Section I

Fundamentals of pediatric neuropsychological intervention

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Introduction

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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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A developmental approach to pediatric neuropsychological intervention

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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