second edition

Neuropsychology of Everyday Functioning

edited by

Thomas D. Marcotte

Maureen Schmitter-Edgecombe

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To Wendy, Kyle, and Kathryn,
who prove that despite its day-to-day challenges,
the real world is a wondrous place to be

And to my parents, Bob and Carol,
who always encouraged and supported me

—T. D. M.

To my parents, Ron and Terry,
who nurtured my curiosity

To my husband, Dennis, and son, Declan,
who continually support and encourage me

And to all my students, who constantly inspire me

—M. S.-E.

To JoAnn Nallinger Grant, my partner in life

—I. G.

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Preface

Life is a neuropsychological test.
—Robert K. Heaton

Some aspects of everyday functioning do not change. Navigating through daily life is a complex and dynamic process. We must constantly filter an overabundance of new information, prioritize minute-to-minute actions, attend to time-sensitive problems while deliberating on others, engage in risky activities (e.g., driving), track appointments and deadlines, interact with others, and change strategies as needed. The human brain, fortunately, is efficient and adaptive, and despite these challenges, it is rare to experience significant failure on most common everyday tasks. But brain damage can profoundly affect these abilities, and even individuals with mild neurocognitive impairments can struggle when completing day-to-day activities.

One aspect that continues to change, and at an ever-increasing pace, is the society in which we live and the types of everyday activities in which we engage. New technology has provided significant benefits in the efficiency with which we can complete daily activities, but it also brings new challenges in terms of adapting to new ways of doing common tasks. Technology has likewise helped advance scientific research into the measurement of the effects various conditions can have on the ability to carry out daily activities. Although our ability to predict performance in the "wild" from assessments in the controlled laboratory or clinic continues to evolve, it nonetheless remains inadequate.

The aims of this book are threefold: (1) to explore the rationale, theory, and practical aspects of assessing everyday functioning; (2) to review the impact of key neurological and psychiatric conditions on the ability to complete real-world tasks; and (3) to provide implications for clinical practice. In this second edition, we highlight advances in technology that have opened up new opportunities for improving our understanding of the relationship between cognition and everyday functioning, and for directly assessing everyday activities within the real-world environment. Our hope is to provide a volume that stimulates critical thinking regarding current methods, ignites ideas about future methods, and fosters thoughtful and innovative research. New to this edition, the authors were asked to provide implications of the reviewed material for clinical practice. As will be evident from reading the clinical implications, these recommendations are derived from the empirical literature alongside years of clinical experience.

This book is divided into two major parts.

Part I addresses general approaches to evaluating the relationship between cognition and everyday functioning. Numerous professions focus on this issue, yet there is often limited dialogue between the groups. Methodologies are sometimes comparable and, at other times, divergent. One goal of this book is to expose the reader to these various methods. In Section A, Chapter 1 begins with an overview of the neuropsychological approach to predicting everyday functioning. This is followed by a new chapter, which critically reviews several models and theories of importance to everyday functioning (Chapter 2). Next, the reader is provided with in-depth overviews of human factors (Chapter 3) and occupational therapy (Chapter 4). This section closes with a chapter focusing on cross-cultural issues in the assessment of functional abilities (Chapter 5). The need to consider culture when making predictions about everyday functioning is an issue relevant to all of the subsequent chapters.

Section B consists of chapters addressing the theoretical bases and practical issues involved in assessing specific components of everyday functioning. Given the significant advances in technology during the past decade, we now include four new chapters covering varying technologies that hold promise for improving understanding of the relationship between cognition and behaviors in the real-world environment. As in the first volume, the following four aspects of real-world functioning that are challenging to assess but common are reviewed in Chapters 6–9: instrumental activities of daily living (IADLs), vocational functioning, medication management, and automobile driving. New to this volume, in Chapters 10–13 we discuss naturalistic assessment methods and provide the reader with information about different technologies being used in the real-world environment (smart homes, wearables, ambulatory assessment) and in the clinic (virtual reality) to try to capture more ecologically valid real-world outcomes.

Part II reviews the impact of specific neurological and psychiatric conditions on real-world performance. This section begins with a discussion of normal aging and everyday functioning (Chapter 14). The remainder of Part II (Chapters 15–21) addresses conditions commonly seen in the clinic: dementia/mild cognitive impairment, vascular dementia, traumatic brain injury, multiple sclerosis, HIV-associated neurocognitive disorders, depression, and schizophrenia. Each chapter includes background on the condition of interest and a discussion of its effects on varying everyday activities as well as guidance for clinicians.

In the final chapter, we review recommendations that were made about future directions in the first edition and consider progress that has been made in the past decade. Then, based on the material presented throughout the book, we provide our opinions regarding directions for future work.

We are grateful to all of the authors for their contributions to this book. We are thankful for the continued support and engagement of researchers who are dedicated to addressing the theoretical and methodological issues associated with the prediction of real-world performance. We were also fortunate to engage additional authors in this volume who could directly address many of the technological innovations that have occurred in the past decade and contributed to our understanding of everyday functioning.

Our knowledge and interest in the importance of using neuropsychological measures to predict real-world functioning have grown in part from work with our mentors (Robert Heaton, PhD, and Charles Long, PhD) and many collaborators. We are also continually inspired by our students and the important contributions that they make to our understanding of everyday functioning.

Last, we'd like to thank Katherine Sommer at The Guilford Press for assisting us through the editorial process, and in particular Rochelle Serwator, our editor at The Guilford Press, who so patiently nurtured both editions into existence.

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PART I

ASSESSMENT CONCEPTS AND METHODS

SECTION A

Approaches to Assessing the Relationship between Cognition and Everyday Functioning

CHAPTER 1

Neuropsychology and the Prediction of Everyday Functioning

Thomas D. Marcotte
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Modern neuropsychology rose to prominence as a discipline during the middle of the 20th century. Armed with a toolkit of cognitive, motor, and sensory tests, neuropsychologists helped localize brain lesions and contributed to the diagnosis of neurological and neuropsychiatric conditions. Over the past decades, the role of neuropsychology in lesion localization has waned considerably, given the improved accuracy of imaging techniques. Neuropsychological assessment is, however, crucial for understanding the nature and severity of any behavioral manifestations that may result from brain abnormalities. Increasingly, a primary reason for neuropsychological referrals is to answer questions about the effects that brain alterations are likely to have on everyday functioning, such as the ability to be successful at work, handle finances, drive an automobile, or live independently (Rabin, Barr, & Burton, 2005). In addition to being a common clinical question, functional status is a focus in forensic referrals, where decisions on financial compensation may depend on estimates of a client's functional levels, and also in referrals that seek to identify treatment targets for rehabilitation efforts.

The neuropsychological approach to assessment, in the psychological tradition, usually integrates results on tests that have been well standardized and carefully characterized in terms of reliability and validity. Such measures can be useful for tracking the effects of disease progression, as well as any beneficial effects of rehabilitation programs or treatment of underlying brain abnormalities. In addition, by delineating an individual's cognitive deficits, as well as strengths, neuropsychologists aim to understand how these might impact functioning in day-to-day life. Such determinations are also an important component of some diagnostic criteria (e.g., interferes with independence; major neurocognitive disorder).

Even though the questions being asked of neuropsychologists have shifted, neuropsychologists continue to use traditional tests (e.g., Wisconsin Card Sorting Test) originally designed to address issues of lesion localization and clinical diagnosis rather than predict how an individual with a particular injury or cognitive decline might function in everyday life (Chaytor & Schmitter-Edgecombe, 2003; Rabin, Paolillo, & Barr, 2016). In addition, tests that were not originally designed to be used as clinical measures, such as the Stroop Color–Word Interference Test and Tower of London, later found their way into the clinical realm (Burgess et al., 2006). These instruments have been used to help predict difficulties with everyday functioning, primarily based on the assumption that they assess functions/constructs that are important to carrying out real-world activities. For example, regarding the Stroop, one might hypothesize that the ability to inhibit an automatic, overlearned response would, at times, be beneficial to the safe driving of an automobile, such as being able to withhold a reflex to press the brakes if a traffic light turns red when the driver is halfway through the intersection.

The approach of predicting everyday functioning using neuropsychological measures designed for other purposes has been questioned because it is not always clear how performance on basic abilities translates to behavior within the varying environments found in the real world (Goldstein, 1996). Further, multiple interacting factors (e.g., emotional, environmental) can impact the relationship between functional and neurocognitive deficits and real-world outcomes. In this chapter we review key issues in the assessment of everyday functioning, including factors that complicate the relationship between performance on laboratory tests and real-world performance. In addition, we briefly summarize the literature on the use of different types of neuropsychological measures to predict real-world performance. We limit our discussion regarding specific neuropsychological predictors and outcomes, as this aspect is covered in other chapters throughout this book.

Ecological Validity

Originally coined by Brunswik (1955), the term *ecological validity* refers to whether the findings obtained within a controlled experiment or environment can be generalized to what we see in the real world, where the organism/person exhibits “free behavior in the open environment” (Franzen, 2000, p. 47). In the context of neuropsychology, Sbordone (1996) defined ecological validity as the “functional and predictive relationship between the patient’s performance on a set of neuropsychological tests and the patient’s behavior in a variety of real-world settings” (p. 15). Although the term *real world* has been criticized as being nonspecific (Rogers, 2008) and as suggesting that behavior in the lab does not count as “real-world” behavior (Goldstein, 1996), we find the term useful to indicate the environment outside the confines of the laboratory/clinic.

Veridicality and *verisimilitude* are two general approaches to ecological validity, as described by Franzen and Wilhelm (1996). Veridicality is “the extent to which test results reflect or can predict phenomena in the open environment” (p. 93). This usually involves using neuropsychological measures or combinations of measures to predict real-world performance (e.g., employment status). Verisimilitude refers to the “the topographical similarity of the data collection method to a task in the free environment” (Franzen, 2000, p. 47). In other words, the test resembles a task people perform in everyday life and is developed considering the theoretical relationship between the demands of the test procedures and the behavior that is being predicted. Because the tests more closely approximate everyday tasks, the inferential leap from test performance to real-world performance can be made more easily (Spooner & Pachana, 2006). Most traditional neuropsychological measures fall into the category of veridicality because they do not directly measure everyday behaviors but do assess some basic requirements of such behaviors; therefore, they may predict functioning outside of the laboratory.

Examples of standardized neuropsychological tests developed with greater verisimilitude include the Rivermead Behavioral Memory Test (Wilson, Cockburn, & Baddeley, 1985; now in its third edition), the Behavioral Assessment of the Dysexecutive Syndrome (Wilson, Alderman, Burgess, Emslie, & Evans, 1996), and the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996; there is also a children's version). Such instruments typically include multiple subtasks that more closely resemble the activities individuals would be expected to undertake in everyday life (e.g., remembering names associated with faces, recalling a hidden object and its location, searching maps, listening to broadcasts of lottery numbers, preparing a letter for mailing, managing medications), with the hope of better predicting real-world functioning. Many of these "performance-based" measures are designed to assess functional capacity—that is, the person's ability to perform tasks under optimal circumstances. The focus is not on differentiating normal and patient groups per se, but on "identifying people who have difficulty performing real-world tasks, regardless of the etiology of the problem" (Chaytor & Schmitter-Edgecombe, 2003, p. 182). Therefore, in theory, these tests should be applicable to many different patient groups and, in some cases, people with normal cognition. Such tests are also often well accepted by patients/participants, given their strong face validity.

Many of the more recent tasks developed with a focus on verisimilitude are leveraging technologies, including computers and the internet. Virtual reality assessment involves administering tasks, in either an immersive (e.g., three-dimensional world via user-worn equipment) or nonimmersive (two-dimensional) environment, that simulate activities that people complete in the real world, such as preparing a cup of coffee (e.g., Virtual Kitchen; Allain et al., 2014) or shopping for grocery items (Virtual Reality Functional Capacity Assessment Tool; Keefe et al., 2016). Other performance-based tasks have been designed to evaluate everyday technology use skills such as filling a prescription by phone (Marshall et al., 2015), performing banking transactions (Woods et al., 2017), or purchasing airline tickets online (e.g., internet-based actual reality; Goverover, O'Brien, Moore, & De Luca, 2010). Although creating tests with verisimilitude continues to be a popular approach, a test based on verisimilitude is not necessarily ecologically valid (Chaytor & Schmitter-Edgecombe, 2003), and such tests need to be validated with respect to their true, real-world counterparts (Rabin, Burton, & Barr, 2007). As an example, in recent work, Ziemnik and Suchy (2019) found that a motor-sequencing task outperformed a laboratory Pillbox Test (high verisimilitude) in classifying participants according to the accuracy of their real-world medication management (weekly pill counts) and in accounting for variance in medication management. Another consideration is the potential trade-off between developing tools with highly specific verisimilitude, in that they closely match a specific task within a specific environment, versus tools with a range of tasks that have greater generalizability to "real-world" situations (e.g., planning routes to different kinds of environments, managing finances in different situations).

Defining "Everyday Functioning" Outcomes

One of the challenges in relating neuropsychological performance to real-world functioning is the lack of agreed-upon best methods for determining impairments in everyday abilities. Should we simply ask patients how they are doing in their daily lives? Should we require documentation of their daily performance, something that is often difficult to come by, if not entirely nonexistent? How about asking a third party who may be prone to bias (positive or negative) and only witness the patient performing tasks under specific circumstances? Or is it best to try to objectively measure the patient's ability to carry out an everyday task (i.e., performance-based task), even though this test would be conducted in a controlled environment and perhaps have limited real-world applicability? Can newer smart environment and wearable technologies be used to capture continuous and in-the-moment performance data and provide meaningful information about real-world abilities?

As noted by Goldstein (1996), "tests or predictors and outcome measures or criteria are both surrogates for actual abilities and behaviors" (p. 84). There is a tendency in the literature to accept various outcome measures as being closely related to real-world functioning, but we must pay as much attention to the outcome, how it is measured, and its relationship to actual real-world tasks/functioning as to the predictors themselves. For example, is slowing on a task in which the individual is required to press a brake pedal when a stimulus on a computer screen changes color evidence of a reduction in "driving ability"? In addition, methods used to assess everyday functioning may at times be used to predict real-world performances and at other times serve as a proxy for real-world performance. For example, some studies have investigated the incremental validity of performance-based tests to predict functional outcome (assessed by self- or informant report) over and above traditional neurocognitive tests (e.g., Robertson, Schmitte-Edgecombe, Weeks, & Pimentel, 2018). In contrast, other studies have examined how well differing cognitive domains predict functional capacity defined by scores on performance-based measures (e.g., Burton, Strauss, Bunce, Hunter, & Hultsch, 2009). Moreover, studies that have directly compared differing functional outcome measures (e.g., self-report, performance-based) have found that these measures do not always correlate highly and can provide differing estimates in their rating of functional ability (e.g., Burton et al., 2009).

The use of outcome measures is addressed in various chapters in this volume; here we touch upon them briefly since they are critical in understanding the relationship, or lack thereof, between performance on neuropsychological measures and "real-world" outcomes.

Self-Report

Directly asking patients/participants how they are functioning in the world is the most relied-upon method for assessing real-world outcomes; in many cases it is the most practical method, given its lower time and cost compared to lengthier objective measures. Self-report may also give a reasonably accurate representation of real-world performance, given that functional abilities can fluctuate across varied environmental situations (Sikkes, de Lange-de Klerk, Pijnenburg, Scheltens, & Uitdehaag, 2009). Self-report is also advantageous because it provides important information regarding an individual's perception of their status, even if it lacks external validity in some cases.

Self-report measures, however, often have a less clear relationship to formal testing than reports from informants or clinical ratings, particularly in neurological populations that may lack insight into their difficulties (Miller, Brown, Mitchell, & Williamson, 2013). In individuals who are cognitively healthy or have mild cognitive difficulties, self-report may be more useful as some types of errors (e.g., self-corrections) or methods of compensation (e.g., more double checking) may not be readily observable by informants. Self-report is also susceptible to biases based on the individual's mood and cognitive status. For example, depressed individuals tend to manifest negative self-judgments across multiple domains and may underestimate their true abilities (see Chapter 20). On the other hand, individuals with impairments in metacognition and self-awareness may be prone to over-confidence in their real-world abilities (e.g., Chiao et al., 2013). In addition, patients may not always accurately identify the likely sources of reductions in functioning, such as attributing declines to physical causes, when they may actually be due to cognitive issues (Obermeit et al., 2017). Other factors, such as litigation and the possibility of secondary gain, may also influence self-report.

Significant Others (Collateral/Proxy)

Another common approach to assessing real-world outcomes is to ask for input from an informant, such as a spouse or caregiver. Such persons may be in a position to give the most accurate reports of how the patient handles everyday activities across multiple environmental contexts, but there are limitations to this approach. The informant may be biased by factors such as caregiver burden or executive dysfunction, may not know the patient well, or may see the person only in situations in which his or her functioning is maximized (or minimized; e.g., Dassel & Schmitt, 2008; Morrell, Camic, & Genis, 2019). Caregivers may be particularly influenced by certain obvious deficits; for example, evaluation of memory difficulties may be more influenced by word-finding difficulties than actual memory deficits (Cahn-Weiner, Ready, & Malloy, 2003). Questionnaire methods can also be impacted by how the rater interprets questions, which might differ based on factors such as level of education, culture, and language (Azar et al., 2017). And, of course, the patient and caregiver may disagree regarding each other's assessments, perhaps making it difficult to determine which view is more accurate, and so clinical judgment must be applied.

Ratings by Clinicians

Clinician ratings are often used as an outcome measure. Examples include the Global Assessment of Functioning, Karnofsky Performance Status Scale, and the Clinical Dementia Rating Scale. A key disadvantage to this approach is that clinicians have only what they see before them in the clinic—a snapshot of the person's functional level. Moreover, clinicians are also subject to biases and often place significant emphasis on input from the patient and/or caregiver. Some studies have found that the clinician's judgment more closely matches performance on neuropsychological tests than the caregiver's reports (Zaidi, Kat, & de Jonghe, 2014), possibly because the neuropsychological and clinical evaluations occur in the same structured environment. Importantly, although the approaches may lead to common conclusions, they still may not reflect real-world performance as closely as reports of an observer in the everyday living environment.

Performance-Based Tests

Performance-based tests range from analog tasks like tying shoes and filling medication dispensers to digital activities such as filling prescriptions online (Czaja, Sharit, Hernandez, Nair, & Loewenstein, 2010) and evaluating online health records (Woods et al., 2016), to simulations of automobile driving (Marcotte et al., 2004). An advantage of these tests over the use of raters is their objective and standardized nature, which allows for clear comparisons of measured functional capacity across individuals and over time. Although most performance-based tests are administered within the clinic or laboratory, some are administered within a naturalistic environment (e.g., Baycrest Multiple Errands Test; Dawson et al., 2009) or in the home (e.g., Assessment of Motor and Process Skills; Fisher, 2003). Performance-based tests can be both time and resource intensive. Performance-based measures also differ on other dimensions, including the population targeted by the test (e.g., mild cognitive impairment, dementia), the domain or domains of function targeted by the measure (e.g., medications, financial etc.), information available about the psychometric properties of the test (e.g., reliability, validity), administration procedures (e.g., open-ended, specific), and scoring procedures (e.g., accuracy, time, error types; Schmitter-Edgecombe & Giovannetti, forthcoming).

Currently, no single performance-based measure has been widely adopted in the literature, likely because of the lack of clarity regarding the ecological validity of performance-based tests. Performance-based tests are typically administered in an environment that is devoid of everyday environmental cues and the ability to engage with typical compensatory strategies. Furthermore, performance-based tasks (e.g., write a check) may not reflect the way an individual completes the task in the real-world environment (e.g., online bill pay). As noted earlier, one of the biggest challenges for performance-based test validation and development is the identification of a gold standard against which to evaluate ecological validity.

Manifest Functioning

Another approach is to seek external documentation of real-world deficits, such as examining employment history, official driving records, or medical records (e.g., for medication adherence measurements). This approach better reflects how people function in their everyday lives and perhaps provides insights regarding whether, due to noncognitive factors, individuals perform better (e.g., using compensatory strategies) or worse (e.g., due to environmental limitations such as distractors) than one would expect, based on their functional capacities as assessed in the laboratory. This approach, however, also can be prone to error. For example, employability or even employment status can be influenced by factors other than capacity (mood disorders, environmental factors such as reduced opportunities, reluctance to give up disability income support, etc.). And in the case of driving ability, crashes are rare, often only reported to authorities in more severe cases and may be related to many external factors (e.g., other drivers, road conditions). Crash history can also be influenced by risk exposure (i.e., driving mileage, urban vs. rural driving, traffic conditions) and may thus not provide an accurate reflection of a person's true driving ability (Janke, 1991).

Actual everyday functioning can be assessed at the "molar" level (e.g., is the individual employed vs. unemployed?) or at a more granular level (e.g., is the individual as effective at his or her job as in the past? Sawamura, Ikoma, Ogawa, & Sakai, 2018; Baughman, Basso, Sinclair, Combs, & Roper, 2015). It appears that composite global cognitive test measures often best predict molar outcomes, perhaps because both types of variables encompass a broad range of abilities (Franzen & Wilhelm, 1996).

Multimodal Approaches

Multimodal approaches that integrate self-report questionnaires, informant-rated measures, performance-based tasks, and objective indicators (e.g., unemployment,) provide another lens to assess global everyday functioning. Such approaches have the potential to increase sensitivity as they allow the clinician to overcome the limitations associated with any one approach (Blackstone et al., 2013; Doyle et al., 2013). These multimodal approaches might provide a more robust assessment of everyday functioning, but the risk of Type I error warrants consideration. To some extent, a multimodal assessment of everyday functioning is utilized in clinical contexts; however, greater empirical attention to standardize their use and maximize their clinical utility is needed.

Technology-Enabled Real-World Assessments

Arguably, the most valid determination of "real-world" outcomes would be direct observation of the person in the real world. Ideally, this observation would occur unobtrusively, without the person's awareness, since the act of being observed can change behavior. The maturing of sensor design, pervasive computing, and machine learning has contributed to new methods for unobtrusively monitoring performances in the real-world environment, both continuously or through the use of in-the-moment assessment. Rather than capturing functional ability under optimized laboratory conditions, the use of sensors in the environment (e.g., home, car), on the person (e.g., smartwatch), and/or on equipment the person uses (e.g., car, phone) can improve understanding of functional abilities across interacting person (e.g., mobility, mood) and environmental (e.g., noise level, time of day) factors, as well as capture variability in performances.

Current sensor technologies differ on a number of dimensions, including the requirements involved in monitoring (e.g., normal routine, charge a battery, respond to questions), types of sensors (e.g., ambient, mobile), and types of data collected by the sensors (e.g., activity level, location, voice, cognition). A few examples of functional behaviors that have been monitored in the real-world environment with sensors include pill box use, vehicle driving behavior, time spent out of the home, overall activity level in the home, and sleep interruptions (e.g., Cook, Schmitter-Edgecombe, Jonsson, & Morant, 2019; Rawtaer et al., 2020). Research also supports the feasibility of using these technologies and machine learning methods with neurologically impaired individuals to capture everyday behaviors and predict function (e.g., Alberdi, Weakley, Goenaga, Schmitter-Edgecombe, & Cook, 2018; Seelye et al., 2017); however, these methods are still in their infancy (see Chapter 10). Psychometric work will be necessary to establish that developed measures are reliable and valid and add value to traditional assessment. Other challenges include usability issues, costs, privacy and security concerns, confidentiality, and challenges associated with analyzing and interpreting large amounts of data. Despite these challenges, these technological advances do represent exciting new options for observing how patients with neurological conditions truly behave in the open environment. (These advances are discussed in more detail in Chapters 9–12 of this book.)

Examples Relating Neuropsychological Performance and Everyday Functioning

A recurring question in the field is whether tests originally developed for the detection and localization of brain pathology can predict real-world functioning (Heaton & Pendleton, 1981). Because of the importance of this question, a considerable amount of research has used traditional neuropsychological tests to predict outcomes such as academic performance, financial management, medication management, and automobile driving. Meta-analyses have also explored the relationship between cognition and functional status, with functional outcome represented by questionnaire and performance-based tests assessing activities of daily living (e.g., Royall et al., 2007). Despite the fact that investigators have used a large variety of neuropsychological tests, ranging from a select number of measures to comprehensive batteries, together with varying operational definitions of functional outcomes, it is clear that basic cognitive functioning (measured via neuropsychological tests) *is* related to one's ability to carry out such real-world tasks. The strength of this relationship can best be characterized as "moderate." Meta-analyses conducted with a variety of populations (e.g., MCI, mixed sample, bipolar disorder) consistently suggest that cognition accounts on average for a modest 21–27% of the total variance in everyday function as assessed by questionnaire and performance-based measures (Depp et al., 2012; McAlister, Schmitter-Edgecombe, & Lamb, 2016; Royall et al., 2007). Similarly, a review article using quality-of-job performance as the outcome concluded that cognitive ability predicted from 4 to 30% of the variance (Sternberg, Grigorenko, & Bundy, 2001). In general, the strength of the relationship between cognition and function varies widely across studies (e.g., 0–80%; Royall et al., 2007), with numerous factors influencing findings, including variables being accounted for (e.g., demographics and global cognitive status), the neuropsychological tests used as predictors, the methods used to measure functional outcome (Schmitter-Edgecombe & Farias, 2018), and the population being studied. Specific examples of this type of research are provided throughout this volume.

