Carol L. Armstrong *Editor*
Lisa A. Morrow *Associate Editor*

Handbook of Medical Neuropsychology

Applications of Cognitive Neuroscience

Second Edition

Springer

Handbook of Medical Neuropsychology

Carol L. Armstrong · Lisa A. Morrow
Editor Associate Editor

Handbook of Medical Neuropsychology

Applications of Cognitive Neuroscience

Second Edition

Foreword by Muriel D. Lezak

Springer

Editor
Carol L. Armstrong
Perelman School of Medicine of the
University of Pennsylvania
Philadelphia, PA, USA

Associate Editor
Lisa A. Morrow
Western Psychiatric Institute and Clinic
Pittsburgh, PA, USA

ISBN 978-3-030-14894-2 ISBN 978-3-030-14895-9 (electronic)
https://doi.org/10.1007/978-3-030-14895-9

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword to the First Edition

This handbook celebrates the abundantly productive interaction of neuropsychology and medicine. This interaction can be found in both clinical settings and research laboratories, often between research teams and clinical practitioners. It accounts for the rapidity with which awareness and understanding of the neuropsychological components of many common medical disorders have recently advanced. The introduction of neuropsychology into practice and research involving conditions without obvious neurological components follows older and eminently successful models of integrated care and treatment of the classical brain disorders.

In the last 50 years, with the growing understanding of neurological disorders, neuropsychologists and medical specialists in clinics, at bedside, and in laboratories together have contributed to important clinical and scientific advances in the understanding of the common pathological conditions of the brain: stroke, trauma, epilepsy, certain movement disorders, tumor, toxic conditions (mostly alcohol-related), and degenerative brain diseases. It is not surprising that these seven pathological conditions were the first to receive attention from neuropsychologists as their behavioral symptoms can be both prominent and debilitating, often with serious social and economic consequences.

However, many diseases affect behavior and cognition without directly involving brain substance. Yet only in the last two decades has a scientifically grounded understanding of the neuropsychological implications of such diseases become available as the neuropsychological enterprise broadened its purview from the common brain disorders to clinical care and research with patients whose medical conditions impaired their neuropsychological functioning. Thanks to the relatively recent emphasis on "holistic" medicine, physicians have increasingly become sensitive to the often subtle but functionally important psychological alterations of medical patients without diagnosable brain disease. This has led many to neuropsychology for reliable knowledge about the behavioral ramifications of these patients' disorders. This recent marriage of traditional medicine and neuropsychology has been

most fruitful, as attested to in the sections that deal with metabolic and endocrine disorders in particular, but also in chapters concerned with specific vascular and immune-mediated disorders occurring outside the brain.

By including sections on developmental disorders and rehabilitation this handbook effectively covers the full range of conditions with neurocognitive ramifications. It will become apparent to the reader that the interplay of medicine and neuropsychology has made possible the science and skills for today's best practices in the care of patients with these conditions.

Of the eight sections in this handbook, the first is devoted exclusively to central nervous system disorders: Four of the six diagnostic categories considered in *primary nervous system disease* concern brain conditions in which neuropsychologists have been involved for more than three decades: movement disorders, epilepsy, traumatic brain injury, and neurooncology (e.g., [1–6]). Although these disorders differ greatly in their etiologies, developmental histories, course, and susceptibility to amelioration, what they have in common is the significant role that their neuropsychological symptoms play in determining the conduct and quality of the patient's life. The large body of scientific literature for each of these categories testifies to the value of medical specialists and neuropsychologists working together on patient evaluation and treatment. Much of the research underlying improved care for these conditions comes from this cooperation and cross-fertilization.

A relative newcomer to the categories of neurological disorders with significant behavioral symptom is *autonomic nervous system disorders*. The recency of neuropsychologists' involvement may account for the paucity of neuropsychologically relevant research into this condition. This chapter and others, such as Hydrocephalus, make it evident that understanding subcerebral disorders. Whether psychological interventions may also ease the cognitive and emotional symptoms of these conditions remains to be seen.

The end product of all *cardiovascular diseases* is reduced availability of oxygen. Thus, by their very nature, these diseases breed neuropsychological disorders as a result of insufficient oxygenation of highly oxygen-dependent brain substance. Their neuropsychological symptoms vary, from the sudden, often dramatic, loss of significant abilities due to stroke or the progressive cognitive withering of vascular dementia to the subtle dampening of cognitive acuity that occurs with primary breathing disorders or the intermittent diminution of function accompanying many migraine headaches. The presentation of the broad range of cardiovascular disorders here should give the clinician an increased awareness of the neuropsychological manifestations of vascular disease, especially those all too common respiratory conditions in which subtle but important neuropsychological consequences have been unsuspected or overlooked, such as chronic obstructive pulmonary disease and sleep apnea.

Unlike some of the other conditions discussed in this handbook, neurobehavioral aspects of (the) most *developmental disorders* are too obvious to have been ignored. Thus, for all of these conditions, some references go

back 30 or more years; in this handbook one on dyslexia was published in 1891. Decades of study have given these disorders a substantial knowledge base which current studies refine but rarely revise. Treatment options are limited or even nonexistant for many of these lifelong conditions. Still, a full appreciation of their genetic, physiological, and cognitive features should enhance clinicians' abilities to work intelligently and sensitively with the patients and their often overly burdened families.

