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The Aging Mind and Brain *Overview*

Matthew Rizzo, Steven Anderson, and Bernd Fritzscht

Introduction

This is an opportune time for studying the aging mind and brain and translating the knowledge gained to improve the quality of life and prolong the independence of older people worldwide. Strategic national and international research efforts are gaining traction into molecules and mechanisms underpinning brain aging. Research programs leveraged by academic, government and industry partners have gained unprecedented insights into normal brain function, as a referent for detecting critical and potentially remediable cascades of dysfunction emerging much earlier in life, that may be harbingers of neurodegenerative diseases such as Alzheimer's, Parkinson's, and related disorders.

Strategic efforts to better understand brain aging need to be understood in view of demographic trends over the next few decades that favor more and longer-living seniors, and relative decline in the proportion and fertility rates of younger people. These changes have huge implications for society. Living, working, spending, and income patterns of seniors differ markedly from juniors', as do healthcare expenditures, ultimately straining government support programs and social networks to their limits. We need to address legislative issues and policies that advance discoveries and technologies and promote access and payment for needed care. We must educate ourselves on the pros and cons of new treatments by analyzing and reconciling moral issues that pit the Kantian wish to provide the greatest good for each person (for example, individualized medicine at some expense) with the Utilitarian goal of relieving disease and suffering as much as possible across the lifespan for the entire population. Personalized medicine (aka, precision, stratified, and P4 medicine) separates patients, putting individuals front and center for medical decisions, practices, or interventions based on predicted disease risk or therapeutic response¹. How can we afford to support these needs, and how can we afford not to?

Reaping the benefits of healthy aging requires mental health for a self-directed life. The silver lining of the Grey Tsunami of aging societies worldwide is increased health of many more seniors, affording a potential "fourth phase" in their lives, inserted between ages 50 and 70 (and perhaps even up to age 100 years or more, should historic trends on increased lifespan continue). Such a phase could allow older individuals to refocus and rebalance their life plans, redefining life strategies in beneficial ways not predicted just a few years ago when expectations for productive workspan ended around age 65 years old, or a century ago, in 1920, when mean lifespan itself was merely 54 years for women and men. Increasing trends toward healthy aging offer personal opportunities to engage in productive life and promise reduced costs of age-related disease to society, assuming medical gains keep pace to preserve the health of the superannuated.

The Wiley Handbook on the Aging Mind and Brain, First Edition. Edited by Matthew Rizzo, Steven Anderson, and Bernd Fritzscht.
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Even with dramatically improved health in the elderly, the growing burden of increased elder care will be a defining issue of all industrialized nations over the next 50–100 years.² In the US, the population of centenarians will rise from 16,000 (2015) to over 1 million (2050) and to even higher numbers by 2100. The number of seniors combined with their increased longevity will strain social security and healthcare systems as senior dependents require caretaking by public and private hands. Society needs alternative strategies to engage seniors in a productive way to maintain the standard of living our society currently enjoys (in line with ongoing efforts in Japan, home perhaps of the world's oldest population). An added benefit of such engaged seniors is to maintain social and intellectual engagement for healthy mind and brain aging, and avert an older and ever-growing cohort of the impoverished, isolated, sick, bored, and despairing.

Goals of this Handbook

This handbook recognizes the critical issues surrounding mind and brain health by tackling overarching and pragmatic needs for better understanding of these multifaceted issues through a convenient source. This includes summarizing and synthesizing critical evidence, approaches and strategies from multidisciplinary research that has advanced our understanding of the neural substrates of attention, perception, memory, language, decision-making, motor behavior, social cognition, emotion, and other mental functions. Basic scientists are discovering molecular, cellular, and genetic underpinnings of neural changes that affect cognitive capabilities over the lifespan. Behavioral researchers are classifying and measuring cognitive functions in multiple domains, tracking specific changes in these over the lifespan, and uncovering factors and treatments that can maintain and improve these functions in aging brains until later in life than ever before. Explanatory models and theories of cognitive processes are being developed to interpret these changes and link them to changes in brain systems that support aging minds. Social scientists and legal experts are demonstrating the key role of cultural supports and life experiences in shaping cognitive content and processes to extremes of the lifespan. These combined advances are furthering our understanding of how aging affects cognitive functioning and informing interventions to maintain cognitive performance to the extremes of superaging.

Popular efforts continue to raise public awareness of the science and opportunities to improve aging brains⁴. To understand and improve the health of the aging mind and brain, a silo-spanning team of interdisciplinary experts in research, teaching, outreach, community engagement, public policy, and the law, has collaborated to write a book on changes in neural health and in behavioral context that occur with aging, understanding differences in cognitive function within and between individuals at baseline and over time, and advancing mind and brain health across the lifespan. The authors tackle principles and practice relevant to “evergreen” challenges posed by the US National Academy of Sciences and National Institute on Aging (NIA)³:

- Build the scientific basis for promoting neural health in the aging brain.
- Improve the understanding of the structure and function of the aging mind, including behavioral and neural mechanisms, and their impact on diseases and their management.
- Evaluate current methods of assessment of higher brain function and behavior and related factors across the lifespan.
- Determine how behavioral, social, cultural, and technological context affect cognitive functioning and real-world performance of aging individuals and how to intervene effectively to augment individual functioning and performance in context.
- Address legal and policy implications for promoting safety and care of persons with cognitive challenges
- Analyze practice and policy issues that impact advancing science, models of care, treatment, outreach, access to care, and quality of life.

