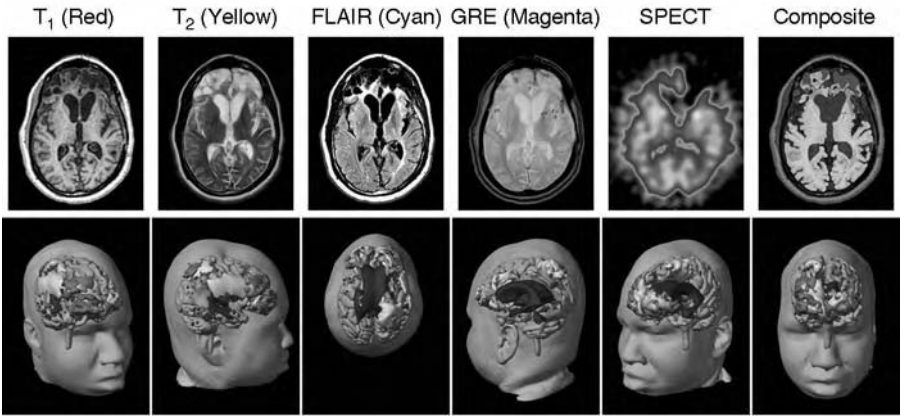

Figure 19.2 This teenager sustained a severe traumatic brain injury (TBI); initial Glasgow Coma Scale (GCS) = 3, with resultant extensive damage. This illustration demonstrates the different sensitivities of various magnetic resonance imaging (MRI) weightings where each weighting is identified by a color. For example, the abnormalities shown in the T1 weighted MRI are highlighted in red. T2 weighted images are more sensitive to cerebral spinal fluid (CSF) changes whereas the fluid attenuated inversion recovery (FLAIR) sequence is sensitive to changes in white matter signal and the gradient recalled (GRE) sequence is particularly sensitive in detecting blood by-products, namely hemosiderin, where micro-hemorrhaging had occurred. The single photon emission computed tomography (SPECT) scan shows where functional metabolic abnormalities reside in the brain, in this case extensively involving the frontal region. The composite image on the right not only shows the integration of the different identified abnormalities, but also depicts the brain segmented into white matter (light pink), gray matter (dark pink), and cerebral spinal fluid (blue). As shown by this illustration, it is best to view pathology across a broad spectrum of imaging studies to best understand the abnormalities, their location, and how that informs the neuropsychological assessment and treatment objectives. (A colour version of this figure is given in the Plate section.)

electroencephalography (qEEG). Most often these functional methods are integrated with structural MRI, so, as an example, the lack of anatomic specificity in functional PET imaging is overcome by co-registration and superimposition of MRI with PET. In this way both structure and function can be shown simultaneously, as depicted in Figure 19.3. As seen in this figure, anatomical detail from the MRI can be seen in the superimposed PET image, and this facilitates identifying what specific brain regions are functionally intact and which are not. The image displayed in Figure 19.3 shows that the entire medial aspect of the temporal lobe are weakly metabolically active.

The neuropsychological implications of the imaging findings in the case presented in Figure 19.3 are quite straightforward. This child, who had sustained

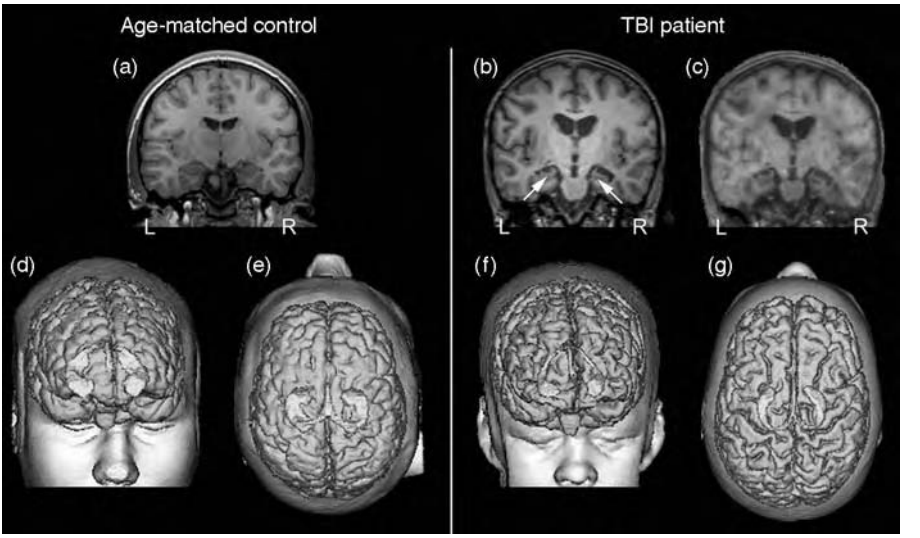

Figure 19.3 The images on the right are from an 11-year-old who sustained a severe traumatic brain injury (TBI), compounded by an anoxic injury, from a motor vehicle accident. The injury had particular effects on the medial temporal lobe, where positron emission tomography (PET) imaging demonstrated reduced activity. PET imaging has been co-registered with magnetic resonance imaging (MRI), so anatomic detail from MRI can be seen in the background of the superimposed PET scan. In PET imaging, the uptake of a radiotracer determines the level of activity of a particular brain region. In this case, the so-called 'warm colors' (orange to red) demonstrate normal activity whereas the 'cool colors' (purple to blue) in the medial temporal lobe regions bilaterally depicts less than normal activity. This child also had very significant hippocampal atrophy (arrows in b point to hippocampus – compare to similar level and normal appearance of the hippocampus in a), where quantitatively hippocampal volume was determined to be 35% of normal. In comparison to the age-matched control, this loss in hippocampal volume can be visibly determined as well. Note also, the brain injury resulted in some generalized volume loss with prominence of the lateral ventricles and cortical sulci. (A colour version of this figure is given in the Plate section.)

a severe TBI a year prior to the imaging, had cognitive deficits, primarily deficits in short-term memory, that related to medial temporal lobe damage; MRI findings clearly depicted hippocampal atrophy and PET imaging shows reduced metabolic activity in the medial temporal lobes bilaterally. While hippocampal atrophy is marked and obvious (see 3-D image in Figure 19.3), PET imaging shows that functionally most of the medial temporal lobe is less active than it should be, implicating far more widespread pathology than just hippocampal damage. Also, functional imaging may reveal disruption in neural systems that otherwise appear normal on structural imaging. This is shown in Figures 19.4 and 19.5. In this case the child suffered a severe penetrating frontal injury from a falling

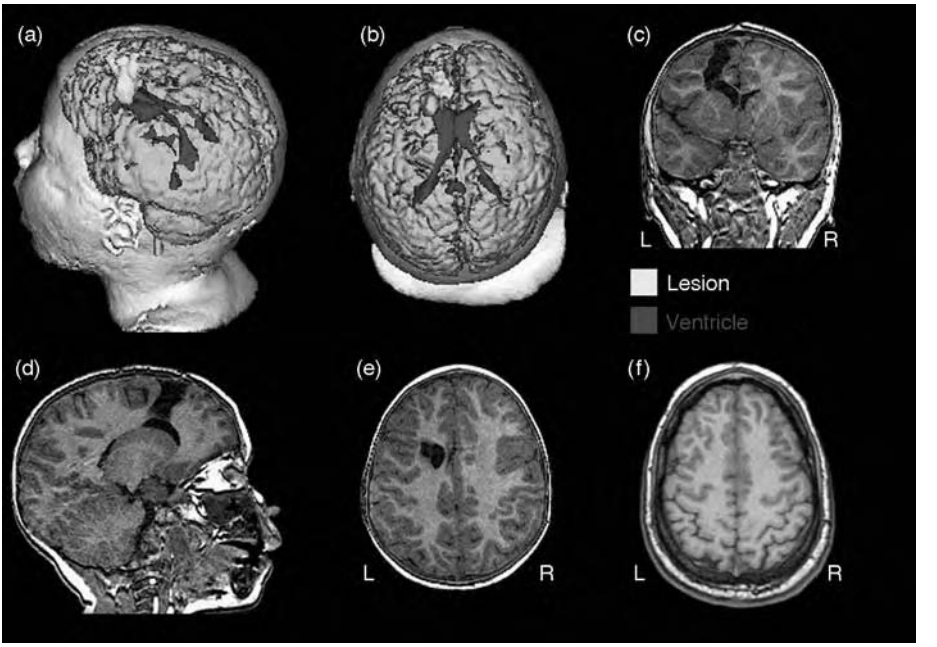

Figure 19.4 As an infant, this child sustained a severe penetrating injury to the left frontal lobe, which is obvious in viewing the T1 weighted images in c to e. Figure f is from an age-matched control child who has typical development with no history of injury. The 3-D perspectives shown in a and b, from the posterior left oblique and dorsally, respectively, show the lesion in yellow and the ventricular system in blue. Note the dilation of the lateral ventricle, in particular, the left anterior horn into the parenchymal space vacated by the lesion. This case also demonstrates an important principle in understanding the neuropsychological consequences of such an injury. Even though the damage is focal and restricted to the left frontal lobe, the left hemisphere damage goes far beyond the focal changes. For example, comparing the white matter and size of the left hemisphere in e to that of the right hemisphere, the size and amount of white matter in the left hemisphere is clearly less than the right. This is also appreciated in the coronal image shown in c. (A colour version of this figure is given in the Plate section.)

object that struck the child when an infant. As seen in Figure 19.4, the frontal damage is unmistakable, but structurally the cerebellum appears within normal limits. However, frontal cortex integrates with the cerebellum via crossed frontocerebellar pathways, and as shown in Figure 19.5, the cerebellar hemisphere contralateral to the damage seen in the frontal cortex shows less perfusion with SPECT functional imaging. This represents the phenomena known as diaschisis, clearly demonstrating that a brain region that structurally appears normal may be functionally abnormal, when its distal but direct input is disrupted.

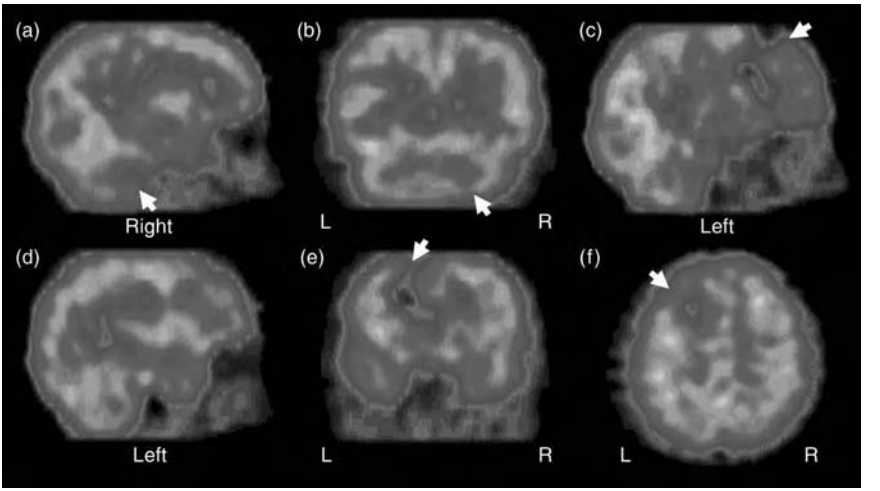

Figure 19.5 Single photon emission computed tomography (SPECT) imaging done the same day as the magnetic resonance imaging (MRI) in the child and case presented in Figure 19.4. The so-called 'warm colors' (orange and red) depict areas of normal radiotracer perfusion, whereas 'cool colors' (blue to purple) show areas of decreased perfusion. Although the focal lesion is in the left frontal lobe, clearly demonstrated by absent activity where the focal, tubular lesion occurred (arrows in c, e, and f), a form of diaschisis occurs where the crossed frontocerebellar pathways are disrupted, resulting in a lowering of activity (arrow in a) in the contralateral cerebellar lobe from the loss of input from the left frontal region. Comparing the right and left sagittal views it is obvious that there is unequal perfusion in the cerebellum, with reduced activity seen on the right. Note also the extensive lowered perfusion in the left frontal region anterior to the lesion (arrow in c) even though as shown in Figure 19.4d, this region has normal signal on T1 weighted MRI. (A colour version of this figure is given in the Plate section.)

Neuroimaging abnormalities: developmental versus acquired and static versus progressive

As already mentioned, there are a host of specific genetic and neurodevelopmental disorders which have characteristic neuroimaging findings (see Osborn, 1994). Knowing the nature and scope of such neuroimaging abnormalities helps in understanding the degree and extent of neuropsychological impairments seen in such pediatric cases, but how neuroimaging information can be used systematically in treatment for the problems identified by neuropsychological testing is new territory. For example, in Williams syndrome there is increased gyrification that can be demonstrated with MRI techniques (Kippenhan *et al.*, 2005; Reiss *et al.*, 2004) which relate to the visuoconstructive deficits commonly seen in that disorder, and in Turner's syndrome a variety of volumetric and fMRI differences have been noted to be associated with intellectual and cognitive

impairments (Kesler *et al.*, 2004; Kesler, Menon & Reiss, 2005). While this information clearly assists in understanding the neuropathology and neurobiology of these disorders and their associated neuropsychological impairments, at this time there are simply no systematic studies that address how to utilize this information in developing treatment strategies.

Focal damage that occurs early in development of life also possess interesting challenges in relating function to outcome and how to treat an identifiable impairment (Moses & Stiles, 2002). For example, the child presented in Figure 19.6 was assumed to have sustained a focal left hemisphere cerebrovascular

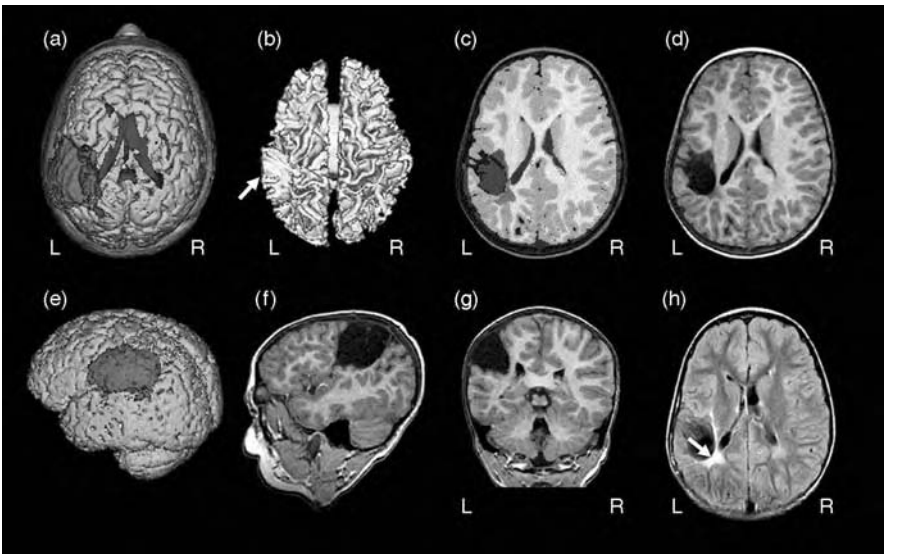

Figure 19.6 This child sustained a focal birth-related injury to the left superior and posterior temporal lobe and parietal cortex, traditional areas critical for language function. The extent of damage is clearly defined by the large cystic lesion that is visible. Despite the extensive damage, when the abnormality is focal like this and in the immature brain, often considerable adaptation and recovery can occur. Unlike the case in Figure 19.8, with a somewhat similar location of extensive left hemisphere damage but occurring in adolescence rather than infancy, this child in Figure 19.6 was showing relatively intact language development. Also, as compared to the child with birth-related injury, but with bilateral damage, the child shown in Figure 19.7 did not show adaptation. (a) 3-D dorsal view, (b) Cerebral white matter has been isolated, with the arrow pointing to the large region of disrupted white matter, (c) color segmented image showing color-coded white and gray matter, CSF and lesion as depicted in the T1 image shown in (d), (e) posterior oblique 3-D view showing the location of the focal lesion, (f) T1 sagittal view depicting the location of the cystic lesion, (g) T1 coronal image showing location of the cystic lesion, and (h) FLAIR sequence showing the sensitivity of this scan in detecting white matter pathology not as readily observed on the T1 scan (compare to d). (A colour version of this figure is given in the Plate section.)

accident (CVA) at birth due to a complicated and prolonged delivery. While the delivery was complicated, the injury was not detected in the newborn infant, and it was not until some months later when concern arose about the child's right side motor problems and language delays. At two years of age, scanning revealed a large cystic formation in the left hemisphere. The follow-up scan shown in Figure 19.6 depicts the various abnormalities at four years of age when he underwent his first comprehensive neuropsychological examination. Interestingly, other than motor deficits and a slight lisp, the child's neuropsychological examination noted generally average abilities and no major deficits. Accordingly, this is a case of focal brain damage in a traditional language area without concomitant language impairment commensurate with the size and location of the lesion, implicating a shift of language areas to regions not traditionally involved in language (Chilosi *et al.*, 2005). From a treatment standpoint, it was felt that the child could handle a regular kindergarten program supplemented with PT and speech therapy, based on neuropsychological testing demonstrating generally average performance on a comprehensive battery of neuropsychological tests. This treatment program and school placement was successfully continued on through the second grade (where the child was at the time of this writing). So in this case, the clinician has to be careful not to over-interpret what looks to be profound structural damage and its effects on neuropsychological function, when neuropsychological testing demonstrates neuroplasticity and adaptation. When focal, lateralized damage occurs to the immature brain, sometimes adaptation develops around focal areas of damage, in essence, a rerouting of function around or away from the focal site of injury (see Als *et al.*, 2004). This sometimes results in a very different pattern of deficits in the pediatric brain in relationship to neuroimaging findings than what occurs with injury and residual structural brain damage in the mature brain.

In a contrasting case of birth injury, Figure 19.7 shows a child with quadriplegia also assessed at age four years. This child's history was different, because rather than a focal injury a diffuse anoxic brain injury at birth had occurred, with neuroimaging abnormalities showing more generalized and global damage, with distinct bilateral abnormalities present. When formal neuropsychological assessment was attempted at age four years, no reliable verbal or nonverbal responses to any aspect of the examination could be determined. In viewing the imaging, as shown in Figure 19.7, marked abnormalities are observed, with SPECT (see 7[D] and 7[E]) imaging showing very little to no activity in regions of MRI demonstrated atrophy. As shown by this case when imaging abnormalities are bilaterally present and diffuse, less resiliency in the brain's capacity to adapt may be present. From a neuropsychological treatment and intervention standpoint, when profoundly impaired neuropsychological findings are coupled with

objective structural and functional neuroimaging abnormalities, poor prognosis is implied.

When typically developing children acquire an injury or disorder, such as a cerebrovascular accident (CVA), the neuroimaging findings may be particularly helpful in understanding the neurobehavioral deficits and assist with treatment planning. An example of this is presented in Figure 19.8. While the centroid

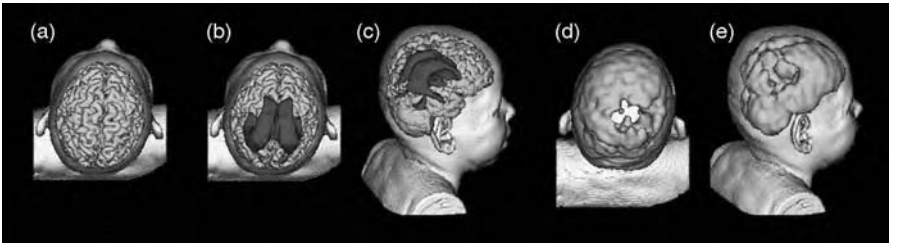

Figure 19.7 This child had hypoxic-ischemic brain injury at birth, with extensive cortical damage shown both structurally and functionally. This child's brain did not show adaptation, resulting in profound deficits at age four when the neuropsychological assessment and neuroimaging studies were performed. (a) Surface 3-D reconstruction depicting mild atrophy but otherwise more normal appearance of surface anatomy however, marked ventricular dilation is shown in (b) and (c) and SPECT imaging, rendered in 3-D surface maps demonstrate large gaps in cortical function (d and e). (A colour version of this figure is given in the Plate section.)