For example, the review of several well-studied developmental disorders —Down, fragile X, and Williams syndromes—relates specific genetic errors to discrete patterns of cognitive and behavioral dysfunction. Other developmental problems have their origins in a variety of structural anomalies, each impinging on different parts of the developing central nervous system with diverse etiologies and neuropsychological consequences. Like its childhood counterpart, adult-onset hydrocephalus bears many etiologic and structural similarities to the developmental condition but, if untreated, can evolve into a classical dementia. And then there are the etiologic puzzles presented by the autism—Aspergers range of neurobehavioral disorders which here are considered as neuropathologic phenomena with associated patterns of neurocognitive dysfunction.

The section on *aging* contains, as one might expect, a *Dementia* chapter which reviews not only the most prevalent of dementing diseases but also one of the rarest forms of dementia—the prion diseases. Although the most common prion diseases progress so rapidly as to be of little neuropsychological interest, neurobehavioral symptoms are prominent in a recently identified variant with a longer course.

Since aging and dementia are so often associated in reviews of neurobehavioral disorders, it is a pleasure to find a separate discussion of normal cognitive aging which not only documents the usual deficits that develop in the seventh and eighth decades, but also emphasizes the variability in cognitive functioning within the aging population. The good news is that high-functioning older people contribute to this variability as well as those whose faculties are exceptionally diminished.

The reviews here of multiple sclerosis and the HIV-AIDS complex are expected in a section on *immune-mediated disease*. An appreciation of the impact of multiple sclerosis on patients and families requires an understanding of how the complexity of the most typical symptoms—motor and cognitive deficits, emotional distress and fatigue—can interact to exacerbate the illness experience. Of especial value is a discussion of the importance of family understanding and support for patients' quality of life which, while focussed on the MS patient, speaks for all neuropsychologically impaired patients and their families.

Rheumatic conditions are widespread with prevalence increasing with age, although many young persons are also affected. The inclusion of chapters on rheumatic diseases may be unexpected but is appropriate and necessary, as cognitive symptoms develop along with the well-known

crippling effects of these diseases. Cognitive issues are complicated by pain and compromised mobility making these conditions almost ideal models for neuropsychological and medical cooperation in treatment as well as research. Included in the section on *rheumatologic conditions* are two disorders whose diagnostic validity has been subject to much debate: fibromyalgia and chronic fatigue syndrome. Whether or not these are distinctive diagnostic entities, persons diagnosed with these conditions do suffer cognitive dysfunction which can, in some cases, seriously compromise everyday life. The now documented neuropsychological repercussions of the Guillain–Barré syndrome have also been mostly ignored as it has been essentially considered to be a peripheral neuropathy.

The contributions of stress to neurobehavioral disorders become apparent in the review of *endocrine diseases*. The stress experiences—particularly repeated stress—with its responsive endocrine imbalances and the resulting behavioral and cognitive dysfunction are linked in a causal chain which should be of interest to society's leaders as well as neuropsychologists and endocrinologists. The direct cognitive consequences of medically well-studied endocrine disorders, such as diabetes, tend to be relatively subtle and thus less likely to be identified in these patients. That these cognitive disorders can compromise daily functioning and quality of life makes their recognition important for appropriate patient care.

Some *metabolic disorders* give rise to disease-characteristic behavioral anomalies that, as yet, have not been explained. One interesting example is visuoperceptual disturbances in hepatic disease which, on appropriate examination, show up as gross drawing distortions. On the other hand, some specific patterns of cognitive dysfunction associated with different toxic sources do have scientifically grounded explanations. Moreover, as in the case of the affinity of organic solvents for fatty tissue or the affinity of carbon monoxide for hemoglobin, these relationships have added to the understanding of brain physiology, tissue vulnerability, and neurobehavioral outcomes. The more or less specific and more or less severe motor abnormalities of mitochondrial disorders have tended to overshadow the associated cognitive disturbances which are—at last—considered here.

Among the latest advances in *rehabilitation* are technological marvels which may substitute for replace, augment, or retrain the impaired functional system. These nontraditional additions or alternatives to more orthodox rehabilitation procedures may open the way for radical rethinking of how to overcome the behavioral impairments due to brain damage.

The inclusion, in many chapters, of assessment recommendations by authors who have had intensive experience in their area of expertise will be appreciated by both newcomers to neuropsychology and older hands confronting patients with unfamiliar conditions. Knowledge of treatment possibilities and procedures—both medical and psychological—is important for neuropsychologists' understanding of and clinical response to these conditions; thus treatment is considered, often extensively, throughout this

handbook. Not least of the many values to be found between these covers are the very current reference lists, most containing over 100 references, several more than 200 making this handbook a treasure trove of knowledge for the active seeker.

Despite the rapidity with which new neuropsychological information becomes available, this handbook will remain relevant for some time as its contents are both current and comprehensive. It will serve clinicians and researchers alike as a ready resource for both the facts and the important references for just about all the brain and nonbrain disorders, conditions, and diseases that can affect cognition.

Portland, OR, USA Muriel D. Lezak

References

1. Aminoff MJ, Marshall J, Smith EM, Wyke MA. Pattern of intellectual impairment in Huntington's chorea. Psychol Med. 1975;5:169–72.
2. Luria AR. Neuropsychological analysis of focal brain lesion. In: Wolman BB, editor. Handbook of clinical psychology. New York, NY: McGraw-Hill; 1965.
3. Lyle OE, Gottesman II. Premorbid psychometric indicators of the gene for Huntington's disease. J Consult Clin Psychol. 1977;45:1011–22.
4. Milner B. Intellectual function of the temporal lobes. Psychol Bull. 1954;51:42–62.
5. Smith A. Intellectual functions in patients with lateralized frontal tumors. J Neurol Neurosurg Psychiatry. 1966;29:52–9.
6. Teuber H-L. Some alterations in behavior after cerebral lesions in man. In: Bass AD editor. Evolution of nervous system control. Washington, DC: American Association for the Advancement of Science; 1959. pp. 267–96.