Overview of Contents

The evidence assembled in this unique handbook is geared toward improving the recognition, diagnosis, prevention, and treatment of many brain-based disorders that occur in older adults and that cause premature disability and death. Our primary aim is to advance the care and quality of life of patients who present with perceptual, cognitive, language, memory, emotional, and many other behavioral symptoms associated with these disorders, as well as aging adults who do not meet criteria for a neurological diagnosis. Materials are presented at a scientific level that is appropriate for a wide variety of learners.

To address the critical topics and challenges in mind and brain aging we have organized this handbook into eight parts (I–VIII) comprising 36 chapters. Between part I. Introduction (containing this chapter) and part VIII. Conclusion (chapter 36), are several sections (II–VII). These are summarized below.

Part II. Theoretical, animal models, social, and humanistic perspectives

Chapter 2. Ashida and Schafer: Social networks, social relationships, and their effects on the aging mind and brain

People, like cells in a person's body, are parts of dynamic systems and a network of support. Ashida and Schafer explore how social interactions at various levels affect healthy aging, much as cells in a body depend on functions of other parts. Mechanistic details of how such social interactions affect mind and brain health remain unclear, and individual variations tend to buck trends, yet common themes of social dependency emerge. Evidence strongly supports that caregiver and care receiver form dyads driven, for better or worse, by interactive dynamics at multiple levels. Social networks and interactions benefit healthy aging, but few attempts have been made to measure these interactions and harness their potential for improving healthy mind and brain aging in a rapidly changing society—where family interactions are progressively replaced by distant social networks in cyberspace. The effects of these dynamic changes on healthy aging of an ever-increasing population of seniors ready and willing to maintain social engagement are critical areas to be explored.

Chapter 3. Prahlad and Chikka: Aging and the brain

This chapter reviews molecular and cellular aspects of aging in the context of the evolution of aging. What is the advantage to humankind of long living? Organismal aging as a postreproductive process is not under strong reproductive selection. Extensions of lifespan may even correlate with reduced reproduction. The oldest known person ever, Jeanne Calment, died at age 122 and had only one daughter. Hers is a prominent human example of a broader inverse relationship between longevity and fertility across species, whose foundations remain unclear. A central theme of aging is the molecular and cellular instability and the role of the brain in regulating these processes. Some proteins are surprisingly long lived and resist proteasome decay, leading in pathological cases to prion disorders such as Creutzfeldt-Jakob disease. The authors review how this works at molecular levels and relates to age-related cellular burden in neurons that never “rejuvenate” through cell division. Parabiosis, or sharing of blood circulation of two organisms of different age, is the best known example of how blood-borne molecules can affect organism vitality and longevity, possibly through additional trophic factors in the brain. This chapter lays biological foundations for interpreting findings on the aging mind and brain covered throughout this book.

Chapter 4. Emmons, Kim, and Narayanan: Animal models of pathological aging

This detailed overview provides insights into the strengths and weaknesses offered by certain model organisms for studying the molecular basis of neuronal aging. Valuable invertebrate model organisms are described first (flies and worms), and their strengths and weaknesses for studying the effects of certain genes/proteins on longevity are provided, including the limits of transfer to

humans. Skipping nonmammalian vertebrate organisms (zebrafish, frogs, chickens), the utility of nonprimate and primate model organisms for studying age-related brain disorders is reviewed. This chapter concludes that no single model organism provides access to all the factors affecting human brain aging. Each is valuable in its own right for gaining insights not obtainable in human studies and, with proper additional testing, may prove applicable to humans.

Chapter 5. Charise and Eginton: Humanistic perspectives: Arts and the aging mind

This overview of humanistic perspectives on aging gives examples of late-life creativity, artistic portrayals of aging and the aging mind, and therapeutic applications of the arts for older persons. With reference to literature and writing, visual arts, and film, we consider how these art forms have given rise to therapeutic practices aimed at improving the lives of older people, especially those with age-related illness or disability. Given the early state of research into arts-based interventions, where possible we refer to effectiveness studies undertaken by humanities and social-science researchers and/or artist practitioners (often in collaboration with neurologists or other health professionals). This chapter argues that aging societies suffer from “Alzheimerization”, preventing use of limited resources of more creative approaches toward humanity of aging. The chapter concludes with a synopsis of critical approaches to clinical neuroscience and aging, followed by new directions for advancing humanistically informed research concerning the aging mind and brain.