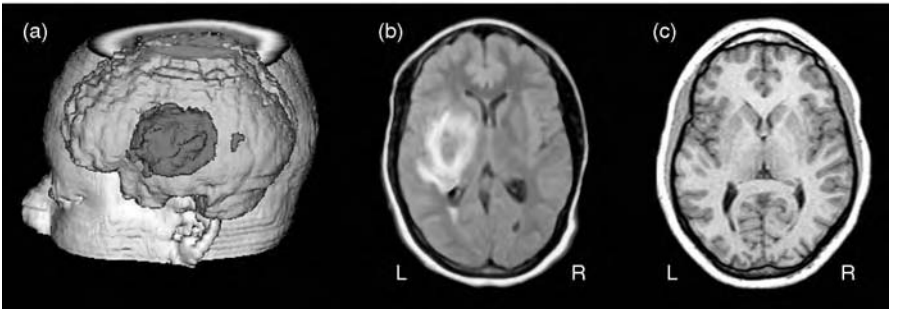

Figure 19.8 This child suffered what was thought to be a spontaneous rupture of an aneurysm involving the left middle cerebral artery. The magnetic resonance imaging (MRI) (middle panel) shows the extensive cerebrovascular accident (CVA) involving the central aspect of the left hemisphere, which when plotted in 3-D space is readily appreciated to be in traditional areas critical for language function. The right panel is an age-match normal control. Note the effacement of the ventricular system by the mass-effect of the lesion, displacing the ventricle. Note also the inflammatory reaction occurring outward from the central lesion site, where white matter in the occipital forceps is abnormal. This is distal disruption caused by the focal lesion. (A colour version of this figure is given in the Plate section.)

location of this left middle cerebral artery CVA (thought to be a spontaneous rupture of an aneurysm) was in the internal capsule/basal ganglia region of the left hemisphere as depicted in Figure 19.8, the damage was extensive in every direction. This damage occurred in a strategic location where the confluence of motor, language, emotion, drive, and motivation are all regulated and integrated. Obviously, motor pathways of the corticospinal tract were compromised, implicating permanent motor deficits (i.e. impaired finger oscillation and strength of grip on motor testing of the contralateral upper extremity). Strategic language areas were also affected; this was consistent with the neuropsychological findings of greater verbal than visual–spatial deficits. Language deficits, as would be expected given the size and location of the original CVA, dominated the neuropsychological impairments in this young teenager as did the right hemiplegic motor impairment. These obvious deficits would be apparent to anyone interacting with this young teenager, but the parents, family and teachers were also concerned with the patient's seeming lack of motivation and her unpredictable emotional lability and questioned whether this child was "depressed." Their rationale for the perception that this was psychologically based assumed the child was emotionally experiencing a perceived loss of function being expressed as frustration and lack of motivation because of the CVA. While these so-called functional or psychological factors may be present, to the astute neuropsychologist, more biologically driven explanations for the emotional changes are also likely to be present, since imaging findings demonstrate frontotemporal involvement – these frontotemporal regions being associated with post-stroke depression and behavioral change (Jorge & Robinson, 2003; Rasquin, Lodder & Verhey, 2005; Robinson, 2003). Accordingly, knowing this neuroimaging information helps in not over-interpreting psychological phenomena in the neurologically impaired child.

When updated neuropsychological consultation three years post-stroke showed little improvement over the past 18 months in the child shown in Figure 19.8, this implied the existence of stable deficits which would be likely to be resistant to traditional treatment and/or further spontaneous recovery. The follow-up neuropsychological assessment had been requested by the family and school to assist in long-term educational and vocational planning. Given the size and location of the CVA, the extent of structural damage, and the fact that her neuropsychological test performance had changed little over the past 18 months, it was suggested that traditional language-based academic therapies likely would not yield much improvement. Her strengths were in non-verbal abilities, and as observed in Figure 19.8, no lesions were present in the right, non-dominant hemisphere. So school and vocational efforts were directed to such therapies. Likewise, combined efforts between various behavioral techniques for emotional

management and psychotropic medications maximized effective treatment strategies for the ''emotional'' problems. This case nicely demonstrates how neuroimaging informs the neuropsychologist, and by knowing the permanency and location of the structural damage, combined with stability in neuropsychological performance over time, assists the neuropsychologist in planning interventions for a child with enduring impairments.

Obviously, primary neoplasms require neuroimaging and monitoring overtime. From a neuroimaging perspective, various brain scan techniques show the primary location of a tumor, and such information can greatly aid the clinician in programming rehabilitation after neurosurgical and/or other interventional treatment. Likewise, some of the treatments for primary neoplasm have their own adverse consequences on cerebral structure and function, often readily detected by neuroimaging. For example, white matter changes secondary to radiation therapy for a focal neoplasm may occur throughout the brain, even though the tumor is localized as is the radiation therapy (Reddick *et al.*, 1998). Thus, while the tumor site may be focal and in only one location, the radiation necrosis may be widespread affecting white matter structures nonspecifically throughout the brain, far from the primary tumor site. Knowing this and being able to visualize or quantify it through neuroimaging helps the clinician know how extensive the secondary damage is and to plan accordingly with regards to neuropsychological interventions. Also, tracking childhood degenerative disorders with neuroimaging helps inform the neuropsychologist about the speed and progression of the disease.

Neuropsychiatric disorders

The most thoroughly studied childhood neuropsychiatric disorder is schizophrenia (Hendren, De Backer & Pandina, 2000). For treatment planning, clinical neuroimaging has relevance if the scan shows cerebral atrophy. For example, the MRI shown in Figure 19.9 is from a young adult, but with adolescent-onset schizophrenia (Weight & Bigler, 1998). When clinical MRI shows this type of non-specific abnormality, and neuropsychological testing demonstrates generalized cognitive impairment particularly in executive function, such findings are often associated with a poorer prognosis. Such patients may have less success with traditional behavioral and pharmacological treatments than those without imaging identified atrophy and neuropsychological impairments (Hoptman *et al.*, 2005; Mitelman *et al.*, 2003; Molina, Sanz, Benito & Palomo, 2004). Unfortunately, standard clinical neuroimaging in most other childhood neuropsychiatric disorders does not provide as much useful clinical information for treatment planning as found in schizophrenia. With the aid of neuroimaging,

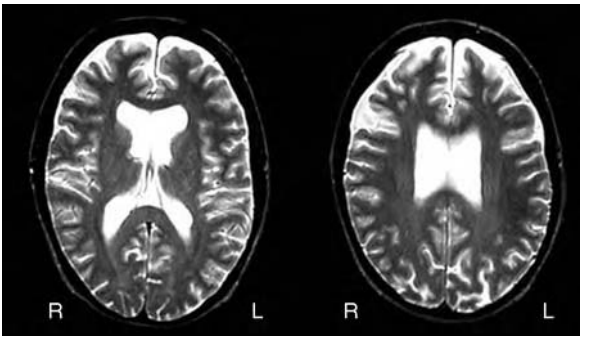

Figure 19.9 This axial T2 weighted magnetic resonance imaging (MRI) obtained at the age of 22, of an individual with early adolescent onset schizophrenia demonstrates prominence of the ventricular system as well as cortical cerebral spinal fluid (CSF), representing significant cerebral atrophy, easily appreciated when compared to the normal axial image at a similar level shown in Figure 19.1b. Also, note that the atrophic changes are more apparent in the frontal areas in contrast to posterior.

tremendous research efforts are underway to better understand the neurobiology of all childhood neuropsychiatric disorders, but in a practical sense the field is mostly empirical rather than applied at this time (Dickstein *et al.*, 2005). For example, most clinical imaging in autism is negative, with no gross morphological abnormalities observed (Bigler *et al.*, 2003). This may change in the future, with improvements in functional neuroimaging and sensitivity of structural imaging to detect abnormalities (see Lainhart *et al.*, 2005) and how such information may inform the clinician for treatment intervention and planning.

Advances in functional neuroimaging will be particularly important for the future; currently, structural imaging that is normal yields little clinical information that helps the neuropsychological clinician plan assessment or treatment (Collins & Rourke, 2003). Since routine structural neuroimaging is typically negative in children with LD, LD will be used as an exemplar of this functional neuroimaging potential and will be discussed in the next section.

Neuroimaging in learning disability: potential treatments and treatment monitoring

MEG and fMRI techniques have advanced to the point where they may be used to examine the brain's response to linguistic stimuli, where characteristic patterns are seen in those with dyslexia (Heim & Keil, 2004; Simos *et al.*, 2000). As an example of this, Figure 19.10 shows the lack of activity in critical receptive language areas of the brain in children with reading disorders (Billingsley-Marshall, Simos & Papanicolaou, 2004; Breier *et al.*, 2003; Simos *et al.*, 2002). However, in response

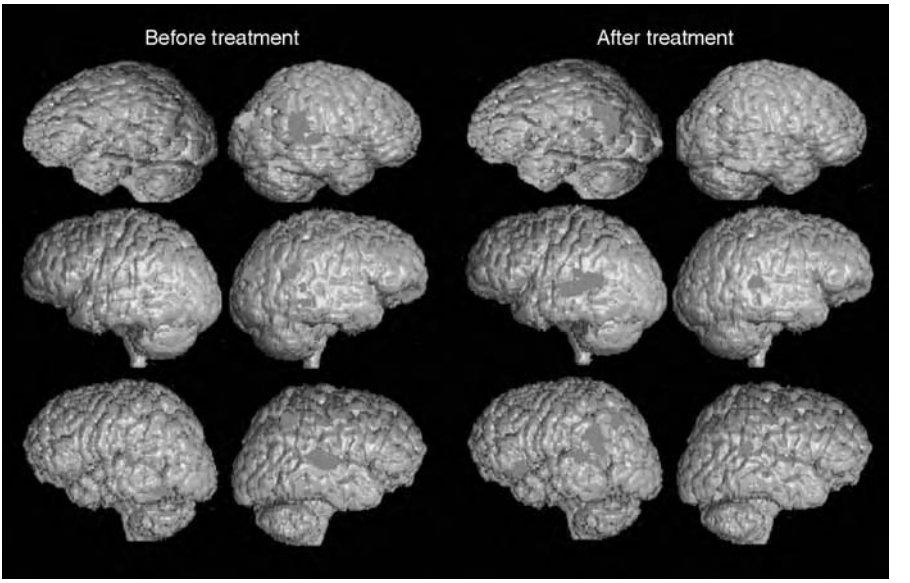

Figure 19.10 Magnetic source imaging where magnetoencephalography (MEG) activation is integrated with 3-D structural magnetic resonance imaging (MRI) is depicted in three different patients with dyslexia prior to intervention. As shown in the 'Before Treatment' column, little activation occurred in the traditional language regions of the left hemisphere. In contrast, as shown in the 'After Treatment' column, increased engagement of left hemisphere language areas occurs. This demonstrates the potential use of neuroimaging to track treatment effects. (Adapted with permission from Simos *et al.*, 2002.) (A colour version of this figure is given in the Plate section.)

to treatment that focused on perceptual timing of linguistic stimuli, improved functional reading ability could be documented and, correspondingly, the brain showed a different activation pattern after treatment. This is, of course, futuristic and a procedure that is experimental in nature, but it is entirely conceivable that such tools will be available for the clinician of the future to plan and monitor specific treatments for various cognitive processing disorders (see Als *et al.*, 2004). This will certainly apply to potential therapeutic treatment programs for children with acquired neurological impairment that affects learning ability; such methods will not only directly allow the clinician to monitor recovery of function after brain injury but to use functional brain imaging to implement therapeutic interventions (Laatsch *et al.*, 2004).

Structural and functional imaging abnormalities have also been demonstrated in ADHD (Konrad *et al.*, 2005; Mostofsky *et al.*, 2006; Silk *et al.*, 2005; Vaidya *et al.*, 2005), a disorder with high comorbidity with LD. Nonetheless, neuroimaging findings associated with ADHD have not yet influenced how the disorder is treated or how neuroimaging may be used in monitoring outcome. This is likely to change

as imaging techniques and research improve our understanding of their clinical significance in these and related disorders. In fact, it is very likely that functional neuroimaging will change the treatment landscape for a variety of disorders that pediatric neuropsychologists see. Further comment on such issues will have to await research, however.

Neuroimaging analysis: qualitative ratings versus quantitative

In children who have sustained a TBI, the degree of cerebral atrophy relates to outcome, particularly in frontal and temporal areas (Wilde *et al.*, 2005). As shown in Figure 19.11 those with greater frontotemporal atrophy had worse outcome, as measured by the Glasgow Outcome Scale (GOS) (Jennett & Bond, 1975), whereas posterior atrophy did not relate systematically to outcome. For the clinician, this means that identification of frontotemporal atrophy may be particularly relevant to treatment planning and intervention. Automated image analysis programs that provide a method to quantify atrophy or lesions and their location as well as quantification for specific brain structures or regions are becoming available (Srivastava *et al.*, 2005). Accordingly, the degree of volume loss or change in the size of a given structure or region or the size of a lesion will become another piece of data the clinician can potentially use on a routine basis.

Figure 19.12 shows three child/adolescent TBI cases with varying degrees of frontal and generalized cerebral atrophy, compared to a normal brain. Using a simple qualitative rating of the degree of cerebral atrophy in frontal and temporal brain regions, Bergeson *et al.* (2004) were able to show how increased atrophy related to increased likelihood of memory, executive and emotional changes with brain injury. The use of Figure 19.12 provides a reference point for rating atrophy by the clinician. This simple rating method can inform the clinician when significant frontotemporal atrophy is present, and such observations combined with neuropsychological impairments in memory and executive function may be useful information for the clinician in treatment planning.

Automated methods for image analysis and display, including 3-D imaging, are becoming more and more available (Kim *et al.*, 2005; Koo *et al.*, 2005; Laird, Lancaster & Fox, 2005; Muzik *et al.*, 2005; Xie *et al.*, 2005), which will permit the clinician to use neuroimaging information more routinely. One such method is voxel-based morphometry (VBM) (Ashburner & Friston, 2000; 2001). A convenience of nature is that at the macroscopic level the brain is readily compartmentalized into gray matter, white matter and fluid-filled cavities or spaces, typically filled with cerebrospinal fluid (CSF) and some of the vasculature. Using a computer program, MRI images can be ''segmented'' into these different compartments as shown in Figure 19.13. Typically what is performed in VBM is

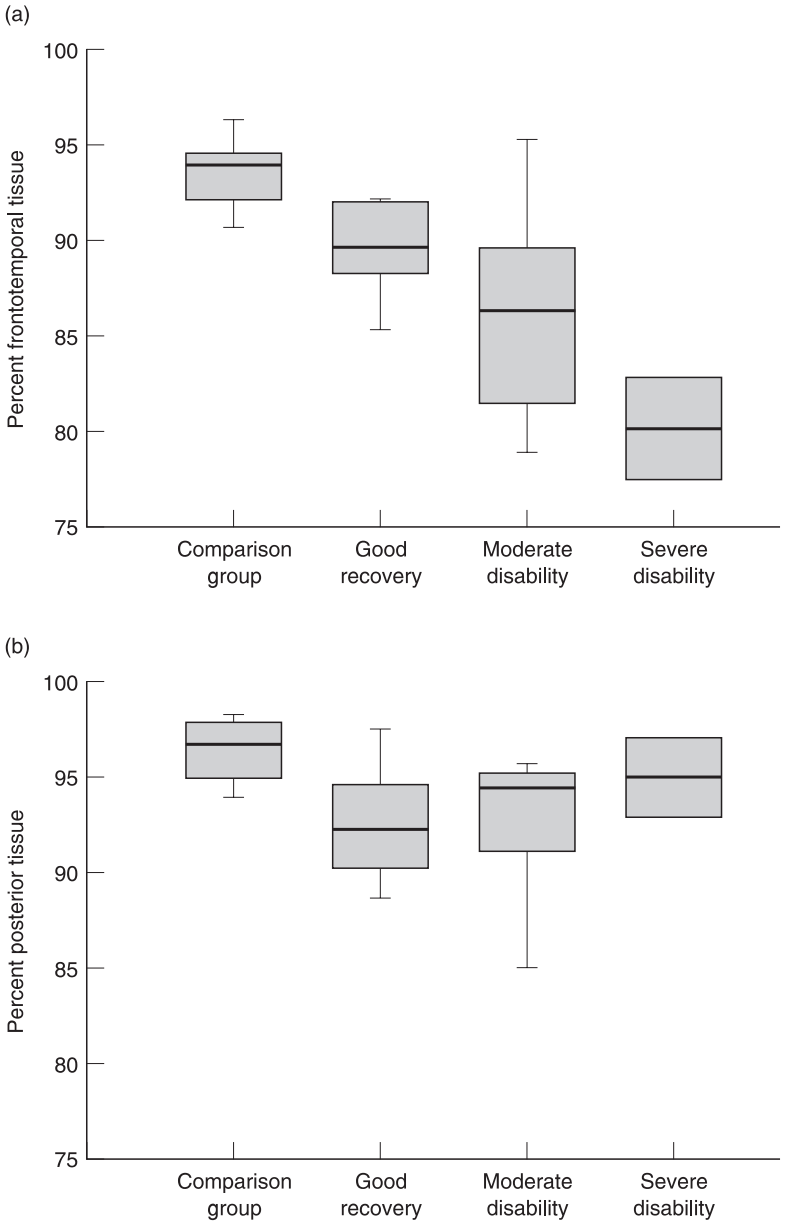

Figure 19.11 The degree of frontotemporal volume loss, as a result of TBI, was found by Wilde *et al*. (2005) to be related to outcome. As seen in a, decreasing amounts of frontotemporal tissue volume were associated with worse outcome, based on a modified Glasgow Outcome Scale (GOS) for children (see Wilde *et al*., 2005; Adapted with permission from the *Journal of Neurotrauma*). (A colour version of this figure is given in the Plate section.)

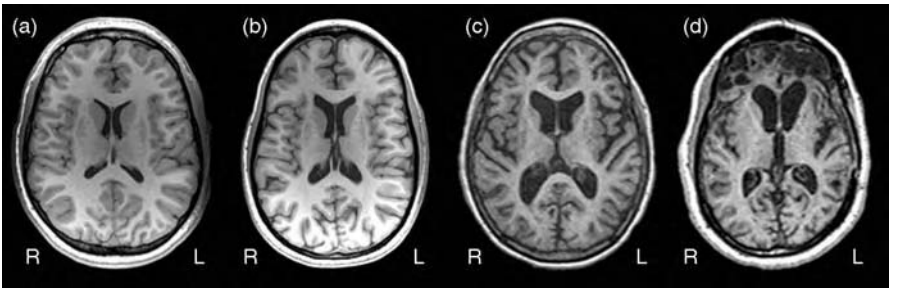

Figure 19.12 Magnetic resonance imaging (MRI) atrophy ratings in child traumatic brain injury (TBI). All images are T1-weighted MRIs in the axial plane at the level of the anterior horns of the lateral ventricles and have been taken from child/adolescent individuals between 10 and 17 years of age. (a) Normal appearance of ventricles and cortical sulci. (b) Mild atrophy – note the ventricle is slightly larger, sulci more prominent, particularly the interhemispheric fissure. (c) Moderate atrophy – note the increased and widespread cortical and intra-sulcal cerebral spinal fluid (CSF) as well as the prominence of the interhemispheric fissure. (d) Severe atrophy – note in addition to the ventricular dilation, there is widespread encephalomalacia and wasting of the frontal lobe, with prominence of the Sylvian fissure. Typically, the more severe the atrophy the greater the impairment in neuropsychological function.

a voxel-by-voxel comparison of the density of white, gray or CSF pixels within a specified voxel. For example, in TBI there is typically a loss of brain parenchyma with compensatory increase in CSF to fill the void. So applying a VBM analysis to the brain will show where there is a decrease in the density of white matter and/or gray matter, with a corresponding increase in CSF. This is shown in Figure 19.13. This teenager was involved in a high-speed side collision with positive loss of consciousness at the scene and an initial paramedic Glasgow Coma Scale (GCS) rating of 9. As can be seen, there is a loss of both white and gray matter pixel density in the frontal lobes, and, likewise, quantitative analysis shows the frontal pole volume to be significantly below what would be expected for an individual of this age. When compared with what was presented in Figure 19.12, his frontal atrophy would be clinically described as mild. His neuropsychological deficits in terms of memory and executive function would also be described as mild. Understanding this was helpful in the clinical management of this adolescent who went on to successfully complete high school.