Preface to the Second Edition

Welcome to the second edition of the Handbook of Medical Neuropsychology: Applications of Cognitive Neuroscience. This second edition continues to take an in-depth approach to the medical conditions and methods of neurorehabilitation found in the first edition. The new chapters for the second edition reflect the changes in prominent problems found in the clinic and thus provide good insights for research investigation, and are described in this Preface to the 2nd Edition. This second edition includes one of the most prominent and difficult to treat conditions, **Substance Use Disorders**, and provides a great deal of guidance for both clinical and research purposes. A subject that has largely been missing from our literature yet affects the entire population is **Nutrition in Neurocognition and Mental Health**, and this rich and comprehensive chapter is critical for guiding work involving developmental and aging populations as well as the general population. Autoimmune diseases are increasing in frequency in the population, and we now include **Hypothyroidism and Hashimoto's Thyroiditis: Mechanisms, Diagnosis, Neuropsychological Phenotypes, and Treatments**, which addresses both endocrine and autoimmune features of these diseases. Few centers are as experienced in early childhood brain injury as the Murdoch Children' Research Institute, and this edition is grateful for their chapter on **Traumatic Brain Injury in Very Early Childhood**. Increasing rates of asthma led to the invitation for a chapter on this very common disorder that encompasses the problem across the lifespan and in the social context: **Cognitive Functioning in Asthma: Central Nervous System and Other Influences**. To learn about a critically important new approach to treatment in neurology, psychiatry, and psychology, meditation is discussed by an author with extensive experience and research, in **The Role of Mindfulness in Neurorehabilitation: From the Monastery to the Clinic**. These new chapters are discussed below, followed by the revisions and additions the reader will find in many of the chapters from the first edition.

Hypothyroidism and Hashimoto's Thyroiditis: Mechanisms, Diagnosis, Neuropsychological Phenotypes, and Treatments: This chapter provides the level of detail needed to understand the thyroid gland, and the role of thyroid hormones in our development and in relation to our anthropomorphic ecological practices and the health of our human communities.

The authors provide a careful analysis of the cognitive and mood findings in studies of individuals with different levels of abnormal thyroid levels. Consistent with other diseases, the authors found that cognitive screenings and brief assessments are less effective in measuring disease outcomes than disease-specific neurocognitive tests. As necessitated by their thorough review of the subject, results across the lifespan are presented. The background for complex interactions of genetics and environmental factors are considered in detail for various thyroid disorders. This chapter is an invaluable primer on the medical, immunological, genetic, and neuropsychological aspects of thyroid deficiencies as models of neurological immune diseases.

Traumatic Brain Injury in Very Early Childhood: The most current concepts in the consequences of childhood traumatic brain injury with an emphasis on preschool children are given in this new chapter. The young child's particular vulnerability to brain injury and the mechanisms that make them particularly vulnerable are well reviewed, including abusive head trauma. The neurocognitive conceptualization of the effects is reviewed in the context of the history and evolution of theory of how brain development of very young children is affected by traumatic injury. The nature of the cognitive systems that are most often damaged are explained as well as the impairments in social skills and attention-deficit/hyperactivity disorders that are so often observed as secondary consequences. The radiographic review demonstrates the cerebral substrate that is most vulnerable in young children. There is relatively sparse literature on treatment, and the authors are from a children's research and hospital who have a history of investigation in treatments, so that the chapter also provides very helpful and in-depth discussions on treatment models and methods, neuropsychological evaluations, and approaches in rehabilitation to the endemic behavioral problems, anxiety, and cognitive impairments, as well as parenting programs.

Substance Use Disorders: Cognitive Sequelae, Behavioral Manifestations, Neuroimaging Correlates, and Novel Interventions: Given that substance abuse is a national crisis, this new chapter is very welcome, and covers many different types of substance use: opioids, alcohol, stimulants, cannabis, benzodiazepines, synthetic substances, hallucinogens, prescription substances of abuse, and polysubstance use. The chapter emphasizes the patterns of neuropsychological deficits that characterize each disorder, the available neuroimaging studies, and the problems resulting from the course of use and abstinence. The authors report on intermediating factors in this field, including the variable response of use during adolescence versus adulthood. A critical issue in this field is that of neural and personality predisposition factors, and studies that have directly addressed predisposition are included.

Cognitive Functioning in Asthma: Central Nervous System and Other Influences: One of the most frequent medical disorders in the United States is asthma, found across the lifespan. This is an emerging field, and the author provides a comprehensive review of the evidence in the aspects of the scope of this public health problem, genetic candidates for the complex asthma phenotype, cognitive problems, the underlying cognitive neuroscience

theories for the associated deficits including the neural and neuroendocrine substrates, and the socioeconomic and ethnic interactions that influence this disease. An important discernment in this chapter is to provide the evidence for mechanisms and outcomes in children and adolescents versus adults and older adults. Finally, the critical clinical parameters and treatment issues are thoroughly reviewed to help clinicians and researches in knowing the state-of-the-art of healthcare for this population.

Nutrition in Neurocognition and Mental Health: Although studies abound of the possible benefits of nutritional status and supplements on brain development, degeneration, and psychiatric disorders, there is not yet much consensus, with some exceptions, and all are reviewed in this chapter. This chapter reviews the state of the science from prenatal to aging and disease considerations. It provides a valuable overview of micronutrients (folate and folic acid, vitamin B12, choline, vitamin D, iron, iodine, zinc, and multivitamins), fats (e.g., long-chain polyunsaturated fatty acids, docosahexaenoic acid (DHA), omega-3 and omega-6 fatty acids), dietary quality and specific diets, and being overweight or underweight on cognition and mood. The association of nutrition with depression, anxiety, attention-deficit disorders, autism, and dementia is reviewed. The authors examine the data on reversibility of the failure of intellectual or cognitive development with improvement in maternal status and temporal stage of development, and on dose effects. The section on polyunsaturated fatty acids is examined carefully and is particularly detailed in reference to neurodevelopment, cognition, mental decline, and psychiatric diagnoses. The authors provide critiques of current research and policy recommendations.