As yet, there is no clear answer as to which neuropsychological tests are most predictive of the many components of real-world functioning, even when we narrow the question down to specific real-world tasks and neurological disorders. Using driving as an example, we find that as with most studies addressing everyday functioning, attempts to summarize the field of driving research are complicated by the variety of populations sampled and methods used across studies. Researchers have used divergent test batteries and different gold standards regarding "driving impairment" (Molnar, Marshall, Man-Son-Hing, & Wilson, 2006; Reger et al., 2004; Withaar, Brouwer, & van Zomeren, 2000). For example, driving impairments have been determined via on-road drives, performance on driving simulators, and reviews of real-world crash or moving violation history. Even though several studies have shown "modest" results in using specific neuropsychological tests to predict driving ability, note that in most cases these studies do not yield cutpoints that can guide the clinician in determining fitness to drive for an individual person. In addition, many factors beyond neuropsychological ability can affect driving performance, including motivation, personality, driving experience, use of medications and other substances with CNS effects, and road conditions (Marcotte & Scott, 2009).

We can have the most confidence in the very general statement that global cognitive impairment is associated with worse performance on everyday functioning measures. Neuropsychologically, overall impairment levels can often be best estimated using summary scores such as the Average Impairment Rating from the Halstead–Reitan Battery, or a Global Deficit Score calculated from a reasonably comprehensive battery (Carey et al., 2004; Heaton, Taylor, et al., 2004). At the domain-specific level, findings from several meta-analyses suggest that executive measures may be the strongest and most consistent predictors of everyday functioning (e.g., Royall et al., 2007; McAlister et al., 2016), in concurrence with the notion that complex measures are more likely to correlate with the complex aspects of real-world functioning (Chaytor & Schmitter-Edgecombe, 2003). Thus, it has been argued that future research should specifically focus on executive functioning as a predictor of real-world performance (e.g., Cahn-Weiner et al., 2003). In addition, learning/memory abilities have also been implicated in predicting real-world behavioral functioning (Heaton, Marcotte, et al., 2004; Van Gorp et al., 2007). But these conclusions are by no means universally true. The utility of specific measures, and even specific cognitive domains, will depend on the pattern of deficits and everyday requirements prevalent in the population being considered.

Factors Further Complicating the Relationship between Neuropsychological Performance and Everyday Functioning

As one considers everyday functioning, a distinction needs to be made between an individual's capacity to perform a task and the actual execution of that capacity. Goldstein (1996) refers to this distinction as the difference between *ability*—a skill or talent within the individual, which is assessable via neuropsychological testing—and *function*—the exercise of that ability in an environmental context (a distinction between what a person *can do* and what (s)he *does do*). A person develops an *impairment* in ability (e.g., attention), which may then lead to *functional deficits* or *disability* (e.g., in driving an automobile). Clinic-based tests typically focus on capacity/ability, whereas in predicting real-world behavior, in addition to understanding what the person is capable of doing, we are also concerned with what the person actually *does*. In order to understand the limitations in using laboratory measures to predict real-world functioning, it is also important to remain cognizant that the person being evaluated must function within a changing environment and under varying contexts (Tupper & Cicerone, 1990), which can make success in the activity more or less likely. The same ability deficit can change from having no effect in nondemanding everyday situations to disabling if the requirements of a person's everyday life increase. Unlike the laboratory testing situation, everyday functioning is not standardized across people and time.

Importantly, even though cognitive abilities are an important determinant of functional capacities, real-world functioning is determined by multiple factors. We have already discussed some of the challenges associated with defining everyday outcomes, including the fact that we currently have no gold standard measure against which we can evaluate clinic-based functional outcome measures to demonstrate that these measures are related to what a person actually does in the real-world environment. As Bilder and

Reise (2019) recently reported, we may need new validation methods in order to best demonstrate associations between real-world outcomes and clinic-based measures. In the following section, we briefly review other factors that can complicate the relationship between test performance and real-world functioning.

Testing Environment

Neuropsychological assessment typically emphasizes the elicitation of "optimal performance" from an individual in order to determine the person's underlying capacity (Lezak, Howieson, & Loring, 2004). By design, external factors (e.g., noise, distracting stimuli), task complexity (e.g., multitasking), and task length (many tests are relatively brief) are kept to a minimum. Even the newer ecologically oriented instruments (Schmitter-Edgecombe et al., 2020; Woods et al., 2017), which may require completion of a variety of ill-structured tasks, are often designed to be carried out within a clinic setting where distractions are minimized. In contrast, in the real world, tasks are typically undertaken in environments where there are variable distractions, no direction, multiple decision pathways, and limited encouragement.

Limited Sampling of Behavior

Neuropsychological testing provides only a brief snapshot of behavior (Chaytor & Schmitter-Edgecombe, 2003), whereas real-world tasks can take place over a long time period. A client may be able to rally resources for a brief testing period but have difficulty when that time is extended, perhaps due to problems with stamina and fatigue (Chaytor & Schmitter-Edgecombe, 2003), limited attentional capacity, or limited ability to exert cognitive control when faced with fluctuating state-dependent factors (e.g., stress, lack of sleep) that can impact compensatory cognitive resources in real-world situations (Small, Jim, Eisel, Jacobsen, & Scott, 2019). Further, some performance-based functional outcome measures exclusively sample one specific functional domain (e.g., medication management, financial capacity) or cognitive process (e.g., multitasking), which limits generalizability given the wide range of activities people carry out within the everyday environment. Similarly, questionnaires may have limited sensitivity to capture more subtle aspects of functional deficits by sampling for broad responses (e.g., independent, needs some help, dependent) or including only one overarching question about a functional domain (e.g., shopping).

Specificity of the Neuropsychological Test

Neuropsychological tests are often cited as measures of specific cognitive constructs. Yet identification of these constructs can vary from author to author, adding to the difficulty in consistently identifying cognitive domains that are critical to real-world functioning. For example, the Trail Making Test Part B (TMT B; Army Individual Test Battery, 1944; Reitan & Davidson, 1974) is often considered one of the measures most sensitive to brain dysfunction. In a recent meta-analysis conducted regarding individuals with mild cognitive impairment (MCI), TMT B emerged as the test most predictive of everyday functioning as measured by questionnaire and performance-based measures (McAlister et al., 2016). In the literature, TMT B has been referred to as a measure of "complex visual scanning," "speed of executive functioning," "cognitive flexibility," "visual–perceptual processing speed," and "set switching ability" (Gunstad et al., 2008; Kennedy, Clement, & Curtiss, 2003; Lezak et al., 2004; Schwab et al., 2008; Wobrock et al., 2007). The truth, of course, is that it has aspects of all of these constructs and receives a label of "X" due to the specific factor analysis that was conducted, the other measures included in the analyses, the subject group (e.g., patients with different clusters of impairments), or the author's own interpretation of the measure.

Domains of Cognition Being Assessed

Also adding to the difficulty of identifying cognitive domains that are critical to real-world functioning, most prior work has focused on traditionally assessed cognitive domains, including episodic content memory, executive functions, attention, speeded processing, language, visuospatial abilities, and general cognitive status. An accumulating body of work (e.g., Bettcher, Giovannetti, Macmullen, & Libon, 2008; Schmitter-Edgecombe, Woo, & Greeley, 2009; Schmitter-Edgecombe et al., 2011; Woods, Weinborn, Velnoweth, Rooney, & Bucks, 2012) indicates that cognitive constructs such as prospective memory, temporal order memory, and error monitoring play important roles in supporting accurate performance of many everyday activities, including remembering to take medication or sequencing events when cooking. Research also indicates that these cognitive constructs account for incremental variance in predicting everyday functioning over and above traditional neuropsychological tasks (e.g., Schmitter-Edgecombe et al., 2009). Therefore, determining the relationship between cognition and real-world task performance will likely involve considering cognitive abilities outside of those typically assessed in neuropsychological evaluations, although assessing such abilities often presents with their own challenges (e.g., evaluating prospective memory over extended time periods).

Multiple Cognitive Determinants of Real-World Functioning

As noted earlier in this chapter, most everyday tasks involve multiple cognitive processes, including tasks that may appear simple, such as making toast (Hart, Giovannetti, Montgomery, & Schwartz, 1998; Giovannetti, Schwartz, & Buxbaum, 2007). Even a simple task (e.g., making coffee) may involve different abilities based on an individual's prior experience or inexperience with the general task or the specific coffeemaker. Thus, determining the relationship between a cognitive ability and performance of a real-world task depends not only on how important the specific ability is to the task, but also the person's degree of impairment in that ability. Some activities may have a threshold whereby significant impairment in a single domain, even if it is not considered critical to the task, can impact the ability to carry out the task. For example, attention and basic arithmetic skills may be key to managing a checkbook, but severe visuospatial or memory impairments may outweigh the relevance of the intact domains.

Environmental Factors and Resources

The ability to carry out everyday functions can be significantly impacted by the environment. For example, being able to safely drive an automobile may differ depending on whether a person is alone in the car, using a cell phone, or transporting a group of middle schoolers. Environmental factors differ between individuals and for a single individual from moment to moment: During the course of a commute, an individual may drive on both a rural roadway and a congested city street, and weather-related driving conditions may change. A person's work environment may also determine if cognitive declines impact vocational functioning: Mild declines may be very evident in a highly demanding or changing work environment, and less so when the responsibilities are more routine and not as challenging (Chaytor & Schmitter-Edgecombe, 2003). Environmental factors can be beneficial as well as detrimental. The availability of resources and support systems, such as electronic reminders or individuals who can guide the person through specific tasks and provide moral/emotional support, may help a person to be more successful in the real world than suggested by a laboratory assessment of functional capacity. Unfortunately, as important as it is to assess environmental demands for each person, few studies incorporate such evaluations in a standardized manner.

Compensatory Strategies

Because clinic/laboratory assessments are typically highly structured and assess only a limited number of abilities, these evaluations may at times underestimate an individual's capacity to perform in the open environment by not providing opportunities to implement compensatory strategies (Franzen & Wilhelm, 1996). Individuals may have learned strategies such as monitoring tasks using a to-do list or setting an alarm as a medication reminder. Thus, they may function adequately in their daily life but do poorly on a clinic-based prospective memory task if they cannot implement their typical strategies. In a recent study that coded for the use of observed real-world compensatory strategies, after accounting for general cognition and proxy measures of functional ability (i.e., questionnaires, performance-based tests), use of compensation accounted for incremental variance in predicting completion of an everyday prospective memory task (Weakley, Weakley, & Schmitter-Edgecombe, 2019). On the other hand, individuals may make a concerted effort to strategize during a testing session but not do so in everyday life. For example, a person might use semantic clustering to remember items on a memory test, but not use such a strategy when trying to remember a shopping list (Chaytor & Schmitter-Edgecombe, 2003). In addition to providing information regarding an individual's deficits, neuropsychological testing can provide valuable information regarding a person's cognitive strengths, which may also suggest ways that he or she could potentially compensate for deficits. This is one reason why neuropsychologists should always consider assessing multiple domains, and not just those in which they hypothesize likely impairment (Heaton & Marcotte, 2000). Questionnaires to assess compensatory behaviors are in development (e.g., Farias et al., 2020).

Individualized Approaches to Problem Solving

Even neurologically normal individuals approach the same task differently (Chaytor & Schmitter-Edgecombe, 2003). For example, some people may spend a great deal of time ineffectively "organizing" their to-do lists, whereas others may focus on completing the tasks that are in front of them. Others may routinely and effectively use shopping lists or map out a driving route ahead of time. These idiosyncratic approaches to everyday life complicate the prediction of real-world performance; in some cases, a well-developed "list-making" approach may help individuals should they suffer a decline in functional capacity in the future.

Physical Impairments and Health Comorbidities

Physical impairments can affect both activities of daily living (ADLs) and instrumental activities of daily living (IADLs) and should be considered in many neuropsychological or functional evaluations. The impact of physical impairments is evident in many neurological conditions (e.g., stroke, traumatic brain injury, multiple sclerosis) and across many real-world tasks (e.g., driving and vocational functioning). A recent study found that although general capability to complete IADLs as measured by multiple methods (i.e., self-reported, informant-reported, performance-based, and direct observation) was similar across groups with MCI and Parkinson's disease, the nature of the error profiles, completion time, and cognitive correlates differed as a result of cognitive and motor difficulties (Schmitter-Edgecombe, McAlister, & Greeley, 2021). Furthermore, greater IADL limitations have been found in individuals with higher levels of physical inactivity, two or more chronic diseases, obesity, and those with frail status (Portela et al., 2020), highlighting the importance of considering health comorbidities.

Neuropsychiatric Symptoms, Psychiatric Disorders, and Substance Use Disorders

Neuropsychiatric symptoms and conditions, such as depression and apathy (Rog et al., 2014), schizophrenia (Green, Kern, & Heaton, 2004), and bipolar disorder (Martinez-Aran et al., 2007), can significantly affect a person's ability to initiate and complete ADLs and impact the reliability of self-reported functioning (Heaton, Marcotte, et al., 2004). Depression in particular is a prevalent condition that can affect everyday functioning (see Chapter 20). Although medications for these conditions often improve functioning, they can potentially have negative effects as well (e.g., on automobile driving). Acute and chronic substance use can also affect key everyday activities such as employment, financial management, and driving ability (e.g., Hser, Huang, Chou, & Anglin, 2007; Johansson, Alho, Kiiskinen, & Poikolainen, 2007), although the literature using objective measures of functional capacity in these groups is limited (Morgan et al., 2014).

Culture, Race, and Ethnicity

People differ in their daily activities and their methods of engagement (e.g., driving versus taking public transportation, using cash versus all-electronic methods for handling finances). Such differences can be found at both the individual level and within larger groups based on factors such as culture, race, and ethnicity. These differences are apparent within the United States as well as internationally (e.g., Labra Pérez & Menor, 2018). Such differences make it difficult to simply adapt functional assessment methods validated primarily within English-speaking subgroups in the Western world to other populations. As noted in several chapters of the present volume, especially Chapter 5, this complicates attempts to characterize changes in everyday functioning in a single, universal matter; it also requires in-depth understanding of such differences and creativity in determining the best way to assess functioning within various groups and societies. This is particularly true when developing instruments emphasizing verisimilitude. In addition, though, the relationships between cognitive and functional measures have frequently not been appropriately validated for individuals of diverse ethnic backgrounds, limiting the inferences that can be drawn from a veridicality approach. Lastly, differences in the prevalence of various health conditions across racial and ethnic groups further impacts our understanding of the relationship between cognition and function. This remains an area in need of much further research.

Education and Literacy

Although educational levels and neuropsychological test performance clearly travel together on many tests, and IQ is closely linked to educational and ultimately job attainment, little attention has been paid to the direct relationship between education and the ability to carry out everyday tasks. At lower levels of education, in particular, literacy (numeracy, reading and writing) may be an issue. Many resource-limited countries have high illiteracy rates. Inadequate numeracy ("the ability to understand and use numbers in daily life") may adversely impact health outcomes and everyday functioning in tasks such as reading food labels, interpreting bus schedules, and refilling prescriptions (Rothman, Montori, Cherrington, & Pignone, 2008, p. 585). However, education and literacy are not completely synonymous, as individuals learn many life skills (e.g., how to count money) without formal education.

Experience/Functional Reserve

It is generally accepted that certain individuals, typically those with higher IQs, educational level, and/or occupational attainment, may be able to withstand greater brain insults before such damage manifests itself clinically (Satz, 1993; Stern, 2003), suggesting cognitive resilience (Stern, Barnes, Grady, Jones, & Raz, 2019). It has been hypothesized that individuals may have a "cognitive reserve" based on innate levels or, alternatively, that such a reserve is expanded by exposure to schooling and other stimulating activities. For most individuals, repeated exposure increases the "automaticity" with which tasks can be completed, enhances their expertise, and perhaps increases reserve. One example of an everyday activity modifying brain structure can be found in a study of London taxi drivers. In this project, the more time the participant spent as a driver, the larger the hippocampal volumes (Maguire et al., 2000), suggesting the possibility of increased reserve. One might hypothesize that more experienced individuals can suffer more brain abnormality prior to reaching a point where they no longer work at a minimally competent level.

Motivation

Clients may be motivated to do their best during testing but perhaps have less motivation in the real world, or vice versa. For example, they may be able to avoid undesirable tasks at home if they feign an inability to do the tasks. In the example of forensic cases, clients may see benefits in not performing their best during an evaluation in order to get increased compensation. Even in nonlitigation cases, clients may simply lack the motivation to try their best across a battery of neuropsychological or everyday functioning tests. These motivational issues suggest a need for skilled examiners, conversant with such problems, even when computerized measures are being administered. A number of instruments assess “effort,” symptom validity, and malingering in the clinic/lab (e.g., Morgan & Sweet, 2008).

Given the many factors that might affect everyday functioning, it is not surprising that, as with most behavioral research, measures of cognitive status alone remain only “moderately” related to real-world performance. Improving assessment in the areas mentioned earlier might enhance laboratory predictions of behavior in the open environment. As an example, the Royal Prince Alfred Prospective Memory Test (RPA-ProMem; Radford, Lah, Say, & Miller, 2011) allows participants to use any strategies they think might help them remember to complete future tasks (e.g., phone and leave a message after they arrive home). Casaletto, Weber, Iudicello, and Woods (2017) proposed a comprehensive assessment model that includes as interacting factors the overlap between the individual’s pattern of deficits and the particular demands of the real-world task, motivation, awareness of cognitive and functional deficits, as well as the availability, effectiveness, and use of compensatory strategies, and the presence and influence of biopsychosocial cofactors. The model accounts for dynamic changes in one area that can impact other areas of functioning as well as reciprocal relationships (e.g., real-world declines negatively impact cognitive functioning, which in turn may exacerbate disability). This conceptualization can guide ongoing efforts by investigators to develop new measures that have a strong neuropsychological bent but focus on cognitive constructs specifically hypothesized to relate to real-world performance—measures designed to assess more directly the abilities needed to carry out everyday tasks.

Selection of Neuropsychological Test Variables

Is a common, underlying set of cognitive abilities necessary in order to adequately perform all everyday activities? Alternatively, is it the case that some key abilities (e.g., attention) are necessary, but perhaps not sufficient, to carry out many tasks, and that specific activities require specific skill sets? Can we predict human behavior by examining performance on cognitive constructs individually and in isolation, or do we need to know how they work in concert? Although these questions remain unanswered, or incompletely answered, practicing neuropsychologists appear to be in general agreement regarding the key abilities that should be assessed when predicting everyday functioning. These include attention, executive functions, intelligence, language, motor skills, verbal and nonverbal (visual) memory, construction, and visuospatial skills. Nevertheless, there remains significant variability with respect to which tests are used to assess these domains (Rabin et al., 2007, 2016), and which normative standards might be most appropriate.

When predicting everyday functioning, most neuropsychologists use traditional neuropsychological tests along with structured interviews/questionnaires and may augment their battery with one or more ecologically oriented measures. A survey of 512 doctorate-level psychologists (Rabin, 2016) revealed that none of the 15 most frequently endorsed assessment instruments were developed primarily with ecological validity in mind. Similarly, across specific cognitive testing domains (e.g., memory, executive functioning), tests developed with high ecological validity in mind (e.g., Brief Test of Attention) were endorsed as being administered by only a small percentage of respondents

(< 8%). Moreover, the most frequently used method for assessing activities of daily living was a structured interview (Rabin, 2016).

Neuropsychological tests can yield a number of performance variables: raw scores, scaled scores, and demographically adjusted scores. To determine whether there has been a decline in functioning, the examiner needs to know the patient's premorbid functional level. However, neuropsychological testing is rarely available for the period prior to an insult (e.g., head injury) or illness. A variety of methods have been developed to estimate prior functioning, including measures based on educational and occupational attainment, as well as performance on tests that are relatively insensitive to acquired brain abnormalities (e.g., Holdnack, Schoenberg, Lange, & Iverson, 2013; Pearson Clinical, 2017). Neuropsychological performance tends to correlate with characteristics such as age, education, gender, and ethnicity (Heaton, Taylor, et al., 2004; Heaton, Miller, et al., 2004), and the use of norms that adjust for these factors are particularly helpful in estimating differences between observed and expected levels of performance.

Although the method of using demographically adjusted normative standards works well for determining whether individuals are impaired relative to expected levels, the use of adjusted scores may not be the best method for predicting performance of activities that most of the population should be able to accomplish routinely. For example, although we might expect a person with a PhD in engineering to perform better on cognitive tests than an individual with a high school education, we would not necessarily expect that person to be a better driver or more adept at managing his or her medications.

When addressing the relationship between cognition and everyday functioning, we are not so much concerned with whether someone has declined from a previous level of neurocognitive performance, but rather whether his or her functioning is adequate for their individual everyday functioning requirements *now*. One approach to predicting competence in everyday skills would be to simply consider raw scores, such as time to complete TMT B, or the learning rate on the California Verbal Learning Test. However, raw scores are difficult to compare across tests and to interpret in relation to expected functioning of the general population. For example, one measure may be timed, in which a fewer number of seconds indicates good performance, whereas higher scores on another measure (e.g., a list-learning test) are indicative of good performance. These differences also make it difficult to combine such variables into summary scores. For these reasons we have recommended the use of scaled scores in predicting everyday functioning (Heaton & Marcotte, 2000). Scaled scores are uncorrected (e.g., for age and other demographics) scores that are generated from a population of normal controls (ideally representing a broad range of demographic characteristics, similar to the society of interest; e.g., based on a national census), and transformed so that they are normally distributed (often with a mean of 10 and a *SD* of 3). Since each test variable is put onto this common metric, one can then compare performance across measures and generate summary scores, such as estimates of overall or domain-specific functioning (Heaton, Taylor, et al., 2004).

There remains a fair amount of variability in whether investigators use raw, scaled, or *T*-scores. One study directly compared the use of adjusted and unadjusted scores (Silverberg & Millis, 2009) in a group of patients with traumatic brain injury (TBI). Real-world outcomes were based on patient and caregiver reports. The authors used the normative data provided by Heaton, Miller, Taylor, and Grant (2004) to generate "absolute scores"—unadjusted scores that were placed upon the *T*-scale metric, where the overall mean of the normative group is 50, with a standard deviation of 10, in order to facilitate comparisons of the two methods. They then created two overall test battery mean scores (for absolute and adjusted scores) in order to predict outcomes on their questionnaires. The authors found that (1) absolute and adjusted scores were often divergent, usually based, as would be expected, on the degree to which the patient differed from the normative group average on demographic factors (age, education, gender, ethnicity); and (2) whereas both measures predicted everyday functioning, the results tended to favor the use of absolute scores. It should be noted, however, that the superiority of absolute scores for predicting everyday functioning may depend on whether the tasks are those that all or most adults would be expected to perform successfully. If the everyday tasks are exceptionally demanding and normally performed only by people with high levels of education (e.g., physicians, attorneys, scientists, university professors), use of education-corrected scores may be better predictive of success or failure.

Additional studies comparing these methods may yield useful insights as to the best way to use neuropsychological test results to predict real-world behavior. For example, such studies might identify absolute levels of functioning in various domains that are needed to accomplish specific tasks, such as medication management. The findings might vary by neurological group. The role of compensatory strategies and other factors that might influence the relationship between neuropsychological test performance and everyday behaviors would also need to be considered. Over time, investigators could build a common base of knowledge that would inform clinicians and future studies.

Challenges in Developing Instruments Focusing on Ecological Validity

A survey of 747 North American doctorate-level psychologists that examined their use of assessment instruments designed with ecological validity in mind revealed that in many cases neuropsychologists emphasized clinical acumen and nonstandardized evaluations rather than published tests (Rabin et al., 2007). According to the authors, the survey "highlights the disparity between the proportion of neuropsychologists who conduct assessments that focus on ecological issues and the proportion who use the instruments designed for ecological purposes" (p. 736). If ecologically oriented instruments hold promise, why have neuropsychologists hesitated to incorporate such measures into their standard test batteries? Spooner and Pachana (2006) propose the following possibilities: (1) the assumption that traditional tests are ecologically valid, despite limited evidence that this is the case; (2) the tendency to stay with those instruments on which one received graduate training or to remain committed to a particular theory of assessment approach; (3) the view that verisimilitude is synonymous with face validity, suggesting a less rigorous or "unscientific" evaluation of the ecological validity of the measure, even though many of these instruments have undergone such evaluations; (4) the belief that tests based on verisimilitude overlap with the occupational therapy approach and thus encroach on another discipline; and (5) the belief that traditional tests measure specific constructs, even though "the application of labels to cognitive domains is not necessarily reflective of unambiguous empirical findings" (p. 334).

Although ecologically oriented instruments hold promise, many of these instruments continue to be most widely used within the context of research. Mimicking everyday tasks in the clinic/lab does not necessarily mean that the findings will directly relate to how patients/participants function in the real world, where they must deal with competing tasks, prioritizing, paying attention in the context of distractions, and so on. Burgess and colleagues (2006) advocated for a function-led approach to creating clinical tasks—models that proceed from a directly observable everyday behavior backward to examine how a sequence of actions leads to behavior, and how that behavior might become disrupted. Ecological validity may be improved because of more specific delineation of cognitive processes, even in seemingly simple behaviors (e.g., making toast and coffee; Schwartz, 2006).