Neuroimaging findings as baseline data

In acquired disorders, the initial scans provide a baseline and then the opportunity for follow-up, so the clinician can determine what changes take place over time and how that relates to outcome. Figure 19.14 is an excellent depiction of the

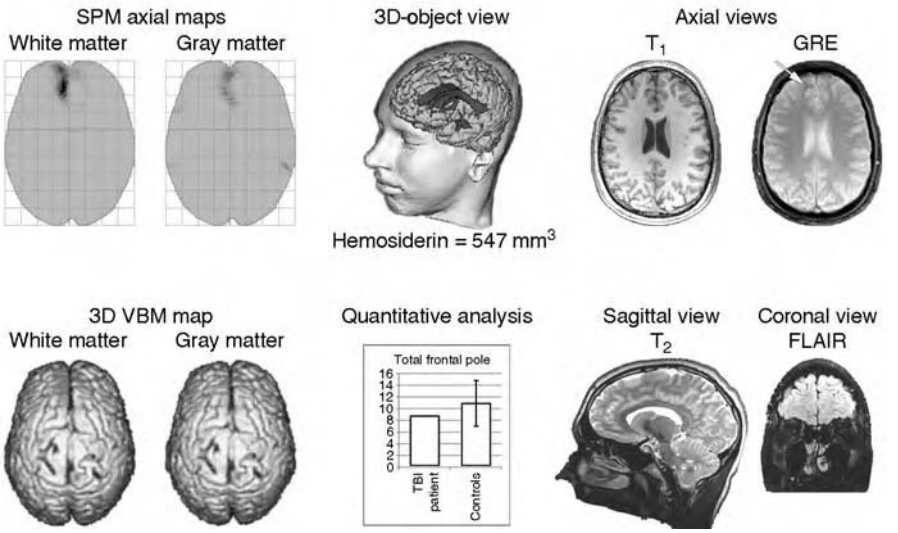

Figure 19.13 These illustrations demonstrate the utility of multiple perspectives of image analysis to best understand what effect an injury has had and also to demonstrate the voxel based morphometry (VBM) technique. The patient had sustained a significant motor vehicle accident (MVA) related brain injury and the gradient recalled (GRE) sequence clearly shows presence of hemosiderin in the frontal region on the left. The statistical parametric mapping (SPM) (upper left) clearly demonstrate differences in the intensity of white and gray matter voxels in the frontal region compared to controls and these areas are then plotted in 3-D for the VBM comparison (lower left). The frontal pole region appears slightly atrophic in the T1 axial view (upper right) and the quantitative analysis demonstrates that the frontal pole volume was, indeed, smaller than control individuals of similar age. The 3-D view shows the location of hemosiderin deposits and their total volume. These types of analyses help identify presence of significant frontal damage in a patient with traumatic brain injury (TBI). (A colour version of this figure is given in the Plate section.)

utility of sequential brain imaging in anoxic brain injury (ABI). This child sustained an ABI from a collapsed ditch that caved in on him. When found, he was unconscious and unresponsive with a GCS rating of 3. Paramedics were able to revive him; he was eventually stabilized at the hospital, however, he did not recover consciousness for several weeks. Consequentially, he was hospitalized for months where he underwent extensive rehabilitation efforts not only for the profound cognitive deficits but also for quadriplegia. As seen in Figure 19.14, the initial scan shows some edema, which is common in anoxic injury. By looking at the size of the ventricular system on or around the day of acquired injury, one is offered a baseline that permits monitoring of the degree of atrophic change overtime. More than a year after injury an MRI shows even more atrophy. This imaging coupled with neuropsychological testing 2.5 years post-injury distinctly indicating

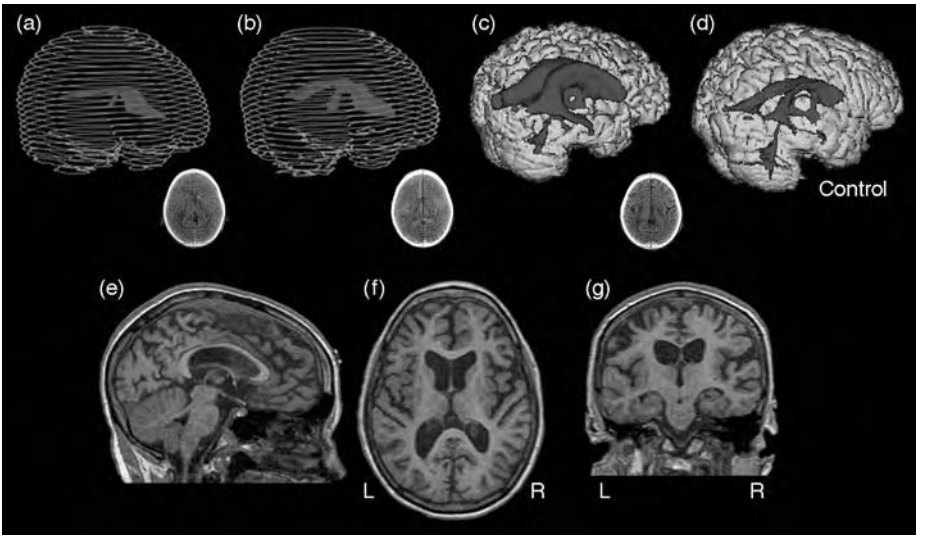

Figure 19.14 The top row depicts right posterior oblique views of the ventricular system following anoxic brain injury (ABI). (a) Day-of-injury computerized tomography (DOI CT) scan, (b) 6 days after injury, and (c) 18 months post-injury. Note the temporal horns can not be identified in a and b, presumably from generalized brain swelling that selectively compresses the temporal extension of the ventricular system. (d) A 3-D image of an age-matched control depicting normal ventricular systems. The bottom row depicts generalized atrophy in sagittal (e), axial (f), and coronal (g) planes in the follow-up magnetic resonance imaging (MRI) at 18 months post-injury. (A colour version of this figure is given in the Plate section.)

presence of memory and executive deficits points to the permanency of the impairment. By tracking the neuropathology shown on imaging with the limited cognitive recovery demonstrated by neuropsychological assessments of the child over time specified the limited possibilities of treatment interventions.

Neurodevelopmental issues in neuroimaging

To use a common phrase, the developing brain is a ''moving target'' at all points from conception through adolescence and early adulthood. This is well exemplified by looking at brain growth curves based on quantitative neuroimaging findings. As already mentioned in discussing the VBM technique, the radiofrequency signal that is the basis for MRI, is readily separated into three classifications; white matter, gray matter and fluid-filled cavities (mostly CSF, but blood and blood vessels as well). This unique feature of MRI technology permits the plotting of growth curves, which show the dynamic changes that occur in the brain from infancy through adolescence. In a general sense, white matter

increases (increased myelin and neuronal connections), gray matter decreases (in response to pruning) and CSF stabilizes from birth to late adolescence/early adulthood (Giedd, 2004). These developmental trajectories are depicted in Figure 19.15 from Courchesne *et al.* (2000).

These constant developmental changes create a real challenge when interpreting the relevance of neuroimaging-identified abnormalities in pediatric disorders. As already seen in Figure 19.6, the brain in some children has an amazing ability to adapt. Figures 19.6.B and 19.6.H from that same child show the disrupted white matter development that occurred in that brain in response to injury. Having an early lesion like this then disrupts all subsequent physical development in that brain region as well as connecting pathways. As demonstrated in Figure 19.6, white matter integrity, predominantly in the left parietal area but to a certain extent affecting the entire left hemisphere, is seriously compromised, but at the time of this writing, most aspects of receptive language function were developing adequately. Therefore, when damage occurs to the infant or child brain during these periods of most rapid growth (i.e. before mid-childhood), the robust growth curves shown in Figure 19.15 are permanently disrupted and may never return to their pre-injury status.

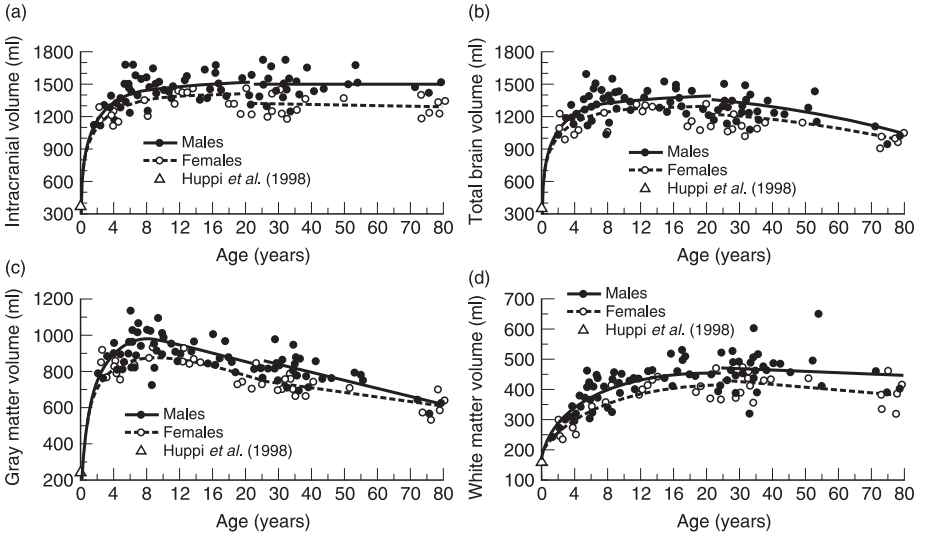

Figure 19.15 The growth curves are taken from Courchesne *et al.* (2000) and depict head growth (a) based on intracranial volume, (b) total brain volume, (c) gray matter volume, and (d) white matter volume. Note the precipitous and rapid peak in head and brain volume, but the dynamic changes in white and gray matter where ostensibly, through pruning, gray matter decreases. In contrast, through myelination and increased interconnectedness, white matter increases. The increase in white matter, yet decrease in gray matter, results in overall stabilized total brain volume.

The new diffuse tension imaging technology can be applied to this problem as well showing developmental changes imposed by an early brain injury. Figure 19.16 is the color-coded diffuse tensor imaging scan clearly showing asymmetry in posterior white matter pathways of the brain that resulted from a significant brain injury when this child was 6 weeks of age. The child was a seat-belted infant in the back seat of the family vehicle, which was struck broadside, wherein the child sustained a right parietoccipital skull fracture. Initial CT imaging demonstrated underlying contusion to the posterior aspect of the right hemisphere. The child also developed post-traumatic epilepsy. Clearly, the diffuse tensor imaging findings demonstrate that white matter development in the posterior right hemisphere was disrupted and did not follow a normal developmental course after injury. Understanding these developmental changes

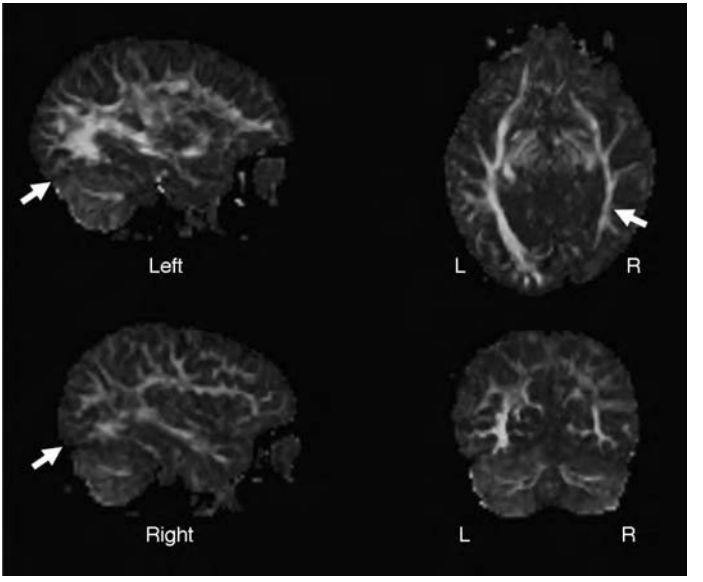

Figure 19.16 As an infant less than two months of age, this child sustained a significant brain injury in a motor vehicle accident (MVA), sustaining a right parietoccipital skull fracture and underlying brain contusion, as demonstrated by computerized tomography (CT) imaging on the day of injury. These diffuse tensor imaging (DTI) images, taken when the patient was a teenager, clearly show that the right hemisphere white matter did not develop normally after this injury and is very asymmetric in comparison to the left (compare regions where arrows are pointing). This is particularly evident in the sagittal images on the left where the left hemisphere shows extensive development of anterior-posterior pathways (green) and dorsal-ventral coursing pathways (blue). Red represents interhemispheric coursing pathways. This illustration nicely demonstrates that once injured, the trajectory brain development may not be normal, with lasting structural anomalies present thereafter. (A colour version of this figure is given in the Plate section.)

can aide the neuropsychological assessment by directing the neuropsychologist to explore likely relationships between the neuroimaging findings and development. In this case, the differential effects of right posterior hemisphere injury would be toward visuospatial impairment, including problems in social perception.

Diaschisis, Wallerian degeneration and the problem of lesion localization in assessment

In the developing brain, the interaction between growth, maturity and experience generally leads to regionalization and lateralization of certain cortical functions, in particular, language (see Szaflarski *et al.*, 2006). Once established, diverse neural networks that subserve cognition and behavior are integrated in complex ways such that a lesion somewhere in the network may disrupt function elsewhere in the network. The term ''diaschisis'' refers to the fact that a focal lesion may have a distal or remote effect because of how that region of the brain connects with others. This may make it difficult to interpret some neuroimaging findings, because the lesion affecting neuropsychological function may be quite distal from brain regions where the functional behavioral consequences occur. The case already presented in Figures 19.4 and 19.5 is an excellent illustration of this. This child sustained a severe penetrating frontal brain injury, but the frontal damage resulted in a functional disconnection of the contralateral cerebellar hemisphere. This form of diaschisis is thought to occur because of disrupted crossed frontocerebellar connections emanating from the damaged frontal lobe that connect with the cerebellum, which has no specific visible structural damage. However, functional activity of cerebellum was rendered impaired by the elimination of pathways originating or terminating in the frontal region where the focal damage occurred.

Related to diaschisis is ''Wallerian'' degeneration, where a focal lesion in one brain region results in atrophy in a distal region. The case in Figure 19.17 illustrates these points, taken from a child who sustained a severe TBI where neuroimaging demonstrated a distinct shear lesion in the right internal capsule–basal ganglia region, as shown in Figure 19.17 clinically resulting in left side paralysis. This lead to downstream Wallerian degeneration that involved the corticospinal track readily appreciated by midbrain asymmetry of the cerebral peduncles, even though no specific lesion is observable in the midbrain. This type of paralysis results in permanent motor impairment, with an inability to carry out coordinated motor movement as depicted in Figure 19.17. So even though the focal lesion in the internal capsule is relatively small, it is strategically located in the pyramidal motor system causing atrophy both above and below where the lesion is located. Thus, the atrophy so clearly observed at the level of the cerebral peduncle is caused

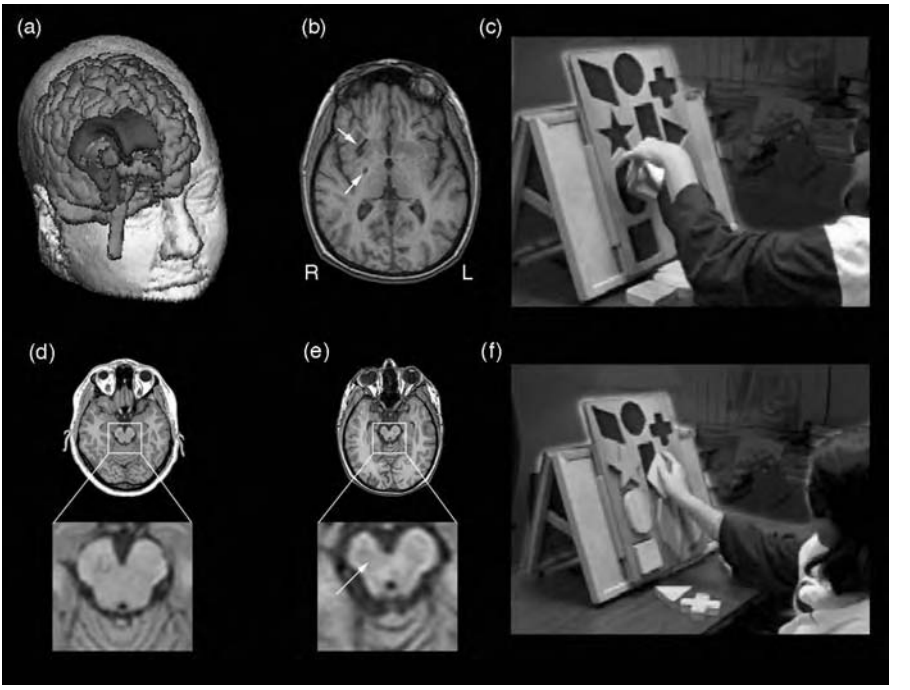

Figure 19.17 This case demonstrates Wallerian degeneration, where the major lesion is in the right internal capsule-basal ganglia region; resulting in left hemiplegia and impaired coordinated motor movement (see c and f). Damage to the corticospinal track at the internal capsule level, results in downstream atrophy of this direct motor pathway, such that at the midbrain level of the cerebral peduncle considerable asymmetry is reflected, indicating the right peduncle has withered (e). The lesion is not in the peduncle, but the effect of the injury is reflected in damaged pathways at the peduncular level resulting in the atrophy. (A colour version of this figure is given in the Plate section.)

by a distal injury instead of a local lesion, so clinicians need to be aware of the origin of atrophy and not misinterpret the source of atrophy.

Innovative neuroimaging methods

Diffusion tensor imaging (DTI) is a relatively new procedure providing insights into the "health" of neural tissue, by studying the diffusion of water molecules (see Figure 19.18). Tightly held and organized tissue, such as aggregate bundles of white matter pathways coursing across the CC permit the identification of pathways and their normal appearance in the typical developing child, using what is referred to as DTI tractography (Lazar & Alexander, 2005; see Figure 19.18.C). In contrast, a child who sustained a moderate-to-severe TBI is shown as a comparison, where a small lesion in the posterior CC can be readily identified. Full

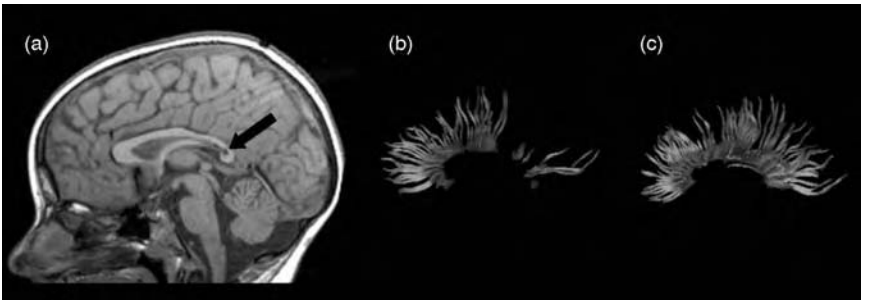

Figure 19.18 The scan on the left (a) is from a child with moderate-to-severe traumatic brain injury (TBI) with clearly atrophic posterior corpus callosum, with a shear hemorrhagic (hemosiderin deposit) lesion in the splenium. (c) shows normal diffuse tensor imaging (DTI) tractography depicting the projections of interhemispheric fiber pathways rather evenly across the corpus callosum (CC) in a normal control individual. (b) represents the child's tractography findings, which demonstrate almost complete dropout of aggregate fiber tracts emanating from the atrophic posterior CC. This type of technology will likely inform the neuropsychologist even further about gross, as well as subtle, pathology that may be present following injury or associated with certain disorders. (A colour version of this figure is given in the Plate section.)