The Role of Mindfulness in Neurorehabilitation: From the Monastery to the Clinic: This field of science has developed a significant database of studies of a critical source of brain plasticity that this author has courageously taken on and analyzed carefully using a critical lens. The approach is very comprehensive, and neuroanatomical, behavioral, emotional, and clinical outcomes are reviewed. Based on the theory and empirical evidence, Dr. Smart has proposed a model of associations of meditation methods with neural plasticity and applications. There is no better source of information on the types and bases for meditation, its track record in a wide range of developmental (e.g., attention-deficit/hyperactivity disorder) and adult neurological diseases (traumatic brain injury, stroke, epilepsy, multiple sclerosis, Parkinson's disease, and late-life cognitive decline), and for applications to rehabilitation. The author handles clearly and with scientific caution the intricate interaction of factors in this emerging field, and the chapter is a pleasure to read. The author's recommendations for research are invaluable. Based on the available corpus of knowledge, this chapter will likely be the authoritative text on this subject. Finally, the chapter ends with case examples that combine meditative practice with cognitive behavioral therapy to demonstrate the potential effectiveness of this type of integrative therapy.

New Material in Chapters from the First Edition

Genetic Syndromes Associated with Intellectual Disabilities: Professor Abbeduto, Director of the MIND Institute at U. C. Davis, is a leading expert on the neurolinguistic features of genetically associated intellectual disabilities, and has focused this updated chapter on neurolinguistic features and prototypical neuropsychological profiles of Down syndrome, fragile X syndrome, and Williams syndrome. The chapter substantially expands on cognitive and linguistic patterns that were already addressed in detail in the first edition, but which provide more assistance to identify key features of the disabilities, and expands the patterns across the years of child development. For example, new studies examining the linguistic development and neuroimages of children with one of these disorders with a comorbid autism spectrum disorder are included in the second edition along with new studies of the social phenotypes. New studies are available that examine the influence of environmental interactions on language and communication. In general, this chapter examines new neurobehavioral and neuroimaging evidence that leads to better understanding of these disorders.

Neuropsychological Problems in Neuro-Oncology: This comprehensive survey of the neurological, neuroimaging, and neuropsychological problems in the assessment, treatment, and study of central nervous system cancers has been updated with a section on the emerging field of immunotherapy treatment in neuro-oncology, including the potential for neuropsychological complications of immunotherapy. New research results are added regarding developmental differences in memory decline following therapeutic irradiation, showing that while memory is vulnerable as early as four years after treatment, different memory systems are at risk for adults versus children, demonstrating the development problem in children, and the particular vulnerability of memory in adults.

Learning Disorders: This chapter by authors with decades of experience in the diagnosis and treatment of learning disorders has been updated in current understanding of diagnoses, and is integrated with the changes in definitions brought by the DSM-V. This is a very comprehensive and theory-based chapter that addresses all the major issues, discrepancies, and problems in identifying and treating individuals with LD. A very helpful level of detailed recommendations is given for a strong and clinically useful evaluation of learning disabilities. The use of performance validity tests for children is now covered in this chapter. Findings from molecular genetics and neuroimaging have been updated.

Chapter on Toxic Disorders and Encephalopathy: This chapter updates the multi-modal neurotoxic effects of organic solvents, lead, and carbon monoxide, and adds manganese toxicity in the new edition. The authors address the specific diagnostic symptom expressions and outcomes, and the nature of the associated cognitive dysfunction. Additional studies since the first edition lead the authors to be able to propose some principles for predicting the permanency and severity of encephalopathy as evidence converges. However, the authors also make clear the areas of research still

needed to understand the risks and protective/exacerbating factors that predict outcomes.

An Introduction to Congenital and Normal Pressure Hydrocephalus: This chapter uniquely contains explanations of ventricular functions, and the etiologies, mechanisms, and treatments of hydrocephalus as a balance of important buffering, signaling, and nutrient pathways "gone bad". This chapter is extensively revised, updated, and truly clarifies these disorders that are frequently encountered but poorly understood by neuropsychologists. A classification, if not taxonomy, of hydrocephalus related to genetic syndromes, and the search for cerebrospinal fluid biomarkers is now included, along with their role in diagnostic identification. Neuropsychological characteristics are described in detail and make this chapter an authoritative analysis of the literature. The diagnostic discrimination, e.g., normal pressure hydrocephalus versus depression or Alzheimer's disease, provided for each disorder is critical for neuropsychologists.

The Continuum of Traumatic Brain Injuries: Subconcussion to Chronic Traumatic Encephalopathy: This chapter provides a context to understand traumatic brain injury in the continuum concept that is based in the principal pathology of diffuse axonal injury, now better understood because of the wealth of studies using diffusion tensor imaging to understand the nature of injury and its evolution in trauma. The chapter includes new sections on blast-induced TBI injuries, chronic traumatic encephalopathy, and subconcussion. Although mood was previously addressed in relation to different trauma scenarios, there is now a new section in which mood disorders and behavioral change are addressed in-depth. Functional imaging has been updated. Expanded detailed emphases on mechanisms of injury, neuroimaging, frontal circuitry, and methods to diagnose damage to frontal systems also make this a very valuable chapter.