Throughout this book, the reader will be exposed to numerous approaches to studying everyday functioning and a variety of ecologically oriented tests developed with the goal of improving the real-world predictive ability of clinic-based tests. Some of these ecologically oriented tests have taken a more function-led approach to development. For example, in addition to coding accuracy and time to completion, to understand how behaviors become disrupted, these tests also code for specific errors being committed (e.g., omissions, commissions) in the actual execution of an action sequence such as making coffee (e.g., Naturalistic Action Test; Schwartz, Buxbaum, Ferraro, Veramonti, & Segal, 2003) or in more complex skills that are ill-structured and involve multitasking (Baycrest Multiple Errands Test-Revised; Clark, Anderson, Nalder, Arshad, & Dawson, 2017). Despite their open-ended and naturalistic nature, such tasks have generally displayed adequate psychometric properties (Knight, Alderman, & Burgess, 2002; Schwartz, Segal, Veramonti, Ferraro, & Buxbaum, 2002) and have shown moderately high correlations with independent outcomes assessing everyday functioning (Dawson et al., 2005, 2009; Schmitter-Edgecombe, McAlister, & Weakley, 2012).

Other aspects of performance being captured by newer ecologically oriented clinic-based tasks include skills such as planning, mid-task planning, self-monitoring, and compensatory strategy use (e.g., Night Out Task: Schmitter-Edgecombe, Cunningham, McAlister, Arrotta, & Weakley, 2021; RPA-ProMem: Radford et al., 2011). "Actual Reality" is an assessment approach that uses the internet to perform real everyday activities such as purchasing an airline ticket (Goverover, O'Brien, Moore, & DeLuca, 2010) or health-related internet searches (Woods et al., 2016). Detecting impairments in navigating technology and the internet might help clinicians and researchers capture potential barriers to optimal quality of life and identify targets for rehabilitation. Newer approaches are also making use of virtual reality to simulate the real world (see Chapter 13, this volume). These computer-administered approaches allow for analysis of more fine-grained details of movement and performance as data is captured automatically and on a continuous time scale. In some cases, individuals may display a number of errors on these ecologically oriented assessment instruments while performing adequately on more traditional measures of similar constructs (Marcotte et al., 2004). To date, many of the instruments that have been developed using a function-led approach are still being used predominantly in clinical research. They await further validation and normative standards before being widely used in clinical care.

These newer instruments may offer ecologically relevant additions to a battery of assessment instruments when such everyday problems are suspected. To this end, we need to demonstrate that ecologically oriented instruments can provide incremental improvement on the prediction of everyday functioning achieved using traditional neuropsychological measures. For example, in a study of the driving abilities of HIV-positive individuals (Marcotte et al., 2004), participants completed a detailed neuropsychological test battery and interactive PC-based driving simulations assessing routine driving and accident avoidance skills, as well as navigational abilities (i.e., using a map, participants were asked to drive to a location within a virtual city and then return to their starting location). Global neuropsychological performance was found to be a significant predictor of passing or failing an on-road drive. However, performance on the simulations explained additional variance beyond traditional testing in predicting on-road performance. This suggested that the simulations may provide information on real-world behaviors that are not captured by neuropsychological measures, such as the ability to anticipate high-risk situations or respond to complex demands when under time pressure. The difficulty in identifying gold standards for evaluating the ecological validity of clinic-based tests, however, makes this work challenging.

Advances in technologies that allow for continuous and in-the-moment assessment within the real-world environment may offer new opportunities for development of gold standard functional outcome measures; these advances may also serve to further augment clinic-based assessment (see Chapters 10–12, this volume). Technology-enabled assessment of real-world function may also improve understanding of the impact of contextual (e.g., environment, mood) and time-varying influences on real-world everyday activities. For example, real-time associations have been found between fluctuations in cognition and behavioral symptom expression, including the side effects of medication (Frings et al., 2008) and fatigue (Small et al., 2019). The ability to capture both variability and trajectories of change in real-world everyday activities could also augment and improve the sensitivity of traditional assessment methods, which typically compare a limited number of assessment points spread out across lengthy time periods to reduce the impact of practice effects.

Ideally, it would be useful to employ ecologically oriented measures that encompass a broad range of skill levels (from easy to challenging), are able to detect subtle declines (in the case of early-stage neurological disorders) or improvements (in the case of pharmaceutical treatments) and are valid across persons of diverse cultural backgrounds. However, it is very difficult to develop measures that reflect everyday functioning—tasks that most people successfully perform in their daily lives—and are still challenging enough to provide a distribution of functioning across "normal" individuals (i.e., so that not everyone either receives a perfect score or fails the test). As the difficulty of a task increases, correlations with education and intelligence increase, and it becomes a challenge to keep the measure from being "test-like" (Goldstein, 1996) or game-like. For example, how much complexity can be added to a money management task before the testee will need to be a certified public accountant to succeed on the test? Or at what point does adding difficulty to a driving simulation (e.g., accident avoidance scenarios) produce the look and feel of an arcade videogame, thus losing the real-world aspects of the measures? The Rivermead Behavioral Memory Test is an example of a measure that was "extended" when the earlier version was found to be insufficiently challenging to delineate functioning within normal individuals (de Wall, Wilson, & Baddeley, 1994). From our own experience, our battery of functional measures (cooking, shopping, financial management, medication management, vocational abilities) underwent a number of modifications before achieving a reasonable balance between task difficulty and real-world applicability (Heaton, Marcotte, et al., 2004). In addition, given that most healthy individuals perform near ceiling on many everyday measures, it is also often challenging to establish test–retest reliability via traditional correlational methods.

What Is the Best Lab- and Clinic-Based Approach to Predicting Real-World Behavior?

As noted earlier, the existing literature suggests a "moderate" relationship between traditional neuropsychological measures and real-world functioning, and no single test, or battery of tests, is predictive of all aspects of everyday functioning across all groups. However, the neuropsychological approach brings many advantages in that many tests have good psychometric properties, established reliability and validity, and norms. In addition, there is abundant evidence that performance on traditional neuropsychological tests relates to aspects of everyday functioning. Few studies have conducted direct comparisons between approaches emphasizing veridicality versus verisimilitude, and comparisons between studies are complicated by the use of different test instruments, different outcome measures, and different samples. However, in a review of studies using one, or both, approaches, Chaytor and Schmitter-Edgecombe (2003) found some evidence favoring the verisimilitude approach in predicting everyday performance, at least with respect to memory and executive functioning. A few studies have also demonstrated that tests with verisimilitude can provide incremental improvement when predicting real-world outcomes after accounting for traditional neuropsychological measures (Marcotte et al., 2004; Robertson et al., 2018). But the matter is still unresolved.

At this juncture, it appears that the best approach remains one in which, in most circumstances, the neuropsychologist uses demographically adjusted scores to determine whether there has likely been a decline from previous cognitive levels. If the decline appears to be of sufficient magnitude to affect everyday functioning, the examination of nonadjusted scaled or absolute scores can be used to predict most real-world activities (Silverberg & Millis, 2009). Greater precision of this prediction is likely to be possible if future studies help clarify basic levels needed to perform specific tasks. In some cases of highly demanding positions (e.g., physician, pilot), it is advisable to continue to focus on expected levels of cognitive functioning, using demographic corrections, since an average level of scaled scores may not adequately encompass the cognitive expertise needed for the most challenging real-world tasks. Based on meta-analytic data, in addition to global cognitive status, a focus on executive functioning and perhaps learning and memory may provide the greatest yield regarding the prediction of real-world functioning (Royall et al., 2007; McAlister et al., 2016). Additional cognitive domains specific to the real-world tasks in question could also be assessed (e.g., prospective memory). As noted earlier, since one is also interested in cognitive strengths (e.g., for potential compensatory mechanisms), we recommend the administration of a comprehensive battery whenever the prediction of real-world functioning is the goal.

It should also be clear that there are benefits to the multimodal assessment of an individual's ability to carry out everyday tasks successfully. Such assessments would include information gleaned from some of the well-developed, ecologically oriented measures discussed here and throughout this book, as well as self- and informant-reported perceptions about how well the individual is functioning in his or her daily life gathered through structured interviews and surveys. Traditional neuropsychological tests and performance-based everyday functioning measures inform us of the individual's capacity, but the clinician also needs to be familiar with other factors (e.g., environmental, emotional, psychosocial) that might cause differences between capacity and implementation.

On the one hand, overestimating functional capacity may result in irreversible negative consequences to a patient, such as financial debt or injury to self. On the other hand, underestimation could lead to unnecessary restriction of daily responsibilities that can diminish independence and sense of self-worth.

The Path Forward

Traditional neuropsychological measures continue to prove useful, as has been described here. However, although measures that assess specific cognitive constructs (e.g., for diagnosis) will always be needed, the field of neuropsychology continues to be faced with the question of how to more effectively use the traditional tests or how to best develop new tests and make use of evolving technology to better predict and assess functioning in the real world. Chapters 2 through 4, this volume, provide information about general theoretical approaches that have been applied to examining the relationship between cognition and function. Chapter 5 draws attention to the importance of considering cultural challenges in the assessment of functional abilities.

As discussed earlier, one needs to pay as much attention to the measurement of outcomes as to predictors. Chapters 6–13 discuss in detail numerous assessment methods, ranging from questionnaires to virtual reality to technology-enabled real-world assessment, that have been employed to improve predictions of everyday functioning. A significant challenge for development of any new clinic-based test is to demonstrate the ecological validity of the test as currently "real-world" outcome is itself poorly defined. In the field of automobile driving, for example, the relationship between cognitive performance and "driving" may differ if driving performance is assessed via reaction time to a video, a fully interactive desktop simulator, a full-motion car cab, a closed-course challenge drive, an open-road assessment, or a tally of real-world crashes. As described in Chapters 9 and 10, newer driving sensor technologies have the potential for unobtrusively collecting continuous data about driving performances and observing important driving behaviors (e.g., off-road glances, driving speed adaptations) and changes in driving behaviors over time (e.g., driving less on highway) in the open, real-world environment. Other technologies described in Chapters 10–13 (e.g., smart environments, wearable) also hold promise for recognizing, describing, and assessing routine behaviors in the real-world environment such as cooking, grooming, pill box use, activity level, and computer use (e.g., Cook et al., 2019; Rawtaer et al., 2020). Although such approaches can raise privacy and security issues and present data informatics challenges, they offer an exciting window for observing how normal and impaired individuals behave in their day-to-day life. They will likely offer new measures of "real-world" outcomes.

As is evident in Chapters 14–21, this volume, where the state of the literature regarding the relationship between cognition and function is discussed relative to specific disorders, additional factors complicate the prediction of real-world behavior. Among these considerations is the fact that an individual's ability to function in the real world at any particular time depends on a complex interaction of a person's neurocognitive deficits with other person-specific and environment factors (e.g., cognitive resilience, compensatory strategy use; Casaletto et al., 2017; Burton, O'Connell, & Morgan, 2018; Delgado et al., 2019). Furthermore, of the ecologically oriented instruments that have been developed, most have yet to gain widespread use, either by different research groups or across different neurological populations. Many tools are "home grown" and are applied within a single laboratory or across only a few patient groups, thus limiting their utility to the field at large. Until these approaches are more widely implemented. which will require greater investment by neuropsychological organizations or government entities, the field will likely continue to progress slowly. Such investments are also important for clinical trials where calls have been issued for better measurement of outcomes relating to everyday functioning and requirements to include co-primary measures that assess clinically meaningful/relevant functional outcomes (e.g., Buchanan et al., 2005; Laughren, 2001). Thus, there may be greater movement toward measures that include a verisimilitude approach to predicting real-world behavior or toward technology-enabled assessment of real-world functioning, if indeed such measures are better predictors.

The ability of neuropsychological testing to predict everyday functioning has been clearly established. However, performance on these clinic-based measures does not capture all of the variance associated with behavior in the open environment. Advances in theoretical conceptualizations, test development, technology, and multimodal methods of assessing predictors and outcomes portend a promising future for our ability to understand the relationship between brain function and behavior in the real world.

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CHAPTER 2

Theories and Models of Everyday Functioning

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Everyday functioning is a deceptively simple term. We can all easily generate a list of the activities that comprise this functioning (e.g., meal preparation, work, parenting). Yet, with very little probing, the complexity of the term becomes apparent. For example, if one takes an annual ski holiday, should this activity be considered part of everyday function? If one continues to complete their daily activities but no longer enjoys them or finds meaning in them, should this be captured in the term everyday functioning? While this term is widely used in the neuropsychology and rehabilitation literature, it is seldom defined, and its boundaries are rarely elucidated. This hampers investigations into ecological validity and obfuscates our endeavors to improve everyday life for our clients. Thus, this chapter aims to explore the meaning of everyday function, critically review the most important models and theories that pertain to everyday function, provide examples of assessments that reflect these models and theories, and consider future directions for work in this area. Our goal is to offer students, clinicians, and researchers language and tools that will enhance and enable their investigation of the neuropsychology of everyday functioning.

In this chapter, we review frames of reference, models, and theories from the fields of occupational therapy, occupational science, and neuropsychology, situating them in the historical development of these professions. The intent is not to provide an overarching unified theory of everyday function but rather to provide further breadth and depth to our understanding. Frames of reference provide a structure for organizing theoretical material and a conduit for putting this information into practice (Hinojosa, Kramer, & Luebben, 2020). Models can be symbolic representations used to provide an explanation of an idea or process and to facilitate the organization of what we know. Models can also be theoretical and representations of hypothetical relationships between concepts. Typically, empirical data are available to support some of the relationships or hypotheses depicted in theoretical or conceptual models. Theoretical models can be useful in fostering a more profound understanding of the relationships depicted in the model and in developing hypotheses that can be subjected to empirical analyses. Thus, they can direct us to different possibilities for mechanisms underlying observations and also to possible targets for intervention.

Frames of Reference: Neuropsychology and Occupational Therapy

While neuropsychologists and occupational therapists use some of the same theories and models, their frames of reference are substantively different; that is, the overarching structure within which they situate their inquiry and practice is dissimilar. Everyday function has always been at the heart of occupational therapy. The field of occupational therapy focuses on enabling purposeful and meaningful occupation in the context of client-centered practice; "occupations refer to the everyday activities that people do as individuals, in families and with communities to occupy time and bring meaning and purpose to life" (World Federation of Occupational Therapists, 2016). Clinicians and researchers understand that occupation is contextual; it shapes and is shaped by environmental and individual factors. In contrast, the primary objective of neuropsychology is to understand relations between the brain and behavior/cognition, typically through the study of brain damage and disease. While neuropsychological research and clinical practice traditionally focused on testing and understanding relatively circumscribed behaviors and cognitive processes, in more recent years the field has recognized that it is critical to understand how the brain organizes everyday activities and interacts with the environment (Burgess et al., 2006).

Why Everyday Functioning Is Important to Neuropsychologists

There are many reasons for neuropsychologists to consider everyday function. Almost every form of brain damage or disease has an impact on some aspect of everyday life. Even subjective cognitive changes associated with typical cognitive aging have been associated with increased difficulties in everyday tasks (Rotenberg, Maier, & Dawson, 2020). Referral sources for neuropsychological assessments often request information about clients' capacity to live and function independently, and improving everyday functioning is the ultimate goal of cognitive rehabilitation. Additionally, because functional difficulties often comprise a core diagnostic criterion of many clinical disorders, including attention-deficit/hyperactivity disorder (ADHD) and dementia, it is important for neuropsychologists to obtain accurate information about the level of functioning in a range of contexts including job, school, home, and so on. As neuroimaging and biomarkers may be used increasingly for diagnosis of clinical disorders in the future (Jack et al., 2018), neuropsychological referral questions may shift to concerns regarding functional abilities (e.g., the ability to live alone, succeed in college-level courses, make decisions about health care). To address these important referral questions, neuropsychologists must, in addition to collaborating with occupational therapists, appreciate the relations among brain function, cognitive processing, everyday functioning, and context. Understanding these complex relations requires comprehensive and empirically validated, conceptual models of everyday functioning that explain the breakdown of everyday functioning following brain damage or disease, as well as moderating variables.

Neuropsychologists also require a firm understanding of everyday functioning, as difficulties with these activities are strongly associated with a wide range of negative outcomes including depression, institutionalization, and increased cost of care (Branch & Ku, 1989; Lehrner et al., 1999; Taylor, Schenkman, Zhou, & Sloan, 2001). Successful performance of everyday activities as a treatment outcome is highly meaningful to clients and families (e.g., McCarron, Watson, & Gracey, 2019). Further, evidence from the cognitive rehabilitation literature supports the view that treatments focusing on specific cognitive processes without providing explicit strategies to support generalization have limited benefit for everyday life (Bowie & Medalia, 2016; Cicerone et al., 2019). Interventions informed by an understanding of the complexities of everyday functioning are likely to be more effective.

Theoretical Models of Everyday Function

Understanding everyday function requires knowledge of several groups of theoretical models and frames of reference. For each group, we provide some historical background for development of the model or framework with at least one example of a key model within the grouping, followed by a discussion of its uses by clinicians and researchers.

Biopsychosocial Models

Historical Perspective

The noted psychiatrist, George Engel (1913–1999) is credited with coining the term *biopsychosocial model* in his seminal paper, "The Need for a New Medical Model: A Challenge for Biomedicine" (Engel, 1977). In this paper, Engel identified two disparate positions within the field of medicine. On one side were those arguing that medicine should focus only on somatic and organic parameters that define disease, while the other side supported consideration of factors such as environment and experience as equally relevant and maintained that these factors were also important in the development of many disease states. Engel believed that all of medicine required a new model of practice.

Engel's ideas were aligned with a growing interest in disability (LePlège, Barral, & McPherson, 2015) among academics in the social sciences, public health, and medical sciences (e.g., Nagi, 1965). The Disability Rights and Independent Living movements were both nascent in the 1970s (LePlège et al., 2015). At the same time, the World Health Organization (WHO) sought to develop a classification system for disablement that would complement the International Statistical Classification of Diseases and Related Health Problems and, in 1980, the I*nternational Classification of Impairments, Disabilities and Handicaps* (ICIDH) (WHO, 1980) was published. Although Engel's ideas were criticized as being too general and the ICIDH was labeled as too focused on the individual while excluding other environmental (social and physical) influences contributing to disability, the groundwork was laid for developing the first biopsychosocial models, arguably the most prominent of which is the *International Classification of Functioning, Disability, and Health* (ICF; WHO, 2001) (see Figure 2.1).

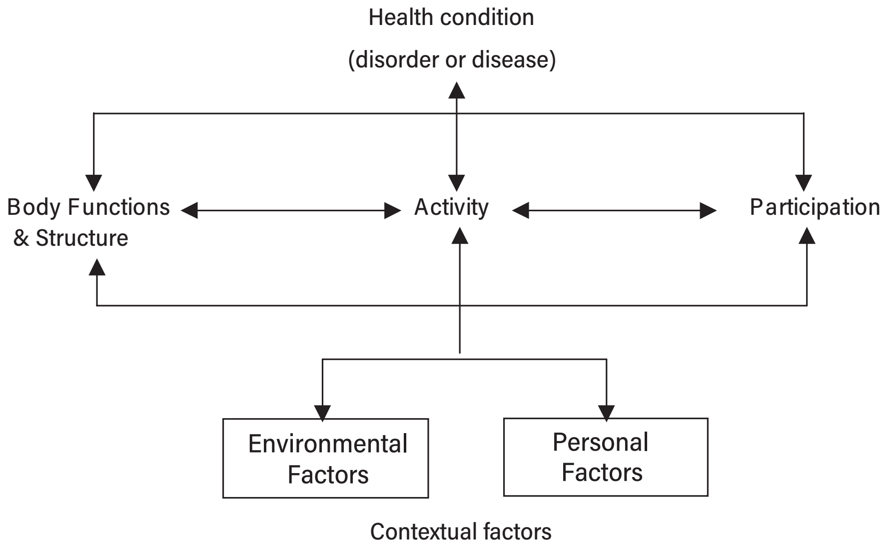

FIGURE 2.1. The International Classification of Functioning, Disability and Health (ICF), WHO, 2001, *www.who.int/classifications/icf/icfbeginnersguide.pdf*. Used by permission.

The ICF is a widely used, internationally known biopsychosocial model with application for many health disciplines, including neuropsychology. It depicts health conditions as affecting individuals as follows. The person as a biological being, that is, the physical aspects of a person, are encompassed in *body structures* and in biological aspects of *health conditions or diseases*. The person as a psychological being is depicted in *body functions*, psychological aspects of health conditions, and in *personal factors* (including gender, learning style, and personality traits). The person as a social being is represented through the interplay of *environmental factors* (physical and social), with all other parts of the model culminating in their ability to *participate* in domains of life situations that are relevant to them. Thus, the model captures the person functioning at three levels: the body (*structure/function*), the whole person (*domains of activity*), and the social being (*participation*). The contrary aspects of these three levels are termed, respectively, impairment, disability, and handicap. Since 2001, substantial work has been done to elucidate the levels of functioning: factors within each of these ICF levels of function are readily searchable online (*https://apps.who.int/classifications/icfbrowser*). For example, searching "dressing" takes one to the category "mental function of sequencing complex movements" within the broader domain of body structure/function or to the category of self-care within the broader domain of activities and participation. This hierarchical organization facilitates considering how a person's difficulty is best described, what might be an underlying impairment, and/or at what level of intervention should be directed. A checklist of the major categories is available for use by clinicians at *www.who.int/classifications/icf/icfchecklist.pdf*.

In addition to depicting the biological, psychological, and social aspects of human functioning, this model shows that activity and participation restrictions (similar to disability and handicap in the International Classification of Impairments, Disabilities and

Handicaps [ICIDH]) arise from the interplay of the condition with the individual person's body structures and functions (how they physically and psychologically respond to that condition) as well as specific personal and environmental factors. For example, problems getting to work may arise from not being able to drive due to a visual impairment and may be compounded by a public transit strike. The way the relationships are depicted implies that activity and participation can influence body structure and health condition, just as body structure and health condition can influence activity and participation. Thus, one can hypothesize that in those with brain conditions, everyday function (activity and participation) may be used as an intervention that positively influences brain and improves day-to-day life. For example, the Cognitive Orientation to Daily Occupational Performance (CO-OP) Approach is based in part on this hypothesis (Dawson, McEwen, & Polatajko, 2017). The CO-OP Approach uses everyday life difficulties (identified by clients as those that they need to or want to do but are having difficulty with) as the "doing" part of the intervention. Strategies are learned in the context of the doing. Data from a series of randomized controlled trials suggest generalization of learning with this approach as improvements have been observed in nontrained goals and in specific areas of cognitive function (e.g., Dawson, Binns, Hunt, Lemsky, & Polatajko, 2013; Dawson et al., 2014; Skidmore et al., 2015). Using a similar form of strategy training, Wolf et al. (2016) reported improved neural connectivity, cognitive performance, and health-related quality of life. Other evidence also supports this hypothesis. For example, studies examining older adults trained as volunteers in elementary schools experienced numerous benefits, including increases in brain activity in the prefrontal cortex and improvements in executive function and memory relative to the controls (Carlson et al., 2008, 2009).

Utility for Understanding Everyday Function

The ICF (and other biopsychosocial models) elucidate the interplay between everyday and cognitive function (in addition to physical and affective function). As a brief clinical example, two people with the same level of impairment in memory functions may have very different levels of participation in everyday life depending on personal factors, including self-efficacy and/or environmental factors such as clutter-free space. In recent years, neuropsychologists have been turning to the ICF to support the development of rehabilitation programs (e.g., Pusswald, Mildner, Zebenholzer, Auff, & Lehrner, 2014), measurement of outcomes (e.g., van Heugten, Caldenhove, Crutsen, & Winkens, 2019), and classification of therapeutic goals (e.g., McCarron et al., 2019). In the study by McCarron et al., goal setting was done as part of the initial assessment. The goals were then coded using the ICF (Children and Youth Version) to provide a broader understanding of the types of goals young people with acquired brain injury (ABI) felt were important. The investigators reported that over half of the goals were in the activity and participation domains, underscoring the importance of these goals to the clients.

The usefulness of the ICF for neuropsychologists is predicated on the view that neuropsychological rehabilitation is not only focused on improving cognition but is concerned with "ameliorating cognitive, emotional, psychosocial and behaviour deficits caused by an insult to the brain" (Wilson, 2008, p. 143). The classification can inform a comprehensive description of clients' status and through this description a more targeted treatment plan. As the entire ICF is large and some would say unwieldy, core sets or short lists of categories have been developed for use with specific populations (available at *www.icf-core-sets.org*). Each core set contains a subset of items from the complete ICF, determined through consensus conferences to be most relevant for a particular patient population (e.g., Bernabeu et al., 2009). Through the website, a clinician or researcher can select a specific core set, and the website will generate a documentation form that can be used to document areas of assessment and/or to guide intervention. Each core set also includes a list of environmental factors (e.g., products and technology for personal use in daily living; personal care providers), allowing the documentation of specific environmental factors that may act as facilitators or barriers in terms of everyday function.

The Relevance of Other Biopsychosocial Models for Neuropsychology

While the ICF is the most comprehensive and universally known of the biopsychosocial models, the development of other biopsychosocial models can enhance our understanding of specific areas of impairment (Woods, 2019). For example, Bol et al. (2010), in trying to understand the factors contributing to fatigue in people with multiple sclerosis, examined the explanatory value of two models: a biomedical model and a cognitive behavioral model. Finding that neither model explained the multifactorial nature of fatigue sufficiently, they proposed a new model that included a fuller set of explanatory variables, both biological and psychological, including disease severity, physical disability, depression, and fear-avoidance. This biopsychosocial explanation of fatigue has been an impetus for others to consider multifactorial explanations for fatigue and investigate more diverse management techniques (e.g., Wijenberg, Stapert, Köhler, & Bol, 2016).

Similarly, Ownsworth, Clare, and Morris (2006) criticized the utility of theoretical models of awareness in the context of chronic brain injury and Alzheimer's disease, as these models did not provide a representation of the complex relationships between biological (neurocognitive), psychological, and environmental (particularly social) factors. They posited an integrated biopsychosocial framework that represents unawareness as arising from neurocognitive factors, psychological factors, or the socioenvironmental context. Ownsworth et al. illustrated how the model could be used to consider the areas of functioning affected and mechanisms through which deficits might arise (e.g., damage to frontal systems, defensive reactions, and influence of cultural values on individual decisions to disclose impairments).