Part III. Methods of assessment

Chapter 6. Diesing and Rizzo: Medical assessment of the aging mind and brain

This chapter reviews essential principles, practice and approaches to assessing older persons with mental, behavioral and mobility changes. These changes are becoming more prevalent with trends toward greater longevity, aging of the general population, and associated age-related neurological disorders. Consequently, healthcare providers of all types are broadly challenged with acute and chronic impairments of mind and brain health. Primary care and cognitive and behavioral health specialists, including neurologists, geriatricians, psychiatrists and psychologists, and others, must be prepared to diagnose, treat, and refer these older patients for appropriate tests, consultation, and treatment. The related history, physical assessment, and laboratory tests in the evaluation of the aging patient are geared toward problems such as changes in mental status, emotion, pain, continence, mobility, and falls.

Chapter 7. Jones: Neuropsychological Assessment of Aging Individuals

The role and practice of neuropsychological assessment for older persons are examined. Aging is associated with decline in various aspects of cognitive function and increased risk of a number of mind-altering diseases. Neuropsychological assessment provides a safe, noninvasive method of evaluating the health of an aging brain and an objective source of information and recommendations regarding cognitive capacities. Key principles of neuropsychological assessment, training models for neuropsychologists, and evolving methods of assessment are reviewed. Neuropsychology is poised to play an ever-greater role in maintaining brain health in our aging population, including widespread screening for dementia, monitoring medication effects, and guiding cognitive rehabilitation after stroke and other age-related events.

Chapter 8. Capizzano, Moritani, Jacob, and Warren: Normal aging: Brain morphologic, chemical and physiologic changes detected with in vivo MRI

Brain morphologic, chemical and physiologic changes detected with *in vivo* magnetic resonance imaging (MRI) are appraised. MRI is a medical imaging technique widely used to assess structural and functional brain changes in aging. MRI scanners use strong magnetic fields and radio waves to form images of the body. The popularity of MRI methods in aging research can be attributed to its ability to probe the brain noninvasively using several different contrast mechanisms that are

sensitive to different properties of the brain tissue (e.g., water content, diffusion environment in the brain, concentration of different metabolites, perfusion, and oxygenation of blood). MRI exams involve minimal risk, and the hardware is now widely available, which makes it an ideal tool in aging research and clinical practice. This review focuses on the changes detected in the brains of healthy elderly subjects as detected by means of state-of-the-art MRI techniques used to assess brain structure and volume (structural MRI), water diffusion (diffusion weighted MRI: DWI), biochemical composition of tissues (MR spectroscopy, MRS), neuronal activity (functional MRI: fMRI) and cerebral perfusion (perfusion MRI). Nuclear medicine functional neuroimaging studies and findings in different types of dementia patients will be reviewed in the corresponding chapters of this book. This chapter complements chapter 9 on positron emission tomography (PET) and chapter 10 on electrophysiologic techniques.

Chapter 9. Boles Ponto: Positron emission tomography (PET) imaging: Principles and potential role in understanding brain function

This chapter provides an overview on PET in terms of strengths and limitations as well as specific use in certain brain pathologies. A limitation of PET is that the use of fast-decaying nucleotides requires proximity to sources of such nucleotides typically justifiable only with a large enough patient basis. Despite these practical limitations, research and clinical roles of PET imaging are well-established, especially for the evaluation of blood flow and glucose metabolism in a variety of neurological and psychiatric conditions. The role of amyloid imaging in the evaluation of an individual's risk for the development of Alzheimer's disease is beginning to be clarified and may become a critical part of the selection of subjects for Alzheimer's disease treatment trials. PET has also proven to be effective in seizure diagnosis. The broad range of potential PET radiotracers and the extensive neurotargets yet to be explored indicate the crucial role that PET can play in our quest to understand the human brain, both its normal function as well as its disease state and during aging.

Chapter 10. Anderson and Taraschenko: Electrophysiological measures of age-related cognitive impairment in humans

Anderson and Taraschenko review current experimental and clinical applications of electroencephalography (EEG) for the assessment of age-related cognitive impairment. EEG records near-instantaneous voltage fluctuations generated by large populations of postsynaptic potentials, providing a measure of neural activity with the high temporal resolution required to study rapid cognitive processes impaired in the aging brain. Quantitative analysis of EEG has revealed age-related changes in properties of oscillatory neural activity across multiple spatiotemporal networks. Event-related averaging methods have demonstrated changes in stimulus-evoked potentials across cognitive modalities in the aging brain. Likewise, longer latency-evoked potentials reflecting neural activity generated by downstream cognitive processes have been shown to be altered in older adults. Studies reviewed here are discussed in the context of existent behavioral and structural imaging data and discussed within a theoretical framework provided by putative compensatory models of cognitive aging. Finally, limitations of current EEG research are discussed, and future directions for the field are described.