Cerebral Palsy: Effects of Early Brain Injury on Development: This chapter that emerges from a dedicated center for the treatment of cerebral palsy now includes new, heuristic methods of assessment that are more robust in measurement of cognition in children with CP-related spasticity that compromises the standardized measurement of verbal and nonverbal skills. The types of cerebral palsy are given in relation to their neural substrates. Neuropsychologists will be well prepared for best practices in clinical and research evaluations of this neurodevelopmental disorder. Updated methods are given for the use of event-related potentials for clinical purposes. The authors' serial studies related reaction time slowness and inaccuracy as some of the underlying causes of cognitive errors, and give new revelations about CP patients' motivation and internal error monitoring.

Current Approaches to Rehabilitation: Rehabilitation approaches have developed and matured greatly in the past 20 years, and fortunately Sarah Raskin is at the center of this development, and has given the reader both detailed methods and the broad picture of cognitive rehabilitation today. Also very helpful, the author has gone into depth into the problems of and approaches for impaired attention, which is central to perception, language, and reasoning, and is one of the most commonly impaired brain systems after brain injury. New to this edition is the review of several strategies that

comprise the corpus of metacognitive approaches to rehabilitation of executive functions and mood, including Von Cramon's training procedure, Marshall's effective problem-solving, Short-Term Executive Plus, Goal Management Training, BrightBrainer, and Advanced Cognitive Training for Independent and Vital Elderly. Very valuable is her review of neurofeedback, repetitive transcranial magnetic stimulation, Brain–Computer Interfaces, and the developing field of virtual reality rehabilitation techniques. The author's review also comes to the conclusion that emotional well-being and regulation need to be included in studies and in treatment programs that use cognitive rehabilitation techniques.

Executive Function Disorders in Pediatric Neuropsychology: Attention–Deficit/Hyperactivity Disorder and Tourette Disorder: This authoritative chapter updates the neuropathology of these disorders, including the most recent data on the implications of the default-mode circuitry and its inhibitory role and problematic reciprocity with other networks, the mechanism of the catecholaminergic neurotransmitter systems, and the abnormal brain volumes in ADHD. ADHD is problematic for the high rate of comorbidities in this disorder, and the chapter provides information on these problems due to the high frequency of ADHD as a secondary disorder to other neurological conditions such as carbon monoxide toxicity. Recommendations—medications and behavior management—and their limitations were impressive in the first edition chapter, and have been made stronger in this second edition. A new component that is especially important for new and experienced neuropsychologists is information on PANS—pediatric acute-onset neuropsychiatric syndrome—that was previously known as PANDAS, and its consideration as an etiology for Tourette Disorder (TD). Finally, the sections on neuropsychological components of TD and on treatments for TD have been greatly expanded.

Cerebrovascular Disease and Disorders: This chapter is unique because it informs and compares the predictable and rare neurocognitive disorders of stroke in both children and adults. In particular, Sabrina Smith is a rare cognitive neurology investigator and practitioner who focused on the cognitive neuroscience of stroke in children, and this chapter provides much needed information to guide assessment. New information is included on the effects of stroke on emotion and on behavior in children. The chapter's updates include unique information on the visuospatial deficits and long-term neurocognitive effects of stroke in the developing brain, areas for which there is little information to guide both assessment and recommendations for families.

Theoretical Perspectives on Cognitive Aging: The authors present much of the new science of aging including the role of life choices and environment on the process of aging. The authors of this chapter bring this critical perspective to this chapter, explaining it as a heterogeneous and dynamic process that is examined through the lens of traditional and new cognitive theoretical models. They propose how neuropsychologists can integrate life course into assessment of aging to inform long-term risks and protective factors. New neuroimaging studies reveal changes in neuronal receptors and volume changes. The authors present current research that examines how the

"relationship among lifestyle factors, environment influences, and cognitive aging … impact the understanding of neuropsychological assessment profiles from a single time point." Cognitive reserve, the scaffolding theory of aging and cognition, and other theories are critically reviewed. The authors pose that the increased variability among older adults is better understood by integrating life course factors.

Autism Spectrum Disorder: A Cognitive Neuroscience Perspective: This chapter has gone through major revisions with an addition of more than 125 references, primarily to add new information, address controversies that have arisen or been researched since the last edition of Handbook of Medical Neuropsychology, or integrate data for new perspectives and priorities for the diagnosis and care of this disorder. The authors' chapter will help to move the field in future directions by engaging with promising contributions from cellular and molecular differences in phenotypes, genetic patterns of transmission, epidemiological risks, neuroimaging, and possible new treatments. The chapter helps the reader to understand that there are networks of genes (and gene/environmental interactions) and variations of ASD phenotypes whose relationships are the subject of ongoing research. For example, ASD etiology may help to elucidate epigenetic mechanisms of neurodevelopmental injury prenatally. The conceptual model of Piven and colleagues is presented that connects the material brain changes in very early childhood with the emergence of autism behaviors. Finally, the neurocognitive features are comprehensively expanded in this edition, for example, the significance of abnormal orientation, reorientation, and attention disengagement, the controversies in findings on facial and affect perception, and the mediating effects of neural complexity.

Neuropsychology of Movement Disorders and Motor Neuron Disease: Parkinson's Disease, Progressive Supranuclear Palsy, Essential Tremor, Huntington's Disease, and Amyotrophic Lateral Sclerosis: This chapter updates five motor neuron diseases—Parkinson's disease, Progressive Supranuclear Palsy, Essential Tremor, Amyotrophic Lateral Sclerosis, and Huntington's disease—in their genetic associations and clinical criteria. Understanding of Parkinson's disease and of Amyotrophic Lateral Sclerosis have undergone significant revisions based on new scientific understandings, which are explained. This chapter also includes more information on the clinical tools and structures used to assess the functional status of individuals with these diseases, and to diagnose comorbid emotional and affective conditions, such as anxiety disorders and impulsivity. Advances in neuroimaging characteristics of the diseases are further elaborated.