Summary

Biopsychosocial models are increasingly being utilized in research and clinical contexts across the lifespan. They are becoming more comprehensive as areas such as epigenetics emerge for consideration in understanding complex functioning (Brecht & Gatchel, 2019). Ultimately, the use of biopsychosocial models greatly enhances understanding of the complexity of everyday function and facilitates achieving a shared terminology and understanding.

Neurocognitive Frames of Reference of Everyday Function

Historical Perspective

Contemporary neuropsychological models of everyday function began with the study of neurological patients with profound difficulties in completing everyday tasks. Neurologists in the early 20th century proposed competing accounts to explain how brain damage or disease impaired performance of relatively simple, multiple-step everyday tasks, such as preparing a letter for mailing. For example, Arnold Pick (1905) described flagrant object use and sequencing errors during everyday tasks in individuals with dementia and attributed the difficulty to diffuse brain damage and a deficit of attention (see also Goldenberg, 2003, for a review). Later, some neurologists attributed these errors to impaired sequencing and organization of task steps (Lehmkuhl & Poeck, 1981; Liepmann, 1908; Luria, 1966) or degraded semantic knowledge for tools and objects (Morlaas, 1928; De Renzi & Lucchelli, 1988).

In the 1980s–1990s, cognitive neuroscientists developed models to explain everyday, routine behaviors and the executive processes that enable control over routine activities when deviations or future planning are necessary. Norman and Shallice (1986) proposed that routine tasks are represented as goal hierarchies called schemata similar to other overlearned skills. They termed the automatic activation of these familiar task goals contention scheduling through which goal activation could occur from other goals (i.e., internal activation) or by triggers in the environment (i.e., external activation). In the circumstances in which one might want to override routine activities, a control mechanism called the supervisory system comes into play. For example, the supervisory system is engaged when we must deviate from our routine evening commute in order to make a stop for groceries or to problem-solve the way home when a car crash necessitates a detour. The supervisory system was hypothesized to consist of at least three complementary component processes: (1) plan formulation/ modification, (2) marker creation and triggering, and (3) evaluation of goals and plans (Shallice & Burgess, 1991). The process of plan formulation/ modification concerns the creation of provisional plans prior to task execution and ongoing modifications during task performance according to opportunities or difficulties that occur (e.g., planning in the morning to stop for groceries on the way home from work). This is partially based on the work of Suchman (1987) and Ellis (1989, both cited in Shallice & Burgess, 1991), who argued that in normal human activity, plans formed prior to task execution do not correspond to completely worked out courses of action. Planning, linked to an individual's intention to perform a certain act at a later time, is hypothesized to operate through the creation and triggering of markers. Markers are defined as messages which, when activated, trigger the initiation of certain behaviors at a certain time or interrupt an ongoing behavior and replace it with another. The third component process, evaluation of goals and plans, is of particular importance in the execution of novel tasks (e.g., mapping a route home de novo; Shallice & Burgess, 1996).

Case reports published by Schwartz and colleagues (Schwartz et al., 1991; Schwartz, Reed, Montgomery, Palmer, & Mayer, 1995) and Humphreys and Forde (1998) used the term *action disorganization syndrome* (ADS) to denote egregious cognitive errors on everyday tasks that could not be explained by lower-level motor difficulties (Schwartz, Reed, Montgomery, Palmer, & Mayer, 1991). Accounts to explain ADS were influenced by the cognitive processing models and proposed problems with the *activation* of everyday task goals in contention scheduling (e.g., premature decay, inappropriate activation by environmental triggers).

Cases of patients with frontal lobe damage and marked difficulties performing everyday tasks also were reported by Shallice and Burgess (1991). Despite their significant everyday life difficulties, these individuals performed well within the average range on traditional tests of intellectual and cognitive abilities. On novel, experimental tasks, one of which simulated (i.e., Six Elements Test) complex and unpredictable daily activities and the other of which (i.e., Multiple Errands Test) required actual performance of these activities, such as shopping for various items in a shopping center, participants showed highly disorganized, inefficient, and generally inadequate performance relative to healthy controls. Shallice and Burgess used the term *strategy application disorder* to describe these behaviors, which they explained as damage to the supervisory attention system according to cognitive processing models (e.g., failure in developing a strategic plan and/or difficulty executing the plan at the right time).

Current Neuropsychological Models Informed by Group Studies

Current neuropsychological models of everyday functioning aim to explain functional difficulties across the entire continuum ranging from errors in healthy people to profound functional disability in individuals with cognitive impairment. In contrast to earlier models, which were based on case reports, newer models have been developed to explain data from group studies. For example, Schwartz and colleagues proposed the resource theory to explain a series of unexpected results from several group studies of people with different forms of brain damage and cognitive impairments—for example, closed head injury (Schwartz et al., 1998a), right hemisphere stroke (Schwartz et al., 1998b), left hemisphere stroke (Buxbaum, Schwartz, & Montgomery, 1998), and degenerative dementia (Giovannetti, Libon, Buxbaum, & Schwartz, 2002). These unexpected findings included (1) striking similarities in everyday error patterns across different patient groups; (2) everyday task performance most strongly predicted by measures of general cognitive ability level; and (3) error totals and error patterns strongly influenced by task and environmental demands (e.g., more errors on more complex tasks). Omission errors (i.e., complete failure in completing task steps) were observed only when resource limitations were markedly taxed, including on relatively simple tasks in people with moderate to severe cognitive impairment or in people with relatively mild impairment who were asked to perform complex everyday tasks (Schwartz et al., 1998a). Schwartz and colleagues explained these results by positing that everyday functioning requires general cognitive resources (e.g., attention, effort) and is highly sensitive to decrements in resource availability, which may result from brain damage/disease, complex tasks, confusing environments, and/or any combination of factors (Buxbaum et al., 1998; Schwartz et al., 1998a, 1998b; Giovannetti et al., 2002). The *resource theory* offered testable predictions, which were not entirely supported by subsequent studies.

A series of studies designed to test the resource theory identified two dissociable components of everyday function difficulties: failures in completing essential task steps (omission errors) versus problems in completing task steps accurately and efficiently (commission errors) (Giovannetti et al., 2008; Giovannetti, Schwartz, & Buxbaum, 2007). Omission and commission errors have been shown to have distinct cognitive and neuroimaging correlates, with omission errors associated with episodic and semantic memory abilities and volumes of the hippocampus and medial temporal lobes obtained from MRI of the brain (Bailey, Kurby, Giovannetti, & Zacks, 2013; Roll, Giovannetti, Libon, & Eppig, 2019). By contrast, commission errors correlate with measures of executive function and neuroimaging measures of the cerebral white matter and prefrontal cortex (Bailey et al., 2013; Giovannetti et al., 2008; Seidel et al., 2013). Further, clinical groups characterized by executive control difficulties (e.g., schizophrenia, Parkinson's disease dementia, vascular dementia) show higher rates of commission errors on everyday tasks as compared to clinical groups characterized by episodic/semantic memory impairment (e.g., Alzheimer's disease dementia) (Giovannetti et al., 2012; Giovannetti, Schmidt, Gallo, Sestito, & Libon, 2006; Kessler, Giovannetti, & MacMullen, 2007). These findings have been described in the literature as the omission–commission model, and more recently the findings have been interpreted in the context of the earlier cognitive processing models and recast as the *goal-control model*. The goal-control model attributes omissions to failures in goal activations and commissions to failures in control over the internal and external goal activations (Giovannetti, Mis, Hackett, Simone, & Ungrady, 2020).

Computational Models. Computational models include a variety of mathematical models designed to simulate human cognition. At least two distinct computational modeling approaches have been proposed to explain everyday task performance, each with different assumptions regarding how task knowledge is represented. One set of models proposed by Cooper and colleagues includes representations of everyday goal hierarchies, as delineated in the cognitive models described above (Cooper, Schwartz, Yule, & Shallice, 2005; Cooper & Shallice, 2000). By contrast, Botvinik and Plaut (2000) proposed a *recurrent connectionist model* that simulates everyday task performance without a formal goal hierarchy. In this model, sequential information about everyday task steps emerges over time within a distributed network of computational units connecting inputs from the environment to possible response options. The Botvinik and Plaut (2000) model may explain how everyday tasks are learned over time, and it simulates the remarkable flexibility that is often observed in human everyday action (e.g., the intention to make coffee may or may not include the goal of adding sweetener depending on the day).

In Cooper and colleagues' models (Cooper et al., 2005; Cooper & Shallice, 2002), goal hierarchy representations are built by the modeler and are activated by objects in the environment, other goals, and noise within the model. Cooper and colleagues designed models for making coffee and for making a lunch and were successful at simulating healthy and impaired task performance. Using their model of making a lunch (Cooper et al., 2005), they demonstrated that different clinical syndromes could be explained by disruption in different parts of the model, with disruption among all the relations between goals in the hierarchy leading to an increase in omission and commission errors, disruption of goal activations from objects in the environment leading to more object substitution errors, and weakened activations from superordinate goals to subordinate goals (i.e., poor top-down control) leading to high rates of omission errors without commission errors.

Summary

Neurocognitive models have evolved from conceptualizing profound problems in everyday activities as a single impairment in a specific cognitive process associated with a specific brain region (e.g., Pick, 1905; DeRenzi & Lucchelli, 1988) to understanding the cognitive mechanisms and brain regions that contribute to specific errors and error patterns (e.g., Giovannetti et al., 2020). Computational modeling has offered a highly controlled approach to evaluate basic assumptions (e.g., need for goal hierarchy representations; Botvinick & Plaut, 2000) and to test specific predictions of contemporary neurocognitive models through simulations of disruption of specific processes (Cooper et al., 2005).

Utility for Understanding Everyday Function

Neurocognitive models focus on specific person-factor mechanisms within the larger ICF framework. Understanding neurocognitive mechanisms will inform intervention strategies that aim to boost the impaired mechanisms (restorative approach) or circumvent them (compensatory approach). For example, according to the resource theory, any attempt to reduce the cognitive resources necessary to perform everyday tasks should improve everyday function in everyone. In fact, environmental changes that reduce clutter and arrange task objects in the order that they should be used have been shown to improve everyday function in a variety of clinical populations (Giovannetti, Schwartz, & Buxbaum, 2007; Kessler, Rhodes, & Giovannetti, 2015). By contrast, the goal-control model, which posits different everyday functional deficits due to different mechanisms, implies that it is important to match the intervention approach to meet a person's action-deficit profile. Indeed, older adults with dementia and everyday action difficulties characterized by high rates of omission errors show significant improvement with cues that remind them of the task goal, whereas older adults with dementia and a commission error profile do not benefit from these types of cues (Giovannetti, Seligman, Britnell, Brennan, & Libon, 2015). These examples illustrate that the detailed understanding offered by neurocognitive models may be used to manipulate nonperson factors to promote function. Restorative approaches also may be informed by these models as interventions may be developed to strengthen goal activations through repeated practice (Foloppe, Richard, Yamaguchi, Etcharry-Bouyx, & Allain, 2018) and increase control over activations through increased attention and deliberation, particularly at critical choice points during the completion of everyday tasks (Divers et al., 2020).

Occupational Science and Occupational Therapy Models

Historical Perspective

Occupational therapy is rooted in ideas that began to emerge in relation to the moral treatment movement, that was founded on the notion that purposeful, goal-directed activity was important for promoting healing in those with mental illness (Peloquin, 1989). In the aftermath of both World War I and World War II in which thousands of soldiers returned home with significant physical and mental difficulties, Adolf Meyer, a psychiatrist and psychobiologist, and one of the founders of occupational therapy, posited that the fundamental occupations in life were work, play, and rest—an idea that has remained central to occupational therapy since that time (Meyer, 1922). In the late 1980s, the field of *occupational science* emerged through interdisciplinary scientists collaborating on understanding humans as occupational beings (Zemke & Clark, 1996) where occupation is understood to refer to all of the goal-directed activities in everyday life and the patterns of activity that occur over the lifetime.

Occupational scientists frame human functioning as *occupational performance* (Christiansen & Baum, 1991), *occupational engagement* (Townsend & Polatajko, 2013), and *occupational participation* (Bartolac & Sangster Jokić, 2019). Occupational performance is defined as the outcome of a transaction between a person (P), their environment (E), and the specific attributes of their occupation (O). Occupational performance can be considered a more involved articulation of everyday functioning, one that requires understanding of each aspect of the core components (PEO), how they interact, and the factors that contribute to ensuring performance is successful. Occupational engagement is viewed as going beyond performance to include the subjective experience of performance and to involve aspects of meaning, interest, motivation, and/or self-efficacy (Kennedy & Davis, 2017). Occupational participation includes participating in established daily patterns and having a sense of belonging and social involvement (Bartolac & Sangster Jokić, 2019). Importantly, it counterbalances the notion of occupational deprivation.

Occupationally focused models have drawn on other historical influences, the most significant being environmental press and flow. The theory of *environmental press*, as posited by Lawton (1982), states that forces in the environment (factors outside the person including opportunities, demands, and challenges) interacting with individual need evoke a response. Optimization of function, understood as adaptation, requires balancing environmental demands and supports with an individual's competence. Lawton's work became the foundation for many other considerations regarding the interaction of the environment and person. Bronfenbrenner (1989) describes environmental systems at meso, exo, macro, and chronos levels. The microsystem refers to persons and their behaviors. Family and religious spheres make up the mesosystem, with government policies and community aspects forming the exosystem. Broader influences at the macrosystem level include such aspects as cultural values, beliefs, and social conditions. Finally, and spanning all systems, is what Bronfenbrenner refers to as the chronosystem, or the influence of time and timing on the developing abilities of the individual. Importantly, this model brings into focus how influences at even the broadest level, such as social values, norms, and attitudes, can influence how an individual performs or engages in an activity.

The work of Lawton (1982), Bronfenbrenner (1989), and others representing disciplines as diverse as geography, environmental and developmental psychology, environmental sciences, critical disabilities studies and gerontology, gave rise to so-called ecologically based models which have, in turn, strongly influenced the development of occupational science and occupational therapy. This way of thinking conceptualizes the individual as an open system that interacts extensively with their environment. Occupationally focused models encompass these broad understandings of the environment.

The concept of *flow* (Csikszentmihalyi, 1975) focuses on the person and their interaction with an activity (i.e., occupation). Flow is the experience of having a "just right fit" or "just right challenge"—that is, flow indicates the point at which a person's skill level is matched with the level of challenge that an activity or task affords and is a mental state that brings happiness and is characterized by intrinsic motivation. Csikszentmihalyi speaks of mental states that are on a range from apathy to flow, with worry, anxiety, arousal control, relaxation, and boredom making up the rest of the continuum, all of which are a function of interactions between skill and challenge level.

Contemporary Occupationally Focused Models

As Baum and Wolf note elsewhere in this text (Chapter 4), there are five prominent models in the occupational therapy literature. Among these, the *model of human occupation* (MOHO) stands out, as it is widely used, has the longest history of publication, and has given rise to a rich body of literature and numerous clinical resources (see *www.MOHO.uic.edu*; Wong & Fisher, 2015). In 1980, Gary Kielhofner published the original iteration of the MOHO, using systems theory to hypothesize how the various factors that contribute to occupational performance are organized together (O'Brien, 2017). The MOHO highlights the person factors of *volition* (e.g., personal causation, values, interests), habituation (e.g., roles, routines), and *performance capacity* (i.e., underlying cognitive and physical abilities, and previous lived experiences), as well as social, cultural, and environmental factors. Volition encompasses a person's individual values and what they consider important. Habituation embraces the notion that roles and routines by their very nature are resistant to change. In the MOHO, the idea of performance capacity includes the objective physical and cognitive capabilities, along with the subjective experience linked to using them. Occupational performance arises from the dynamic interaction of these person factors with the environment. In the context of the MOHO, the environment is understood to be multilayered and to place constraints and demands on performance as well as provide opportunities and resources.

Use of the MOHO provides clinicians and researchers with an organized way of considering multiple factors that may be contributing to disruption in everyday functioning related to some type of injury or illness. This model is the basis of numerous assessments (e.g., Occupational Performance History Interview [OPHI-II], Kielhofner et al., 1998; Occupational Circumstances Assessment Interview and Rating Scale [OCAIRS], Forsyth et al., 2005), including a screening tool (Model of Human Occupation Screening Tool [MOHOST] Version 2.0, Parkinson, Forsyth & Kielhofner, 2006). The screening tool assesses most of the concepts in the model, providing an overview of an individual's functioning. In addition, it identifies the need for occupational therapy (OT) services and specifies areas where further assessment would be helpful. Together, these assessments allow for targeted interventions depending on the source(s) of difficulty and the client's preferences in relation to how the functional difficulty will be addressed. For example, frequent foci in stroke rehabilitation are gait training, promotion of upper extremity function, and neurocognitive training. However, after completing an OPHI-II, the therapist learns that the client's strongest motivation (i.e., volition) is to return to valued family roles, including assisting with house maintenance and parenting. Through the interview, the therapist also learns that the two primary barriers to resuming these roles are not the client's physical abilities but rather the anxiety of the client's spouse and physical environmental barriers. Interventions would then be targeted toward working with the spouse and home modifications.

Utility for Understanding Everyday Function

The MOHO and other occupationally focused models fall clearly within the domain of occupational therapy and occupational science. Understanding how these models depict everyday functioning will contribute to assessment and intervention plans by neuropsychologists and other clinicians who take a holistic view of their client and practice. For example, Pereira, Fish, Malley, and Bateman (2017) cite Kielhofner's work in their suggestions for improving cultural competence within the practice of neuropsychology. These models provide a broader understanding of everyday functioning that is contextualized within layers of environment, inclusive of the subjective component of lived experience. The models also emphasize that as each culturally embedded individual brings unique meanings to their engagement in a particular everyday functional activity, the essential nature of that activity is changed. For example, the activity of eating a meal encompasses eating lunch at one's work desk, having a family dinner, and so on. Different people experience the same activity differently at different times, across different life stages and contexts. These models emphasize that knowing that a particular type of cueing is successful in ameliorating a specific cognitive difficulty within an experimental context is only one part of supporting successful performance.

Relevance of Other Occupationally Focused Models for Neuropsychology

Other occupationally focused models highlight several additional concepts that are relevant for the neuropsychologist's understanding of everyday functioning. *The Canadian Model of Occupational Performance and Engagement* (CMOP-E) integrates the concept of the person as a spiritual being (Townsend & Polatjko, 2013). Within this model, spirituality is characterized broadly, including as "a pervasive life-force, manifestation of a higher self, and/or a sense of meaning, purpose and connectedness that people experience within the context of their environment" (Canadian Association of Occupational Therapists, 1997, p. 182). Thus, everyday functioning becomes imbued with much more than independence and successful completion, and goal setting within the context of rehabilitation must consider what is purposeful and meaningful for the client. For the interested reader, Collicut (2019), a neuropsychologist and Anglican priest, grapples with this link between spirituality, meaning, and everyday functioning in presenting a case history in a recently published text, *Neurology and Religion*.

As a group, occupationally focused models provide the foundation for considering a variety of concepts related to everyday functioning and occupational performance, participation, and/or engagement. Scholarly work on the CMOP-E and other occupationally focused models has resulted in the investigation of many aspects of everyday functioning, including (1) the meanings attributed to the activity by a specific individual at a specific point of time and in specific environment; (2) the concept of engagement, which encompasses the notion that to be engaged does not necessarily mean physically or cognitively doing the activity; (3) the notion of occupational balance, which encompasses the idea that our activities are balanced; and (4) occupational disruption, a term that encompasses the overall change in everyday functioning that can be brought about by an event that affects a single individual, such as a traumatic brain injury or a global, environmental incident such as a pandemic. Lack of meaning, engagement, balance, and/or occupational disruption can all have substantive and deleterious effects on health and well-being (Townsend & Polatajko, 2013). Anecdotes from clinical practice provide exemplars of how considering these factors allowed for rehabilitation. In relation to attributing meaning to an activity, one of the author's (DD) clients in stroke rehabilitation was very reluctant to participate in gait training because he was discouraged that his gait was not fluid and symmetrical. During the course of his rehabilitation, his daughter announced her engagement to be married. Because it was important to him that he walk her down the aisle, he began doing the work necessary (and was successful). A colleague described a teenaged client who had sustained a traumatic brain injury. Their primary goal was to attend an upcoming concert for a favorite pop star and for which they had tickets. While members of the clinical team initially shrugged this wish off as either unrealistic or beyond the scope of their program, they were eventually convinced that the concert was key to engaging the client in rehabilitation. Using clients' goals is a key part of the Cognitive Orientation to Daily Occupational Performance (CO-OP) Approach, an occupationally focused intervention that was developed in line with the CMOP-E (Dawson et al., 2017).

Occupationally focused models also provide for a broad understanding of the environment and allow consideration of how environments may or may not be supporting occupational performance and engagement. For example, working on community integration skills with clients from different ethnicities may require very different approaches despite similarities in cognitive functioning. Critics of biomedical and reductionist understandings of everyday functioning by disability groups and others who embrace a social model of disability and/or those espousing critical disability theory have influenced not only the ICF but also the further development of occupationally focused models (e.g., Pereira et al., 2017; Restall, MacLeod Schroeder, & Dubé, 2018). With the perspective that disability can arise from the environment, the environment becomes a target for intervention. For example, a senior citizen may be unable to engage in political advocacy as she has no access to accessible transportation or online technology. From this perspective, ageism (as expressed in community designs that assume that all people are able-bodied young people) may be seen as the key barrier to engagement and a target of intervention.

In sum, as a group, occupationally focused models highlight characteristics of everyday functioning that elucidate important aspects of the complexity of how an individual "functions" contextually, that is, in relation to what they are doing (their occupations), the meanings they attribute to their occupations, and where and why they are doing it (the environment). These models recognize that dysfunction can arise not only from impairments but also from disengagement, imbalance in areas of occupation and/or disruption in roles and routines, and deprivation where the environment does not afford the opportunities to participate in meaningful/purposeful occupations.

Future Directions: Toward a More Comprehensive Understanding of Everyday Functioning

Humans have functioned in the everyday since the beginning of time. The meaning of the term *function* has also evolved over time. A thesaurus check reveals a long list of synonyms, including purpose, role, job, occupation, task, and utility. Synonyms for everyday function found in the rehabilitation literature include abilities, capacities, and skills, all of which, in some way, refer to how well people can or do perform or *function*. These terms encompass what are assumed to be an objective and observable set of (basic) activities of daily living (ADLs, e.g., eating, dressing, grooming) and instrumental activities of daily living (IADLs, e.g., shopping, cleaning, laundry) or enhanced activities of daily living (EADLs—i.e., activities performed in relation to adapting to a changing environment such as learning to manage a new cable TV system) and learning new skills to cope with these challenges. In this chapter, we have reviewed and discussed three ways of understanding everyday function, each way emphasizing different aspects of the multidimensional concept of function. We encourage neuropsychologists and other clinicians to consider the breadth of everyday function when defining the scope of their research and clinical practice. For example, neurocognitive and biopsychosocial models of everyday function generally ignore the subjective experience of engaging in observable everyday activities, that is, the meanings that individuals bring to them. While great efforts have been made in advancing these models, no single theory adequately explains the complexities of human functioning. We believe that a more complete awareness of these theories of everyday function will yield improved interdisciplinary practice and collaboration and that some unifying principles will emerge that may lead to important revisions in existing models and/or to a new unified framework.

The first section of the chapter discussed biopsychosocial models and more specifically the International Classification of Functioning, Disability, and Health (ICF). The ICF depicts functioning as comprised of increasing levels of complexity of behaviors, in terms of their interaction with the environment and the personal factors an individual can draw upon. The ability to engage in increasingly complex daily activities of everyday life is an iterative process between body structures and functions (e.g., neurons, memory), activities at the level of the individual (e.g., practicing scanning in a workbook), and participation at the level of society (e.g., successfully finding everything at the grocery store). It provides a common language that is increasingly used within the health community and a taxonomy of function that can inform and be used in documentation for clinical and research purposes. Building on the ICIDH (WHO, 1980), the ICF introduced the notion that functioning went well beyond the absence of disease and/or pathology and highlighted the importance of personal and environmental factors in individuals being able to participate in everyday life.

The second section of this chapter reviewed neurocognitive frames of reference of everyday function, specifically contemporary neuropsychological models and computational models. Their focus is primarily on the body structure and function part of the ICF, and these models greatly enhance the ability to examine in depth how specific cognitive processes contribute to performance of everyday tasks. In addition, they provide direction for researchers and clinicians to consider how manipulation of the environment may promote function for a specific individual and task.

The third section of the chapter considered the value of occupationally focused models for understanding everyday function. These models emphasize that everyday function arises from the dynamic interactions between humans, their environments and their occupations (a term that should be read as inclusive of the subjective component or meaning an individual brings to that activity). These models provide for examination of how these transactions occur and how they can be influenced through changing any of the parameters.

Each group of models brings something unique and necessary to the understanding of everyday function, and, as discussed, gives rise to specific assessment and intervention approaches. However, drawing on more than one group of models can be enormously fruitful. For example, building on the work of Shallice and Burgess, neuropsychologists and occupational therapists have developed various iterations of the Multiple Errands Test (MET), including versions for “real-world” environments such as large department stores (Antoniak et al., 2019) and homes (Burns et al., 2019). The MET, devised as an experimental tool to illuminate everyday life difficulties not detected in standardized neuropsychological testing, is now being used by clinicians and researchers in the fields of cognitive neuroscience, neuropsychology, and occupational therapy to characterize the neurocognitive processes that are critical for everyday function under different environmental demands and contexts (for further information see *https://cognitionandeverydaylifelabs.com/multiple-errands-test*).