Chapter 11. Rizzo and Rizzo: The brain in the wild: Tracking human behavior in naturalistic settings

Measuring brain activity is critical to understanding the mechanisms and controls of behavior and require tracking "the brain in the wild." Researchers have been tracking activity in the brain for several centuries, in model organisms and in human test subjects, and many of these investigations have depended on the control afforded by a laboratory setting. While laboratory research can provide unparalleled opportunities to explore the brain in isolation, researching in these controlled settings can also create drawbacks in the pursuit of an accurate understanding of the who, what, when, where and why of brain activity in naturalistic (real-world) settings. Human behavior observed in laboratory settings may differ markedly from that exhibited in nature ("the wild"). Test subjects may be

frustrated by the task at hand and underperform on clinical testing as a result. Conversely, test subjects may be acutely aware measurement is taking place and may overperform on clinical tests. One solution to this problem is to use self-reporting or interviews to glean insights on what activity actually occurs in naturalistic settings. However, memory isn't a foolproof record of reality, and biases or lack of training on the part of the observer or subject can create filtered reporting that results in a lack of actionable data. Even when self-reporting is accurately able to capture behavior in field conditions, proxy measurements produce additional complications. Whether the data being examined is an accurate determinant of a behavior or outcome is a difficult question. If an individual scores well on an IQ test, this does not guarantee he or she will succeed in terms of choices and activities at home, work, or play. To address these considerations of validity, we need metrics of the "ground truth" of everyday life. Rizzo and Rizzo explain how they examined older life gains from emerging technology in terms of healthy brain aging, independence, and quality of life.

Chapter 12. Wolinsky and Andresen: Quality of life assessment

This chapter traces the intellectual origin of the concept of *quality of life* (QOL), offers the World Health Organization (WHO) conceptualization of QOL and criteria for its measurement, and a perspective of QOL and health-related QOL (HRQOL) discussions. Standards for QOL methods and measurement advocated by several groups are presented in the second section as well as special considerations for older adults like cognitive impairment and dementia, the end of life, and the use of proxy-respondents. The third section of the chapter focuses on the two main families of generic QOL and HRQOL measures, those of the WHO and the Medical Outcomes Trust and QualityMetrics partnership. In the fourth section one preference (utility) measure for each of these two families of generic QOL and HRQOL measures is outlined. In the final section three QOL measures specifically constructed for the special circumstances of older adults are presented.

Part IV. Brain functions and behavior across the lifespan

Chapter 13. Eslinger and Flaherty: Executive functions and behavior across the lifespan

Executive functions (EF) are here defined in conceptual and practical behavioral terms. A framework is developed that broadly describes the maturational trajectory of EF across the lifespan and how EF relate to the primary cognitive constructs of intelligence, language, spatial perception, and memory. Most importantly, the linkage between EF and continuing adaptation in adulthood and especially aging is emphasized. The "frontal executive" theory of aging is presented and related to the broader cognitive aging and cognitive reserve literature. In this way, specific aspects of working memory, decision-making, and social cognition can be highlighted. Distinctions between executive aging and executive dementias are addressed with pragmatic assessment and management recommendations.

Chapter 14. Warren, Rubin, Shune, and Duff: Memory and language in aging: How their shared cognitive processes, neural correlates, and supporting mechanisms change with age

This chapter provides an overview and discussion of two quintessential human abilities that change over the course of our lives: memory and language. The chapter begins with a summary of cognitive aging findings focused on memory abilities, and following that section is a similar summary of cognitive aging findings addressing language abilities. Several relevant theories of cognitive aging that are applicable to the study of memory, language, or both are then considered. The chapter concludes with a discussion of the promise of research probing the intersections of memory and language through behavior, neuropsychology, and neuroimaging, which point towards possible shared mechanisms.

Chapter 15. Owsley, Ghate, and Kedar: Vision and aging

Vision impairment is among the top 10 causes of disability in the United States and is particularly prevalent among older Americans due to common problems such as presbyopia, cataract,

glaucoma, macular degeneration, and, less commonly, brain disorders such as stroke, tumor, and neurodegenerative disease. A million Americans are blind and millions more have low vision—irreversible vision impairment (best-corrected visual acuity worse than 20/40 or field loss of less than 10 degrees from fixation). Vision impairment not only causes difficulties with the visual activities of daily living such as reading and mobility, but also has been associated with a number of adverse outcomes including depression, loss of personal independence, social isolation, transportation challenges, unemployment, placement into long-term care, and death.

Chapter 16. Fattal, Hansen, and Fritzsche: Aging-related balance impairment and hearing loss

An overview of the structure, function, pathology and countermeasures of the motor system related to balance, as well as the major input via the vestibular system and the closely associated auditory system is provided. The motor control system of human bipedal walking and its levels of spinal, brainstem, and cortical control as well as loss of control in different pathological states is first described. This is followed by the detailed analysis of the vestibular system, including how that system ties into the motor control of balance and loss thereof, leading to falling in the elderly. The auditory system is included here, as it is closely related to the vestibular system of the ear and shows similar but more accelerated age-related decline. The auditory system is unique among all sensory systems, as an electronic prosthesis, the cochlear implant, can restore some hearing in deaf patients. Similar vestibular implants are in advanced stages, making the ear unique among all senses in terms of electronic substitution.

Chapter 17. Lester, Vatterott, and Vecera: Attention and processing speed

Aging and degeneration of the brain can result in forgetfulness and difficulties interacting with complicated or novel environments, including instrumental activities of daily living. Many aspects of these difficulties are rooted in impairments of speed of processing and attention. The chapter by Lester and colleagues examines the interaction of aging and selective attention, which depends on the integrity of cortical and subcortical structures, including the reticular activating system of the brainstem. Modern concepts of aging and attention have expanded considerably beyond a processing speed account into models of distributed functional connectivity in the brain. The chapter concludes with interventional approaches to cognitive aging and attention decline through various “neuroenhancement” techniques.