Philadelphia, PA, USA Carol L. Armstrong

Preface to the First Edition

The burgeoning of molecular and genetic studies of neurological and developmental disorders has contributed to the continuing relevance of neuropsychological studies of medical disorders. Neuropsychologists who follow science have updated and expanded the tools of our field to increase understanding of the functional consequences of disease, disease progression, and treatments. Equally important are the theoretical models of neurocognition that have been developed and refined in conjunction with functional imaging and other tissue or neurotransmitter-specific neuroimaging techniques. Contributing to clinical neuroscience, neuropsychiatry, and developmental neuroscience requires a sophisticated understanding of the medical and biological elements and future directions in which progress is being made in order to remain relevant. The purpose of this book is to provide a current and cutting edge understanding of the various diseases and disorders covered within and their neuropsychological effects. The authors are academic clinicians and researchers who bring insight and carefully constructed explanations about their respective fields of research. The neuropsychological findings of the diseases and disorders that comprise this book are given in the context of the disease mechanisms. Rather than taking the route of quick summarization, the chapters are meant to be intently studied, as they are dense with information. These chapters should remain useful for a long time.

Handbook of Medical Neuropsychology: Applications of Cognitive Neuroscience aims to provide understanding of some topics that neuropsychologists confront frequently, such as cerebrovascular disease, dementia, learning disability, normal aging, and traumatic brain injury. These chapters provide incisive reviews of the state of the science, reveal the controversies in diagnosis, and give the current opinions about the most critical factors that characterize these diseases and variations of "normal" brain states (autism, cerebral palsy, and genetic disorders could also be characterized this way). All of the chapters will make the reader who immerses him/herself in the material ready to design a study or understand a clinical evaluation, by helping the reader to be oriented to the key issues, areas that lack clarity, and future directions.

Other diseases covered in this book are confronted less frequently, but are the focus of intense investigation, such as autism, cardiovascular disease, endocrine disease (diabetes), epilepsy, and HIV-AIDS. These chapters are particularly rewarding because of the wealth of information contained in them and the insights that the authors have given us. Those who wish to participate in the cognitive neuroscience of these fields through grant-funded research will find these chapters very valuable. Clinicians will be better able to understand the purposes of treatments and the neuropsychological behaviors of their patients.

Some diseases are included because they are actually relatively common, yet their neuropsychological symptoms and mechanisms are not often examined closely, such as various autoimmune diseases and endocrine disorders, hydrocephalus, migraine, neuro-oncologic disorders, stress disorders, stress/post-traumatic stress disorder, and toxic disorders/encephalopathy. These chapters are reviews that are broadly encompassing yet also focused on the inconsistencies and generalizations that are possible, based on the state of the science.

Today, neuropsychologists must integrate knowledge about neurodevelopmental disorders into their work, whether their focus is adults or children. We are fortunate to have such knowledgeable and elegant chapters about cerebral palsy, pediatric frontal lobe disorders, learning disability, and the language impairments of genetic disorders. These chapters are elucidating and will give the reader new insights.

There are also the chapters on classic, and in some cases not well-known, medical diseases that have direct effects on brain functions: autonomic nervous system disorders, hepatic encephalopathy, movement disorders, respiratory disorders, and rheumatologic conditions. Again, these chapters remain true to analyzing their fields through the mechanisms of the disease and how these mechanisms encompass cognitive dysfunction.

There is one other subject of great interest that is still emerging and that is neuropsychologically understudied: mitochondrial disorders. I am grateful to the author, Kevin Antshel, who has taken the proverbial bull by the horns and given us knowledge about the biomedical tools we need to approach the neuropsychological investigation of these diseases.

Last, but most certainly not least, is rehabilitation. This book views this field from two perspectives. One gives the conceptual underpinnings of cognitive rehabilitation as it is carried out in the best brain injury cognitive rehabilitation centers extant. The other approach is the integration of neural brain mechanisms with human perception, to alter the way humans control their movements and balance. The chapter entitled *Sensory Reweighting: A Rehabilitative Mechanism* is included to inspire our present and future generations of neuropsychologists to use neuroscience technologies that integrate sensory information to modify behavior.

Another intent for this book is to provide critiques of the neuropsychological tests that are useful in tracking these diseases. The authors have striven not only to indicate what the tests have shown but also to show that recent research demonstrates that the most informative measures are those with high specificity even in relatively diffuse diseases. The goal was to point

to the tests of cognition that are most informative regarding a disease process or disorder.

Finally, we will leave the reader with the insight of a scientist of the past, to remind us that we all can see most clearly if we stand on the shoulders of those who came before us. Neils Bohr, a physicist of the twentieth century whose work was critical for the development of quantum theory, said that the opposite of a truth is a falsity, but the opposite of a deep truth is often another deep truth.