Improving the well-being of those with neuropathology is a key goal for neuropsychologists and demands a comprehensive understanding of everyday function. This chapter provides an introduction to concepts and language that we believe will be useful for students, clinicians, and researchers. While neurocognitive and occupationally focused models are the primary domain of different professional groups (i.e., cognitive neuroscientists and neuropsychologists, and occupational scientists and occupational therapists), biopsychosocial models provide a common framework and terminology within which many collaborations and discussions can prosper. Readers are encouraged to consider how their studies, research, and/or clinical practice may be enhanced through a more comprehensive understanding of everyday function. This chapter provides the foundation through which, we hope, this will occur.

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CHAPTER 3

Human Factors/Ergonomics

Relevance to Assessments of Everyday Functioning

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Understanding human–system interactions is the broad goal of the field of human factors/ergonomics (HF/E). The characteristics of the human that are relevant to such interactions include physical, perceptual, and cognitive capabilities. The "system" can range from an item as simple as a can opener to something as complex as the cockpit of a jet airplane or the control room of a nuclear power plant. The present chapter focuses on the cognitive capabilities of humans that influence their interactions with systems encountered in the context of everyday activities such as computers, medical devices, medications, and transportation systems.

HF/E practitioners investigate the capabilities and limitations of people and the demands placed upon them when they are performing activities ranging from the most basic everyday functions to the most complex vocational tasks. Our goal in this chapter is to illustrate the relevance of the knowledge base and the tools of the field of HF/E to issues faced by neuropsychologists and their patients. For example, neuropsychologists and occupational therapists could use HF/E tools and techniques to obtain a more complete understanding of the cognitive and perceptual functioning of a traumatic brain injury patient. This knowledge could then guide interventions to facilitate everyday functioning for that individual. These tools can guide development of strategies designed to assist individuals with general memory deficits in performing demanding tasks such as managing a medication regimen. One of the major benefits of the HF/E tools and techniques discussed herein is their potential applicability to a wide range of people and systems.

This chapter provides an overview of the field of HF/E and describes the tools and techniques used in HF/E to understand human–system interactions, identify problems, and develop solutions (e.g., asking the right questions and answering them). We also provide illustrative examples of these tools and techniques as they have been applied in various domains. The domains we have selected mirror the activities of everyday functioning addressed in the other chapters of this volume.

Defining the Discipline of HF/E

HF/E is a “unique and independent discipline that focuses on the nature of human–artifact interactions, viewed from the unified perspective of the science, engineering, design, technology, and management of human-compatible systems, including a variety of natural and artificial products, processes, and living environments” (Karwowski, 2012, p. 3). In the United States, a distinction is often made between *human factors*, referring to perceptual and cognitive characteristics of people and the systems with which they are interacting, and *physical ergonomics*, referring to anthropometry and biomechanics. In other nations, the broad term *ergonomics* is used to refer to the whole discipline. In the present chapter, we use the abbreviation HF/E to represent all aspects of the discipline.

HF/E practitioners are generally interested in three goals: to enhance system performance, to improve safety, and to increase user satisfaction (Wickens, Hollands, Banbury, & Parasuraman, 2012). These goals are generally achieved by analyzing and understanding the cognitive and physical capabilities and limitations of the user as well as the physical and information systems with which they are interacting through the use of appropriate analysis tools. Adding HF/E tools to neuropsychologists’ and occupational therapists’ toolkits will provide them with the means to better understand neurological populations and the systems with which they interact.

The breadth of the field is illustrated by the range of technical specialties within it. The Human Factors and Ergonomics Society (HFES), founded in 1957, has approximately 4,500 members and 26 technical groups that support the exchange of knowledge within specialty areas (see Table 3.1). This list demonstrates the range of application areas of HF/E (e.g., aging, communication, health care, the internet, and transportation), as well as the varied research methodologies used in the field (e.g., cognitive engineering, human performance modeling, usability/system evaluation).

Asking the Right Questions—and Answering Them

HF/E is a diverse discipline that ranges from transportation to health care and from nuclear power plants to the football field. How can the tools and techniques used by HF/E practitioners span such a seemingly broad spectrum of domains? Simple: By asking the right questions in the right situations.

The purpose of asking the right questions is to identify user–system problems, to pinpoint the source(s) of the problems, and to understand and identify potential solutions. Although there is no formula to guide the question-asking process, certain commonly asked questions may serve as a starting point (see Table 3.2). Given the HF/E focus on the person, the system, and the interaction between them, the relevant questions encompass these variables. The basic tenet of HF/E is to “know thy user.” The corollaries are to understand the system and the context of use.

TABLE 3.1. Technical Groups of the Human Factors and Ergonomics Society

Aerospace Systems	Human Performance Modeling
Aging	Individual Differences in Performance
Augmented Cognition	Internet
Children's Issues	Macroergonomics
Cognitive Engineering & Decision Making	Occupational Ergonomics
Communications	Perception and Performance
Computer Systems	Product Design
Cybersecurity	Safety
Education	Surface Transportation
Environmental Design	System Development
Forensics Professional	Usability and System Evaluation
Health Care	Training
Human–AI–Robot Teaming	Virtual Environments

Note. Data from *www.hfes.org.*

The first step is to understand the person. What are the capabilities and limitations in terms of the physical, perceptual, and cognitive characteristics of the people who will be interacting with the system? This question can be answered through observation, interviews, and surveys, as well as through an understanding of the typical capabilities and limitations for the user group (e.g., children, older adults, visually impaired). The person analysis must be specific. For example, we would not assess engineers to ascertain the problems individuals with cognitive impairments would have navigating through an environment or interacting with a system; we would assess individuals with cognitive impairments. This may seem obvious, but unfortunately, decisions are often based on the beliefs of designers rather than on specific user capabilities and limitations. The technical performance of a product may take precedence in the design process, thereby overshadowing the assessment of user needs. Moreover, there may be multiple user groups for a particular system, and thus the differences between users must be considered.

The system characteristics must also be analyzed. What are the physical, perceptual, and cognitive demands imposed by the system itself? Does it require fine motor control, processing of multiple sources of information, or the comprehension of complex instructions? Is monitoring of automated components required? System analysis may be accomplished through task analysis and process diagrams (described later in this chapter). An understanding of the characteristics of the system is essential to link the users' capabilities and limitations to the system's demands and requirements.

It is also important to understand more about interactions between the person and the system. What is the context of use (e.g., time-stress), what types of instruction and feedback are provided during the interaction, is the situation static or is it dynamically changing? Consider an analysis of a person using an in-vehicle navigation system. It is important to know if the user is an experienced driver, is familiar with the system, can process both visual and auditory information, has constraints on attention or working memory, and so on. Details of the system must also be understood, such as the type of

TABLE 3.2. General List of Questions Relating to the User, the System, and the User–System Interaction

Questions relating to the user

General characteristics

- Who are the users?
- Is the design for a single user or for multiple users?
- What are the cultural differences between users?
- What is the average age of the intended user population?

Physical characteristics

- What is the average body size of the user population?
- Do users have mobility problems that restrict normal body movements?
- What are the strength characteristics of the users?

Perceptual characteristics

- What are the visual capabilities of the users?
- What are the auditory capabilities of the users?
- Do important perceptual differences exist between users?

Cognitive characteristics

- What are the users' memory capabilities and limitations?
- What are the users' attentional capabilities and limitations?
- What decisions does the user have to make?
- What learning is required of the user?

Questions relating to the system

Environmental characteristics

- What are the lighting conditions of the environment?
- How much clutter is in the environment?
- How much noise is in the environment and what are its sources?
- Is the system operating indoors or outdoors?
- What is the temperature of the system environment?

System characteristics

- What is the purpose of the system?
- What tasks are involved?
- Is the system automated?
- What are the system inputs and outputs?
- What sort of feedback is provided by the system?
- What instructions have been provided?
- What is the context of use?

Questions relating to the user–system interaction

- What are the cognitive (memory, attention, information-processing) demands on the user?
- What are the perceptual (visual and auditory) demands on the user?
- What are the users' experiences in relation to the system?
- What are the task demands?
- Are multiple users interacting?
- How much workload is placed on the user?

input device that is used to interact with the system, the amount of information that is displayed, and the format in which it is displayed, among other factors. It is also relevant to understand the context of the interaction: if the system will be used while the person is driving, the display can only be viewed for limited amounts of time (while taking eyes off the road), input can only be made with one hand, and decisions may have to be made quickly. The context of the interaction includes the environment in which the person is using the system, such as weather affecting driving conditions, other cognitive distractions in the car created by passengers or the radio, and the like. The person, the system, the context, and their interactions must all be analyzed to understand where, why, and how errors might occur and to develop solutions that will minimize errors and lead to a safe, effective, and efficient person–system interaction.

HF/E Tools and Techniques

To meet the goals of HF/E, various techniques are used to identify problem areas within a user–system, describe the problems and their sources, and suggest solutions to remedy those issues. In the following sections, we will highlight a few techniques that are widely used throughout the field and across various domains.

Surveys and Questionnaires

Surveys and questionnaires are often used in descriptive studies to gather data from the user's perspective (e.g., Jacko, Yi, Sainfort, & McClellan, 2012; Stanton, Salmon, Rafferty, Walker, Baber, & Jenkins, 2005; Vu, Proctor, & Garcia, 2012). An advantage of surveys and questionnaires is that the data can be qualitative or quantitative either by asking open-ended questions or by ranking responses on a numerical scale. These techniques also offer flexibility to assess a wide range of variables, and data can be obtained from a large group of users in a relatively short time. However, it may be difficult to obtain a representative sample of respondents for a survey, and the development of materials and analysis of qualitative data can be time consuming and laborious. Moreover, both the developers' and the users' biases may affect the validity of the results.

Individual and Group Interviews

Interviews with individuals or with small groups may be used to collect descriptive data from users (Mitzner et al., 2010; Stanton et al., 2005; Vu et al., 2012). Interviews conducted in a one-on-one environment are appealing in that the interviewer can direct the questioning to elicit responses, especially about cognitive components of an activity. Small-group interviews are ideally conducted with four to eight individuals of similar backgrounds; in such environments, ideas can emerge that may not have been realized by an individual. Interviews conducted in the home can provide additional information to understand the users' contexts, including artifacts, such as post-it notes to remind users of medication scheduling.

An example of an interview study is the Aging Challenges, Concerns, and Everyday Solution Strategies (ACCESS; Koon, Remillard, Mitzner, & Rogers, 2020; Remillard et al., 2018) in which individuals aging with disabilities were interviewed about the difficulties they encounter in their everyday activities. People who were Deaf, blind/low vision, or had a mobility impairment (60 in each group ages 60–79) provided in-depth information about their challenges, allowing a rich needs assessment to guide interventions and technology solutions.

A focus group study by Mitzner et al. (2010) included 18 sets of focus groups with four to nine participants each. After creating interview scripts, they pilot-tested the questions to ensure the clarity of questions and the relevance of responses. The final interview script consisted of two broad discussion questions with a series of follow-up prompts. The main procedure of the focus groups was as follows: (1) introduction of the study goals, (2) an icebreaker question for participants to become comfortable with discussion, (3) the two general discussion topics, separated by a break, and (4) the study debriefing. This study provided a range of insights about technology use, preferences, and difficulties for older adults from varied backgrounds.

Although the data collected from interviews and focus groups are rich in detail and thus very informative, the analysis of such qualitative data can be challenging and time consuming. One common approach for analyzing qualitative interview data is a thematic analysis to identify categories that represent the participants' responses (e.g., Howitt & Cramer, 2011). Researchers can create a coding scheme for categorizing responses through a top-down approach (e.g., hypothesized themes based on the literature), a bottom-up approach (e.g., common interviewee remarks), or a combination top-down/bottom-up approach.

Task Analysis and Process Diagrams

No matter how simple a task may seem, there are often several unseen steps that a casual observer may never consider. To fully understand human–system interactions, it is imperative that all user activities, physical and/or cognitive, required in a user–system process are understood. A valuable tool for developing such a detailed understanding is a *task analysis,* which can be used "to identify and characterize the fundamental characteristics of a specific activity or set of activities" (Hollnagel, 2012, p. 385).

Task analysis is a broad term that includes many techniques to collect, organize, and analyze information about user–system activities (for details, see Kirwan & Ainsworth, 1992). Generally, an activity is selected, the goals of that activity are defined, and then there is a delineation of each step that must be performed to attain the final goal of the activity. Example task analysis techniques reviewed by Kirwan and Ainsworth (1992) include (1) hierarchical task analysis, where each task is divided into a hierarchy of subtasks with goals, operations, and plans defined; (2) link analysis, where the relationships between a user and parts of the system are identified; (3) operational sequence analysis, where the sequence of movements and information acceptance and/or dissemination are detailed; and (4) timeline analysis, where the time for each task element is recorded. Different task analysis techniques can be selected depending on the goals for understanding the user–system activities and the administrator's expertise in administering a task analysis; Adams, Rogers, and Fisk (2012) provided a guide for choosing the right approach to achieve a particular goal. For example, using a hierarchical task analysis is appropriate when people can achieve the same goal in different ways.

Although a task analysis is often necessary for developing an understanding of human–system interactions, the analysis may require resources, such as time and video or audio equipment (Stanton et al., 2005). Moreover, conducting a task analysis properly requires training (Adams, Rogers, & Fisk, 2013). Given the detail required for an accurate task representation, it is often useful to have multiple raters analyze the task because each analyst may create different representations of the same activity. Ideally, multiple analysts should independently conduct the task analysis with consideration for the varying users and contexts.

Aspects of the task analysis can be compiled into pictorial representations called process flow diagrams. Standardized symbols that depict the required actions, decisions, movements, information flow, time, and effort of an activity can convey the process in an easy to understand format (Kirwan & Ainsworth, 1992). Figure 3.1 provides an example of a flow diagram for the relatively simple task of making coffee. This approach provides a detailed overview of the task, with every step indicated in the order in which it should be performed. Moreover, a flow diagram can illustrate the actual complexity (number of steps involved) of tasks and indicate why such tasks may be overwhelming for individuals with diminished cognitive capacity. For example, Giovannetti et al. (2008) studied errors people with Alzheimer's disease made in completing task steps for three everyday tasks. Task completion was scored using the Naturalistic Action Test (NAT), which essentially assessed people's ability to complete the sequential steps of a task through a variation of a task analysis.

Perhaps the most important advantage of process diagrams is that an entire user–system activity can be visualized easily without the need for pages of text describing each step. However, the more complex the task is, the more visually overwhelming the diagram becomes. These diagrams are easy to learn and use, and they can depict a range of tasks. However, they represent only one aspect of a task analysis in that they do not indicate where errors are likely to occur and what the potential error sources are.

Workload Analysis

The task analysis and process diagrams provide general overviews of task requirements. However, the same task may impose different demands across individuals and contexts of use. Workload analysis is a means to measure workload at the individual level. Workload can be broadly defined as "the amount of work that a machine, employee, or group of employees can be or is expected to perform" (Costello, 1998, p. 2189).

Workload may be measured using physiological techniques such as heart rate, measures of brain activity, or pupil dilation (Vidulich & Tsang, 2012). However, such techniques may be costly or interfere with the tasks being performed. Another approach to workload analysis is to measure subjective workload. Two commonly used methods have been extensively tested for both validity and reliability: the National Aeronautics and Space Administration-Task Load Index (NASA-TLX) and the Subjective Workload Assessment Technique (SWAT).

The NASA-TLX assesses six categories and uses the ratings to derive an overall workload score (Hart & Staveland, 1988; *NASA Task Load Index,* retrieved March 20, 2015). Users quantitatively rate six factors: (1) mental demand, (2) physical demand, (3) temporal demand, (4) performance, (5) effort, and (6) frustration. For each factor, participants are asked to provide a rating on a seven-point scale ranging from very low/

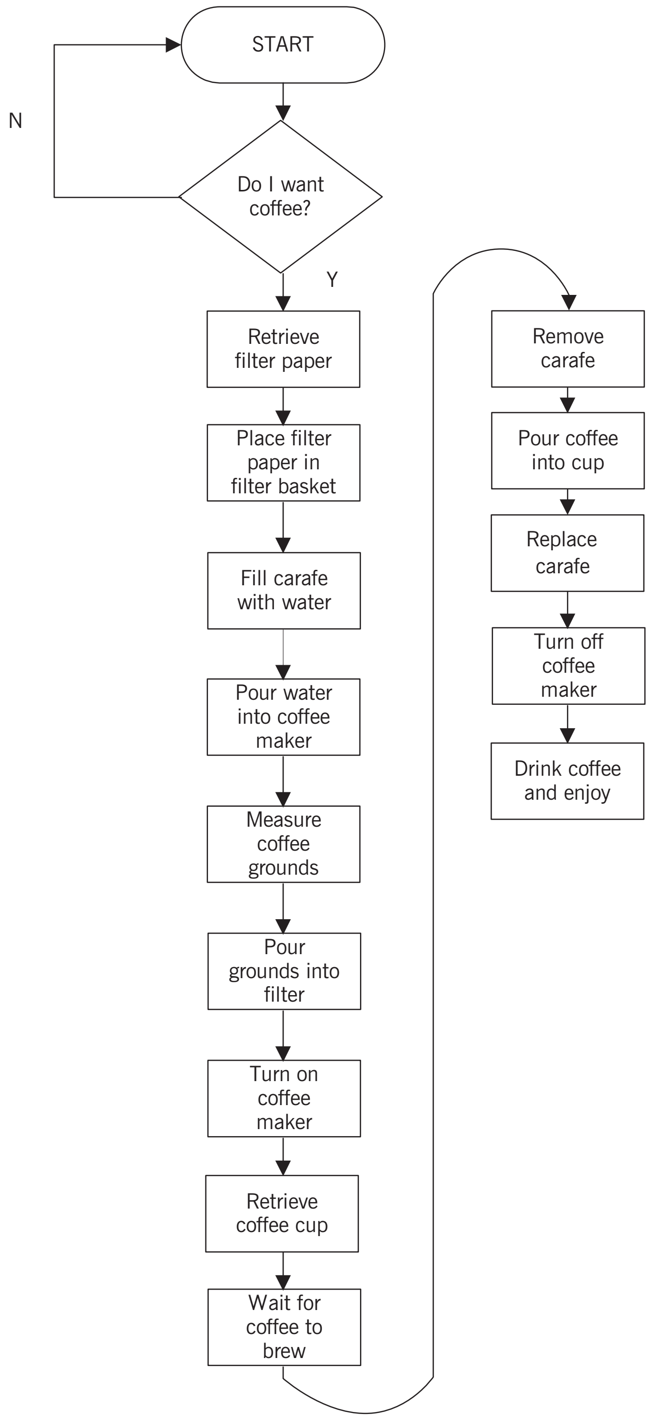

FIGURE 3.1. Process diagram for making coffee.

imperfect to very high/perfect (e.g., "Mental Demand: How mentally demanding was the task?"). Advantages of the NASA-TLX are that it is quick and easy to use, and the general categories allow this technique to be applied across various domains. Its disadvantages are that the data from the six categories are complex to analyze, and it only applies to individual workload assessments (Stanton et al., 2005). See Table 3.3 for an example application of the NASA-TLX and the type of output it provides. Note that the individual dimensions can be analyzed independently to identify the specific sources of workload for an individual.

The SWAT is also a multidimensional self-report questionnaire scale like the NASA-TLX, but it considers different categories (Reid & Nygren, 1988). The dimensions measured are time load, mental effort load, and psychological stress load. Like the NASA-TLX, the SWAT is quick and easy to use and is generalizable across domains; however, some studies have suggested it is less sensitive than the NASA-TLX (Stanton et al., 2005).

Usability Assessment Tools

Thus far, we have described tools that are useful for understanding the user and the system. There are also techniques that focus specifically on the interaction of the user with the system. For example, usability testing can reveal critical features of the user–system interaction.

One method of usability testing is the user trial, wherein users perform representative tasks with a product or device to evaluate specific user difficulties in context (Stanton et al., 2005). For example, websites can be assessed for usability by providing people with information to search for on the site and assessing where they get lost or when they fail to

TABLE 3.3. Using the NASA-TLX to Assess Subjective Workload for Two Hypothetical Diabetes Management Systems

Step 1:	Have patient interact with first device or system of interest
Step 2:	Have patient complete NASA-TLX
Step 3:	Have patient interact with second device or system of interest
Step 4:	Have patient complete NASA-TLX

	System 1: Diabetes management system using directive instructions		System 2: Diabetes management system using cooperative instructions	
Scale	Value	Weight	Value	Weight
Mental Demand	25	0.13	80	0.27
Physical Demand	20	0	35	0
Temporal Demand	50	0.33	80	0.13
Performance	30	0.20	65	0.13
Effort	25	0.13	80	0.33
Frustration	20	0.20	75	0.13
Total workload	33.33		77.33	

Note. The overall subjective workload is clearly lower for System 1; consequently, that support system might be selected for this particular patient. However, even for System 1 the reported temporal demand is high, and the system might thus be redesigned to reduce that aspect of demand.

find the information (e.g., Olmsted-Hawala, Bergstrom, & Rogers, 2013). The flexibility and simplicity of user trials are appealing advantages, but the time-consuming nature of this technique must be considered. Often, user trials involve a lengthy analysis as large amounts of data are collected; these data are extremely informative for identifying issues and assessing how the system will be used.

Another approach is a cognitive walkthrough analysis "whereby experienced system operators perform a walkthrough or demonstration of a task or set of tasks using the system under analysis" (Stanton et al., 2005, p. 479). The actual system is not required in a walkthrough analysis, as the operator can simply describe the steps of the tasks performed. This technique allows assessment without interrupting real-time system operations. Although this technique is very useful, the reliability of the method is not well established because there is no prescribed technique for conducting a walkthrough analysis. Consequently, it is useful to have more than one person perform the walkthrough and then to compare the results.

Knowledge Engineering

Another approach to understanding the human–system interaction is knowledge engineering, which can be used to understand the users, their goals, their tasks, the system, and the interaction of these components. Knowledge engineering involves developing a complete understanding of the system and system goals, and then using focus groups, interviews, and other knowledge acquisition techniques to understand users' knowledge (Bowles, Sanchez, Rogers, & Fisk, 2004; Cullen et al., 2012). Knowledge engineering may reveal how operators actually use systems (perhaps in contrast to their intended use), how skilled operators differ from novices, task demands imposed on users, gaps in operator knowledge about system functions, and information requirements for successful system use, which can be used to ultimately inform technology design and training.

Modeling

Complex tasks have multiple steps, and the order in which they are completed may vary across individuals. Task scheduling models can provide insights into the decision-making process to identify whether some people are more efficient, which might guide training programs. For instance, Barg-Walkow, Thomas, Wickens, and Rogers (2021) evaluated task scheduling decisions in the context of emergency departments by comparing patterns of emergency physicians' task scheduling models across levels of experience. The experts' level of experience influenced their task-scheduling decisions; the scheduling decisions of more experienced experts were consistent with a more frugal decision process. These findings have implications for training and evaluation.

Developing Solutions

Asking the right questions is the first step in an HF/E analysis, for example: Who are the users? What will they be doing and in what context? What kinds of difficulties are they likely to encounter? The next step is to develop solutions. Three general classes of solutions are training, environmental support, and system redesign.

Training

Training the individual is one way to alleviate problems identified or to prevent problems from occurring. Training may be broadly defined as "any systematic efforts to impart knowledge, skills, attitudes, or other characteristics with the end goal being improved performance" (Coultas, Grossman, & Salas, 2012, p. 491). Training can be particularly worthwhile when people are learning to use complex systems.

However, there is no single training method that can be applied to all tasks. Training can include the use of instructional materials, feedback, simplification of the task, or other methods. For example, part-task training involves dividing a complex task into component tasks for training (Kirlik, Fisk, Walker, & Rothrock, 1998). Part-task training can be accomplished in different ways (e.g., by segmenting the task or by simplifying the task). The decision of which approach will be optimal will depend on the specific task demands. It is therefore important to conduct a training needs analysis before beginning any training program (Coultas et al., 2012). Training needs can be identified using the aforementioned HF/E techniques (e.g., task analysis, knowledge engineering). Once training needs have been identified, the appropriate training technique can be implemented.

Another critical component of training is the provision of feedback to guide performance and learning (Coultas et al., 2012). The feedback must be timely, informative, and task-relevant. The feedback should also allow the trainee to learn to adjust and improve behavior for future interactions. Task demand and the learner's cognitive abilities, which may change with age, need to be considered when providing feedback (Kelley & McLaughlin, 2012).

There is a large literature on training and instructions (for reviews, see Alvarez, Salas, & Garofano, 2004; Czaja & Sharit, 2012) that can provide guidance for the development of training programs. One general principle to remember is that the training must be tailored to the task goals, the context of use, and the capabilities and limitations of the user (Rogers, Campbell, & Pak, 2001).

Environmental Support

Another method of solving human–system interaction problems is providing an environmental support to aid the cognitive aspects of a task (see Morrow & Rogers, 2008). An environmental support can be a map or an outline of material on a webpage, a stimulus that promotes recall of a particular characteristic, or a technological aid such as an app on a smartphone. Environmental supports have proved particularly beneficial to people with limited cognitive abilities such as memory and attention (Boot, Nichols, Rogers, & Fisk, 2012). Environmental supports can remind and guide individuals, improving their function in everyday situations.