Source: Adapted from Wilde *et al.* (2006) with permission from the Journal of Neurotrauma

appreciation of the significance of this finding, however, comes from viewing the DTI tractography of the CC white matter projections, which clearly demonstrates a significant loss of fiber pathways in that region (see Figure 19.18.B).

Guidelines for the clinician in utilizing neuroimaging data in treatment planning

Since neuroimaging is widely performed in pediatric neurodevelopmental or acquired neurological disorders, neuroimaging becomes integral to the assessment process and should help to inform the clinician in making neuropsychological inferences and treatment recommendations. However, systematic study of how neuroimaging findings may best relate to and predict outcome are just emerging (Blackman *et al.*, 2003; Grados *et al.*, 2001; Levin *et al.*, 2004). As at the time of writing, there are no comprehensive evidence-based treatment studies that provide intervention recommendations and their effectiveness for neuropsychological disorders based on how neuroimaging findings inform the clinician. Undoubtedly, such studies will be forthcoming and will tackle these clinical issues, providing clinicians with procedures that best guide intervention strategies for pediatric conditions with neuropsychological sequelae (Herbert, 2004).

For now, understanding relationships between developmental issues, as described above, and areas of damage, certainly helps to direct clinicians with

intervention strategies. As shown by Wilde *et al.* (2005), the presence of frontal and temporal damage seems to have the most adverse impact of recovery from brain injury, and, therefore, knowing that frontal and temporal damage is present informs the clinician that greater intervention challenges may be in store for children with such damage. Likewise, as shown by several cases reviewed above, the confluence of impaired neuropsychological function and specific areas of damage suggests permanency of deficit.

Future directions

As this chapter is written, numerous neuroimaging research centers are focusing on functional brain imaging as the tool for cognitive assessment (Moritz *et al.*, 2004; Schmitz *et al.*, 2006; Zakzanis, Mraz & Graham, 2005). Structural neuroimaging will always have limitations in predicating outcome and informing the clinician about intervention strategies. However, rapid image 3-D display and analysis of brain structure will become commonplace tools for the clinician in the not-too-distant future. In addition, functional neuroimaging permits direct assessment of cerebral function during the recovery process following injury (Laatsch *et al.*, 2004), or of some acquired deficit (Crinion & Price, 2005), and/or of how the brain responds to treatment (Noppeney *et al.*, 2005; Straube *et al.*, 2005). Within the next decade, the integration of structural and functional imaging will probably result in significant advancements in the development of interventional strategies in children and adults with neuropsychological impairments.

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20

Cognitive rehabilitation

Robert W. Butler

Overview

Pediatric brain injury rehabilitation is at a crossroads. At times a treatment stepchild within rehabilitation, most pediatric outpatient brain injury rehabilitation programs have gone into decline. While not ignored, perusals of rehabilitation journals clearly indicate that most work is directed toward adult populations. Inpatient treatment remains a mainstay, but is typically characterized by quite brief stays, largely due to the rapid physical healing that occurs in childhood. While the 1980s and early 1990s were characterized by adequate medical insurance support for outpatient pediatric brain injury rehabilitation, this is no longer the case. In the United States, we have, largely, left the task of cognitive rehabilitation to educational professionals. Unfortunately, while these individuals are quite skilled in working with children who have a learning disability, with some exceptions they have minimal background in brain injury rehabilitation. Thus, the child who suffers a central nervous system (CNS) insult such as traumatic brain injury, or a brain tumor, will frequently receive services similar to that of a child with a learning disability, whom does not necessarily have the specific medical, neuropsychological, and remediation needs associated with a brain injury. This chapter will present the current status of education-based standards of care for cognitive rehabilitation secondary to a brain injury. I will then review recent literature on specific cognitive rehabilitation programs designed to improve functioning in children following a brain injury. These interventions are somewhat loosely characterized as ''behavioral'', ''cognitive'', or ''holistic'' which combines the approaches of the previous two treatment modalities, and also emphasizes psychosocial adjustment and functioning. I will describe an approach developed by my own research and treatment team which, while initially directed toward survivors of childhood cancer who had experienced CNS impairment, is now being pilot tested on other pediatric patients with brain injury. Finally, new innovations and directions that hold

promise for improved quality of life in not only patients, but also their family members will be reviewed.

Brain injury rehabilitation standard of care

Initial cognitive rehabilitation efforts for adults were based on theoretical and practical ideas that came from neuropsychologists and neurologists (Ben-Yishay, 1983; Luria, 1963). Theoretical principles were developed from those adult patients with a brain injury, and treatment approaches were directed accordingly. It has only been in the past 10–15 years that increased attention has been applied to brain injuries in childhood. This is partly due to an initial conceptualization of children as being much more resilient to the effects of a CNS insult. Early evidence suggested that cortical re-organization following brain damage was associated with less eventual impairment. This was termed the Kennard principle (Kennard, 1942). This principle, however, was developed on studies using primates, and restricted to motor functioning. It has now become apparent that brain injuries, particularly those of a diffuse nature, may be more likely to result in greater degrees of impairment when they occur in infancy and early childhood, and the age/plasticity relationship is far more complex than initially proposed (Stein, Brailowsky & Will, 1995). Moreover, we are learning that age at injury is not the most single relevant mediator/moderator on eventual neuropsychological impairment (see Donders, Chapter 1, this volume). This is particularly important for pediatric cognitive rehabilitation because most CNS insults in childhood are global in nature.

The child with a brain injury who is in need of cognitive rehabilitation may not receive appropriate and comprehensive standard of care services because they have not been efficiently identified, and resources may be limited. This is becoming an increasingly apparent and significant problem. Public schools are, almost universally, undergoing budgetary and financial struggles which are Herculean in proportion. Typically, only the children and adolescents with the most severe disabilities receive services, and the quantity and quality of these services decline annually. It is important to emphasize, however, that there are regional differences, and some school systems have worked to develop programs for students with a brain injury; but, budgetary limitations remain a governing force. Therefore, subtle to mild disabilities are oftentimes not identified, or even actively ignored. On a very optimistic note, a growing body of psychological, medical, educational, and allied rehabilitation specialists are working to "make more with less". Pediatric brain injury rehabilitation studies, particularly Phase III clinical trials, are beginning to emerge in the research literature. Pediatric specific texts on rehabilitation are being published. While obstacles to

effective treatment are prominent, progress is being made, and innovative approaches are emerging.

I will now describe school-based special education services directed towards rehabilitation. These services were originally developed for children and adolescents with specific and general learning disabilities. They were not necessarily structured to meet the needs of a student with brain damage, but can be extremely therapeutic for rehabilitation.

School-based rehabilitation services

Educational interventions that are applied mainly to students with learning disabilities, but also to children/adolescents with CNS involvement, typically involve either a 504 plan or an individualized education plan (IEP). The difference between these two approaches is one of involvement. The 504 plan is generally less formal, whereas the IEP results from team meetings and includes reasonably comprehensive assessments, and extra written work plans.

504 considerations refer to informal interventions, such as seating the child in the front of the class, a reduced workload, and untimed testing. These are usually reserved for children who have minimal cognitive impairment. They can be quite appropriate as a brain injury treatment, if the nature of the neuropsychological dysfunction is extremely mild, or if provided in conjunction with other rehabilitation methods. These services are typically readily available for children because they do not require significant efforts and expense on the part of the school.

Individualized education plans (IEP) do require considerable cost and effort on school personnel, who, by federal guidelines include, at the minimum, a special education expert, speech/language pathologist, occupational therapist, and school psychologist. They are based on a federal law, the Individuals With Disabilities Act (IDEA), that identifies the manner in which children with disabilities need to be identified, taught, and provided with rehabilitation services. There are a number of different criteria for what defines a child with disabilities. Many, if not most, states allow for traumatic brain injury (TBI) as a specific disability category. If TBI is not a designated category, the student with a brain injury will most commonly be placed within the other health-impaired category. This category also includes CNS health impairments such as irradiation to the brain, metabolic disturbances, and stroke associated with sickle cell disease. There are overviews published on the nature and structure of the IEP (Siegel, 2004). The IDEA, however, is complex and often confusing. Using parent-directed texts as simple bibliotherapy may be unwise, but they can be effective learning tools.

While readily apparent to most professionals in the field of rehabilitation, and with parents who have gone through the IEP process, it is important to emphasize that only schools who receive federal funds are required to follow these guidelines. Thus, a private school does not need to provide special needs assessments or to develop 504 and IEP plans. Nevertheless, depending upon state regulations, the parent may be able to access specific special education services even though the child remains in a private school. The above-referenced IEP text contains a wealth of information, including contact information by state, specific federal regulations, and also sample request and assessment forms.

In our own childhood brain injury rehabilitation practice, the current emphasis has been directed toward developing a model which actively teaches parents to be effective advocates for their children within the public school system. Unfortunately, the relationship between parents and public school personnel regarding a student who suffered a CNS insult can become adversarial rather than cooperative. There are a myriad number of reasons for why this occurs, but the most important point is that it is detrimental to the rehabilitation process. The rehabilitation model that myself and collaborating colleagues have been working toward is one of complementary rather than redundant services. More specifically, I view brain injury rehabilitation as a series of specific intervention strategies that are designed to promote the efforts that school personnel direct toward special education. Our approach is not one in which specific academic skills are taught. Rather, we attempt to improve upon the student's ability to manage neurocognitive functions, such as attention, memory, and processing speed, with the expectation that improvement in these neurocognitive functions will facilitate the efforts of special education and IEP professional efforts.

In sum, this represents a brief review of standard of care for the vast majority of pediatric patients with a brain injury. Very few outpatient cognitive rehabilitation programs and centers are available for this population: where present they are quite expensive, and insurance companies have been increasingly reluctant to fund these interventions. Also of concern, only recently have brain injury rehabilitation research efforts directly involved the educational domain. Nevertheless, there remains a small but active group of clinicians, educators and researchers who are attempting to develop effective and potent acquired brain injury treatment programs that involve educators. These are largely designed to work in concert with special education standard of care that typically addresses academic learning, and the integration of these efforts with neurocognitive and psychosocial impairments (Glang, Singer & Todis, 1997). This is, in my opinion, the potential strength of cognitive rehabilitation in the pediatric

population, and a team approach is generally accepted as essential for effective treatment. The team needs to include not only the patient and parents, but also educational professionals, and other relevant individuals, including, in certain circumstances, members of the extended family.

Pediatric cognitive rehabilitation

Cognitive rehabilitation has been defined as "a systematic effort to assist brain damaged individuals in developing ways to compensate for cognitive deficits" (Brett & Laatsch, 1998). The most common cognitive deficits following a childhood brain injury include attentional dysfunction, memory problems and self-control difficulties. Depending upon the severity and location of the injury, language involvement, visual–motor integration difficulties, and other specific impairments may also be present. As noted above, the most frequent brain injury in childhood is one that is global rather than location-specific. Thus, multiple cognitive deficits are the rule with children, and therapy has traditionally been interdisciplinary. The formative model was of one of enrollment in a rehabilitation institution that the individual attended for a portion of a day where speech/language, occupational, psychological, neurological, and brain injury services were all administered. This is no longer the case, and if the child is receiving school-based rehabilitation services along with outpatient medical services, communication channels among all treatment professionals are essential.

Traditional brain injury interventions were primarily based on an exercise model. It was thought that having the patient exert various cognitive functions would promote the development of "new neural neuropathways", and also stimulate the brain to heal itself. Again, much of this older research is based on adult patients (Lynch, 1982), and this restricted approach began to be perceived as reductionistic. Work on developing and assessing rehabilitation programs extended into the 1990s, and a more holistic approach began to be advocated (High, 2005). The application of these early adult models was initially, somewhat ineffectively, directed toward the pediatric population. As an example, pilot testing of exercise-based cognitive rehabilitation with patients who had brain damage secondary to a childhood cancer did not result in significant beneficial effects (Butler & Copeland, 2002). Subsequently, while initially committed to a drill-based exercise approach to cognitive rehabilitation, Sohlberg and Mateer (2001) have become increasingly holistic in their approach to both adults and children.

The holistic emphasis directed toward multimodal interventions has been promoted by somewhat disappointing treatment results from the application of pure massed practice (Wilson, 1997). Regardless of orientation, pediatric brain

injury rehabilitation efforts have been mainly applied to two populations; traumatic brain injury and CNS insults secondary to disease/treatment for a pediatric malignancy. The basis of the therapeutic effects of these treatments, albeit largely from adult studies, is documented in a National Institutes of Health (NIH) consensus statement (National Institutes of Health, 1998) which supported the use of various cognitive rehabilitative methods.

In early individual studies with the pediatric population, behavior methods tended to be emphasized, likely due to concerns over cognitive development, parental involvement, and the child's inability to effectively use methods such as metacognitive strategies. Nevertheless, there is initial evidence that efforts to remediate cognitive functions such as attention, memory, and mental flexibility, particularly in adults, can be effective (Cicerone *et al.*, 2000), and it is hoped that these will translate to the pediatric population. I and my co-workers have been actively attempting to translate these remediation efforts so as to be applicable to the pediatric population, and other researchers are also involved in these endeavors.

Even given the above concerns, retraining of cognitive abilities using a drill approach has been documented by a number of researchers (Sohlberg & Mateer, 1987; Thomson *et al.*, 2001). While positive results have been reported, effect sizes are typically quite modest. This is not surprising given the nature of brain injury rehabilitation. There is a growing body of research demonstrating that cognitive rehabilitation does stimulate functional changes in the brain (Laatsch *et al.*, 2004; Levin & Grafman, 2000; Ogg *et al.*, 2002). Nevertheless, it needs to be emphasized that the task of brain injury rehabilitation is daunting. The therapist is trying to stimulate improvement in an organ that has reduced and limited healing capabilities. Further, brain imaging changes need to be correlated with real world quality of life improvements.

Traumatic brain injury is the most common cause of neuropsychological deficits in childhood. There is an edited text on rehabilitation with children and adolescents who have suffered a traumatic brain injury that embodies the holistic model (Ylvisaker, 1998). While reasonably current, there have been additional advances in techniques since the year 2000 (Ylvisaker *et al.*, 2005; Ylvisaker, Jacobs & Feeney, 2003). The text and these later summaries make a number of important points. It is essential that the cognitive rehabilitation therapist strive for generalization to the real world and every day activities. Most rehabilitation specialists will readily acknowledge that documentation of improvements in therapy is necessary, but translation into the real world is paramount. Thus, rather than intervening with a massed practice or behavioral approach, a combination of these two orientations, along with instruction in methods such as mnemonic strategies and metacognitive strategies is advocated. Organizational skills,

generally thought to be deficient due to frontal brain injury, are quite common in pediatric traumatic brain injury, and specific activities designed to improve planning in the systematic approach toward activities of daily living are likely to be helpful. These children/adolescents can manifest the aforementioned complications of language disturbances and deficits in visual–spatial awareness, and visual–motor integration. Thus, assessments and interventions from speech pathologists and occupational therapists may be necessary. School re-entry is frequently a problem area, and psychological/adjustment disorders can be expected (Butler & Satz, 1999). As Ylvisaker and colleagues' work has progressed, there has been a continued evolution into holistic rehabilitation that attempts to address all areas of the patient's life: the school, the rehabilitation team, the family, self-awareness, the use of cognitive–behavior modification, and peer relations. Increased use of primary providers as the deliverers of services, with specialists providing support is being advocated. Individualizing rehabilitation efforts to the specific needs and situation of the child/adolescent is also viewed as important. While this may be clinically appropriate, it does make the scientific methodology of clinical trials very problematic.

Even though the outpatient traumatic brain injury treatment center for children has largely disappeared, there remains a need for a team approach. Within these early centers, staff typically included a neurologist or physiatrist, speech pathologist, occupational therapist, and neuropsychologist, along with other personnel. Thus, the institution, itself, represented the team approach. Given that these centers are unavailable for most children who are in need of cognitive rehabilitation, it is extremely important for there to be a primary team leader who coordinates communication through various individuals and institutions, and the neuropsychological rehabilitation professional is well positioned to assume this role. Public school systems will provide speech and occupational therapy to children in need of these treatments (Siegel, 2004). Alternatively, some parents may wish to seek these services through private practice professionals. There may be ongoing medical issues such as chronic pain, and the treating professionals in these areas need to be apprised of therapeutic activities and endeavors. Informing the schoolteacher about treatment gains and methods, preferably through communication with the parent is also necessary. Overall, it can be seen that while a team approach remains viable, there are clearly complications with logistics and communication that must be taken into consideration, and planning should begin at the onset of cognitive rehabilitation.

There is no "gold standard" for the frequency and duration of brain injury rehabilitation implementation. In the 1980s, the standard of care for adult patients involved approximately six months of intensive treatment that occurred five days a week, and typically lasted approximately the length of a standard work day.

Currently, treatment is less intensive. Thus, most childhood cognitive rehabilitation programs advocate weekly or bi-weekly sessions of therapy that involve one to two hours of treatment over a period of four to six months, at best. An important consideration is the level of functioning of the patient. Younger patients, as well as those with greater levels of initial impairment, may demonstrate less improvement, and correspondingly need both increased treatment sessions, and reduced, realistic expectations. Older and less impaired individuals may progress at a more rapid rate.

Ecological and environmentally based interventions with children/adolescents whom have neurodevelopmental complications are under-appreciated. Few studies have addressed this important perspective. Baron and Goldberger (1993) wrote an excellent article advocating for the integration of environmental manipulation, and attention to factors such as basic nutrition in children. For example, as part of 504 considerations, not only will many children need extended time limits for examinations, but the use of true–false and multiple-choice formats in testing may be preferable to essay examinations. Digital recording of classroom lectures for later review is often helpful. Using written handouts rather than copying from a whiteboard should be considered. One also needs to account for adequate sleep, a healthy diet, and acceptable levels of environmental stimulation. In a very large family with working parents, schedules may become very complex, particularly as children emerge into adolescence and extracurricular activities increase. This can result in a high degree of confusion, even for children/adolescents without a brain injury. Family counseling designed to assist the development of a structured routine that emphasizes consistency can be of great benefit. In terms of sleep, for example, the reader should recall the last time he/she suffered several nights of poor sleep. I suspect that most will immediately identify with the impact that sleep deprivation has on cognitive function, such as memory and attention/concentration. Assisting parents with routine, as identified above, and also consultation with physicians for potentially helpful medications are encouraged.

An innovative concept that involved training schoolteachers to administer cognitive rehabilitation exercises and activities has been pilot tested (Brett & Laatsch, 1998). The project involved ten high school students who had suffered a traumatic brain injury. Cognitive rehabilitation occurred twice a week for twenty weeks, and was administered by trained schoolteachers, who were supervised by psychologists who had been trained in cognitive rehabilitation. There was no control group, but on pre- and post-treatment neuropsychological testing, the students did demonstrate a significant improvement in memory functioning. The gains were associated with increases in verbal learning. The authors, not surprisingly, identified obstacles to this approach that generally involved the

reluctance of school administrators to reduce teaching time, coordination of student schedules, and other logistic problems. Our own work with school personnel will be described below. We are considering alterations in our treatment approach, and greater involvement of teachers would, in my opinion, be likely to improve the efficacy of our treatment. We are hesitant, however, to implement this because of the above noted difficulties that the authors experienced.