Chapter 18. Darling, Cole, and Ashton-Miller: Motor functions and mobility

This chapter provides an overview of the effects of aging on motor function and mobility in healthy individuals, focusing on gross and fine movements of the upper limb, whole body posture, and locomotion. The chapter details the motor changes associated with aging, pointing out the progressive slowing of movement with increasing age. Subsequently, the chapter highlights many of the attempts made to mechanistically understand the age-related slowing and their neurosensory control mechanisms. Both cortical and subcortical motor control areas show age-related alterations that could play a role in the slowing of movement, but little evidence exists to pinpoint exactly how each of these various motor control pathways relates to the slowing of movements.

Chapter 19. Kreder, Faris, Rao, and Rizzo: Incontinence and sexual dysfunction

The diagnosis and treatment of incontinence and sexual dysfunction, conditions that are particularly prevalent among the elderly, are discussed. These troublesome and costly healthcare problems can be caused by lesions at several levels of the nervous system in association with lesions in the peripheral nerve, spinal cord, and brain. Some patients have neural lesions at more than one level, as in diabetes, alcohol abuse, and multiple sclerosis. Vascular pathology, medication effects, and psychiatric factors further complicate the assessment and treatment of these patients. Incontinence is a significant threat to independent living and an important factor in nursing home placement. Neural substrates and treatments of these complex biological and psychosocial phenomena are active areas of multidisciplinary research and keen public interest.

Chapter 20. Chen and Anderson: Aging and emotional functioning

Changes in emotional function associated with aging are reviewed, including profiles of change, factors that appear to shape these profiles, and implications for successful aging. Emotional function in older age is strongly associated with quality of life, physical health, and mortality risk but remains poorly understood. This chapter first describes age-related changes in discrete negative emotions (anger, sadness, fear, and disgust), positive emotions, social cognitive and self-conscious emotions, and in the intensity and complexity of emotions. Then, factors are reviewed that may mediate/modulate changing emotional status in older age, including sex differences, culture, personality, and the social/work environment. The third part of the chapter reviews contemporary theories and models of aging and emotion. Finally, a new integrated perspective on aging and emotion is presented, which brings together a number of features from existing theories and models, with an emphasis on the compensatory interactions between age-related strengths and weaknesses. The model incorporates age-related differences between various types of discrete emotions, different levels of emotional challenge, stages of emotion generation and regulation, and phases of the dynamic process of emotion.

Part V. Brain disease and dysfunction

Chapter 21. Jones, Bruns, and Petersen: Alzheimer's disease and mild cognitive impairment

Dementia is a primary concern for many elderly individuals, and among the dementias, Alzheimer's disease (AD) is by far the most common cause. While AD is not an inevitable consequence of aging, its frequency increases dramatically among people over the age of 70. There were approximately 4.5 million people with AD in the United States in 2000, and this number may increase to 14 million by 2050. Greater attention is merited on possible precursors to AD, such as mild cognitive impairment (MCI). Growing evidence supports gradual progression of the pathologic process from normal aging to MCI to clinically probable AD. Individuals experiencing this progression must be identified and monitored through a variety of means including neurological examination (see chapter 6), imaging (see chapter 8 and chapter 9) and other biomarkers, and through new technologies and approaches for real world monitoring (see chapter 11). Jones et al. review these issues and relevant evidence, opinions, and practice parameters from the American Academy of Neurology concerning MCI, diagnostic issues concerning AD and other dementias, and related treatment recommendations from the National Institute on Aging–Alzheimer's Association (NIA-AA) workgroups on diagnostic guidelines.

Chapter 22. Nagaraja and Leira: Cerebrovascular disease and white matter disorders.

About a third of blood pumped by the heart with every contraction circulates through the brain, which critically depends on this steady supply for normal neuronal function. Nagaraja and Leira detail in their chapter the multiple facets of vascular-related brain dysfunction, ranging from stroke to white matter atrophy due to limited blood circulation. As expected, strong correlations of vascular diseases of the brain exist with age, weight, and diabetes. Arguably, vascular diseases are likely the largest single cause of dementia and certainly play a major role in Alzheimer's disease. Countermeasures in terms of various treatments after stroke or to prevent vascular diseases are discussed and put in the context of well-known preventive measures such as exercise, reduced blood pressure, and low levels of cholesterol related to appropriate dietary intake such as the Mediterranean diet.

Chapter 23. Lamichhane and Uc: Movement disorders

This review of motor disorders categorizes such disorders into those with excessive, abnormal, decreased, slow, and loss of movement. For each of these categories, overviews are provided of the clinically relevant disorders and how these disorders relate to aging (most show a strong age dependency in frequency of occurrence). This chapter provides a detailed account of diagnostic features of various movement disorders (e.g., Parkinson's, Huntington's), and points out similarities

and dissimilarities between disorders that fall overall into the same categories. The preferred therapeutic intervention is provided for each movement disorder and put into the perspective of side effects. The authors also present side effects caused by certain treatments of a given disorder that mimic other disorders, thus clearly relating the complexity of intervention with currently available treatments.