Philadelphia, PA, USA Carol L. Armstrong

Contents

Contributors

Leonard Abbeduto MIND Institute and Department of Psychiatry and Behavioral Sciences, University of California, Davis, CA, USA

Julie A. Alvarez Department of Psychology, Tulane University, New Orleans, LA, USA

Eric Anson Department of Kinesiology, Neuroscience and Cognitive Science Program, University of Maryland, College Park, MD, USA

Kevin M. Antshel Department of Psychiatry and Behavioral Sciences, State University of New York – Upstate Medical University, Syracuse, NY, USA

Clara Chavez Arana Child Psychology, School of Psychological Science, University of Melbourne, Parkville, VIC, Australia
Autonomous University of Mexico, Mexico City, Mexico

Carol L. Armstrong Department of Pediatrics, Perelman School of Medicine, The University of Pennsylvania, Philadelphia, PA, USA

Peter A. Arnett Department of Psychology, The Pennsylvania State University, University Park, PA, USA

Jasmohan S. Bajaj Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University and McGuire VA Medical Center, Richmond, VA, USA

Fiona H. Barwick Department of Psychology, The Pennsylvania State University, University Park, PA, USA

Joseph E. Beeney Department of Psychology, The Pennsylvania State University, University Park, PA, USA

Sue R. Beers Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Jean B. Belasco Department of Pediatrics, Perelman School of Medicine, The University of Pennsylvania, Philadelphia, PA, USA
Division of Oncology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA

Allison Berman Neuropsychology Division, and Cognitive Neuroscience and Brain Imaging Laboratory, Thomas Jefferson University/Jefferson Medical College, Philadelphia, PA, USA

Sonia Y. Bernal Bellevue Hospital Center, NYC Health and Hospitals, New York, NY, USA
Department of Psychiatry, New York University School of Medicine, New York, NY, USA

Juliana Sanchez Bloom The Levin Center, Atlanta, GA, USA

Baily M. Bonura Psychology Department, Tufts University, Medford, MA, USA

Kirk R. Bryant Clinical Neuropsychologist, WellStar Medical Group, Marietta, GA, USA

Lauren Bullard MIND Institute and Department of Psychiatry and Behavioral Sciences, University of California, Davis, CA, USA

Cathy Catroppa Child Neuropsychology, Murdoch Children's Research Institute, Parkville, VIC, Australia
School of Psychological Science, University of Melbourne, Parkville, VIC, Australia

Leanne Chukoskie Qualcomm Institute and Institute for Neural Computation, University of California, San Diego, CA, USA

Jared Conley Case Western Reserve University School of Medicine, Cleveland, OH, USA

Rosalia Costello Department of Psychiatry and Behavioral Neurosciences, University of Chicago Medical Center, Chicago, IL, USA

Louise M. Crowe Child Neuropsychology, Murdoch Children's Research Institute, Parkville, VIC, Australia
School of Psychological Science, University of Melbourne, Parkville, VIC, Australia

William C. Culbertson Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

Jennifer B. Dave Capital Institute for Neurosciences, Pennington, NJ, USA

Robert N. Davis Houston Neuropsychology Associates, PLLC, Houston, TX, USA

Gayle K. Deutsch Department of Neurology and Neurological Sciences, Stanford Comprehensive Epilepsy Center and Stanford Center for Memory Disorders, Stanford University Medical Center, Stanford, CA, USA

David M. Frim Department of Neurosurgery, University of Chicago Medical Center, Chicago, IL, USA

Suzanne L. Gharib Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Jennifer M. Glass Department of Psychiatry, Institute for Social Research, Addiction Research Center, University of Michigan, Ann Arbor, MI, USA

Anna C. Graefe Psychology Service and VA National Center for PTSD, VA Boston Healthcare System, Boston, USA

Laura Grande Psychology Service, VA Boston Healthcare System and Department of Psychiatry, Boston University School of Medicine, Boston, MA, USA

Carol M. Greco Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Michelle M. Greene Department of Psychology, Virginia Commonwealth University, Richmond, VA, USA

Marc W. Haut Departments of Behavioral Medicine and Psychiatry, Neurology, and Radiology, West Virginia University School of Medicine, Morgantown, WV, USA

Clarissa S. Holmes Department of Psychology, Pediatrics and Psychiatry, Virginia Commonwealth University, Richmond, VA, USA
Department of Psychiatry, Georgetown University, Washington, DC, USA

Ramona O. Hopkins Psychology Department, Neuroscience Center, Brigham Young University, Provo, UT, USA
Pulmonary and Critical Care Division, Department of Medicine, LDS Hospital, Salt Lake City, UT, USA
Pulmonary and Critical Care Division, Department of Medicine, Intermountain Medical Center, Murray, UT, USA

Megan M. Hosey Department of Psychology, University of Maryland, Baltimore, MD, USA

Farzin Irani Department of Psychology, West Chester University, West Chester, PA, USA
AAA Neuropsychology, Malvern, PA, USA

John Jeka Department of Kinesiology, Neuroscience and Cognitive Science Program, University of Maryland, College Park, MD, USA

Amy H. Kao Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Melanie Katrinak Department of Psychology, West Chester University, Philadelphia, PA, USA
Children's Hospital of Philadelphia, Philadelphia, PA, USA

Leslie I. Katzel Division of Gerontology and Geriatric Medicine, Department of Medicine, School of Medicine, University of Maryland, Baltimore, MD, USA

Geriatric Research Education and Clinical Center, Baltimore Veterans Affairs Medical Center, Baltimore, MD, USA

Dana Kelly Department of Psychiatry and Behavioral Neurosciences, University of Chicago Medical Center, Chicago, IL, USA

Sandra L. Kerr Department of Psychology, West Chester University, West Chester, PA, USA

Kinga Kertesz Center for Neurological Imaging, Brigham and Women Hospital, Boston University Medical School, Boston, MA, USA

Maureen A. Lacy Department of Psychiatry and Behavioral Neurosciences, University of Chicago Medical Center, Chicago, IL, USA