One way to provide environmental support is through automation, which involves reallocating functions previously performed by a human to a computer or an electronic device (Sheridan & Parasuraman, 2006). Automation of tasks can free up memory resources by reducing the number of items the user must remember (e.g., an automated appointment reminder on a smartphone). By alerting users of when to focus attention instead of requiring them to sustain attention (e.g., an alarm in the car indicating the oil is low), automation can free up attentional resources. Automation has the potential to support aspects of everyday life, but it is not a panacea. Issues such as trust and reliance and how they interact with system reliability, error type, error consequences, and how people manage errors are not yet well understood (Sanchez, Fisk, & Rogers, 2006; McBride, Rogers, & Fisk, 2014).

Redesign

Human–system interactions can be optimized through design. For example, Rogers, Mykityshyn, Campbell, and Fisk (2001) used a task analysis to analyze a blood glucose monitor whose manufacturer claimed it was "as easy as 1, 2, 3." However, rather than requiring 3 easy steps, there were 52 substeps to perform. Based on this analysis, Rogers et al. (2001) were able to provide redesign suggestions along five dimensions: (1) modify the test strips (e.g., make them longer), (2) modify the meter (e.g., reduce amount of programming required), (3) modify the features (e.g., reduce processing time), (4) modify the blood-sampling procedure (e.g., reduce required amount of blood), and (5) modify major systems (e.g., eliminate need for calibration). Opportunities for system redesign abound (see Norman, 1988; Xie & Carayon, 2015, for examples).

Summary of HF/E Tools

HF/E provides guidance for understanding human–system interactions by asking the right questions, assessing user-system interactions, identifying problems, and providing solutions. The first step is to ask the right questions about the user and the system. What are the perceptual and/or cognitive demands on a user? What are the characteristics of the system being used? The next step is to choose an approach to answer the question. Many techniques can be used, ranging from task analyses to interviews to usability testing. However, one must carefully consider both the advantages and disadvantages of each approach. The final step is to provide a solution. Training, environmental support, and redesign are all potential solution options.

We have provided only a brief introduction to the discipline of HF/E. We recommend the following texts for more details:

- *Engineering Psychology and Human Performance* (4th edition; Wickens, Hollands, Banbury, & Parasuraman, 2012)
- *"Extra-ordinary" Ergonomics: How to Accommodate Small and Big Persons, the Disabled and Elderly, Expectant Mothers, and Children* (Kroemer, 2006)
- *Handbook of Human Factors and Ergonomics* (4th edition; Salvendy, 2012)
- *Human Factors Methods: A Practical Guide for Engineering and Design* (Stanton, Salmon, Rafferty, Walker, Baber, & Jenkins, 2005)
- *Usability Assessment: How to Measure the Usability of Products, Services, and Systems* (Kortum, 2016)

Illustrative Examples

The following sections illustrate the application of the HF/E methods described in this chapter. These examples demonstrate how HF/E is applied to diverse domains, including everyday activities, work, health promotion, and navigation. Cultural differences are discussed as a person characteristic that must be considered at all stages of analysis.

Everyday Activities

Everyday activities can be broadly defined in terms of three categories: (1) activities of daily living (ADLs), which can be defined as activities such as bathing, toileting, and eating, that a person must perform to live successfully by oneself (Clark, Czaja, & Weber, 1990; Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963); (2) instrumental activities of daily living (IADLs), which include activities such as doing housework, managing medication, and preparing nutritional meals (Lawton, 1990); and (3) enhanced activities of daily living (EADLs), which are the activities that individuals perform in adapting to changing environment (e.g., using an in-store kiosk, learning a new app) and learning new skills to cope with these challenges (Rogers, Meyer, Walker, & Fisk, 1998; Rogers, Mitzner, & Bixter, 2020). IADL impairments, for example, are a strong predictor of mortality (Bowling et al., 2012).

Declining cognitive and physical functioning can hamper performance of these activities, and much of the research in this domain has focused on aging. Researchers have assessed how people's abilities change with age and how these changes impact independence in the home (Czaja, Boot, Charness, & Rogers, 2019; McLaughlin & Pak, 2020). Despite the focus on aging in this area, the research approach is relevant to all ages.

HF/E Questions Relevant to ADLs, IADLs, and EADLs

What difficulties does a person with arthritic hands encounter in performing activities of daily living? How do they open a jar of spaghetti sauce, insert a key into a lock, or type on a keyboard? What if a person has limited leg mobility? How will that person climb stairs, make the bed, sweep the floor, or take a shower? The physical demands of daily living activities should not be overlooked; see Clark et al. (1990) for a direct assessment of the physical demands required to perform various ADLs.

Also relevant is developing an understanding of the cognitive component of everyday activities. For example, a specific question relevant to EADLs might be, What is the relationship between strategy use and internet search success for experienced younger and older users? (Stronge, Rogers, & Fisk, 2006). Researchers have also studied the frustrations and difficulties older adults experience in the context of performing ADLs, IADLs, and EADLs (Rogers, Meyer, Walker, & Fisk, 1998). Another HF/E question relevant to these activities is, What are the attentional demands of cooking a meal? There may be multiple ingredients to track, events that must be sequenced properly, as well as timing of various components and monitoring to prevent burning. HF/E analysis can provide insight into these issues.

HF/E Techniques

Using task analysis technique, Clark et al. (1990) detailed the physical demands associated with ADLs by videotaping older adults performing tasks. Via this method, tasks such as making the bed were divided into elemental physical units such as bending, reaching, grasping, and pulling. Additionally, for one specific ADL task, namely, cooking, the methods of interviews, questionnaires, and usability assessments, as well as knowledge engineering via role playing, were used to better understand physical difficulties (Ibrahim & Davies, 2012). Although both of these studies focused on the physical actions required of ADL tasks and the capabilities and limitations of older adults, these techniques can be used for assessing cognitive and perceptual components of ADL tasks for users of any age or ability. For instance, the cognitive demands of preparing a meal can be identified using task analysis. This method can illustrate how an individual remembers what ingredients have been added or how a person monitors meal preparation progress.

To understand the task components of strategies in searching the internet, participants were asked to execute specific queries and were monitored (Stronge et al., 2006). Process diagrams were created based on how participants executed queries to visualize the various search strategies used, and knowledge engineering was used to assess the declarative knowledge of the users. These methods provided detailed descriptions of each step in a complex process. Another study used eye tracking to uncover differences in participants' strategies and performance in navigating websites (Romano Bergstrom, Olmsted-Hawala, & Jans, 2013). These studies illustrated different strategies and processes that can be used to successfully find information on the internet.

Group interviews were conducted to collect descriptive data about the frustrations older adults encounter in ADLs, IADLs, and EADLs (Rogers et al., 1998). The questions centered on the constraints of interacting with devices and performing everyday tasks. The benefit of this technique is that the group dynamic can move the conversations into a data-rich domain that the interviewer may not have considered. These HF/E methods yield valuable data relevant to solving user problems in the domain of everyday activities.

Solutions or Potential Solutions

Environmental supports, assistive technologies, and support services were identified by Clark et al. (1990) as solutions to remedy the physical problems experienced by older adults when performing ADLs. Current solutions to overcoming challenges in the home are mostly focused on adapting the person, as opposed to the environment (Fausset, Kelly, Rogers, & Fisk, 2011), although this approach may not always be optimal. The data collected from the Rogers et al. (1998) focus groups indicated that nearly 40% of the problems encountered in ADLs, IADLs, and EADLs by older adults were a result of physical limitations, whereas 30% were attributable to cognitive limitations. Redesign of the kitchen workspace could reduce physical problems associated with cooking (Ibrahim & Davies, 2012). Automated aids such as the Cook's Collage, which gives the user feedback about what ingredients have been added to a recipe, may assist those with memory deficits in the realm of everyday activities (Sanchez, Calcaterra, & Tran, 2005). Training was identified by Rogers et al. (1998) and Stronge et al. (2006) as a solution to aid older adults in EADLs. Other suggested solutions included redesign for the internet search engines studied by Stronge et al.

Work and the Workplace

The workplace can be anywhere. For taxi drivers it is the car, for accountants it is an office, for golf course maintenance teams it may be riding a mower. No matter the occupation, several aspects of work must be considered and assessed to reach optimal work performance. With the diversity of work and workplaces, it is important to understand the physical and cognitive aspects of a job to make it safer and more efficient.

HF/E Questions Related to Work and the Workplace

Physically fitting the workspace to the human operator is important to prevent injury and to increase work efficiency (Spath, Braun, & Meinken, 2012). Some HF/E questions relating to physical considerations involve the users' diversity of size. For example, in any office environment it is critical to ask how users differ in size and shape, and what their physical capabilities and limitations are. Do any of the users have injuries or deficits that restrict movements? Other issues relate to the layout of the workspace—for example, the placement of items required for the job such that they are physically accessible to the users. This leads to questions such as what are the most important items and what items are most frequently used?

In addition to physical considerations, the cognitive aspects of a job must be addressed. For example, consider the cognitive aspects of using a riding mower at a golf course. Relevant cognitive questions might be, What are the decisions that the operator must make while operating the mower (e.g., navigating through varying terrain, recovering from a vehicle's slip)? What cues does the operator have available on which to base those decisions (e.g., terrain, obstacles)? What are the memory demands of the task (e.g., things that have already been done and things that still need to be done)? What does the operator need to pay attention to, and where does attention need to be placed? How much workload is placed on the operator while completing the task?

HF/E Techniques

Knowledge engineering techniques have been applied to the analysis of commercial mowing at a golf course (Sanchez, Bowles, Rogers, & Fisk, 2006). Product manuals, subject matter experts, interviews, and process flow diagrams were used to understand the task of mowing a golf course. The interview data gave insight into what operators do when faced with a specific problem (e.g., slipping in wet grass), the decision sequence that takes place to solve the problem (e.g., reduce pressure on gas, lift blades), and the reasons behind the decisions. Knowledge engineering also provided insight into areas where the operators' understanding of the system was inaccurate. This was accomplished by comparing the actions of the operators to the information available in the instruction materials. The comparison revealed that operators were unaware of the benefits of a key mower feature (e.g., the traction control knob) that was described by the subject matter expert as essential for successful operation. How a user operates a piece of machinery (such as a golf course mower) or makes a decision within a system is influenced by the amount of workload placed on the user.

The amount of workload will differ depending on the tasks that must be completed or monitored at a given time, the complexity of the tasks, or the amount of time available to complete tasks (Gonzalez, 2005). Different individuals will have different workload capacities, and people with limited cognitive abilities are likely to be more affected by workload. The subjective workload associated with the task can be measured for each individual using one of the methods discussed previously (e.g., NASA-TLX, SWAT). For example, during dynamic decision-making tasks, decisions made in real time are affected by the environment in which they are being made; they will be negatively impacted under high workload and when individuals have limited cognitive abilities (Gonzalez, 2005). Thus, when designing tasks and jobs for individuals, it is important to examine, understand, and if appropriate, adjust the workload placed on the user.

Solutions or Potential Solutions

The knowledge engineering study conducted by Sanchez et al. (2006) provided insights into the potential for solution in the three categories described above (training, environmental support, and redesign). Training could help operators learn to use the current mower to its maximum efficiency, for example, by teaching operators how to use the traction control system. Environmental support might be provided through automating the traction control such that it automatically engages when the mower slips. Future redesigns of the mower could make the traction control feature more salient either by emphasizing it in the instructions or by placing the control in a visible location. Other solutions might reduce or manage workload, notably: training to improve the user's skill so that the task becomes easier, environmental support to aid memory or other taxed cognitive resources, or redesign of the system to reallocate functions from the person to the machine.

Health Promotion

Health improvement is an important everyday activity that can benefit from HF/E analysis. For example, medication adherence is a serious problem for noncompliant individuals as well as for the entire health care system. A 2013 report by the National Community Pharmacists Association found high levels of medication nonadherence from medication users who suffer from chronic illnesses (*Medication Adherence in America: A National Report*, retrieved March 20, 2015). Using HF/E techniques, researchers have identified problem areas and suggested solutions to improve adherence. However, medication adherence is only one area that HF/E researchers have examined in the health domain. Other areas include medical device use, teamwork, and communication with health care professionals, and nutrition label effectiveness (e.g., can consumers appropriately understand the contents of a nutrition label and apply this understanding to their own nutritional goals?).

Much research in this domain has focused on an aging population, likely because older adults take more medications and have more health issues than younger adults. As the average expected lifespan increases, people are more likely to have chronic diseases that they must manage (Mitzner, McBride, Barg-Walkow, & Rogers, 2013). However, this research is relevant to all ages and all conditions because the same HF/E techniques can be used to identify issues, suggest solutions, and direct future research.

HF/E Questions Related to Health Promotion

Managing one's health is easy when one is very healthy. However, how does health management change when one is not very healthy? For instance, what are the demands of managing multiple medications when a person's health declines? How difficult is it to piece together all of the data coming from increasing use of technologies in home health care? How effective are external cognitive aids, such as pill organizers, organizational charts, scheduling tools, and other reminders, such as emails or text messages, in facilitating adherence to a medication regimen (Kannampallil, Waicekauskas, Morrow, Kopren, & Fu, 2013; Park, Morrell, Frieske, & Kincaid, 1992)? What is the best way to train individuals to use a sequential, multiple-step device, such as a glucometer (Mykityshyn, Fisk, & Rogers, 2002)? How simple are "simple" medical devices (Rogers et al., 2001)? How should a label be designed to ensure optimal reader comprehension (Marino & Mahan, 2005; Wolf et al., 2011)?

HF/E Techniques

Rogers et al. (2001) used a task analysis to assess the physical and cognitive steps required in using a medical device. This analysis clearly demonstrated that a medical device (a glucometer) has multiple steps that must be performed in a specific sequence to attain the end goal of proper use. These steps can tax the user's working memory and because of the importance to their health, likely increase the stress they feel. To assess the mental workload of using a medical device, participants in the Mykityshyn et al. (2002) study completed the NASA-TLX after each step. This provided the researchers with a subjective measure of the mental workload placed on the users.

In another study, a usability assessment was employed to evaluate cognitive comprehension of prescription labels (Wolf et al., 2011). In this assessment, adult patients had to interpret different types of label instructions for prescriptions, which is an example of a user trial. The redesigned prescription labels included more explicit, organized instructions, which can reduce cognitive demand. This analysis provided evidence of comprehension attained with different instructions.

Solutions or Potential Solutions

Training, support, and redesign are all potential solutions to health promotion issues. Video training led to more successful medical device use than a text manual in the Mykityshyn et al. (2002) study. The video training provided more environmental support by minimizing the working memory load and visualization demands placed on the user compared to what is required in reading a manual. Training and differences in the visibility of features in a glucose meter's design were potential contributors to errors when using a new glucose meter (Mayhorn & Carpenter, 2012). Reducing cognitive demands led to more successful comprehension of prescription labels in the Wolf et al. (2011) study. By supporting comprehension, working memory, long-term memory, and prospective memory, Park et al. (1992) found that combining a pill organizer and an organizational chart resulted in the highest medication adherence. By following HF/E information display principles, Marino and Mahan (2005) showed that current nutrition labels are inadequate in the demands they place on readers. They found that information integration of current labels imposed working memory demands on readers; participants made more correct judgments about nutrition when the label design was displayed pictorially. Moacdieh and Sarter (2015) used eye tracking to identify clutter in electronic medical records (EMRs), which can distract from performance. Applications of this work can include display redesign to reduce clutter and improve the abilities of health care providers to quickly and accurately digest information about a patient using EMRs. Further, Drews and Doig (2013) improved nurses' speed and accuracy with a display that was explicitly designed to support the task of comprehending patients' vital signs (compared to the existing display). Device redesign was suggested by Rogers et al. (2001), as the usability testing revealed that the "user-unfriendly" device design could not be remedied by training alone.

Getting Around: Issues of Navigation and Driving

Most people think about "getting around" as simply jumping into a car and driving to a destination. However, transportation issues arise when one is navigating through an environment on foot or using public transportation. In this section, we discuss not only driving and the cognitive factors involved in driving, but also wayfinding and navigation.

HF/E Questions Related to Navigation and Driving

Navigating through the environment or finding one's way can be reasonably easy if a person is in a familiar environment and perceptual or cognitive resources are not being overly taxed. However, when a person is in an unfamiliar place, with the added complexities of driving, navigating the environment can become very demanding. For individuals with cognitive impairments, these problems may be exacerbated (Sohlberg, Todis, Fickas, Hung, & Lemoncello, 2005). Relevant questions then relate to understanding the capabilities and limitations of individuals with respect to the task of navigating an environment or driving a vehicle. System analysis is also critical: What are the characteristics of the environment and the vehicle that are placing demands on the user, and what exactly are the demands? The questions should address all aspects of navigating an environment or driving a car, from determining a route to reading street signs and from visually searching an environment for hazards to deciding to proceed through an intersection.

HF/E Techniques

Task analysis indicates that three domains of ability or human functioning relate to successfully getting around: sensory-perceptual (vision and audition), cognitive (attention, memory, spatial processing), and movement control (Watson, 2001). Being able to see or hear is crucial to successful navigation. Vision deficiency can be problematic when navigating. The ability to read street signs and directions and to adjust to differing light conditions (such that occur when going from outside to inside) are important to finding one's way. Visual attention, the visual information that can be attended to during a brief period of time, has a significant effect on one's ability to drive and avoid accidents (Goode et al., 1998). Visual attention can be measured using the Useful Field of View (UFOV®), which measures the size of the area to which individuals can visually attend. The size of the UFOV predicts crash involvement and risk of crashing in older adults, who generally have smaller useful fields of view (Goode et al., 1998). Visual attention—or rather, the lack of it—to the leading vehicle relates to rear-end automobile accidents (e.g., Dingus et al., 1997). Advanced in-vehicle crash warning systems are one intervention being used more frequently by the automotive industry to cue drivers to shift their visual attention to the leading car. This intervention can improve drivers' reaction times and thus ultimately prevent accidents (e.g., Lee, McGehee, Brown, & Reyes, 2002).

Given the nature of driving today, with the demand of performing multiple tasks at a given time, the driver's capacity to divide attention is particularly relevant. Drivers may simultaneously talk on a cell phone, adjust the radio, listen to music, or talk to a passenger (not to mention put on make-up or eat lunch). Individuals with fewer attentional resources will have more difficulty performing multiple tasks successfully and may put themselves and others at risk (Caird, Edwards, Creaser, & Horrey, 2005). Research shows that if attention is divided during driving, people react more slowly, show greater speed variation, follow at a greater distance, and are involved in more rear-end collisions (Strayer & Drews, 2004). For example, sending and receiving messages on a mobile electronic device while driving is associated with less time spent looking at the road, less ability to maintain lanes, and increased variability in following distance (Hosking, Young, & Regan, 2009). In addition, when searching for objects in the environment, such as street signs and other vehicles, drivers are slower and less accurate when attentional resources are being taxed (McPhee et al., 2004). Dividing attention can leave less time for evasive action (McPhee, Scialfa, Dennis, Ho, & Caird, 2004) but also negatively impact decisions while navigating complex environments such as intersections (Caird et al., 2005). Individuals whose attention is taxed will rely on fewer cues in the environment on which to base driving decisions.

Looking forward, the shift in the automotive industry toward hands-free voice-activated controls and devices in cars may not actually reduce driver distraction as they can increase cognitive load on operators (e.g., Strayer et al., 2013, 2019). Additionally, the shift in technology toward increasingly automated cars, including self-driving cars, means that additional consideration is needed regarding human operators' situation awareness and ability to successfully transition to manual control of cars (Hancock et al., 2020; McDonald et al., 2019).

To assess these effects for individuals from specific populations, surveys, interviews, and focus groups with populations of interest may be used. These methods are an excellent way of ascertaining the source and subsequent outcomes of many functional limitations associated with navigation and wayfinding. For example, Sohlberg et al. (2005) used these techniques to assess the challenges faced by individuals with cognitive impairments. Such individuals expressed concerns with getting lost and the challenges associated with problem solving while en route; their concerns resulted in fewer medical and business visits and reduced social interaction. The interviews and focus groups enabled the researchers to delve more deeply into problems and to discover strategies used to overcome them and potential areas for solutions to these problems.

Solutions or Potential Solutions

Human beings are very good at adapting and overcoming obstacles, up to a point. Although some people may experience problems navigating an environment, many develop "survival" strategies. Sohlberg et al. (2005) found that people will often use explicit written directions received in advance to reduce memory demands. Landmarks were found to be unhelpful because, when memory is a problem, individuals with cognitive impairments do not remember having passed landmarks. The authors also found that it is important for individuals with cognitive impairments to have backup plans if the primary strategy fails (e.g., if the directions are lost). Such plans include continually asking people for directions, carrying a cell phone to receive directions from family or friends, or using a global positioning system (GPS)—either on a cell phone or as a standalone device. From these survival strategies, we can inform solutions to navigational problems.

Training has proved effective for improving problems associated with UFOV and risk awareness in drivers. For example, the size of UFOV was expanded when participants were trained on speed of processing, a fundamental ability influencing UFOV (Ball, Edwards, & Ross, 2007). Risky driving behavior was decreased by training inexperienced drivers to reduce their exposure to dangerous situations and to detect hazards (Fisher et al., 2002; Fisher, Pollatsek, & Pradhan, 2006). Actively training individuals to focus attention in appropriate locations while driving has a long-term effect, which can enable drivers to compensate for taxed attentional resources in complex driving situations (Romoser, 2013). Other solutions can include designing the automobiles and their environments to support drivers' cognitive capabilities, such as providing advanced warning before a green light turns yellow (Gugerty et al., 2014).

Cultural Considerations: Globalizing HF/E

With the increased cultural interactions in the present global economy, considering the user beyond the cognitive, perceptual, and motor differences of Western society is essential for the acceptance and integration of systems and technology worldwide. Important cultural distinctions—physical, perceptual, and cognitive—must be made. Such distinctions may be relevant to proposed HF/E solutions (e.g., Rau, Plocher, & Choong, 2012; Harris, Nie, & Rogers, 2020).

Anthropometric data used by human factors specialists are based primarily on measurements derived from Western populations. However, there are significant physical differences between cultures. For example, on average, Japanese people are shorter than Western people (Lippa & Klein, 2005). A mismatch between the physical size of users and the physical size of where they are operating can lead to reduced efficiency in the workplace and increased safety risks. But cultural differences go beyond physical characteristics.

Cultural differences can also be seen in differences of perception. Culture is the belief system and values of the society in which one is raised and can have a significant influence on how one perceives the world. A quantitative review of 26 studies of ethnic group differences showed moderate to large effect sizes for pain tolerance differences between groups (Rahim-Williams, Riley, Williams, & Fillingim, 2012). One study showed that Nepalese people exhibited significantly higher pain thresholds compared to Western people (Clark & Clark, 1980). These differences were not attributed to neurosensory differences, but to differences related to pain-reporting criteria, produced by a different cultural value system. It is therefore important to be cognizant of cultural differences in the context of human–system interaction. These differences might impact the ability of the patient and health care providers to track and manage pain (e.g., Barg-Walkow et al., 2013).

Physical and perceptual differences exist between cultures, but research also indicates that there are cultural differences in the way we think. For example, a comparison of Asian and American cultures revealed distinct differences in the way each uses intuition versus formal reasoning to overcome conflict (Norenzayan, Smith, & Kim, & Nisbett, 2002). Americans were more likely to use formal reasoning compared to Chinese and Koreans, who relied more heavily on intuitive strategies for solving conflict. Nisbett, Peng, Choi, and Norenzayan (2001) found that Westerners were more analytic compared to East Asians who tended to be more holistic in their systems of thought. These fundamental cultural differences can influence cognition and motivation.

In a study comparing American and Asian cognitive styles, Rau, Choong, and Salvendy (2004) found that the American cognitive style tends to classify stimuli based on inferences about stimuli or the functions of stimuli. In contrast, some Asian cultures tend to classify stimuli based on their interrelationships. The Asian way of thinking is more relational compared to that of Americans, who are more analytical. As a result, Asian cultures tend to rely on thematic structuring of processes (e.g., what are the relationships between products?), whereas Americans tend to rely on functional structuring of processes (e.g., what are the attributes of a product?). An example of different mental structuring would be a thematic structure of separating household items by room of use (e.g., kitchen, bedroom) versus a functional structure of separating household items by attributes (e.g., appliances, decoration). An implication of cultural differences in cognition is that the mental models on which designs are based may not work for people from other cultures; in fact, they may be detrimental to their efficiency and safety interacting with the product/system.

Cultural differences can play a big role when applying HF/E tools and techniques. For example, Chavan (2005) pointed out that the Indian culture generally accepts the current state of a situation and then looks for ways around it. This approach can pose a problem when conducting usability studies in that people from the Indian culture do not like giving negative opinions. Even the idea of "usability" was found to have different meanings and priorities for users from China (e.g., high value of visual appearance) versus users from Denmark (e.g., high value of efficiency; Frandsen-Thorlacius, Hornbæk, Hertzum, & Clemmensen, 2009), which needs to be considered when conducting studies and deciding how to phrase questions. In addition, people from collectivist cultures (e.g., most Asian cultures) may have trouble providing an individual opinion and will likely give an opinion they think the collective would hold. Therefore, when applying HF/E tools it is important to consider cultural differences and how they affect the collection and interpretation of data.

Summary of Illustrative Examples

As the above examples have illustrated, HF/E techniques have been employed in a wide range of domains. From task analysis to interviews and from driving a car to managing medications, HF/E techniques have been used to identify problem areas; describe the user, the system, and their interaction; and suggest solutions. These tools can be applied to any domain or any system that involves a human user. HF/E techniques consider the user's capabilities and limitations and the context in which the user is interacting with the system.