Chapter 24. Wengel, Cervantes, and Burke: Psychiatric disorders

Many psychiatric disorders found in younger adults extend into the senior years. Beyond this obvious discernment, Wengel et al. present in their chapter a more detailed insight into late-appearing psychiatric disorders and their relevance as warning signs of underlying brain dysfunction. Such late-onset psychiatric disorders may be the result of early life experiences, may be related to neurologic disorders as compromising additional effects or may manifest themselves as side effects of pharmacological treatments of seemingly unrelated disorders. In many of these late-onset disorders it is essential to understand the patient's life history to evaluate the likely causes and conclude with proper treatment. While certain treatment may result in easy relief of the symptoms, other cases, in particular of personality disorders, require long-term care to reduce the symptoms, with no cure yet in sight. Both family and professional caregivers need to be properly informed about those diseases to endure the stress associated with caring for such elderly patients.

Chapter 25. Serrano-Pozo: Encephalopathy

This chapter on encephalopathy (Greek, from *enkephalos* – brain and *pathos* – disease) includes coverage of clinical manifestations, etiologic classification, specific subtypes, and diagnostic work-up. Encephalopathy implies an anatomical correlate in the brain and a functional correlate in terms of brain dysfunction or failure. *Altered mental status* and *delirium* fall under the larger umbrella of encephalopathy and describe functional manifestations. Encephalopathies can be classified as acute (hours to days), subacute (weeks to months) or chronic (>6 months) as in Alzheimer's disease. Serrano-Pozo focuses on the acute and subacute encephalopathies that require prompt inpatient diagnostic work-up and pose immediate challenges to clinicians. Chronic encephalopathies, addressed in other chapters, are mostly irreversible dementing processes typically seen in the outpatient setting, including Alzheimer's disease and related disorders (see chapter 21), vascular disease (see chapter 22), chronic traumatic encephalopathy (see chapter 26), Parkinson's disease (see chapter 23), and other disorders.

Chapter 26. McGuire: Traumatic brain injury and neurodegenerative disease

Moderate or severe traumatic brain injury (TBI) has been linked to an increased risk of Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. In contrast, mild TBI (or "concussion") has only recently been considered a risk factor for progressive neurodegenerative disease, except for "punch drunk" syndrome, or *dementia pugilistica* which was presumed to be confined largely to professional boxers. In 2002, Bennet Omalu, a forensic pathologist, identified changes of dementia pugilistica in the brain of a retired National Football League (NFL) player, and subsequent autopsy series found this pathological fingerprint in veterans of ice hockey, wrestling, soccer, and other contact sports players with histories of concussions. Chronic traumatic encephalopathy (CTE), now the preferred term, has been confirmed in football players with no reported concussions, but with predictable exposures to head trauma in practice and play, and in military veterans with histories of blast-related or other mild TBI sustained in combat. McGuire underscores that cognitive, motor, and neuropsychiatric manifestations have emerged years after mild TBI, usually repetitive, in confirmed cases of CTE. Decline in memory, poor judgment, executive function impairment or frank dementia may be preceded or accompanied by neuropsychiatric symptoms such as depression, increased aggression, and suicidality. Gait abnormalities, Parkinsonism, weakness, and dysarthria are well-described features in some affected individuals. Hence this clinically heterogeneous spectrum may imitate several dementing illnesses in older individuals. Common comorbidities such as vascular disease, diabetes, and alcohol and substance abuse,

undoubtedly influence presentation and progression. As yet, CTE remains a postmortem diagnosis with unknown incidence and prevalence, and there are no consensus-based or prospective, validated clinical diagnostic criteria. Increased public awareness has led to legislation in all 50 states on detection and evaluation of concussion in school sports along with partnership among the National Institutes of Health (NIH) NFL, and Foundation for the NIH.

Chapter 27. Tippin: Sleep and sleep disorders in older adults

Complaints of poor sleep and daytime sleepiness are common in older adults. Frequent nocturnal awakenings, early morning awakening, excessive daytime sleepiness, and daytime napping are often encountered. Many older adults have a phase advance in their circadian rhythm leading to a tendency to go to sleep and awaken earlier than usual. Some of these changes may be the consequence of aging-related changes in the brain, but often they are the result of potentially reversible medical and psychiatric illnesses. Neurodegenerative disorders such as Alzheimer's and Parkinson's diseases may exaggerate these issues. In addition, there are sleep disorders that are either specific to this age group or become more prevalent with aging, such as restless leg syndrome, obstructive sleep apnea, and rapid eye movement sleep behavior disorder. Attention to potentially reversible comorbidities and conditions commonly seen in the elderly is crucial for proper management of sleep-related problems in older adults.