While primarily directed toward the adult brain injury population, the approach of Sohlberg and Mateer (2001) has been applied to the pediatric population. Their text contains a chapter addressing rehabilitation and cognitive remediation efforts with children and adolescents who have, typically, suffered a traumatic brain injury. Therapeutic training exercises based on the attention process training (APT) approach have been specifically developed for the early childhood population. These are hierarchically organized into a system labeled "Pay Attention" (Thomson *et al.*, 2001). These methods are primarily based on massed practice and drill exercises for the various forms of attention and concentration (e.g. divided, sustained, alternating, etc.), but specifically designed for use with very young children. There is an emphasis on the need for adjustment of goals and approaches, with developing patience on the part of the entire team. Children often cannot sustain involvement in extended cognitive remediation activities at the same level expected with adolescents and adults, and this is particularly true of younger children. Rarely is remediation administered to preschoolers. The program is directed toward attentional deficits, but cognitive impairment within the area of memory is also addressed.

The work of a research consortium based in Ohio, largely led by Yeates and Taylor, (Yeates, 2000; Yeates *et al.*, 1997; 2001) has been documenting very significant implications for childhood brain injury rehabilitation. These studies are establishing the critical importance of family integrity for recovery from traumatic brain injury in children. More specifically, reduced family chaos, effective communication among parents and children, and the absence of psychological adjustment disturbances are clearly associated with more effective recovery from brain injury, not only within the psychosocial realm, but also the neurologic and neuropsychological arenas. These effects do not appear to be entirely dependent upon access to rehabilitation services. Using these pioneering assessment findings as a foundation, Wade and colleagues (Wade *et al.*, 2005a; 2005b) have developed a very original and innovative family-oriented rehabilitation program that is Internet based. Thus, treatment is available to individuals who live in rural areas or have difficulty in reliably attending treatment sessions at the hospital. The Internet web-based site allows parents to access treatment interventions at their convenience, and the approach is strongly focused toward improved family functioning. Access to inexpensive treatment services is an

obvious and ingenious response to the fact that insurance companies are not funding pediatric brain injury rehabilitation outpatient services at a growing rate, and this trend is unlikely to change in the near future.

With all pediatric brain injury rehabilitation interventions, the importance of homework exercises which are connected to actual remediation activities is critical. In this respect, therapists in this field need to stay current with resources not directly academically based, but still educationally relevant, and not necessarily produced by rehabilitation professionals. Examples of these resources include the *Are they thinking* manual (Rasmussen & Rasmussen, 1996). This book has numerous exercises designed to improve problem-solving, visual–spatial awareness, and visual–motor integration processes. Another resource is the *Think good–feel good* workbook assembled by Stallard (Stallard, 2002). This is a text directed toward assisting children and adolescents in acquiring cognitive–behavioral skills. The exercises also involve identifying affect and emotion, and promote learning in how to cope with adjustment disturbances and life challenges.

The international rehabilitation community has been increasing their attention toward cognitive remediation with children who suffer acquired brain injuries. While positive findings exist, it has been suggested that there is no definitive evidence for the efficacy of cognitive rehabilitation with pediatric patients who have suffered a CNS insult (Limond & Leeke, 2005). This is primarily due to very few Phase III clinical trials on rehabilitation programs, not only with children, but also with adults. This lack of research is changing. A randomized clinical trial directed toward a remediation program compared to a control condition was recently conducted, and the results were reflective of significant improvement in the treatment group on a number of neuropsychological tests of attention and memory (Hooft *et al.*, 2005). While the sample size of this study was modest ($n = 38$), it represents the beginnings of definitive scientific efforts to identify and document effective rehabilitation treatments and techniques. Unfortunately, no measures of treatment generalization were obtained. A much larger randomized controlled trial was recently conducted in Brazil (Braga, Da Paz & Ylvisaker, 2005). The study compared clinician delivered family support interventions, and both groups received intensive services for one year. Thus, this rehabilitation intervention required a level of involvement that would make it difficult to apply on a clinical basis due to expense and treatment compliance. The study describes a very ambitious family-based intervention which involved family members meeting with rehabilitation specialists on a daily basis, interdisciplinary assessments of the child who had suffered a brain injury, group parental meetings and family training sessions, and visits to the patient's home by rehabilitation specialists. Physical and cognitive outcome variables

improved in the family supported intervention group at a statistical and, apparently, clinical level. Other countries have also been expanding efforts to meet the needs of the pediatric brain injury community (Gillett, 2004; O'Flaherty, 2004). The overall outlook is extremely positive and optimistic, as the childhood brain injury rehabilitation literature is clearly growing on an international level. Mitigating this enthusiasm is the need to account for culturally specific treatment approaches. Additionally, interventions which are not reasonably brief may not be feasible to implement.

The cognitive remediation program (CRP)

Two significant collaborators and I (Butler & Copeland, 2002; Butler & Mulhern, 2005) have developed a neurocognitive rehabilitation program which was designed to be not only programmatic, but also individualized. It is important to also recognize the contributions of other colleagues, post-doctoral fellows and students, who are, unfortunately, too numerous to name. Treatment length was based on generally recommended rehabilitation schedules, that are typically in the three to six month range. Therapy was programmatic in that traditional brain injury rehabilitation techniques were used, as identified earlier, and described by professionals in the adult disciplines of brain injury rehabilitation (Prigatano, 1999; Sohlberg & Mateer, 2001).

Recognizing the need for both a necessary structure with clearly identified goals regarding brain injury rehabilitation, in addition to individually implementing exercises/interventions that would include memory improvement, attentional advancement, and also self-awareness and motivation, the cognitive remediation program (CRP), was developed based on a tripartite model.

Firstly, brain injury rehabilitation techniques were used, and largely based on the methods developed by Sohlberg and Mateer (2001). Secondly, metacognitive strategies were introduced, based on work from researchers in educational psychology and special education. Thirdly, clinical psychological techniques were also introduced into the intervention plan, largely based on the seminal writings of Meichenbaum (1977), in addition to the research of Kendall (1991). The Butler, Copeland and Mulhern approach has been specifically directed towards pediatric patients who are of school age. Thus, techniques were developed designed to be appropriate to both children and adolescents. Our methods have been described previously in considerable detail (Butler & Copeland, 2002; Butler & Mulhern, 2005). The therapeutic approach is individual, and a team format is advocated. The team includes not only the therapist and participant, but also the parents, school personnel, and other relevant

individuals. Specific strategies are taught, and the participant is expected to not only memorize the metacognitive strategies, but also understand how, why, and when they are to be used. The parents are responsible for reinforcing strategy use, not only in the home, but also in interacting and working with teachers to further emphasize the generalization of strategy application. Our approach is strongly directed towards applying treatment results outside of the clinic environment, and the ultimate goal is not only to improve cognitive functioning in therapy sessions, but also to promote treatment advances to the home and school environment. We believe that this is critical in regard to childhood brain injury rehabilitation.

The CRP is programmatic in that all participants and patients are expected to have achieved individual goals at certain time periods over the course of the 20-week therapeutic sessions. However, therapy, as identified earlier, was also designed to be individualized. More specifically, whatever issues that might present, perhaps, organizational problems or temper tantrums, were clearly viewed as ''grist'' for the treatment ''mill''. While this approach has been criticized from a scientific methodological standpoint, it was also lauded as a clinical innovation based on an NIH study section review. We continue to advocate for a combination of programmatic and individualized treatment for our patients.

In the spirit of individualized treatment, a 60–80% treatment guideline is followed, in that cognitive remediation activities are administered to individuals so as to be challenging, but not associated with excessive failure. Thus, activities are administered at a level of difficulty during which children and adolescents achieve at least 60% success, and once 80% success is reached, the next level of difficulty is promoted. A cognitive–behavioral therapy orientation is advocated, and each child/adolescent is encouraged to become their own ''best coach'' as opposed to their own ''worst enemy''. This becomes particularly relevant with children who endure a significant length of time in which they suffer and fail in school. The techniques are designed to counteract an associated self-failure mentality, and promote communication with teachers and parents, in order to foster a positive teaching approach that encourages success.

Metacognitive strategies in the CRP are divided into three general approaches: (1) Task preparation, (2) On-task performance, and (3) Post-task behavior. Table 20.1 summarizes examples of various metacognitive strategies that are commonly taught to individuals in our CRP. By mid-therapy, the approach expects that the individual will have incorporated, depending upon his/her level of functioning and age, at least 7 to 20 specific strategies. While a number of strategies that appear effective and relevant for most students have been identified, therapists are also encouraged to individually develop strategies by observing the patient's progress. With most children/adolescents, it is reasonably easy to

Table 20.1. CRP metacognitive strategies

I. Task preparation strategies	Description
1. Magic/special words	This strategy is designed to help the individual become motivated. Children/adolescents are encouraged to pick one or two word cues to stimulate maximal effort.
2. Soup breath	This is a very brief relaxation exercise which can be helpful in preparing the patient to do their very best work. It is an exercise that is very relaxing, and it should also be prescribed as homework.
3. Game face	This is best used as a sports analogy. Describe the concept of a 'game face' to the patient in terms of looking like they will produce his/her best performance.
4. World record	The world record strategy is used to encourage the child to perform at his/her highest level. When using this strategy it can be helpful to encourage the child to keep a personal record of his/her own performances.
5. Warm up my brain	The child should be taught about brain function at an age appropriate level. The important idea to convey is that his/her brain is activated during a cognitive task. This is a strategy that is very conducive to the use of visual imagery.
II. On-task strategies	**Description**
1. Talk to myself	This is a cognitive–behavioral-oriented strategy that should be used to have the child use both self-encouraging and self-alerting internal dialogues. The patients should continually remind themselves what they are supposed to be doing. This strategy serves not only as a self-monitoring function, but also as a self-alerting process.
2. Mark my place	Frequently children will lose their place when working with complex visual arrays. If this is the case, the patient can be taught to make small tick marks at the end or beginning of each row in order not to lose his/her place.
3. Start at the top, one row at a time	This is another strategy that is used with visual–spatial stimulus materials. The child may need to be specifically taught to start in the top left corner, and complete the task in a systematic, one row at a time fashion.

Table 20.1. (*cont.*)

II. On-task strategies	Description
4. Look for shortcuts	The child should be taught to analyze a problem or task and determine the most effective way that it can be completed. The patient should also be encouraged to use the 'look for a shortcut' strategy in his/her everyday life.
5. Time out/start over	The child should be encouraged to self-monitor and be aware when he/she is making errors. If a task becomes confusing or the patient begins to become 'lost', he/she should learn how to ask the therapist, and then parents and teachers to please stop, take a brief rest break, and start over again.
6. Look at the floor	Many children engage in self-distracting behavior. With these children it can be very helpful to teach them to stare at a blank surface, or directly at the instructor's face so as not to become distracted.
7. Ask for a hint	If the child is struggling, they should be taught how to ask for assistance. Many children simply continue to flounder rather than request help.
III. Post talk strategies	**Description**
1. Check your work	The importance of this time-honored procedure cannot be overemphasized. All children with attentional impairment need to check their own work, and the eventual goal of this strategy is for it to be completely internalized.
2. Ask for feedback	The child should be encouraged to ask the therapist, and then parents and teachers about his/her level of performance, and if there is anything that they could be doing to improve their performance.
3. Reward yourself	This is a most important strategy. The child should always reward him/herself for effort.

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incorporate the names of the strategies into his/her cognitive repertoire, particularly if this is done in a "bullet" fashion. By "bullet" fashion, attempts to identify the strategies by two to three words in order to assist in memory encoding are enforced. What is more difficult, and critical to treatment effectiveness, is teaching the children why they are using the strategy, how the strategy is

to be used, when the strategy should be applied, and the overall purpose of the metacognitive strategy. This is a clear challenge to cognitive remediation with children/adolescents, especially those who are younger, lower-functioning, and have significant memory and learning problems. With younger and lower-functioning patients, we will often schedule treatment sessions that occur at two to three week intervals, and instruct parents to work closely with their child in order to assist with skill acquisition. Effective strategy incorporation in accord with the above parameters appears critical for cognitive rehabilitation.

We have recently concluded a Phase III randomized clinical trial designed to test the effectiveness of the CRP. As of the publication of this book chapter, these results have been submitted for publication in a peer reviewed manuscript (Butler *et al.*, In review). To summarize, the CRP does appear to be associated with beneficial effects in children who have an attentional deficit associated with childhood cancer. The CRP may also be relevant to children who have other brain injuries, such as that described with a traumatic brain injury, or other CNS insults. In accord with the results of brain injury rehabilitation clinical trials, the obtained effect sizes are positive, but modest. This is the rule rather than the exception. Treatment efforts were associated with statistically significant increases in academic functioning, parental self-report of attentional abilities in their children, and also teacher self-report on improvements in attention in the classroom. While there were no statistically based group differences when CRP versus wait list control comparisons were conducted on the global neuropsychological indices, directionality was consistently as predicted, and there was clear evidence of generalization to everyday, real-world functioning. These results are very encouraging.

Our orientation to rehabilitation research is to use additive strategies. More specifically, the difficult nature of this work dictates that one needs to continually amplify therapeutic methodology, as opposed to the traditional dismantling techniques that are used in psychotherapeutic research. While cognitive rehabilitation is an exciting and daunting endeavor, progress can be expected to be limited and slow, because of the complex nature of brain function, and this is particularly true for children and adolescents.

Future directions

Much work remains to be conducted in order to improve brain injury rehabilitation programs, and there is evidence of new directions that are exciting. Clinical researchers have been implementing increasingly innovative methods, such as teaching classroom educators brain injury rehabilitation methods. Therapeutic exercises specifically designed for young children have

been produced. Functional brain imaging is being used as a dependent variable for treatment success. Family interventions hold much promise in the childhood brain injury rehabilitation field. The important point is that continued strivings need to be exerted towards improving our methodology in brain injury rehabilitation. Greater communication is needed to promote the integration of advances in the cognitive neurosciences with clinical interventions. Of paramount importance is the paltry number of Phase III clinical trials directed towards proving the efficacy of brain injury rehabilitation methods, and the paucity of programmatic therapeutic models that can be readily incorporated by various institutions.

In support of the need to move from the "bench to the bedside", the National Institutes of Health have recently dedicated funds to support the development and ongoing accomplishments of major clinical research centers which specifically integrate the work of basic scientists with clinical researchers. This is a reasonably dramatic addition to funding policies which have typically resulted in the separation of cognitive neurosciences from clinical trials of brain injury rehabilitation. It is hoped that the funding of these centers will promote more effective neuropsychological assessment methods, in addition to greater treatment gains from remediation interventions. The NIH recently sponsored a brain injury rehabilitation symposium which took place in the fall of 2004 (National Institute of Neurological Disorders and Stroke, Department of Health and Human Services, & National Institutes of Health, 2004). This two-day symposium brought together researchers from the areas of stroke, brain tumors, and traumatic brain injury. Working sessions were held, and each of the three committees presented the current state of the art in their own field, along with recommendations for the manner in which rehabilitation should progress. A review panel then critiqued all three presentations. It is obvious that the NIH is committed towards efforts in brain injury rehabilitation, and is aware that children and adolescents are being underserved. Thus, clear progress is occurring in this field.

Research from the traumatic brain injury population is documenting that family integrity is an extremely important variable that impacts the child/adolescent's recovery. Structured family interventions outside the brain injury rehabilitation field should be evaluated for relevance. Kazak (2005) has been developing brief, family-based interventions directed toward improving psychological adjustment in children who were newly diagnosed, as well as with long-term survivors. These interventions are designed to improve psychosocial adjustment and family integrity. Preliminary research is supportive of a methodology involving weekend group sessions which are brief and intensive. Treatments such as this may be very important and effective supplements to

current cognitive rehabilitation efforts with children/adolescents. The relevance of the family, particularly the parents, as interfaces between brain injury rehabilitation professionals and educational/school professionals cannot be overemphasized. Within the pediatric/adolescent population, an emphasis needs to be applied to parental interventions, not simply therapy, but instruction in problem-solving skills, particularly in regards to navigating the increasingly complex educational environment. The effectiveness of a brief, six- to eight-session intervention designed to decrease negative affectivity and stress in mothers of newly diagnosed children with cancer has recently been established (Sahler *et al.*, 2005). This intervention involves a skills acquisition approach directed toward teaching parents the steps of superior, efficient, and advanced problem-solving skills. The treatment also has a cognitive–behavioral component, and encourages an optimistic approach to problem-solving. Teaching not only the parents of a child/adolescent with brain damage, but also the patient him/herself these steps may prove to be of therapeutic efficacy. This approach should be directed toward effective interactions with not only rehabilitation professionals, but also experts in the educational environment.

Increased efforts should be applied to pharmacological interventions. Cost-effective, beneficial medication regimens, perhaps combined with briefer rehabilitation therapies may provide an acceptable balance for the average family. Studies investigating the potential effective effects of methylphenidate (MPH) on cognitive functioning in children who had undergone treatment for a brain tumor have recently been summarized (Butler & Mulhern, 2005). It is becoming apparent that stimulant medications may be appropriate for children with a brain injury. Research has begun to demonstrate that stimulant medication can improve attentional functioning in those who have received a CNS insult. Results indicate that the necessary dose for effective treatment is typically lower than that used with patients with ADHD; however, individuals with a cancer-based brain injury appear to manifest a greater number of side effects. Studies on MPH in the traumatic brain injury populations do not document this increased vulnerability to adverse effects (Jin & Schachar, 2004). The medication appears to be particularly helpful with behavior abnormalities following a head injury rather than cognitive functions. Research has been criticized, however, on the basis of relatively short drug trials.

New generations of medications designed to improve attentional functioning are being introduced, and side-effect profiles are becoming less severe and more manageable. Clinical trials with medications such as Strattera need to be conducted with pediatric patients who have CNS impairment because this drug appears to be characterized by very mild side-effects. The combination of stimulant medication with concurrent brain injury rehabilitation interventions

may result in synergistic treatment effects. Studies comparing the continued administration of stimulant medication following completion of a brain injury rehabilitation intervention versus cessation of pharmacological treatment at the end of remediation need to be instituted. Another unexplored direction at this time involves the therapeutic potential of periodic ''booster'' sessions of rehabilitation that might be as easily administered as annual clinic visits to review progress and identify continuing problems, involving only one to two treatment sessions.

Further approaches need to be developed. For example, pharmacological agents apart from the stimulant medications may be beneficial, including antidepressants and mood stabilizing drugs. Overall, the field of brain injury rehabilitation has experienced, unfortunately, some degree of stagnation, and there is clearly a need for innovative thinking.

Summary

What at times seem to be insurmountable challenges, given poor funding and difficult clinical challenges, can also be conceptualized as a ''call to action'', and a charge to professionals to raise their research methodology and treatment efforts to a new and higher level. It is distressing that fewer than a handful of Phase III clinical trials have been conducted on brain injury rehabilitation interventions for children and adolescents. On a pragmatic level, the dearth of these clinical trials is understandable given their expense, especially with the need for very large samples because of expected modest effect sizes. Nevertheless, these studies are the true test of therapy effectiveness, and their emergence in the literature must become more prominent. This is even more important for the pediatric population, which is typically underserved.

Cognitive rehabilitation with children/adolescents can be a very frustrating clinical endeavor, but this is buffered by the rewards of improved school performance, however modest; appreciative parents; the emergence of satisfaction in a patient who had begun to view school as a punishing environment; and working with teachers who further extend their already overburdened workload in order to assist an individual student. It should be remembered that school is to child/adolescent as work is to adult. Schooling is a child's/adolescent's job. Children/adolescents need to learn foundation skills to prepare themselves for university education, if appropriate, for work, and for life. The cognitive and behavioral abilities which are taught over the course of primary and secondary education are critical to the development of an individual who will be productive in society, and who will enjoy a satisfying life. Within this context, pediatric brain injury rehabilitation is one of our most pressing concerns, on not only an individual, clinical level, but also on the overall societal level.