Looking to the Future: Advanced Technologies

The discipline of HF/E has much to offer the practice of neuropsychology. In fact, there is an emerging area, called neuroergonomics, that represents the intersection between HF/E and neuropsychology (see Parasuraman & Wilson, 2008). Neuroergonomics analyses involve understanding the neural bases of perception and cognition as they relate to human–system interactions underlying performance. Specific methods related to neuroergonomics are varied and can include techniques such as neuroimaging (e.g., functional magnetic resonance imaging [fMRI], electroencephalography [EEG]), noninvasive brain stimulation, and genotyping, usually in conjunction with other HF/E methods described in this chapter. Parasuraman and Wilson (2008) provided examples of how this approach may involve assessments of cognitive workload, attention, and vigilance. Such measures may prove useful to detect—for individual patients, for example—when workload is overloading them while they are performing a particular task. Neurological measures would be particularly useful if the person were unable to provide an accurate report of subjective workload. Neuroergonomics methods can be used in training to improve cognitive task performance (Parasuraman & McKinley, 2014).

The concept of adaptive automation also has potential for supporting patients' needs. In adaptive automation, functions are assigned (allocated) either to the technology/system or to the person based on different parameters such as workload, stress, goals, or ability in real time. In other words, adaptive automation systems "appropriately modify their behavior to fit the current context" (Feigh, Dorneich, & Hayes, 2012, p. 1008). This type of adaptive system could support learning by the patient during the rehabilitation process and yet recognize situations of overload, providing technological support as needed. For example, in a low-stress or low-workload situation, it may be desirable to have the human perform a task (e.g., wayfinding) so that they can maintain and improve their functional abilities. However, in high-stress or high-workload situations, it might be critical to have an automated system provide the needed information, such as autonomous braking in automobiles immediately prior to an accident (e.g., Kusano & Gabler, 2012). Adaptive automation is reliant on valid and timely assessments of workload; neuroergonomics can be used to assess the person's current abilities and identify points when the adaptive automation should shift tasks between the system and the person (e.g., Christensen & Estepp, 2013; Hancock et al., 2013).

Robotics, similar to adaptive automation, can play a role in supporting users' needs. In human–robot interactions, functions are assigned (allocated) either to the robot or to the person, based on different parameters such as preference or ability. For example, older adults expressed a preference for robot assistance over human assistance for home-based tasks with a higher physical demand, such as maintaining a lawn (Smarr et al., 2014). Additionally, one animal-like robot has been found to improve physical and sociocognitive well-being (Kidd, Taggart, & Turkle, 2006; Robinson, MacDonald, & Broadbent, 2014; McGlynn, Kemple, Mitzner, King, & Rogers, 2017). This form of advanced technology has the potential to aid aging-in-place through the support of ADLs and IADLs (Mitzner, Chen, Kemp, & Rogers, 2014; Stuck & Rogers, 2018).

The broad discipline of HF/E has well-developed methods to enable understanding of human–system interactions in a variety of contexts. These methods provide ways of asking questions that lead to the development of solutions through training, provision of environmental support, or technology/system redesign. Such solutions may be implemented for groups of people or for single patients. In either case they have the potential to improve the safety, efficiency, and effectiveness of human–system interactions.

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CHAPTER 4

The Relationship between Cognition and Function

The Occupational Therapy Perspective

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Occupational therapists (OTs) are core members of the team that addresses the cognitive issues that people with neurological injuries, chronic diseases, and mental illness face as they are required to learn the strategies needed to manage the complexity of their daily lives. The OT's lens is focused on occupational performance, which requires the OT to have an understanding of how psychological, cognitive, sensory, motor, and physiological factors support the capacity of the person; the person's occupations, defined as what the individual needs and wants to do to maintain themselves as they engage in work, family, and community activities; and the environment, which includes social support, social capital, the physical environment, and culture).

This chapter highlights the approach, assessments, and interventions that occupational therapists use to address people with cognitive impairment. The OT works with the person while in the hospital or health system and often works with people in their homes and communities as they learn to build action plans and use strategies to continue their recovery and engage in the activities that support their roles and are meaningful to them.

The Occupational Therapy Approach

There are five main contemporary models in the occupational therapy literature that support the clinician's understanding of occupational performance: the person–environment–occupational performance model (Christiansen & Baum, 1991, 1997, 2005, 2015); the model of human occupation (Kielhofner, 1985, 1995, 2002, 2008); the Canadian model of occupational performance-enabling occupation (Townsend et al., 1997; Townsend & Polatajko, 2007), and the KAWA model (Iwama, 2006). Each of these models includes all three central elements: person, occupation, and environment, and all the models reflect the stage of development of the person as they influence the person's motivation, skills and roles. Moreover, these OT models share views of the individual that emphasize the complex relationship of biological, psychological, and social phenomena and the importance of a satisfactory match between the person, the task, and the situational characteristics. This interaction is known as *occupational performance*; occupational therapists use this term to describe the function of an individual interacting with the environment while doing the activities that are important for them to do.

The person, environment, and occupation (PEO) concepts were articulated by scholars in occupational therapy throughout the 20th century (Meyer, 1922; Reilly, 1962; Fidler & Fidler, 1973; Mosey, 1974). Today these concepts form the basis for views of OT practice that address the occupational performance issues of individuals. All of the PEO models are supported by research and knowledge from the behavioral and social sciences (psychology, anthropology, environmental science, and sociology) and the neurosciences, as well as from work in newer areas such as rehabilitation science, disability studies, and occupational science.

Occupational therapy intervention is viewed as a process of using a broad range of purposeful client-centered strategies that engage the individual to develop or use their capacities and resources to enable successful performance. The use of such strategies points out that the satisfactory performance of occupations is a consequence of individual goals and environmental characteristics that either limit or support participation. Intervention strategies involve an individual's direct engagement in occupation, and it is possible to modify environments to make them accessible and provide necessary physical or cognitive support. The client's active involvement may consist of working with the therapist and the family to identify goals and strategies that will remove barriers and enable participation in tasks and roles. OTs almost never do things *to* people; they more frequently enable people to do things.

Many people with chronic health conditions and disabilities have cognitive problems that limit their performance of daily life activities. Daily life requires the individual to formulate goals, plan how to achieve them, and carry them out. OTs work with children and adults who have difficulties formulating and maintaining the focus on their goals. Such goal-directed activities include care of self and others, home maintenance, work, fitness, leisure and sport activities; as well as community, social, and spiritual activities. These goal-directed activities give meaning to people's lives. Performing goal-directed activities requires the individual to use higher-level cognitive processes to be able to self-correct, make decisions, use judgment, and make wise choices as they navigate through life's challenges and difficulties (Lezak, 1982; Goel, Grafman, Tajik, Gana, & Danto, 1997; Lezak, Howieson, & Loring, 2004). Thus, impairment or loss of these functions compromises the ability to fully participate in society.

Emphasis on both occupational performance and participation requires the practitioner to employ a client-centered strategy (Trombly, 1992; Mathowetz & Haugen, 1995; Fisher, 1998; Baum & Law, 1997). The practitioner must determine with the client what he or she perceives to be the issues that are limiting participation and causing difficulty in carrying out tasks that include those related to productivity and work, personal care, home maintenance, sleep, and recreation or leisure. This approach is defined as a top-down approach because it starts with the individual's goals and needs to learn how the physiological, psychological, cognitive, neurobehavioral and spiritual factors may be supporting or interfering with the individual's performance. It also identifies the environmental factors that may serve as enablers or barriers to performance.

It is important to determine an individual's capacity for real-world or everyday performance (Alderman, Burgess, Knight, & Henman, 2003; Fisher, 1998; Giles, 2005; Gioia & Isquith, 2004; Keil & Kaszniak, 2002; Levy & Burns, 2005; Shallice & Burgess, 1991; Morrison, Edwards, & Giles, 2015). Capacity is determined by having the person demonstrate that he or she can perform the activity. Performance-based testing is originally based on environmental psychology theory and the concept of ecological validity proposed by Egan Brunswik (1955). Brunswik advocated for research that would allow free behavior in an unrestricted environment to help better explain behavior beyond that of a strictly controlled laboratory experiment, which only examined the influence of one variable on behavior (Brunswik, 1955). He referred to this type of experiment as "ecologically valid," meaning representative of real-world performance, which regularly requires multitasking and occurs in environments that may or may not be supportive. Because occupational therapists work with people to help them achieve occupational performance in the activities important in their own lives, the concept of ecological validity was introduced into rehabilitation testing with Tim Shallice and Paul Burgess's introduction of a multitasking assessment called the Multiple Errands Test (MET; Shallice & Burgess, 1991). The MET was built on the notion that the testing of real-world performance requires behavioral observations in the environment in which the person will actually perform the task. Occupational therapists have been building performance-based measures since the early 1990s based on the need for ecological validity to assess the interaction of the person, doing an activity, in an environment. The information occupational therapists obtain from such assessments enables therapists to work with individuals and their families to maximize function in those with cognitive loss as they face the challenges of setting goals, planning and implementing tasks that are necessary and important as they return to their daily lives. Occupational therapists assess cognition to determine the person's capacity to be safe, live alone, work, or do any task that is important and meaningful for them. Thus, testing addresses the impact that executive function has on performance by assessing a person's cognitive capacity in the performance of daily tasks. It is possible to observe key executive constructs in the performance of daily life (Baum & Edwards, 1993; Baum et al., 2008). These include initiation, the process that precedes the performance of a task (DePoy, Maley, & Stranaugh, 1990; Kaye, Grigsby, Robbins, & Korzun, 1990; Lezak et al., 2004); organization, the physical arrangement of the environment, tools, and materials to facilitate efficient and effective performance (Weld & Evans, 1990; Lezak et al., 2004); judgment (Lezak, 1982; Goel et al., 1997); and completion (Goel et al., 1997).

The occupational therapist approaches the measurement of cognition and function not just to know what a person can do, but to know what to do to foster the individual's engagement in daily life because occupation is a basic human need, a determinant of health and a source of meaning (Meyer, 1922; Reilly, 1962; Townsend, 1997; Hasselkus, 2011; Christiansen, 1999).

How OTs Address Cognition from a Performance and Environmental Perspective

Occupational therapists gather information to build a client-centered plan that will not only maximize the capacities of the person but also help families understand what has happened to their family member who has experienced a cognitive impairment and provide knowledge of how to minimize their burden as they support their needs. The therapist will collect background information about the person and their activities and conduct a cognitive screening to determine if further assessment is necessary. They will measure the person's cognitive capacity to perform a task to determine the level of cue or support they need and will determine the environmental context in which performance may need to be supported for safety. As well, they will collect the observations of the informant's behaviors. All five areas will be presented, and some measures that can be used for each area will be described. With the exception of the screening tools, the measures discussed in this chapter were developed by occupational therapy scientists to identify the occupational performance issues of people so that appropriate interventions can be employed to help people with cognitive impairment continue their recovery and live their lives.

Interview and Background Information

The OT uses the initial interview to create a profile or a summary of the person's activities, interests, and roles. Such information helps the occupational therapist understand what is important to the person. At this time, it is necessary to know of their habits and if their daily lives require them to respond to novel tasks. It is also important to understand their motivations for activity, as such information forms the basis for establishing goals and interventions (Wolf & Baum, 2018).

The following measures provide information about the person's occupational history and the activities they perform that support their daily functioning. These tools help the therapist determine the person's interests and experience with activities that can be used to build daily routines and set goals. The Occupational Questionnaire (OQ; Smith, Kielhofner, & Watts, 1986) asks the person to list activities during a 24-hour typical day. The Activity Card Sort (ACS; Baum, 1995; Baum & Edwards, 2001; Katz, Karpin, Lak, Furman, & Hartman-Maeir, 2003; Sachs & Josman, 2003) records the activity participation of adults and older adults in instrumental, leisure, and social activities. It requires the individual (or with the family support) to sort photographic cards depicting typical activities that fit into the categories of instrumental, leisure, fitness, and social activities. Using the pictures of people actually performing the activity prompts the person to recall the level of their engagement with the activity and provides an occupational profile of the types of activities the person is engaged in or has given up. Such information is central to planning the care of a client who needs occupational therapy. The ACS has been validated, with culturally appropriate versions reflecting the activities of older adults in the United States, Israel, Australia, Hong Kong, Singapore, Puerto Rico, the Netherlands, Great Britain, and Malaysia. The Canadian Occupational Performance Measure (COPM; Pollock, McColl, & Carswell, 2006) measures performance and satisfaction in self-care, productivity, and leisure. It is designed to capture a client's self-perception of their performance and satisfaction over time and structures the goal-setting process. The performance changes and satisfaction can be used to determine effectiveness of interventions. The COPM has been translated into over 30 languages.

It is common for persons with suspected cognitive deficits to lack awareness of their cognitive challenges; therefore, it cannot be assumed that they have a realistic view of their condition. There may be several reasons for this lack of awareness, including a neurocognitive deficit, a psychological issue, and perhaps a lack of understanding of the cognitive implications of their condition (Fleming & Ownsworth, 2006; Toglia & Maeir, 2018). The first step in cognitive assessment is to determine the client's level of awareness. There are different methods to evaluate awareness, such as interviews with questionnaires, comparison between the answers of the individual and a proxy (relative, other caregiver, or therapist), comparison to test performance, and prediction before and evaluation after task performance (Fleming, Strong, & Ashton, 1996; Katz, Hartman Maeir, Ring, & Soroker, 2000; Prigatano, 1986; Toglia, 1993, 2005). Three tests for awareness are as follows: (1) The Self-Awareness of Deficits Interview (SADI; Fleming et al., 1996) collects both qualitative and quantitative data as the person is asked about their self-awareness of deficits and limitations and their ability to set a realistic goal; (2) The Awareness of Errors in Naturalistic Action (Hart, Giovannetti, Montgomery, & Schwartz, 1998) asks the person to report on their performance after completing a complex task that has been observed by the clinician; and (3) The Assessment of Awareness of Disabilities (AAD; Tham, Bersnpang, & Fisher, 1999; Tham, Ginsburg, Fisher, & Tenger, 1999) can be used to assess the discrepancy between the client's observed ADL ability and their perceived ability using the AAD, which is a guided interview (Tham et al., 1999). The interventions to address awareness are discussed in the intervention section of this chapter.

Cognitive Screening

The screening instruments described in this section are standardized, and their psychometric properties are established. In order to acquire a basic knowledge of the client's cognitive abilities and deficits, the occupational therapist will choose the appropriate tests depending on the client's age, diagnosis, stage of illness, setting, and so on.

The Mini Mental Status Examination (MMSE; Folstein & Folstein, 1975) and the Short Blessed Test (SBT; Katzman et al., 1983) are used extensively as screening tools for dementia by health professionals, and clock drawings tests are used in a variety of ways to assess visual spatial neglects, spatial organization, memory, and executive functions (Freedman et al., 1994; Royall, 1998).

The Montreal Cognitive Assessment (MOCA; Nasreddine et al., 2005) is a brief cognitive screening test designed to detect mild cognitive impairment. It assesses visuospatial abilities, task alteration, memory, naming, attention, verbal fluency, abstraction, delayed recall, and orientation. A validation study has shown the MOCA to be superior to the Mini Mental State Examination for detecting mild cognitive impairment with a sensitivity and specificity of 90% and 87%, respectively (Nasreddine et al., 2005). It has been recommended by the National Institutes of Health for the identification of vascular cognitive impairment. A final total score of 26 and above is considered normal.

The St. Louis University Mental Status Examination (SLUMS; Tariq, Tumosa, Chibnall, Perry, & Morley, 2006) is a tool that screens for dementia but includes a screen for mild cognitive impairment to indicate further testing of executive functions. The MMSE (Folstein & Folstein, 1975) and the Brief Interview for Mental Status (BIMS; Saliba et al., 2012) are used to determine orientation, recall, and short-term memory and are good screening tools if dementia is suspected.

The Menu Task (MT; Edwards et al., 2019) is a brief performance-based screening task that requires the person to select what they want to eat from a menu, while following a set of rules that relate to their dietary restrictions. It is particularly useful as it can be part of the menu selection where food service is provided.

At this stage of the process, the occupational therapist should have a good idea about the client's level of self-awareness, their previous and current occupational performance and participation, and whether further testing will be needed to determine how cognitive problems are impacting performance. Although screening tools may have reduced sensitivity to subtle impairments, when paired with performance-based assessments, they do give a clinical indication of problems that require attention if the person is having difficulty performing tasks. Individuals with subtler neurological impairments associated with mild stroke have been known to perform well on screening assessments of cognition but have higher-level cognitive impairments that are often underdetected in the acute care settings (Edwards et al., 2006; Wolf et al., 2010). If suspected, the next step is to measure cognition as they actually perform a task.

Measures of Cognition in Task Performance

The performance of a task requires executive function, as individuals must plan, initiate, and modify actions when problems are encountered and to be successful, they must process feedback from their environments (Fitzpatrick & Baum, 2012). Occupational therapists have developed valid, standardized tools to assess cognitive function in the performance of a task. Performance tasks are typically performed in a life skills area of a clinic or in the home.

For an individual who is not independent in the basic activities of daily living, the A-ONE (Arnadottir & Fisher, 2008) is an assessment based on naturalistic observation of ADL task performance. The A-ONE directly links functional performance (basic activities of daily living and mobility) to neurobehavioral deficits, including cognitive-perceptual and motor impairments. This assessment tool is appropriate to use for clients over the age of 16 who present with damage to the central nervous system. It utilizes standardized and structured observations as the method of assessment during the following ADLs: feeding, grooming, and hygiene (upper body washing, oral/hair care, shaving, etc.), dressing (upper and lower body), transfers and mobility (bed mobility, transfers, maneuvering in a wheelchair or during ambulation), and functional communication (comprehension and expression).

The Kitchen Task Assessment (KTA; Baum & Edwards, 1993) is a performance-based standardized assessment of cognition and executive function. The investigator records the level of support needed to perform a simple cooking task (making cooked pudding or oatmeal). This support is in the form of a verbal cue, physical assistance, or an indication that the person is not capable of the task. Individuals are scored on their ability to initiate, execute (including organization, sequencing, judgment, and safety), and complete the task. The KTA serves three purposes: (1) to determine which executive functions are causing performance problems (initiation, organization, sequencing, judgment and completion); (2) to assess an individual's capacity for independent functioning; and (3) to find the level of assistance required to support completion of the task (Baum & Edwards, 1993), which can inform caregivers of the level of cue the person needs in order to be successful with a simple performance task.

The Kettle Test (Hartman-Maeir, Armon, & Katz, 2005) uses the task of preparing two cups of hot beverage using an electric kettle to boil water and either tea bags or an instant drink mix. Following completion of the task, the therapist engages the client in a debriefing that focuses on the client's evaluation of their own performance. Task selection is designed to require basic cognitive abilities such as attention, perception, praxis, and memory, as well as higher-order executive functions by providing unusual conditions of the materials and context, planning, and regulations of mistakes.

The Actual Reality (AR; Goverover, O'Brien, Moore, & DeLuca, 2010) is a performance-based assessment that involves use of the internet to perform actual everyday life activities. The person is required to do an everyday task (e.g., order an assortment of cookies or an airline ticket) online using a credit card. These steps involve critical actions required to complete the task, such as clicking on certain internet icons when necessary, choosing the time and date for departure and arrival or delivery and, paying for the plane ticket or order. Participants are required to go through all of the steps in order to complete the task, and the score is formed by the errors and need for and use of cues.

The Revised Observed Tasks of Daily Living (OTDL-R; Diehl et al., 2005) is a performance-based test that requires problem solving in IADL tasks. It includes nine tasks in three areas: medication use, telephone use, and financial management. The test is able to discriminate between groups of cognitive impairments and to predict performance on the OTDL-R from categorization and deductive reasoning measures.

The Assessment of Motor and Process Skills Scale (AMPS; Fisher, 2001) was developed to assess the motor and cognitive process of the individual. The instrument includes a list of about 50 ADL and mostly IADL tasks from which the client and therapist choose two to three daily tasks (making a sandwich, packing a lunch, washing a plate, etc.) that are familiar to the person; the therapist observes as the person performs these tasks. The scoring yields both a motor and a process scales score, and it also describes four levels of independence. The instrument was developed using a Rasch model, and it was studied with large and diverse populations (Fisher, 1993; Fisher, Liu, Velozo, & Pan, 1992; Kizony & Katz, 2002).

The Contextual Memory Test (CMT) and the Toglia Categorization Assessment (TCA) were developed by Toglia and Kirk (2000). The unique feature of these tests is their dynamic component in which a graded cueing system is incorporated, allowing the clinician to observe the person's cognitive capacity to perform tasks. Also incorporated in these tests is the evaluation of online or emergent awareness that enables the therapist to see whether the clients' level of awareness changed while they performed a task in correspondence to the level of performance. Both tests were developed for clients following traumatic brain injuries (TBIs), but they were later also evaluated in clients with schizophrenia and in children with TBI and attention-deficit/hyperactivity disorder (ADHD; Goverover & Hinojosa, 2004; Josman, Berney, & Jarus, 2000a, 2000b; Josman, 2005).

The ADL Checklist for Neglect (Hartman-Maeir & Katz, 1995) reports the expression of neglect in activities such as grooming, dressing, and eating, as well as reading, writing, and mobility. This test answers the question, "Does the client neglect the left or right side of his personal or extra personal space without the knowledge that it occurs?" This phenomenon is one of the most detrimental to the rehabilitation outcome of clients following stroke (Heilman, Watson, & Valenstein, 2003; Katz, Hartman-Maeir, Ring, & Soroker, 1999).

The Executive Function Performance Test (EFPT; Baum et al., 2008) was developed based on the scoring rubric of the Kitchen Task Assessment. It records executive functions in the performance of four standardized IADL tasks (cooking, telephone use, medication management, and money management). The therapist provides graded cues (no cue needed, a verbal prompt, a gestural prompt, a direct verbal cue, or physical assistance) to record a score for the cognitive components of initiation, planning, execution of the task with error detection and correction, safety and judgment, and task completion. It has been validated in individuals with stroke (Baum et al., 2008), head injury (Baum et al., 2017), and schizophrenia (Katz, Tadmor, Felzen, & Hartman-Maeir, 2007).

The Multiple Errands Test (MET) by Shallice and Burgess (1991) evaluates how an individual performs errands by using real-world tasks like purchasing and paying for specific items, collecting and writing down specific information, or arriving at a specific location. It has been studied with TBI clients (Alderman et al., 2003; Knight, Alderman, & Burgess, 2002) and clients following stroke (Dawson, McEwen, & Polatajko, 2005) using a complicated task performed in a shopping district.

The Complex Task Performance Assessment (CTPA; Wolf, Morrison, & Matheson, 2008) is a performance-based assessment that was developed with the theoretical framework from the MET, while addressing some of the limitations of the MET when used in a clinical context (e.g., need for a community-based setting, no time limit). The CTPA requires that a person simulates working in a library with two primary work tasks—(1) Current Inventory Control and (2) Telephone Messaging—which are administered simultaneously. The Current Inventory Control requires that a person calculate the current fines and replacement costs for books and videos that are overdue. The Telephone Messaging activity requires the person to listen to recorded telephone messages, with three varying levels of difficulty. Messages have three levels of difficulty: (1) Declarative—no interaction with other tasks. Messages are recorded only; (2) Interactive—require interaction with other tasks; and (3) Reasoning—require interaction with other tasks and for the participant to make decisions that will impact how they complete the other tasks. Secondary tasks are also involved in order to meet the multitasking criteria used in the MET, including a time-based task and event-based task.

The Performance Assessment of Self-Care Skills (PASS; Rogers, Holm, & Chisholm, 2016a) allows the clinician to observe and document systematically the skills of the person being observed. It supports a test–intervention–retest paradigm that is typically used in the intervention of persons where a learning paradigm is being employed and the person is given indirect cues to correct the error. The therapist records the independence, safety and adequacy of the performance.

The Weekly Calendar Planning Activity (WCPA; Toglia, 2015) is a performance-based measure of functional cognition that requires the test taker to enter items of appointments into a blank weekly schedule, while adhering to rules, monitoring time, and recognizing and reconciling conflicting task demands. This test allows for observation of cognitive strategies as the subjects learn, problem-solve, and perform the task.

Evaluation of Environmental/Contextual Factors

Occupational therapists understand that an individual's abilities can be optimized by environments that support their ability to use their skills. Environmental assessments identify the facilitators and barriers to performance.

Many practitioners visit the client's home to determine the safety of the physical environment. Persons with cognitive loss need to have the environment assessed to determine if they have the cognitive capacity to live alone. Assessments that focus on home safety include the Home Occupational Environmental Assessment (HOEA), the Safety

Assessment of Function and the Environment for Rehabilitation (SAFER Tool), and the In-Home Occupational Performance Evaluation (I-HOPE).

HOEA (Baum & Edwards, 1998) is a checklist designed to identify how the home environment supports occupational performance and the safety of the person being assessed. It is particularly useful for clients with visual and cognitive impairments. It is completed by a therapist while in the client's home, and it requires approximately 20 minutes. The HOEA checklist covers issues such as accessibility within the home, sanitation, food storage, safety issues, and lighting at the point of common tasks. The scoring indicates the independence of the person.