Yimei Li Department of Biostatistics, Perelman School of Medicine, The University of Pennsylvania, Philadelphia, PA, USA
Division of Oncology, The Children's Hospital of Philadephia, Philadelphia, PA, USA

Cynthia Lippincott-Stamos Neuropsychology Division, and Cognitive Neuroscience and Brain Imaging Laboratory, Thomas Jefferson University/Jefferson Medical College, Philadelphia, PA, USA

Michelle London Department of Psychiatry and Behavioral Neurosciences, University of Chicago Medical Center, Chicago, IL, USA

Kara Lonser Department of Behavioral Medicine and Psychiatry, West Virginia University School of Medicine, Morgantown, WV, USA

Kathryn Maher Department of Psychology, Virginia Commonwealth University, Richmond, VA, USA

James J. Mahoney III Department of Behavioral Medicine and Psychiatry, West Virginia University School of Medicine, Morgantown, WV, USA

Andrea McDuffie MIND Institute and Department of Psychiatry and Behavioral Sciences, University of California, Davis, CA, USA

Michael R. Meager Department of Psychology, New York University, New York, NY, USA
Department of Neurology, New York University School of Medicine, New York, NY, USA

John Stirling Meyer United Neurology Headache and Pain Clinic, Houston, TX, USA

Liv E. Miller Department of Behavioral Medicine and Psychiatry, West Virginia University School of Medicine, Morgantown, WV, USA

Nancy Minniti Department of Physical Medicine and Rehabilitation, Temple University Hospital, Philadelphia, PA, USA

Maria T. Moran Department of Physical Medicine and Rehabilitation, Pennsylvania State University, Milton S. Hershey Medical Center, Pennsylvania, PA, USA

Kari L. Morgan Department of Psychology, Virginia Commonwealth University, Richmond, VA, USA

Terri Morris Department of Clinical Psychology, Widener University, Chester, PA, USA

Kevin D. Mullen Division of Gastroenterology, MetroHealth Medical Center, Cleveland, OH, USA
Case Western Reserve University, Cleveland, OH, USA

Sarah Nelson MIND Institute and Department of Psychiatry and Behavioral Sciences, University of California, Davis, CA, USA

Karol Osipowicz Cognitive Neuroscience and Brain Imaging Laboratory, Thomas Jefferson University/Jefferson Medical College, Philadelphia, PA, USA

Robert H. Paul Department of Psychology, Behavioral Neuroscience, University of Missouri, St. Louis, MO, USA

Cecilia Peralta Department of Neurology, Centro Neurológico, Fundacion Alfredo Thomson, Parkinson's Disease and Movement Disorders Clinic, Hospital Cesar Milstein, Buenos Aires, Argentina

Silja Pirilä Department of Pediatrics, Tampere University Hospital, Tampere, Finland

Priscilla Powell Department of Psychology, Pediatrics and Psychiatry, Virginia Commonwealth University, Richmond, VA, USA

Sarah J. Pulaski Department of Clinical Neuropsychology, Barrow Neurological Institute, Phoenix, AZ, USA

Sarah A. Raskin Department of Psychology and Neuroscience Program, Trinity College, Hartford, CT, USA

Anthony L. Rostain Departments of Psychiatry and Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

Troy Russell Center for Neurological Imaging, Brigham and Women Hospital, Boston University Medical School, Boston, MA, USA

Cynthia J. Schmus Division of Oncology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA

Stephen L. Seliger Division of Nephrology, Department of Medicine, School of Medicine, University of Maryland, Baltimore, MD, USA

Paula Shepard Department of Psychiatry and Behavioral Neurosciences, University of Chicago Medical Center, Chicago, IL, USA

Colette M. Smart Department of Psychology and Institute on Aging and Lifelong Health, University of Victoria, Victoria, BC, Canada

Sabrina E. Smith Division of Pediatric Neurology, Kaiser Permanente Oakland Medical Center, Oakland, CA, USA

David F. Tate Harvard Medical School, Brigham and Women Hospital, Boston University Medical School, Boston, MA, USA

Ayanna K. Thomas Psychology Department, Tufts University, Medford, MA, USA

Angela John Thurman MIND Institute and Department of Psychiatry and Behavioral Sciences, University of California, Davis, CA, USA

Jeanne Townsend Department of Neurosciences, University of California, San Diego, CA, USA

Joseph I. Tracy Neuropsychology Division, and Cognitive Neuroscience and Brain Imaging Laboratory, Thomas Jefferson University/Jefferson Medical College, Philadelphia, PA, USA

Alexander I. Tröster Department of Clinical Neuropsychology and Center for Neuromodulation, Barrow Neurological Institute, Phoenix, AZ, USA

Jaap J. van der Meere Department of Clinical and Developmental Neuropsychology, University of Groningen, Groningen, The Netherlands

Jennifer J. Vasterling Psychology Service and VA National Center for PTSD, VA, Boston Healthcare System, Boston, USA

Shari R. Waldstein Department of Psychology, University of Maryland, Baltimore, MD, USA
Division of Gerontology and Geriatric Medicine, Department of Medicine, School of Medicine, University of Maryland, Baltimore, MD, USA
Geriatric Research Education and Clinical Center, Baltimore Veterans Affairs Medical Center, Baltimore, MD, USA

S. Carrington Rice Wendell Department of Psychology, University of Maryland, Baltimore, MD, USA

Marissa Westerfield Department of Neurosciences, University of California, San Diego, CA, USA

Christine E. Whatmough Department of Neurology and Neurosurgery, McGill University, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis Jewish General Hospital, Montreal, QC, Canada

Steven Paul Woods Department of Psychiatry, School of Medicine, University of California, San Diego, USA

Part I
Primary Nervous System Disease