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21

Neuropsychological rehabilitation of school-age children: an integrated team approach to individualized interventions

George P. Prigatano and Sylvie Naar-King

Acquired neurological disorders commonly result in a complex set of physical, cognitive, behavioral, and affective disturbances, which require an integrated team approach to actualize a child's rehabilitation potential (Andrews, 2005; Naar-King & Donders, 2006; Prigatano, 1999; Ylvisaker *et al.*, 2005). The need for an integrated rehabilitation team approach is most clearly seen in the acute care of children who have suffered significant brain injury, when not only cognitive deficits but also child behavioral and family dynamic issues must be considered (Michaud, Duhaime & Jaffe, 1999; Yeates et al., 1997; Wade *et al.*, 2005). Assisting and involving families and teachers in the care of these children is an important part of such rehabilitation. This chapter summarizes the literature on integrated team approaches to the management of children with special healthcare needs, and also provides a description of a pilot neuropsychological intervention program for children with traumatic brain injury (TBI), from development to implementation and evaluation.

Support for an integrated approach

A substantial body of medical literature endorses the importance of an integrated, collaborative, cross-discipline approach in the assessment and management of children with special healthcare needs. This approach is necessary because of the broad spectrum of biomedical and psychosocial problems present in this population (Drotar, 1995; Haas, Gray McConnell, 1992). In addition to being consistent with family-centered care, interdisciplinary team approaches also allow for the integration of medical and psychological services. A substantial body of literature endorses the importance of integrating medical and psychological services, as opposed to behavioral health "carve outs," in the assessment and management of children with special healthcare needs (Drotar, 1995; Haas, Gray & McConnell, 1992; Walders & Drotar, 1999). Walders and Drotar (1999) define

integration as "a continuum of the extent to which mental health services are interwoven into the medical management of a child's chronic illness" (p. 119). The most integrated services offer health and mental health services at the same time and in the same setting. As opposed to a consultative model where the physician must identify a concern and ask for psychological assistance, in an integrated model the psychologist is a member of the team and is responsible for identifying concerns and intervening.

There are several advantages of the integration of services that in an interdisciplinary team approach. Concerns may be identified before they become diagnosable disorders. Brief interventions within the clinic setting may alleviate these subclinical concerns. The model allows for access to mental health services by families who either would not normally have coverage for such services or who would not normally seek out such services. The mental health provider is able to form a rapport with families over time, and the integration of services within the medical setting may increase acceptability and decrease the stigma associated with mental health care. Despite the hypothesized benefits of an integrated model of service delivery; there is a paucity of systematic assessment of integrated models of service delivery.

A few studies have documented the effects of collaborative approaches on satisfaction with services, parent outcomes, and child outcomes (see King *et al.*, 2004 for a review). Naar-King, Siegel, and Smyth (2000) documented parent, child, and provider satisfaction with an interdisciplinary, family-centered care program for children receiving specialty care for a wide range of chronic conditions. Responses were compared to an a priori defined minimum standard of 80 % satisfaction. More than 80% of parents were satisfied with care. Even though collaborative team approaches may take up more time in clinic than do traditional services, families felt that the time involved was worthwhile. However, child satisfaction approached but did not meet criterion, suggesting that collaborative programs must not only focus on parents but must also help children to feel included in decision-making. Staff satisfaction met the 80% criterion for quality of care and for components of the interdisciplinary team approach, but staff members were less satisfied with training, a potential barrier to implementing collaborative interdisciplinary approaches.

Williams and colleagues (1995) found that the best predictors of parent satisfaction with epilepsy clinic services were parents' experience of staff attitudes as positive and the amount of information which they received about the condition. Other studies have confirmed that components of collaborative interdisciplinary team approaches, particularly parent perceptions of supportive and collaborative communication with providers, are associated with increased

satisfaction with services (Carrigan, Rodger & Copley, 2001; DeChillo, Koren & Schultze, 1994). Studies have consistently found that parents are more satisfied when they feel that they are part of the team (King *et al.*, 1999; King, Rosenbaum & King, 1996).

There are a few controlled studies of the effect of interdisciplinary approaches on child outcomes. Stein and Jessop (1984) compared children with chronic conditions who received a home-based, interdisciplinary, family-centered program with children receiving standard hospital care. The intervention group not only showed higher satisfaction with care, but higher levels of child and parent psychological adjustment. Even stronger support for the program was demonstrated by a dose-response effect and long-term follow-up. Families who were in the program for the longest period of time had the best outcomes. Data from a 4–5 year follow-up showed even greater differences between the intervention and the control condition (Stein & Jessop, 1991).

Naar-King *et al.* (2003) compared families who attended interdisciplinary clinics with families attending clinics that followed a traditional model in the same hospital setting. Children had a wide range of chronic conditions. There were no differences between groups on demographic variables or health status. Children in the interdisciplinary clinics had significantly fewer behavioral symptoms than children attending traditional clinics. Significantly fewer children from the interdisciplinary clinics were in the clinical range for poor school functioning compared to children in non-integrated clinics.

A recent randomized control study has argued that well-trained families may provide equal if not better care than a traditional clinic-based approach to children with brain injuries (Braga, da Paz Júnior & Ylvisaker, 2005). A careful reading of this study and a supporting document (Braga & da Paz Júnior, 2005), however, reveals that parents were well trained by an interdisciplinary team to work on a child's cognitive, physical, and emotional difficulties within the context of a family environment. Thus, an interdisciplinary influence was present, even though the context of the therapy was family-centered.

In summary, there is some evidence to suggest that collaborative approaches where care is family-centered and integrated, are associated with greater parent satisfaction and improved child psychosocial outcomes. Further studies are warranted assessing the effects of these approaches on illness management (i.e. adherence to treatment recommendations as well as parents' efficacy to manage at home) and on healthcare utilization (i.e. hospitalizations and emergency department visits). These data are necessary to advocate to third-party payers and companies who purchase insurance for the integration of psychological services into the healthcare of children with chronic and handicapping conditions.

A summer neuropsychological rehabilitation program for school-age children with TBI

A ''pilot'' summer neuropsychological rehabilitation program for school-age children (NRP-C) with TBI was conducted in 1999. The program was staffed by two clinical neuropsychologists, one resident in clinical neuropsychology, a school psychologist seeking specialized training in neuropsychology, a special education teacher, and an occupational therapist. Only the special education teacher was employed full-time in this program. The other personnel had additional responsibilities during the course of a ''clinical'' day, but ''carved out'' time to provide services within the context of the NRP-C program (usually —three to four hours a day for each staff member). The treatment program existed for six weeks.

In this pilot program, six (6) children were identified and agreed to participate. Only four (4) were able to sustain involvement throughout the summer program. It was difficult for some families to commit to such a treatment regime. Two of the four children had Glasgow Coma Scores between 3 and 8. For the other two children, GCS scores were not available, but they had evidence of residual hemiparesis and/or space-occupying brain lesions. Children were between ages 6 and 11 years and were at least six months post-injury.

Staff members met each morning to review progress of the previous day and to prepare for the coming day. Each child received individualized cognitive rehabilitation aimed at improving learning, working memory, and speed of information processing. These children often required a ''rest break'' from such work and a snack was provided. Children were also engaged in a social skills training group. This was conducted by one neuropsychologist and a teacher. The goal was to have the child carry out educational and/or cognitive tasks while attempting to be cooperative with their peers.

This was followed by individual academic training which focused on the child's specific strengths and weaknesses. All therapists (except the occupational therapist) participated in this activity. This was followed by a small, brief special education classroom experience. The aim was to improve the child's capacity to work with others on various educational tasks. It simulated a classroom environment. This was conducted by two neuropsychologists and one teacher.

After this activity, lunch followed. Children then were involved in physical activities that focused on athletic skill and social interaction. This was conducted by the occupational therapist. The goal was to improve motor skills within the context of cooperation and normal competition that children experience when interacting with one another. After this event (which occurred at another location on our campus), the children walked back to the rehabilitation environment with the occupational therapist. They then prepared to think about what occurred

Table 21.1. Essential ingredients of a children's neuropsychological rehabilitation program

Establish a protective learning environment (and milieu).
Teach academic skills to the child (with an understanding of their underlying cognitive deficits).
Teach cooperative behavior without losing the child's individuality (with an understanding of the personality and behavioral disturbances that are present).
Teach the child to establish and maintain friendships.
Teach the child appropriate athletic skills (to improve motor development and social competency).
Teach the teacher to teach the child (and reduce their distress).
Teach the parent to parent the child (to reduce their distress).
Manage the rehabilitation staff's reactions to the child and parent.
While many of the above activities include psychotherapeutic interventions, formal psychotherapy may be needed for different children and their parents when the indirect symptoms preclude full involvement in the rehabilitation process.

throughout the day. This was done by the occupational therapist and a neuropsychologist. The children then participated in a child's version of milieu therapy (see Prigatano, 1999). The children were asked to reflect on the day's activities and their behavior. The child was reinforced for behaviors that were considered to be adaptive. The child was encouraged to think about what needed to be improved on the following day.

Starting at the third week of rehabilitation, parents met with the treatment team regularly. There were also discussions with the teachers, when possible. Efforts were made to share information concerning the child's functioning, both at home and within the rehabilitation environment. Parents often report their need for such information (Aitken *et al.*, 2005). In addition, extensive neuropsychological reports were prepared that could be utilized by both teachers and parents. The neuropsychological/educational reports were written in conjunction with the special educator. Table 21.1 lists the "essential ingredients" which formed the approach to this Summer NRP-C Program.

What was learned and why was a team approach necessary?

This sample of children who had a history of moderate to severe TBI, showed unequivocal difficulties in speed of information processing, working memory, and inefficiency in new learning. They had difficulties with social judgment and therefore, difficulties knowing how to interact with one another. Three of the four children had considerable difficulty engaging in the various tasks involved in the day treatment program. Two of the children had evidence of pre-existing

psychiatric problems. Our experience taught us that larger numbers of children with noncompliant or belligerent behaviors are difficult to manage within the context of this kind of program.

Multiple professional views were needed as to how to best approach a child over their given educational/retraining tasks. This is a time-consuming effort, but without it therapists often did not know how to best re-approach a child's cognitive and behavioral problems. They needed support from one another in order to continue this type of work with the child. One thing we learned from this pilot project was that all team members should really be committed fully to the program: having other job responsibilities while trying to do this work produced too much fragmentation and insufficient preparation for continued interventions.

Commitment by families is equally needed. Parents typically want the "best" treatment for their child but may have difficulties (for various reasons) in making the sacrifice to consistently bring their child in, and to participate in the program. It became clear that it is important to prepare families for this commitment much earlier in the process, and also to assist them in dealing with the logistic problems in getting the child to the day treatment program.

Having a special educator as part of the treatment team proved to be crucial for the success of the program. Educators have recognized that neuropsychologists and special educators need to work together to help the TBI child in the school environment (Glang, Singer and Todis, 1997). There has not been, however, a recognition that a Summer NRP-C staffed by multiple disciplines would potentially help to prepare the child for the academic year and improve the child's performance and adaptation in the school. The impact of such a program for helping school personnel to prepare for the child has also not been recognized. This project suggests that such a program may indeed be helpful, but further empirical studies are needed to test this hypothesis.

Expected outcomes from a Summer NRP-C

An NRP-C is costly from an economic and professional time point of view. It is crucial that clinicians providing this service clarify for third-party payors, school districts, and family members, exactly what are the outcomes that are being sought. Four outcomes should be achieved. As a result of this form of treatment, the child should improve in their ability to obtain and maintain friendships. Friendships are most likely to decline after TBI (Prigatano and Gupta, in press). If a child is able to obtain a friendship and maintain it, it is indirect evidence that there is improvement in the child's social skills.

A second outcome is to improve a child's academic performance and their engagement in various academic activities. Often children with significant brain injury are placed in educational settings in which they cannot properly cope. As a consequence, they often avoid school or school activities. If a child's academic performance increases and their willingness to go to school improves, this is an important outcome finding.

The third desired outcome is to reduce parental distress when caring for these children. Parental distress is notoriously not related to the severity of initial brain injury (Hawley *et al.*, 2003), but it is related to the child's difficulties in school as well as to problems with social integration (Prigatano, 2004). A Summer NRP-C program should help families cope with their children better, and thereby reduce their distress level.

The fourth major outcome is to reduce the teachers' distress level when educating children with TBI. While not systematically studied, it is well known that teachers have their own emotional reaction to the formidable problems that brain-dysfunctional children present with. If the Summer NRP-C Program is effective, teachers should report being better prepared to educate the child during the up and coming academic year, and their distress level should also decrease. We are in the process of developing potential measures for each of these outcomes.

Concluding comments

The neuropsychological rehabilitation of school-age children with moderately severe to severe TBI is a challenging task. It clearly requires an integrated team effort in order to individualize treatment programs. This pilot project may illustrate the practical challenges when trying to build such a new program. The major challenge for future research is to provide long-term follow-up, preferably through case-controlled or randomized clinical studies, to verify the incremental and persisting benefits of these kinds of programs.

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Section IV

Future directions

22

Reflections on present and future interventions for neurodevelopmental disorders

Eileen B. Fennell

As many of the preceding authors have noted, there have been tremendous advances occurring in the field of pediatric neuropsychology over the past decades. Increasingly, the phenotypic expression of a variety of neurodevelopmental disorders is being described, whether these disorders result from genetic perturbations, adverse perinatal events, acquired brain insults or unknown etiologies (Baron, Fennell & Voeller, 1995; Goldstein & Reynolds, 1999). What the clinical discipline of pediatric neuropsychology additionally brings to our understanding of these disorders and their outcomes is a shared fundamental perspective about, and accompanying emphasis on, the interaction of neural development, medical treatments, environmental context, educational experiences, and family factors. This approach yields an elucidation of consistent and variable patterns of cognitive and emotional behaviors throughout the course of growth and development, which is crucial to our development of approaches for intervention and rehabilitation. Reliance upon, and promotion of, such a biopsychosocial model of development is the theme in this text; most clearly because this model holds the promise for future knowledge about what is needed to improve the functional outcome for affected children and their families.

Complementing a recent work focused on treating neurodevelopmental disabilities (Farmer, Donders & Warchausky, 2006), Hunter and Donders have edited this clinical text in three parts with the goal of helping practitioners and clinical researchers better identify and understand relevant empirically supported interventions for a number of congenital and acquired neuropsychological disorders affecting children and their families. To review, while the first section is focused on several fundamental issues in pediatric neuropsychological practice and intervention planning, the second section covers specific childhood onset neurodevelopmental disorders, summarizing what is known about the biological bases of these disorders, their clinical presentations, neuropsychological findings and existing intervention approaches.

The third section covers a more eclectic mix of chapters related to procedures relevant to intervention, including the consideration of pharmacological interventions for cognitive and behavioral symptoms; the use of physiological and neuroimaging technologies for diagnostic confirmation and treatment planning and monitoring; and exemplar recent school- and community-based approaches to pediatric cognitive remediation. Throughout the component chapters in each section, clear attention to the biopsychosocial interactionist model has been paid, whether the authors are discussing assessment or treatment issues. As such, each chapter makes clear that this model is the most useful guide, either when seeking to identify relevant variables which can affect or moderate assessment findings and treatment outcomes, or when seeking how to best support and remediate the impact of neurodevelopmental disorders on children and their families.

In the remaining portions of this discussion, I will highlight what I believe are the important issues and findings that emerge from the collective writings of the contributors to this volume, to in effect emphasize what are ''the take home lessons'' that the authors seek to provide. Spevack (Chapter 2) opens the second section, highlighting organizing principles of brain development and stressing that interventions for childhood disabilities cannot be, nor should be, extrapolated from adult models. She offers some common approaches to thinking about available age-relevant assessment methods and techniques which reflect a developmental approach to neuropsychological assessment of children's cognitions and behaviors. In this explication, core competencies of a pediatric neuropsycholgist are enumerated and these reinforce the central importance of clinical assessment based upon a developmental model. An important cautionary note is raised in reminding the reader that efforts to correlate brain structural changes with concomitant behavioral and cognitive development are still in their infancy. As such, Spevack's chapter sets forth the important issues necessary for considering the chapters that follow.

Sparrow (Chapter 3) focuses on the two primary goals of neuropsychological assessment: first, accurate diagnosis of the child's cognitive and behavioral status and second, treatment planning. She notes that diagnosis is a necessary but not sufficient condition to enable treatment planning. She asserts the need for involvement of the parents of an affected child in order to address their worries about their child's developmental problems, their fears about the future and the intent and limitations of treatment interventions. This emphasis on parental concerns helps to form a needed alliance between professionals and parents, which is required to facilitate cooperation in planning and compliance with the demands of intervention strategies (Yeates *et al.*, 1997). Her review

also points out the continued need for careful research that empirically demonstrates how neuropsychological assessment lends incremental validity to treatment planning. Such empirical support, however, must be able to address the potential differences in response to treatment that are related to the cultural and ethnic differences children present.

As Ries, Potter and Llorente (Chapter 4) demonstrate, acculturation, race and ethnic/cultural diversity have as major an impact on the outcome of neurodevelopmental disorders as do subject demographics (e.g. socioeconomic status). However, simply expanding the number of cultural/ethnic or racial minorities in normative samples of newly revised cognitive tests such as the Wechsler Scales will not adequately address how cultural variance, language fluency, family structures, and cultural values influence outcomes in assessment and treatment interventions for many neurodevelopmental disorders. These issues require a much greater emphasis in clinical neuropsychology research and practice, in order to more effectively support the development of effective empirically based approaches to pediatric assessment and intervention.

The final chapter in this first section highlights the fact that pediatric neuropsychologists who work with school-age children, adolescents, and young adults need to be aware of legislative changes in providing services under the IDEA-2004 and other federal legislation that affects classification for services and treatment planning for children from elementary through post-secondary education. Maedgen and Semrud-Clikeman (Chapter 5) comprehensively review the interaction of neuropsychological assessment and practice with the changing federal and state laws affecting classification for, and provision of, services to individuals with developmental disabilities. In particular, they emphasize several areas of significance for the pediatric neuropsychologist, including outlining the impact of the required assessment of ''Response to Treatment'' (RTI) as part of the determination of learning disabilities placements; the contrasts that exist between formulating ''Section 504'' plans and individualized education plans (IEPs), and their implementation; and the concept of ''average range of performance'' as it relates to learning disability determination at the post-secondary level. Here, too, the fit between neuropsychological assessment outcomes and treatment outcomes in educational interventions is strongly emphasized; as such, Maedgen and Semrud-Clikeman emphasize that there is a significant role to be played by pediatric neuropsychologist beyond just articulating how to treat reading disorders. Instead, a multiply informed approach to intervention, based on knowledge of the state and federal legislation, may become a more salient focus of clinical practice.

In Section II, the variety of childhood neurological and neuropsychiatric disorders covered is testimony to the sheer volume of information that has accumulated about both common and more rare childhood neurodevelopmental syndromes. What is striking about the eleven chapters that make up this section is the recurring theme of the need for methodologically sound empirical studies of treatment efficacies and outcomes. Whether the topic is traumatic brain injuries, childhood cancers, epilepsy, movement disorders, disorders of motor control and coordination, attentional problems, dysexecutive disorders, disorders of right hemisphere functioning, or autism spectrum disorders, each chapter discusses the available literature on interventions in these disorders, and argues that much remains to be clarified and outlined in terms of effective approaches to take. While some disorders clearly possess a wealth of data to date, there remains an overdependence on case vignettes and small sample studies of the effectiveness of intervention methodologies. Clearly, a broader approach to demonstrating efficacy is needed. Additionally, as one examines these various chapters, one cannot help but be cognizant of the imbalance between the number of studies employing pharmacological interventions as compared with behavioral treatment efforts. And even more rare are studies that employ neuropsychological variables as treatment outcome measures when examining the available modes of intervention. This situation occurs despite our awareness that IQ levels and academic achievement do not sufficiently capture the subtle changes in cognitive function which can accompany treatment intervention. Development of appropriate assessment batteries to assess for treatment intervention effects, such as those proposed for studies in treatment of childhood cancers (see discussion by Nortz, Hemme-Phillips & Ris, this volume) have the potential to allow for a finer resolution between group studies of differing treatment interventions and their efficacy.