Chapter 28. Herr, Gibson, and Hadjistavropoulos: Pain

This chapter reviews key points on the experience of pain, strategies for identifying and assessing pain, and approaches to treatment in persons with dementia. Over the past decade considerable advances have been made in knowledge and approaches to addressing the many challenges faced by clinicians caring for persons with dementia and pain. However, the evidence to guide practice is still limited, leaving clinicians to make judgments by extrapolating information from studies on adults and/or older adults without cognitive impairment. As the population of persons with dementia rapidly grows over the next 30 years, targeted research that includes sufficient representation of this vulnerable group to judge treatment effects is essential to provide a rational basis for their treatment. Specifically, understanding the mechanisms and etiologies of pain in various forms of dementia, discriminating pain better by unifying language describing pain, standardizing observation tools, and implementing long-term cost-effective care are needed to manage pain.

Part VI. Optimizing brain function in health and disease

Chapter 29. Voss: The benefits of physical activity on brain structure and function in healthy aging and age-related neurological disease

Voss presents an overview of the positive effects of physical exercise on brain function, including some potential molecular explanations for the exercise effect. Interestingly, the data derived from human and mammalian animal models clearly demonstrate consistency of this correlation even in cases of neurological disorders. The century old statement “Mens sana in corpore sano” (a healthy mind in a healthy body) is bestowed with new meaning through these thorough and controlled studies. Importantly, most evidence points to mild exercise as being sufficient to generate the benefit of added neuronal plasticity. The absolute quantification of how physical exercise correlates with long-term mental benefit remains to be elucidated. Importantly, given the overall similarities in mouse and human on this benefit, it seems to be possible to use the power of the mouse model to unravel the molecular pathways leading to this benefit.

Chapter 30. Czaja: Aging, mind and brain: A human factors engineering perspective

This chapter addresses the key role of human factors engineering (HFE) for addressing growing challenges and opportunities associated with population aging, with a focus on an older user-

centered design approach. This includes examples in the realms of task and equipment/product design, training and instructional design and a précis on assessment and evaluation, and discussion of needed research in this area. HFE can greatly enhance the development of strategies to address normative age-related and disease-related changes in cognitive abilities and function experience. HFE examines the interactions of humans with products, equipment and environments during the performance of tasks and activities. This improves the “fit” between the characteristics, abilities, needs and preferences of the person with the demands associated with tasks, activities, products and environments to maximize performance potential, safety, user satisfaction and comfort and minimize the likelihood of errors, inefficiencies, fatigue and injuries. This might include ensuring that the labels on medication bottles are legible to an “aging eye” (see chapter 15) or providing environmental support aids to reduce demands on working memory or provide adequate training and instructional support. It might include designing electronic health record interfaces that consider visual capabilities and training needed to accommodate older healthcare workers (for an ethical and legal perspective see chapter 35).

Chapter 31. Williams and Jao: Community and long-term care supports for older adults with cognitive decline

This chapter reviews the current status of senior care with a projection of future needs based on demographic trends. Meeting self-care and family caretaker needs in progressive dementia can be financially and emotionally draining. Family caregiving ability is often undermined by changes in family structure and the progressive needs of demented family members. Professional care, resources and facilities are needed to accommodate these problems, with a range of costs and benefits. The chapter emphasizes the importance of assisted living facilities for early stages of professional caregiving needs in transitions to more intense and costlier hospice care. Successful care plans depend on knowledge of individual patient and family characteristics and proper diagnosis and staging of disease. With the aging baby boomer cohort, a comprehensive strategy is needed to support burgeoning annual dementia costs, which are expected to exceed \$1 trillion by 2050.

Part VII. Legal and ethical issues

Chapter 32. Anderson: Neuroethics of aging

This review discusses a number of neuroethical issues raised by the rapid scientific advances in our understanding of the aging human brain, and by the care of individuals with aging minds. Many of these issues stem from the fact that aging often is accompanied by suboptimal neurocognitive function, which can appear in a dynamic fashion with an infinite number of variations in time course, severity of deficits, and profile of change. The implications of this for personal autonomy, sense of self, and self-determination cut across medical care, public health and safety, and the conduct of aging research involving human subjects (see chapter 34 on competency and capacity, and chapter 33 on public policy). Additional ethical questions have arisen because the ability to predict age-related neurologic disease has outstripped the ability to treat these conditions—an imbalance which is not likely to change in the near future. Continued scientific advances in the neuroscience of aging must be accompanied by ongoing consideration of the thorny ethical issues involved. Aging with autonomy and dignity is a universal goal that arouses considerable general interest and provides fertile ground for public engagement, education, and discussion of the neuroethics of aging.

Chapter 33. Kaskie and Stamy: The public health challenge presented by the growing population of persons with Alzheimer’s disease and other forms of dementia: A survey of American public policy activity

This overview of activities to counteract the demographics of dementia, estimated by the World Health Organization (2014) to be about 35 million people worldwide, presents policy approaches to the most common chronic and disabling conditions among the elderly. Dementia became

defined as a national public health problem in the late 1970s, being among the most costly Medicare beneficiaries. The federal administration has steadily expanded efforts to address the challenges presented by dementia through Medicare, Medicaid, and the Older Americans Act. By 2014, every state had enacted at least one policy that identifies persons with dementia as a protected class and/or supports dementia-specific programs and services, but no single type of law has been enacted by every state and no single state has enacted every type of law. Despite considerable progress, much remains to be done to advance dementia policy at both federal and state levels. Through the assembly of task forces, the development of strategic plans, the identification of legislative champions, the support of bureaucratic agencies, and the empowerment of private enterprise and advocacy organizations, dementia policy will be moved forward to counterbalance the demographic predictions of the “silver tsunami” of elderly.