A second emerging theme throughout this section is an increased appreciation of the need to study the role of the family in treatment compliance and efficacy. In childhood, there are two critical contexts in which children develop: the school and the family. What is needed in future studies is not simply inclusion of family demographic features but instead the development of better family functioning measures that are sensitive to cultural/ethnic variation. Similarly, understanding how differences in culture/ethnicity can affect perception of target symptoms on parent child-behavioral questionnaires and potentially impact parent investment and compliance with treatment plans is needed for methodologically sound treatment outcome studies. Ways to enhance parent involvement in their child's treatment form an area of continuing need in outcome studies, as is the need for disease-specific quality-of-life assessment. If, indeed, the goal of intervention is to enhance the affected child's adaptive outcome, then further development

of models of disease-specific functional living skills, functional social skills and community integration abilities for vocational and educational attainments might better define the specific intervention needs of a child with a disorder such as ADHD-Combined type versus a child whose attentional problems follow radiation and chemotherapeutic treatment for a brain tumor. Similarly, if, as Butler suggests (Chapter 13), cognitive rehabilitation is increasingly being shifted from outpatient Pediatric Rehabilitation Centers to the school systems, then the pediatric neuropsychologist must develop a more comprehensive working alliance with educators regarding treatment design and implementation, in order to better assist clients. Whether through patient-specific consultations, in-service educational programs for school personnel, or through the role of an advocate to the local School Administrative Board, the pediatric neuropsychologist may have to become a more active voice regarding the role of neuropsychological factors on an affected child's ability to positively benefit from traditional educational therapies.

In Section III, Owley's (Chapter 12) discussion of the critical steps needed to identify and evaluate the potential for pharmacological treatment of target symptoms; the importance of cost–benefit analysis of drug therapies; and the role medications may serve as an adjunct to social, behavioral and educational interventions in Autism Spectrum Disorders is particularly important. In my clinical practice, I see an increasing emphasis on the use of polypharmacy to treat a variety of behavioral symptoms which often accompany the neurodevelopmental disorders. At a time when financial constraints of insurance carriers leads to have limited access to psychotherapeutic and other behavioral interventions, reliance upon drug treatments alone is increasing. At the same time, the risk of adverse side-effects and drug interactions needs close monitoring in childhood disabilities to avoid misattribution of negative treatment outcomes to the characteristics of the disorder rather than to the adequacy of the treatment approach. Improving the design of drug treatment studies with children by the use of appropriate neuropsychological behavioral measures is clearly needed in future research studies.

Methodological flaws in the selection of subjects, variations in the techniques of analysis, and the absence of appropriate control groups are some of the problems that Krull, George, and Strather (Chapter 13) assert have weakened support for the use of qEEG for the effective diagnosis of clinical disorders affecting children. Problems of sensitivity and specificity abound in many qEEG studies of pediatric TBI and ADHD. While the authors assert that this is a promising technology, its application to target symptoms such as attentional problems in the extant neurotraining studies remains flawed by faulty research methodology. Future research that corrects many of these design problems may allow the promise

of electrophysiological recording and analysis for treatment interventions to be fulfilled, analogous to the large literature on the utility of biofeedback training for pain and stress-related disorders in adults.

Bigler (Chapter 14) makes a cogent argument for the ability of newer brain structural and functional imaging techniques to not only confirm findings from neuropsychological assessments but also to monitor recovery of function and the likelihood of successful interventions for various rehabilitative strategies.The case examples used to illustrate his position are compelling. However, knowing whether the newer imaging technologies alone, or in combination with such approaches as MRI, fMRI and Diffusion Tensor Imaging (DTI), will become the standard of care in the current climate of decreasing insurance support for expensive investigational techniques or traditional outpatient rehabilitation for the pediatric age group (Chapter 15), is problematic. While federal government research funding has supported development of these methodologies for clinical applications in rehabilitation (e.g. Constrained Movement Therapy) as well as supported the acquisition of normative imaging data on brain development in children, translation from research applications to standard of care for monitoring treatment outcome is still in its formative stages. There is also only limited federal support for Phase III clinical trials of rehabilitation programs for children and adults. Even studies that examine the effectiveness of specialized Pediatric Trauma Centers vs. General Trauma Centers typically utilize survival as a primary outcome indicator, rather than reduction of neuropsychological sequelae. This would suggest that pediatric neuropsychologists may need to take an active role in the development of policies for research support, educational programs, and healthcare services at state and federal levels to enhance opportunities for the continued research with and service to children with neurodevelopmental disorders.

A final issue relates to the adequate preparation of the pediatric neuropsychologist for future practice and research. As the future emphasis on empirically supported outcome studies expands, involving both educational remediation, and or family- or community-based interventions, graduate and post-doctoral training in pediatric neuropsychology need to respond to these changes. For example, coursework and practical experience in the application of well supported behavior therapies for children and adolescents, including methods such as experimental analysis of behavior (EAB) and parent−child interaction training (Hersen, 2006) should be provided. Experiences in pediatric rehabilitation settings that promote appreciation of a multidisciplinary model of treatment and transition planning should be offered. Coursework in the application of federal and state legislation governing the classification and accommodation requirements for educational and vocational/workplace settings

for individuals with developmental disabilities should be required for doctoral and post-doctoral subspecialty training. Similarly, recognition that clinical and research training in neurodevelopmental disorders is needed, beyond the current emphasis which exists on learning disabilities and other childhood behavioral disorders, is crucial to the further development of methodologically sound and empirically tested neuropsychologically based interventions for the myriad of child neurological and neurobehavioral disorders that affect the processes of normal development.

This volume, while providing the reader with comprehensive reviews of many disorders and preliminary data on existing interventions, clearly demonstrates that although there are many limitations of current research on intervention with neurodevelopmental disabilities, the likelihood of improved research designs and innovative intervention approaches promise to accelerate the very real possibilities of the future.

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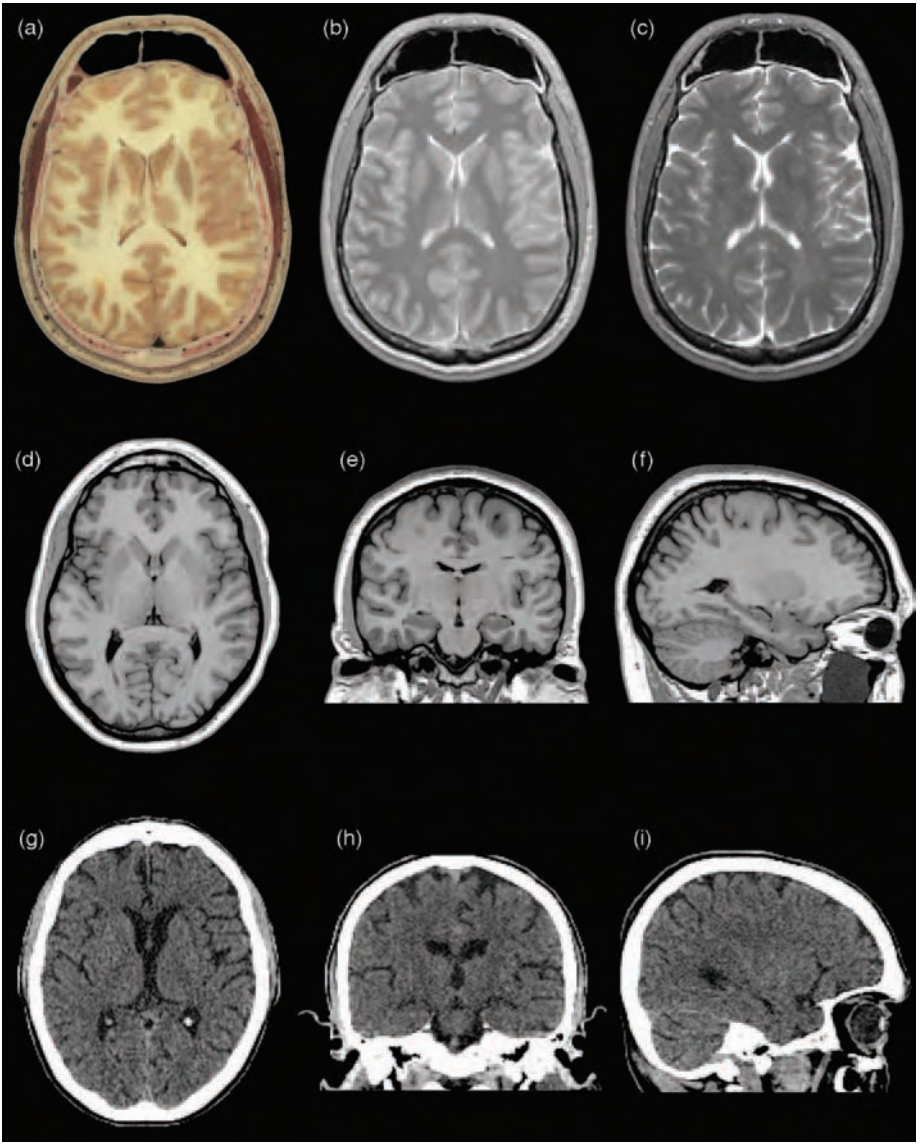

Figure 19.1 The top left axial cut (a) was performed at post-mortem, to compare to the pre-mortem imaging done at precisely the same level in (b) (a mixed weighted image) and (c) (a T2 weighted image). From a different individual, the middle row are all T1 weighted images in different planes: axial (d), coronal (e); and sagittal (f); Also, from a different individual, the bottom row depicts axial (g), coronal (h); and sagittal (i) images from CT scans. Note the differences in tissue differentiation between MRI and CT imaging, but that both provide good approximation of the actual brain as shown in (a).

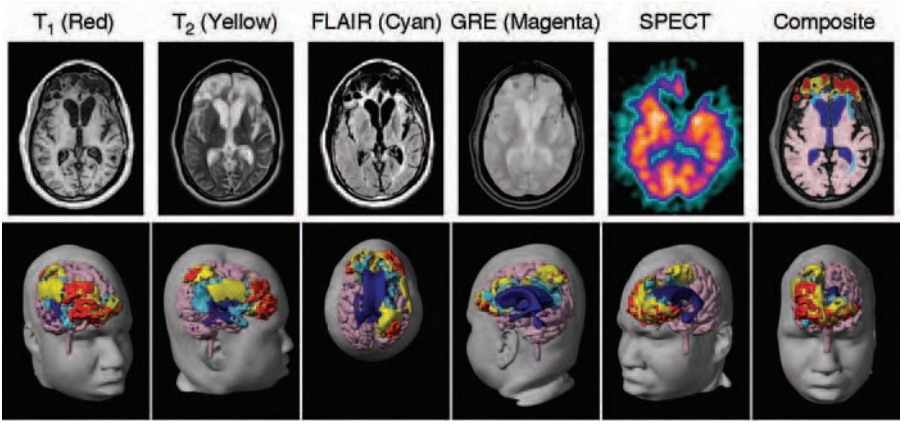

Figure 19.2 This teenager sustained a severe traumatic brain injury (TBI); initial Glasgow Coma Scale (GCS) = 3, with resultant extensive damage. This illustration demonstrates the different sensitivities of various magnetic resonance imaging (MRI) weightings where each weighting is identified by a color. For example, the abnormalities shown in the T1 weighted MRI are highlighted in red. T2 weighted images are more sensitive to cerebral spinal fluid (CSF) changes whereas the fluid attenuated inversion recovery (FLAIR) sequence is sensitive to changes in white matter signal and the gradient recalled (GRE) sequence is particularly sensitive in detecting blood by-products, namely hemosiderin, where micro-hemorrhaging had occurred. The single photon emission computed tomography (SPECT) scan shows where functional metabolic abnormalities reside in the brain, in this case extensively involving the frontal region. The composite image on the right not only shows the integration of the different identified abnormalities, but also depicts the brain segmented into white matter (light pink), gray matter (dark pink), and cerebral spinal fluid (blue). As shown by this illustration, it is best to view pathology across a broad spectrum of imaging studies to best understand the abnormalities, their location, and how that informs the neuropsychological assessment and treatment objectives.

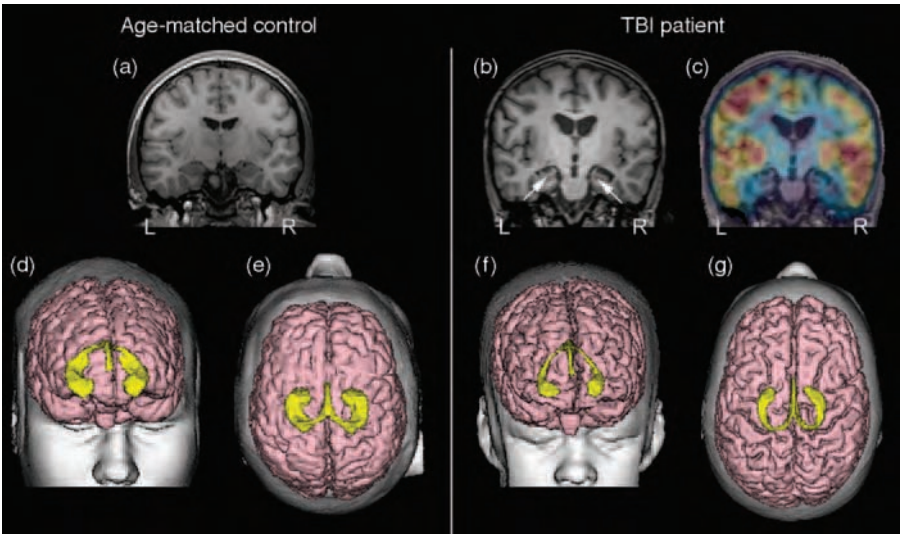

Figure 19.3 The images on the right are from an 11-year-old who sustained a severe traumatic brain injury (TBI), compounded by an anoxic injury, from a motor vehicle accident. The injury had particular effects on the medial temporal lobe, where positron emission tomography (PET) imaging demonstrated reduced activity. PET imaging has been co-registered with magnetic resonance imaging (MRI), so anatomic detail from MRI can be seen in the background of the superimposed PET scan. In PET imaging, the uptake of a radiotracer determines the level of activity of a particular brain region. In this case, the so-called 'warm colors' (orange to red) demonstrate normal activity whereas the 'cool colors' (purple to blue) in the medial temporal lobe regions bilaterally depicts less than normal activity. This child also had very significant hippocampal atrophy (arrows in b point to hippocampus – compare to similar level and normal appearance of the hippocampus in a), where quantitatively hippocampal volume was determined to be 35% of normal. In comparison to the age-matched control, this loss in hippocampal volume can be visibly determined as well. Note also, the brain injury resulted in some generalized volume loss with prominence of the lateral ventricles and cortical sulci.

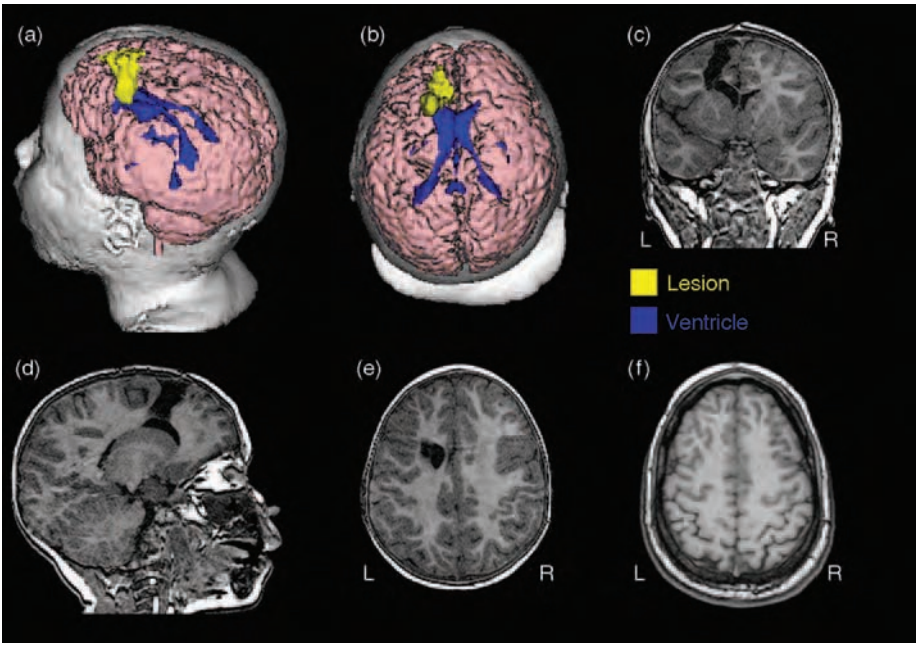

Figure 19.4 As an infant, this child sustained a severe penetrating injury to the left frontal lobe, which is obvious in viewing the T1 weighted images in c to e. Figure f is from an age-matched control child who has typical development with no history of injury. The 3-D perspectives shown in a and b, from the posterior left oblique and dorsally, respectively, show the lesion in yellow and the ventricular system in blue. Note the dilation of the lateral ventricle, in particular, the left anterior horn into the parenchymal space vacated by the lesion. This case also demonstrates an important principle in understanding the neuropsychological consequences of such an injury. Even though the damage is focal and restricted to the left frontal lobe, the left hemisphere damage goes far beyond the focal changes. For example, comparing the white matter and size of the left hemisphere in e to that of the right hemisphere, the size and amount of white matter in the left hemisphere is clearly less than the right. This is also appreciated in the coronal image shown in c.

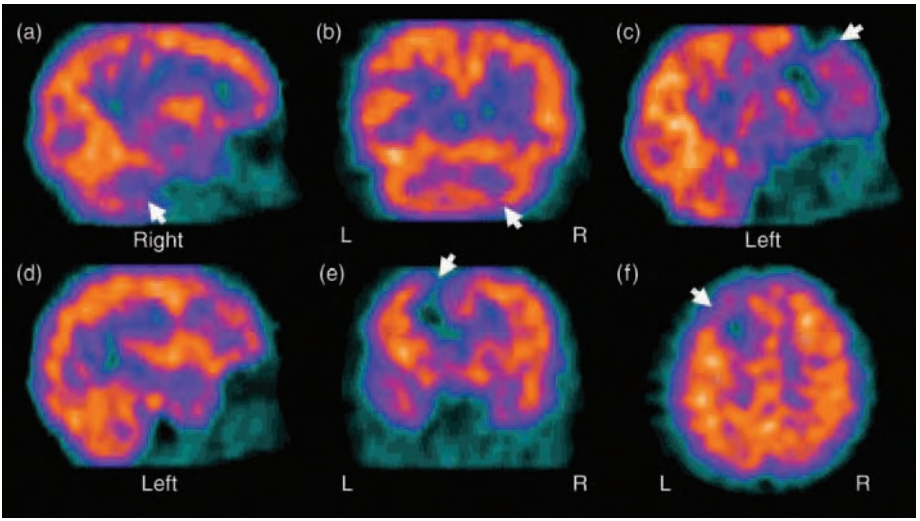

Figure 19.5 Single photon emission computed tomography (SPECT) imaging done the same day as the magnetic resonance imaging (MRI) in the child and case presented in Figure 19.4. The so-called 'warm colors' (orange and red) depict areas of normal radiotracer perfusion, whereas 'cool colors' (blues to purple) show areas of decreased perfusion. Although the focal lesion is in the left frontal lobe, clearly demonstrated by absent activity where the focal, tubular lesion occurred (arrows in c, e, and f), a form of diaschisis occurs where the crossed frontocerebellar pathways are disrupted, resulting in a lowering of activity (arrow in a) in the contralateral cerebellar lobe from the loss of input from the left frontal region. Comparing the right and left sagittal views it is obvious that there is unequal perfusion in the cerebellum, with reduced activity seen on the right. Note also the extensive lowered perfusion in the left frontal region anterior to the lesion (arrow in c) even though as shown in Figure 19.4d, this region has normal signal on T1 weighted MRI.

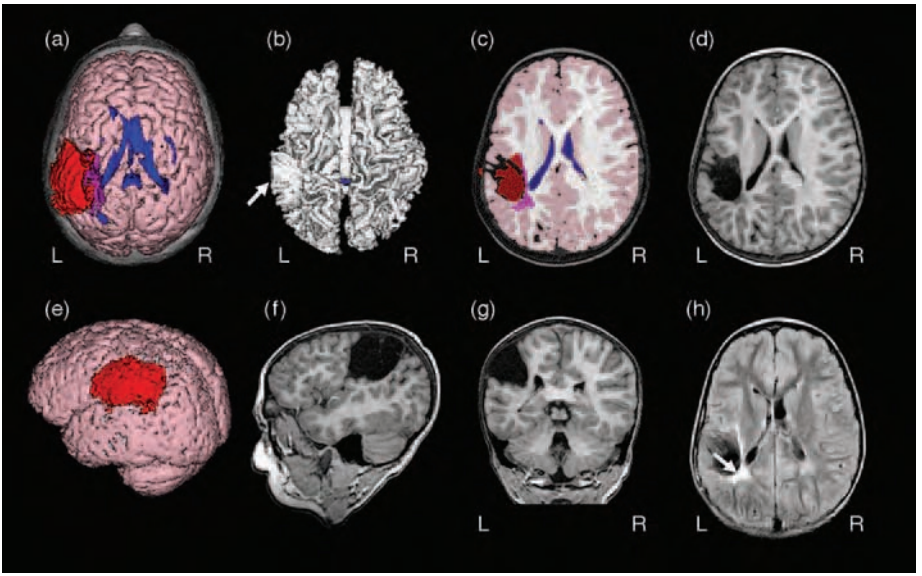

Figure 19.6 This child sustained a focal birth-related injury to the left superior and posterior temporal lobe and parietal cortex, traditional areas critical for language function. The extent of damage is clearly defined by the large cystic lesion that is visible. Despite the extensive damage, when the abnormality is focal like this and in the immature brain, often considerable adaptation and recovery can occur. Unlike the case in Figure 19.8, with a somewhat similar location of extensive left hemisphere damage but occurring in adolescence rather than infancy, this child in Figure 19.6 was showing relatively intact language development. Also, as compared to the child with birth-related injury, but with bilateral damage, the child shown in Figure 19.7 did not show adaptation. (a) 3-D dorsal view, (b) Cerebral white matter has been isolated, with the arrow pointing to the large region of disrupted white matter, (c) color segmented image showing color-coded white and gray matter, CSF and lesion as depicted in the T1 image shown in (d), (e) posterior oblique 3-D view showing the location of the focal lesion, (f) T1 sagittal view depicting the location of the cystic lesion, (g) T1 coronal image showing location of the cystic lesion, and (h) FLAIR sequence showing the sensitivity of this scan in detecting white matter pathology not as readily observed on the T1 scan (compare to d).

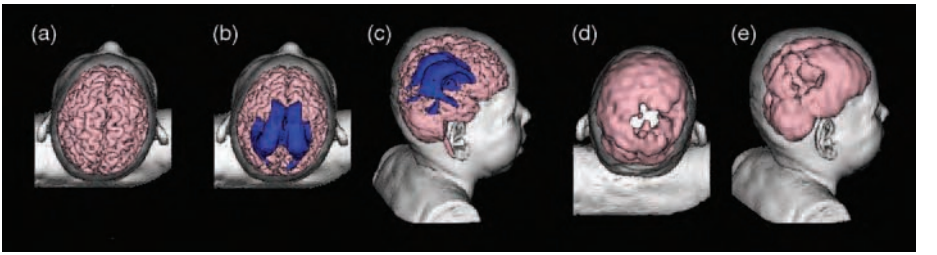

Figure 19.7 This child had hypoxic-ischemic brain injury at birth, with extensive cortical damage shown both structurally and functionally. This child's brain did not show adaptation, resulting in profound deficits at age four when the neuropsychological assessment and neuroimaging studies were performed. (a) Surface 3-D reconstruction depicting mild atrophy but otherwise more normal appearance of surface anatomy however, marked ventricular dilation is shown in (b) and (c) and SPECT imaging, rendered in 3-D surface maps demonstrate large gaps in cortical function (d and e).

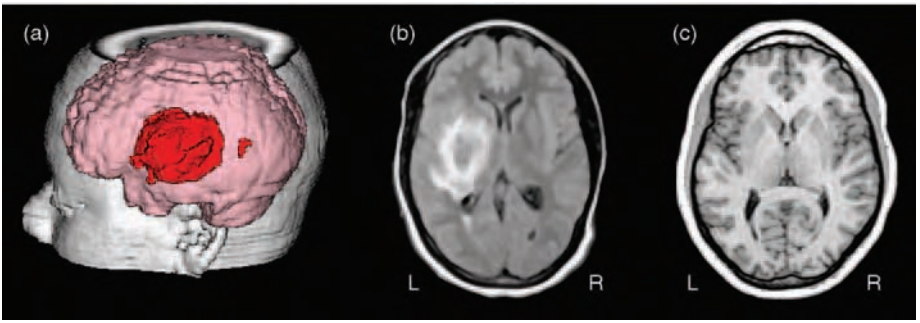

Figure 19.8 This child suffered what was thought to be a spontaneous rupture of an aneurysm involving the left middle cerebral artery. The magnetic resonance imaging (MRI) (middle panel) shows the extensive cerebrovascular accident (CVA) involving the central aspect of the left hemisphere, which when plotted in 3-D space is readily appreciated to be in traditional areas critical for language function. The right panel is an age-match normal control. Note the effacement of the ventricular system by the mass-effect of the lesion, displacing the ventricle. Note also the inflammatory reaction occurring outward from the central lesion site, where white matter in the occipital forceps is abnormal. This is distal disruption caused by the focal lesion.

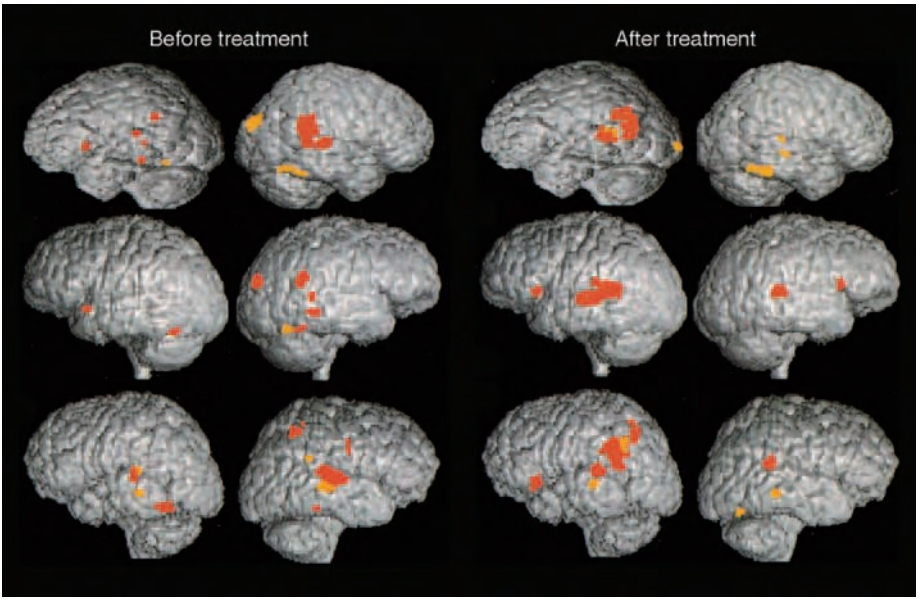

Figure 19.10 Magnetic source imaging where magnetoencephalography (MEG) activation is integrated with 3-D structural magnetic resonance imaging (MRI) is depicted in three different patients with dyslexia prior to intervention. As shown in the 'Before Treatment' column, little activation occurred in the traditional language regions of the left hemisphere. In contrast, as shown in the 'After Treatment' column, increased engagement of left hemisphere language areas occurs. This demonstrates the potential use of neuroimaging to track treatment effects. (Adapted with permission from Simos *et al*., 2002.)

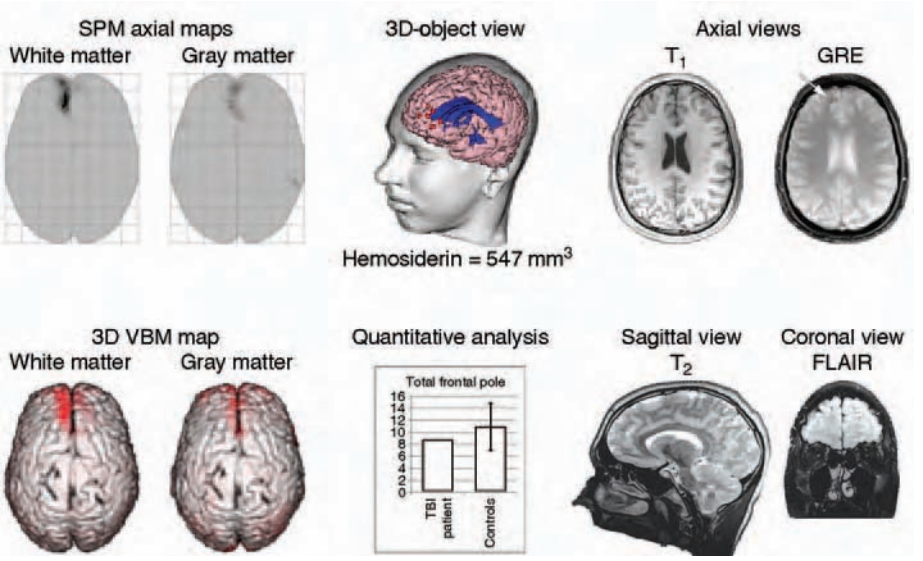

Figure 19.13 These illustrations demonstrate the utility of multiple perspectives of image analysis to best understand what effect an injury has had and also to demonstrate the voxel based morphometry (VBM) technique. The patient had sustained a significant motor vehicle accident (MVA) related brain injury and the gradient recalled (GRE) sequence clearly shows presence of hemosiderin in the frontal region on the left. The statistical parametric mapping (SPM) (upper left) clearly demonstrate differences in the intensity of white and gray matter voxels in the frontal region compared to controls and these areas are then plotted in 3-D for the VBM comparison (lower left). The frontal pole region appears slightly atrophic in the T1 axial view (upper right) and the quantitative analysis demonstrates that the frontal pole volume was, indeed, smaller than control individuals of similar age. The 3-D view shows the location of hemosiderin deposits and their total volume. These types of analyses help identify presence of significant frontal damage in a patient with traumatic brain injury (TBI).

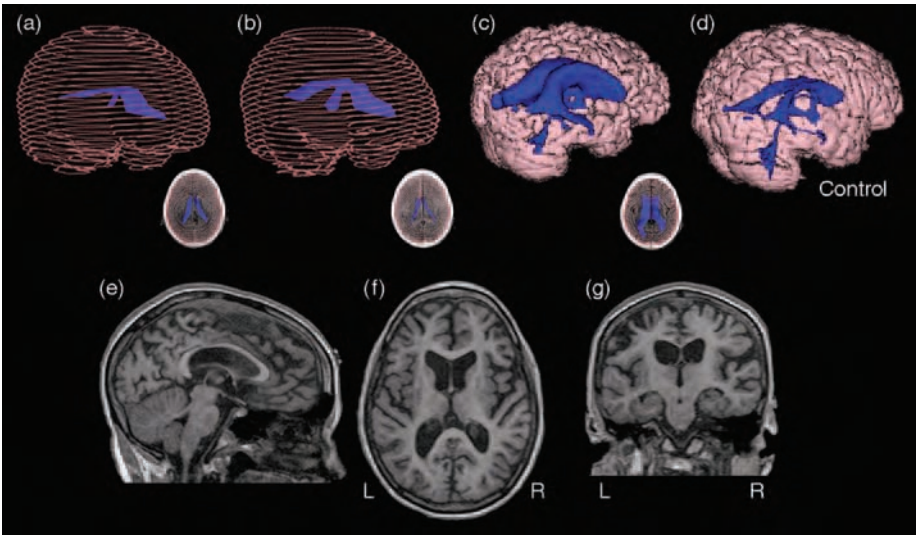

Figure 19.14 The top row depicts right posterior oblique views of the ventricular system following anoxic brain injury (ABI). (a) Day-of-injury computerized tomography (DOI CT) scan, (b) 6 days after injury, and (c) 18 months post-injury. Note the temporal horns can not be identified in a and b, presumably from generalized brain swelling that selectively compresses the temporal extension of the ventricular system. (d) A 3-D image of an age-matched control depicting normal ventricular systems. The bottom row depicts generalized atrophy in sagittal (e), axial (f) and coronal (g) planes in the follow-up magnetic resonance imaging (MRI) at 18 months post-injury.

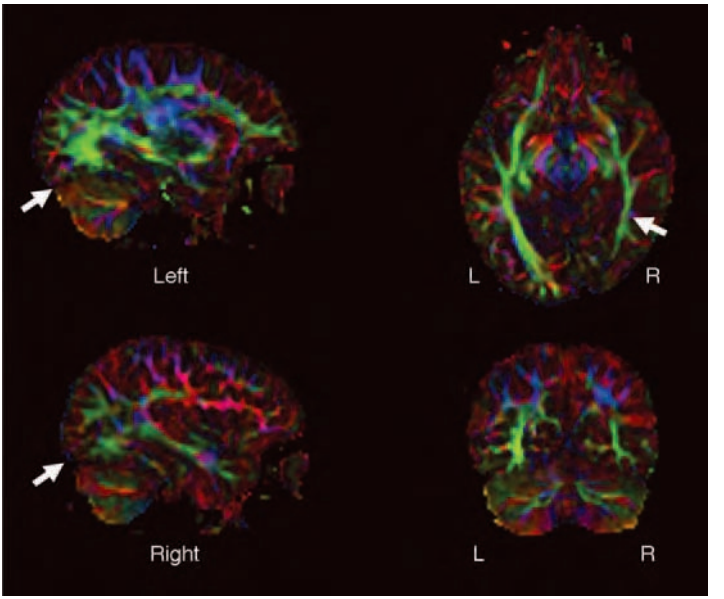

Figure 19.16 As an infant less than two months of age, this child sustained a significant brain injury in a motor vehicle accident (MVA), sustaining a right parietoccipital skull fracture and underlying brain contusion, as demonstrated by computerized tomography (CT) imaging on the day of injury. These diffuse tensor imaging (DTI) images, taken when the patient was a teenager, clearly show that the right hemisphere white matter did not develop normally after this injury and is very asymmetric in comparison to the left (compare regions where arrows are pointing). This is particularly evident in the sagittal images on the left where the left hemisphere shows extensive development of anterior-posterior pathways (green) and dorsal-ventral coursing pathways (blue). Red represents interhemispheric coursing pathways. This illustration nicely demonstrates that once injured, the trajectory brain development may not be normal, with lasting structural anomalies present thereafter.

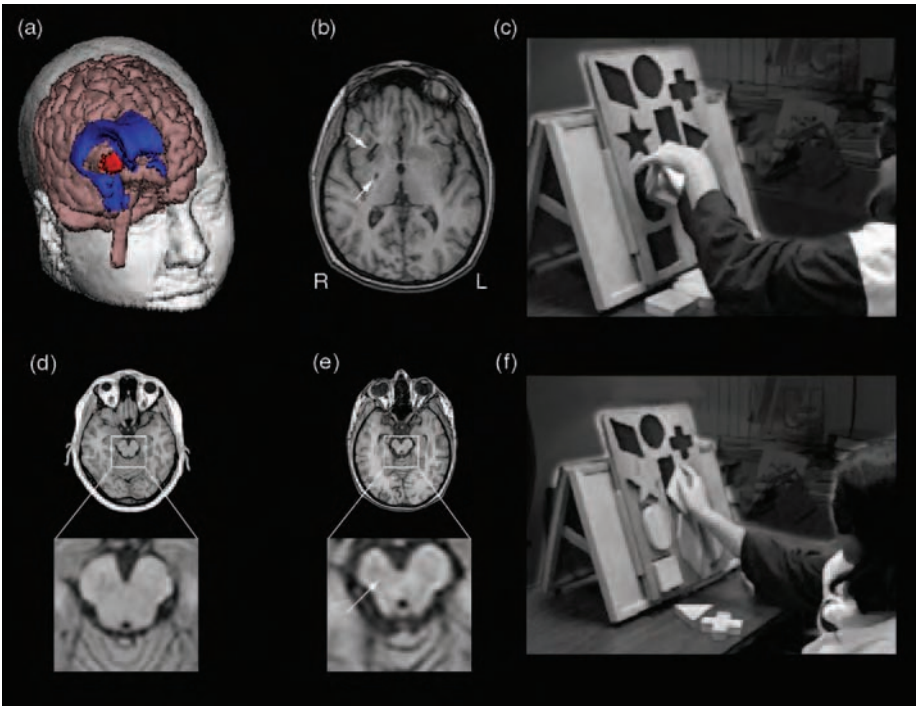

Figure 19.17 This case demonstrates Wallerian degeneration, where the major lesion is in the right internal capsule-basal ganglia region; resulting in left hemiplegia and impaired coordinated motor movement (see c and f). Damage to the corticospinal track at the internal capsule level, results in downstream atrophy of this direct motor pathway, such that at the midbrain level of the cerebral peduncle considerable asymmetry is reflected, indicating the right peduncle has withered (e). The lesion is not in the peduncle, but the effect of the injury is reflected in damaged pathways at the peduncular level resulting in the atrophy.

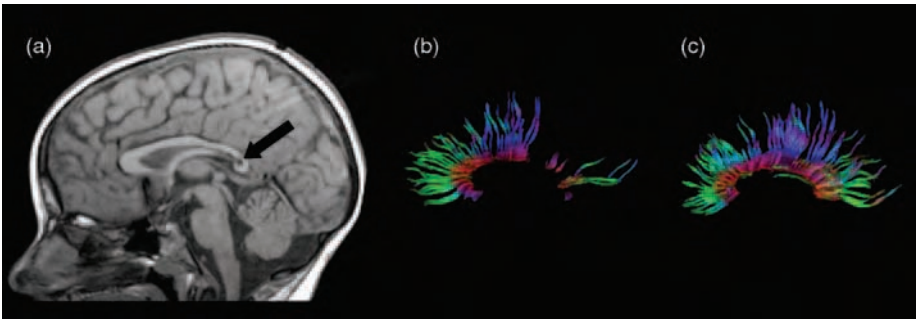

Figure 19.18 The scan on the left (a) is from a child with moderate-to-severe traumatic brain injury (TBI) with clearly atrophic posterior corpus callosum, with a shear hemorrhagic (hemosiderin deposit) lesion in the splenium. (c) shows normal diffuse tensor imaging (DTI) tractography depicting the projections of interhemispheric fiber pathways rather evenly across the corpus callosum (CC) in a normal control individual. (b) represents the child's tractography findings, which demonstrate almost complete dropout of aggregate fiber tracts emanating from the atrophic posterior CC. This type of technology will likely inform the neuropsychologist even further about gross, as well as subtle, pathology that may be present following injury or associated with certain disorders.