Chapter 34. Barrash: Competency and capacity in the aging adult

This chapter focuses on the myriad factors involved in determining an elderly individual’s capacity for decision-making and other complex activities. The historical and legal roots of competency determination, and the distinction between competency and capacity are reviewed. The specific cognitive and functional capacities required to meet legal standards for various forms of capacity, and the wide range of specific neuropsychological capabilities underpinning them, are also reviewed. The clinical evaluation of capacity for specific activities is outlined, with particular attention to factors affecting cognitive and functional abilities in the elderly (medical/neurological status, emotional and psychiatric status, medications, environment, social support—each of which may impart positive or negative influence), as well as other factors relevant to capacity (e.g., personal values and cultural influences). Emphasis is placed on conceptualizing capacities not in a dichotomous “present/absent” fashion, but instead tailoring nuanced impressions and recommendations to the specific individual. The factors promoting and compromising capacity identified from the evaluation should contribute to a judgment that is minimally restrictive, balancing the patient’s rights and independence with protection of the patient and society. The evaluation also should provide a blueprint for the individual, family and other care providers, and professionals to implement approaches to remediation and accommodation that optimize the individual’s capacity and level of functioning.

Chapter 35. Reavis and Park: Boomers after the bust: Ageism and employment discrimination after the Great Recession

This overview of the national context of labor force participation and employment provides trends after the Great Recession and associated societal challenges. This chapter explores the significance of the continual growth of the “55-plus” workforce as well as the impact of gender in employment, particularly for older workers. It demonstrates the impact of ageism and age discrimination throughout the employment cycle of older workers, offering a review of relevant federal and state laws and procedural avenues and their limitations, and concludes with recommendations on protecting and incorporating older workers in the labor market. The chapter can be read in the context of the many physical and health challenges reviewed in other chapters including measures for better design of tools to support work-related tasks (as in chapter 30) and Kaskie and Stamy’s review of public health challenges presented by the growing population of persons with functional and cognitive decline (chapter 33).

Key points, key readings, and Glossary

Each chapter includes key points and key readings to make this handbook more transparent and accessible to readers. Increasing precision of terminology and agreement on meanings is an essential dimension of advancing the recognition, diagnosis, treatment and research of mind and brain health and the Glossary section at the beginning of this book is meant to identify and clarify this common vocabulary with working definitions. These terms have grown in number and importance in step with the blossoming of behavioral neurology, neuropsychology, neuropsychiatry, and connections to

technology and the social sciences. Related growth of public discourse, awareness, interest, and understanding is also attributable to healthcare policy and initiatives. These include the Decade of the Brain initiative, Alzheimer's Disease Initiative, Human Connectome Project, Patient Protection and Affordable Care Act, 21st Century Cures Act, along with burgeoning public exposure and fascination with research findings amplified through modern news and social media, and a general desire to understand and cure disorders of brain and behavior across the lifespan.

Audiences

We are not aware of any single current source such as this handbook that so broadly addresses the needs of potential audiences interested in the aging mind and brain. Topics span psychology (cognitive science, social science), cognitive neuroscience, physiology, biology (genetics, molecular biology), neuroimaging, computer science, human factors/ergonomics and human systems integration, medicine, nursing, social work, ethics, law, humanities, and public policy.

Potential audiences span academia, industry, and government. This includes researchers and practitioners wanting to undertake studies of aging and cognition, state and federal program managers wanting to fund relevant research, and public health officials charged with decisions on funding research projects at the state and national levels. Potential readers also include pharma industry researchers testing drugs to mitigate cognitive aging and dementia, scientists and engineers developing sensors to measure physiology and behavior (at home, work, and hospitals and in cars across the "internet of things" and in "the wild"), and faculty teaching graduate programs who want to supplement the material on mind and brain aging available to their students.

The healthcare audience includes professionals who are often called upon to advise patients with a wide range of age-related impairments. These include physician assistants, nurse practitioners, occupational therapists, pharmacists, physical therapists, social workers, and doctors, such as neurologists, psychiatrists, internists, family practitioners, psychologists, and geriatricians who care for patients in routine and specialty practices, as well as their students, who include interns, residents, fellows, postdoctoral scholars and others students at all levels, for whom interdisciplinary curricula are being developed, more and more, around the world. We understand that the audience can also include curious laypersons, patients, families, and community members interested in advancing mind and brain health for older citizens in their own communities.

We hope this handbook is useful to you. To quote the as-yet-to-be-born Star Fleet Officer Spock and his departed earthly vessel, Leonard Nimoy, "Live long and prosper," or, if you prefer the biblical, "Long life to you! Good health to you and your household! And good health to all that is yours"! (1 Samuel 25:6).

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