The SAFER Tool (Chui, Oliver, Marshall, & Letts, 2001) was designed to guide a therapist's report on the client's ability to safely carry out functional activities at home. The therapist conducts an interview and uses observation to record 97 items in 14 areas of concern, including mobility, kitchen use, fire hazards, wandering, and communication. The SAFER Tool provides a comprehensive list of activities and environmental issues that need to be considered to support safety at home. It also provides useful ideas for environmental interventions.

The In-Home Occupational Performance Evaluation (I-HOPE) uses a card sort to identify in-home activities, prioritizes and rates the client's performance for each activity rated to be important, and rates the barriers that can influence their safety by observing the person perform activities they have identified as important. This approach can account for the tremendous variability that can occur across homes by focusing on person–environment fit. I-HOPE is a reliable and valid measure of performance in the home environment and can be used to determine the activity patterns of older adults in their homes, performance of daily activities, satisfaction with that performance, and the influence of environment. This instrument is conducted in the participant's home, takes approximately 45 minutes to complete, and is helpful to client-centered care planning.

Informant-Report Measures for Observed Performance

It is important to remember that family members care for and live with the person with cognitive impairments. It is always good to have a way for them to report their observations to those who can help them. The following are validated tools that can be help facilitate important discussions.

The Functional Behavior Profile (FBP; Baum, Edwards, & Morrow-Howell, 1993) reports the observations of a caregiver on the person's task performance, problem solving, and social interactions. The clinician can use this tool in discussions with the caregiver and help the person providing care to identify important information regarding the behaviors they observe to the health team.

The Behavior Rating Inventory of Executive Function—Adult Version (BRIEF-A; Roth et al., 2005) can be self-administered or recorded by an observer. It identifies issues with inhibition, shifting, emotional control, and self-monitoring as well as initiation, working memory, planning and organization, and monitoring. Such information may help the caregiver understand the brain-related behaviors their family member is experiencing.

The Alzheimer's Disease Cooperative Study-ADL Inventory Scale (ADSCS; Galasko et al., 1997) is a self-administered or informant report measure that describes the behaviors they have experienced or observed as the person with cognitive impairments performs an ADL or IADL task. It is helpful to share such information with a member of the health team.

The occupational therapist's assessment provides information to the client, the team, and the family about the person's performance in tasks and interaction with the environment. The occupational therapist does so by using the person's occupational history, making it possible to help them set goals and learn strategies to do the things they consider important. The next section introduces four interventions that occupational therapists use to address persons with cognitive impairment—all with the goal of maximizing their performance and participation, helping them to live their lives.

Occupational Therapy Interventions to Address Cognitive Problems

The last decade has fostered the development of occupational therapy treatment models for persons with cognitive loss. Four treatment approaches used by occupational therapists are reviewed here: (1) strategy learning and awareness, the work of Toglia (A Dynamic Interactional Approach to Cognitive Rehabilitation); (2) Cognitive Orientation to Daily Occupational Performance (CO-OP), as developed by Polatajko; (3) adaptive and functional skill training (A Neurofunctional Approach), the work of Giles; and (4) the need for environmental interventions designed to enhance occupational performance and limit burden on care providers, the Advancing Caregiver Training (ACT), the work of Gitlin, Winter, Dennis, Hodgson, and Hauck (2010).

A Strategy Learning and Awareness Approach: Theoretical Foundations for a Dynamic Interactional Model of Cognition

Traditional cognitive rehabilitation approaches have been guided by the assumption that cognition can be divided into subskills (Trexler, 1987). Toglia (1993, 2005) proposes an alternative to syndrome-specific approaches and encourages the clinician to discover the underlying conditions and processing strategies that can influence performance. The approach uses cues and task alterations to compensate for deficits. Treatment focuses on helping the person develop strategies and become aware of how deficits require the modification of activity demands and the environment. The approach is based on cognitive and educational psychology literature as well as on cognitive rehabilitation and neuroscience that address how people process, learn, and generalize information (Toglia, 1991, 2005; Toglia & Kirk, 2000).

Lidz (1987) defines cognition as the capacity to acquire and use information to adapt to environmental demands. This definition encompasses information processing, skills, learning, and generalization. Individuals must take in, organize, assimilate, and integrate new information with previous experiences; adaptation involves using information that has been previously acquired to plan and structure behavior for goal attainment. Using this definition, one does not divide cognition into subskills such as attention, memory, organization, or reasoning. Instead, the approach requires understanding the person's ability to use strategies and monitor performance and the potential to learn. Such an approach is necessary as cognition is not static or stable; it changes with the interaction with the external world (Feuerstein & Falik, 2004; Lidz, 1987; Lidz & Elliot, 2000). This model conceptualizes cognition as an ongoing product of the dynamic interaction among the person, activity, and environment, and cognition is modifiable under certain conditions. Because there is a fixed or structural limit in the capacity to process information. capacity can be used in different ways. The same activity can require different amounts of processing capacity, depending on how it is performed; thus, it must be used efficiently. The efficient allocation of limited processing resources is central to learning and cognition (Flavell, Miller, & Miller, 1993). This treatment approach focuses on changing the activity demands, the environment, and the person's use of strategies and level of awareness. It requires the occupational therapist to present opportunities for the individual to experience different environments and different levels of demands of the activity, and bring to consciousness a new level of awareness.

The measurement methods developed for this model include a dynamic graded cueing approach to assess the current abilities of the individual and the potential performance with mediation, as well as steps to identify the level of awareness for the performance requirements within the assessments. Literature to support use of the dynamic interaction model is young and consists of early-stage, small-scale designs. The positive effects of this model have been demonstrated in individuals with TBI on measures of cognition and activity performance in trained and untrained goals (Toglia, Johnston, Goverover, & Dain, 2010; Toglia, Goverover, Johnston, & Dain, 2011). More recently, the approach has been found to be feasible for use with individuals with Parkinson's disease, with positive changes in activity performance from pre- to postintervention (Foster, Spence, & Toglia, 2018).

Performance-Based Problem-Solving Approach

Cognitive Orientation to Daily Occupational Performance (CO-OP) is a client-centered, performance-based, problem-solving approach that enables skill acquisition through a process of strategy use and guided discovery (Dawson et al., 2017; Sangster, Beninger, Polatajko & Mandich, 2004, 2005). CO-OP fosters skill acquisition, cognitive strategy use, and generalization and transfer of learning. The foundational theories are drawn from behavioral and cognitive psychology, movement science, and occupational therapy. The application of CO-OP results in the individual learning skills that support occupational performance. The performance of tasks requires motor skills, and this approach is based on theories of motor learning. Motor learning is an internal process that leads to a change in the learner's capacity for skilled motor performance (Rose, 1997). The process of learning a new skill is not observable but can be inferred by observing the individual's motor performance. The learning of a motor skill also requires the individual to interact with the environment in which the task will be performed. Dynamic systems theory emphasizes the relationship between the person and the environment (Turvey, 1990; Thelen, Kelso, & Fogel, 1987). This theory supports the belief that behavior arises from a hierarchical, dynamic interaction of the sensory, motor, perceptual, and anatomical systems (Thelen, 1995). The Fitts and Posner (1967) model of motor learning provides theoretical support for CO-OP. Their three-stage model of motor learning guides the process. In the *cognitive stage*, the individual seeks to understand the task and how to perform it; in the *associative stage,* the individual focuses attention and performs with greater speed and precision; and in the *autonomous stage,* the skill is performed consistently and in a coordinated pattern. CO-OP is based on a learning paradigm that acknowledges that new skills emerge from an interaction with the environment; the occupational therapist creates the learning environment to support optimal learning. In this approach, cognition acts as the mediator between the individual's ability and the performance that is the goal of the individual; as such, a certain level of cognitive abilities is required in order to develop the new desirable skills. Such an approach creates a learning paradigm that helps the individual develop skills to support their daily occupations.

CO-OP has seven key features: cognitive strategy use, patient-chosen goals, dynamic performance analysis, guided discovery, enabling principles, parent/significant other involvement, and a specific intervention format (Polatajko, McEwen, Ryan, & Baum, 2010). The foundation of the approach is cognitive strategy use, inasmuch as CO-OP is built on a metacognitive problem-solving strategy—GOAL, PLAN, DO, CHECK—adopted from Meichenbaum (1977, 1994). This strategy serves as a framework for guiding the discovery of self-generated domain-specific strategies that support skill acquisition. For example, an adult with stroke who is learning to cook with residual cognitive and motor symptoms associated with their stroke would learn the GOAL, PLAN, DO, CHECK strategy. They would first state the goal of the activity (e.g., make a sandwich). Next the occupational therapist would use guided discovery (asking questions/cueing) to guide the patient to develop a specific plan to accomplish their goal. After the activity, the occupational therapist would again use guided discovery to check/review how the plan worked and modify the plan as necessary to continue to work toward the goal.

Several additional theories/skills built into the administration of CO-OP are necessary for administration. Behavioral theories focus on the relationship between stimulus, response, and consequence. In this view, learning is viewed as a permanent change in the form, duration, or frequency of a behavior. Reinforcement is seen as an integral component of learning. CO-OP uses reinforcement, modeling, shaping, prompting, fading, and chaining techniques to support skill acquisition (Polatajko & Mandich, 2004). CO-OP also builds on a cognitive view of learning as an active mental process of acquiring, remembering, and using knowledge. The mental organization of knowledge (problem solving, reasoning, and thinking) plays an important role in the acquisition and performance of skills (Schunk, 2000).

CO-OP was originally developed for pediatric use. A body of research has demonstrated its association with improved skill performance in children with developmental coordination disorder, cerebral palsy, and Asperger's syndrome (Miller, 2001; Rodger, Springfield, & Polatajko, 2007; Thornton et al., 2015). This approach has also been successful with adults with acquired brain injury (Dawson et al., 2009; Dawson, Binns, Hunt, Lemsky, & Polatajko, 2013; Hunt, Paniccia, Mah, Dawson, & Reed, 2019). A multiphase research program to evaluate the adaptation of this approach for adults with chronic stroke demonstrated successful skill acquisition in two case studies (Henshaw, Polatajko, McEwen Ryan, & Baum, 2011), two single-case experimental series (McEwen, Polatajko, Huijbregts, & Ryan, 2010; McEwen, Polatajko, Huijbregts, & Ryan, 2009), and a small trial with comparison (Polatajko et al., 2010). The CO-OP treatment approach was associated with transfer to an untrained task in a single-case experimental series (McEwen et al., 2010. It was also found to have a greater effect on skill acquisition and transfer of training effects to untrained tasks in individuals with subacute stroke in an early-phase clinical trial (McEwen et al., 2014; Wolf et al., 2016).

Functional Skill Training

The aim of functional skill training is to enhance abilities and participation by training each activity the person needs to perform and modifying the activity demands and contexts of persons with severe cognitive impairment. This approach develops habits and routines by retraining real-world skills, with the goal of developing behavioral automaticity and placing greater reliance on the environment, including cueing (Giles, 2005). Such an approach seeks to train clients in behavioral routines when there is little expectation of generalized application of strategies to novel circumstances encountered in the real world. For example, it may train clients in a specific morning routine, repeating the sequence and activities over many days until it becomes automatic. Or it may seek to train a person to walk to the same restaurant on the same route, showing specific points of where to turn, how to look before crossing a street, how to obey street lights, and so on. When getting to the restaurant, clients would become familiar with the staff and the menu and would be trained in how to use the menu and order a dish. The aim is to maintain a schedule that can become routine through repeating the same activities in the same sequence each day.

Neurofunctional retraining considers the person's learning capacity in the design and implementation of programs. Memory, attention and frontal lobe impairments create problems for individuals that make it difficult to achieve community independence. Although the specific cognitive capacities are not the target of direct interventions, capacities must be considered in the design of functional skills training. Memory is central to performance, as the individual must both remember to do and execute skilled behaviors. Knowing how memory systems are affected may improve performance. Nondeclarative (procedural) memory is important to support performance as it is central to habituation and learning may occur without the client's awareness (Giles, 2005). Attention is central to sustaining performance and orienting oneself to surroundings for both doing appropriate tasks and achieving safety. It is important to know the individual's ability to exhibit cognitive control, as the process is crucial for new learning to occur (Schneider, Dumais, & Shiffrin, 1984), and to both focus attention and divide attention when multitasking is required (Stuss et al., 1989). If individuals have a divided attentional deficit, they may be unable to do more than one thing at a time; even walking and having someone speak to them may cause them to lose their balance (Giles, 2005). Task performance is influenced by the competing demands on attention (Kewman, Yanus, & Kirsch, 1988); the person's ability to attend must be understood. It is also important to determine the individual's metacognition, for it is central to learning compensatory strategies.

The individual's executive functions as impairments may contribute to the increased environmental dependency (Lengfelder & Gollwitzer, 2001). Norman and Shallice (1986) propose that two systems, the supervisory attentional system and contention scheduling, are involved in selecting and controlling action. Contention scheduling is drawn upon during the routine behaviors of everyday life that require little conscious thought. The supervisory attentional system provides conscious attentional control of novel actions and selects automatic behaviors, making it responsible for conscious decision making, planning, and monitoring of behavior. The supervisory attentional system is involved in the management of novelty and contention scheduling that occurs without awareness and is initiated and executed automatically (Shallice & Burgess, 1996). Such impairments make it difficult for an individual to organize everyday activities because they may not have the internal behaviors necessary for planning and executing complex sequences. They may also not have the ability to perceive cues that will be offered from environmental support.

The term *anosagnosia* describes the failure to recognize limitations. An awareness of a combination of deficits of attention, memory impairment, and executive control have to be integrated into a new view of self after brain injury. There may be a distinction between a motivated lack of awareness (embarrassment) and an organic lack of awareness (McGlynn & Schacter, 1989). To support daily life, it is important to integrate awareness into interventions. A direct skill training approach, such as the neurofunctional approach, may be best indicated for those with a severe lack of awareness. However, if mild–moderate awareness deficits are present, a strategy learning and awareness approach (as described above) may enable improvements in activity-related awareness. For example, having a person predict performance of an activity, perform an activity, and then evaluate performance after the activity with the verbal guidance from the therapist may improve awareness of task-related errors. Other strategies, such as observing oneself in a mirror or a video recording may also be implemented.

The individual's memory, attention, and executive function deficits create constraints that must be overcome as the occupational therapist addresses the occupational performance needs of the person with brain injury. The neurofunctional approach considers these constraints in developing treatment programs that will train an individual in routines and use of environmental affordances that will support their daily life function. The behavioral treatment approach used in this model is also in line with an errorless learning training method in which errors are prevented as much as possible (Wilson, Baddaly, Evans, & Shiel, 1994; Ylvisaker, Hanks, & Johnson-Green, 2003) compared to trial-and-error learning where errors are corrected. The model uses a range of assessment techniques for initial screening of neurofunction, specifically in the areas of metacognition, attention, memory and executive functions. However, the primary mode of evaluation is observation in real-life functioning according to client needs.

Comparison of the neurofunctional approach with a cognitive-didactic approach in a randomized controlled trial with veterans yielded similar outcomes immediately postintervention. However, at 1-year follow-up, participants from the neurofunctional group demonstrated significantly better outcomes (Giles, 2009, 2010; Vanderploeg et al., 2008). The neurofunctional approach has also demonstrated positive results in chronic stroke in occupational performance (Rotenberg-Shpigelman, Erez, Nahaloni, & Maeir, 2012). It has also been applied with individuals experiencing posttraumatic amnesia, with a group receiving usual care plus neurofunctional training demonstrating improved performance of activities of daily living as compared to usual care alone (Trevena-Peters et al., 2018).

Environmental Approaches

Occupational therapists work with the families of those who have cognitive impairments. The previous three descriptions of interventions are with the person; an environmental approach requires someone to create an enabling environment (organization of tasks or tools); help with getting started with a task (initiation); and assist in task shifting or sequencing, creating a safe environment, and supervising a task when there could be safety concerns, or helping a person complete a task (Baum, 1991). Families are the backbone of the health care system as they provide the care for those with cognitive impairment who are living at home. Many times, the family is left with the responsibility of providing care without the necessary knowledge and resources to fulfill the role.

People with cognitive impairment are often difficult to manage. In addition to memory problems, some have limited ability to comprehend or express language (aphasia) (Faber-Langendoen, 1988); others have difficulty recognizing objects, sounds, and images (agnosia) (Mendez, Mendez, Martin, Smyth, & Whitehouse, 1990; Namazi, Rosner, & Calkins, 1989); and still others have difficulty in performing motor skills, particularly those that involve organizing and executing complex movements (apraxia) (Edwards, Baum, & Deuel, 1991; Edwards, Deuel, & Baum, 1991). It is very important to help the family understand the consequences of these neurobehavioral deficits because the family members often think the person's behavior is willful.

Laura Gitlin and her colleagues (Gitlin et al., 2010) created and tested an intervention using occupational therapists and nurses to help families manage these distressful behaviors. They built on work they had previously done in a randomized clinical trial, the Environmental Skill-building Program, which improved caregivers' skills in providing care but did not reduce behavioral symptoms. The Advancing Caregiver Training (ACT) was developed to target problem behaviors. The intervention conceptualized problem behaviors as a consequence of three domains: patient-based (unmet needs, discomfort or pain, incipient medical condition), caregiver-based (stress, communication style), and environment-based (clutter or hazards). The behavioral part of the ACT program was administered by occupational therapists as they sought to identify and modify potential triggers in each domain to help caregivers eliminate, reduce, or prevent the problem behavior. They used problem-solving approaches to help caregivers identify antecedents and consequences or potential modifiable triggers of the behaviors, and together they built an action plan. The action plan included adapting the physical environment, using assistive devices, simplifying communication and tasks, and engaging the patient in activity. The caregiver was also instructed in stress reduction and self-care techniques. The advanced practice nurse worked with the caregivers to understand medical conditions (e.g., pain, dehydration, constipation) that may exacerbate problem behaviors and to uncover possible undiagnosed illness. The ACT showed both immediate and long-term benefits in symptom reduction, caregiver life quality, and social acceptability (Gitlin et al., 2010). Further research showed financial stability, therapeutic engagement, and perceived benefits of the intervention to increase the probability of improvements (Gitlin & Rose, 2014). ACT demonstrated the value of a targeted problem behavior approach that can be carried out with a clinic nurse to follow the medical conditions and an occupational therapist trained in ACT to do skill building sessions in the home.

Summary and Clinical Implications

An intervention is selected based on a person's awareness. A high level of awareness allows for recognition and prediction of activity-related errors; thus, a strategy-based approach may be indicated. Strategy-based approaches offer the greatest flexibility, as their goal is to be broadly applicable without respect to environment or activity. In contrast, when self-regulation is limited due to decreased awareness, a functional skill training approach and/or an environmental approach may best serve to improve performance within specific activities and context, with limited expectation for generalization of skills.

The management of cognition requires a team approach. This chapter highlights the contribution of the occupational therapist and demonstrates how the clinical contribution of the OT can build on the neuropsychologist's identification of cognitive problems by adding the performance dimension. The occupational therapist uses the person's capacities and the affordances offered by the environment to foster the individual's occupational performance. They work with people in hospitals, in rehabilitation hospitals, in the home, and in the work environment to help people gain the skills that will support their recovery and learn strategies to manage any residual cognitive impairments. A cognitive profile provides a description of cognitive strengths and weaknesses and their implications for occupational performance; recommendations concerning the type and amount of assistance currently required for safe and meaningful occupational performance; and the basis for clinical reasoning in selecting a cognitive model for intervention and a treatment approach. The factors that enter into the decision-making process are following the three perspectives of a PEO model.

1. *Person*: severity of cognitive deficits, variance of cognitive profile (areas of strengths and deficits); learning potential (declarative, procedural); awareness of deficits and disabilities; psychological factors; disease/injury variables (time post-onset, severity, progressive, etc.).
2. *Environment*: human, physical, economical, cultural, resources, safety of the environment, or barriers to rehabilitation.
3. *Occupation*: previous and current activities that can be used in the intervention to sustain independence and health; support the individual's sense of self and identity; promote social interaction; and give the person meaningful activities to engage their time.

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CHAPTER 5

Cultural Considerations in the Assessment of Functional Abilities

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The need to assess disability in persons of diverse cultural backgrounds continues to increase, as a result of both immigration patterns around the world and the impetus to transfer available technologies from more developed countries to resource-limited settings. Occupational scientists have devoted significant effort to developing awareness about the delivery of culturally competent rehabilitation services, making care providers cognizant of potential mismatches between the professional and the patient with regard to health-related views, generalizability of activities of daily living, nonverbal communication, and cultural norms (see, e.g., Jezewski & Sotnik, 2001, for a listing of issues and resources pertinent to rehabilitation settings). Similarly, work in cultural psychology and psychiatry, as well as medical anthropology, highlights cultural and sociodemographic differences in the understanding of health, disease, and disability (James & Foster, 1999; Reynolds Whyte & Ingstad, 1995; Truscott, 2000; van der Geest & Reis, 2002). In neuropsychology, we have been concerned with the applicability of cognitive assessment methods that were developed and validated primarily in the Western world, and most often in English, to other populations. Increasingly, neuropsychologists have also been interested in the correspondence between performance on cognitive tests and "real-world" functioning, as the latter is not only of practical interest for determining a patient's ability to live independently and pursue goals, but it is also a requisite for diagnosing most types of dementing disorders.

One reason to adapt instruments for use in a different cultural or linguistic context, as opposed to creating a brand-new measure based on the population of interest, is the ability to compare the phenomenology of disability constructs across settings. Efforts to adapt functional assessment instruments for use across different populations have led investigators to address certain basic dimensions that determine equivalence between the original and the adapted instrument. These dimensions pertain primarily to aspects of construct validity; that is, does the adapted instrument indeed measure what it was intended to measure? Once construct validity can be reasonably demonstrated, then the resulting instrument is ready for pilot testing, which may lead to further adjustments. Next, the psychometric properties of the instrument need to be examined, leading to other potential adjustments. Finally, the instrument can be subjected to norming with representative samples of interest. In this chapter, we discuss methods for adapting measures for cross-cultural use and ways of ascertaining the construct validity of the resulting instrument.

The Adaptation Process

Effective adaptations are accomplished by successive approximation. “Adaptation,” in this context, is the overall process of making an instrument appropriate for use in a setting that is different from its original. This process may involve translation into another language, translation into regional variants of the same language, and/or replacement of certain concepts in an instrument to harmonize with a different cultural, regional, or linguistic context. The section that follows uses translation into a new language to detail the iterative process required to achieve a sound instrument, but the steps involved apply to other mentioned aspects of adaptation and are reflected in the subsequent sections on construct validity.

Translation

The method of forward translation into the new language or variant followed by back translation into the original language (typically English) was long advocated by many researchers as necessary to achieve an accurate translation (Brislin, 1970). However, arguably more critical steps are required in order to obtain a usable instrument. First, it is important to identify the words that best convey the intended meaning, which may not correspond to a literal translation. Here, it is important to determine whether the selected word is common in the new language and will be understood by all likely respondents. In some cases, a translated word will be accurate but infrequently used in the language, and thus be unfamiliar to many. The translation phase is also a time to examine whether some concepts are not relevant to a particular cultural context or translatable in the new language. (We discuss this matter further in the section on conceptual equivalence.) Once the translation is performed, it should subsequently be examined by truly bilingual/bicultural individuals with relevant expertise (e.g., neuropsychologists, medical professionals, occupational therapists) who can determine linguistic and conceptual equivalence and adjust the original translation, as needed. Bonomi and colleagues (1996), and later Eremenco, Cella, and Arnold (2005), exemplify the use of these strategies in their translation of the English version of the Functional Assessment of Cancer Therapy (FACT) into multiple languages. Two translators produced the first translation to the target language; then a third independent translator was used to reconcile the two versions; and a fourth translator performed the back translation into English. Next, a panel of three to four bilingual health professionals evaluated the translations and resolved any discrepancies. Finally, the newly translated scales were pretested on a small cohort of the target population to ensure their comprehensibility and make any final changes.

These methods are echoed in the findings of a task force appointed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), which reviewed a number of methods employed by several organizations and distilled a 10-step set of guidelines for the translation and adaptation of patient-reported outcome measures (Wild et al., 2005): (1) preparation, (2) forward translation, (3) reconciliation, (4) back translation, (5) back-translation review, (6) harmonization among multiple-language versions and the original instrument, (7) "cognitive debriefing" by testing the instrument on a relevant target group, (8) review of the cognitive debriefing results and finalization, (9) proofreading, and (10) production of a final report detailing the adaptation process. In their review of standards for the development of cross-cultural quality-of-life instruments, Schmidt and Bullinger (2003) also added that the preparation stage should include literature review and focus groups with the aim of arriving at a list of test items judged to be possible candidates, which are then pared down after pilot testing and cognitive debriefing. Additionally, the interval properties and item response characteristics of the resulting scales need to be ascertained, along with their psychometric properties of reliability and validity. Finally, Schmidt and Bullinger advocated norming the instrument with a representative sample of the target population.

A great deal of literature already exists regarding the translation of instruments to measure psychological, educational, and other human traits and outcomes (e.g., Hambleton, 2005), the details of which are beyond the scope of this chapter. The reader is referred to the International Test Commission (ITC; *www.intestcom.org*) and the associated *International Journal of Testing* (*www.leaonline.com/loi/ijt*) to keep abreast of developing guidelines on cross-cultural test adaptation and administration, as well as discussions on statistical methods derived from item response theory, such as differential item functioning analysis and Rasch analysis (van der Linden & Hambleton, 1997; Reise & Waller, 2009), designed to address the psychometric equivalence of adapted instruments. The most recent *ITC Guidelines for Translating and Adapting Tests* (International Test Commission, 2017) provides best practices for test adaption in the form of 18 guidelines organized into six categories—precondition, test development, confirmation, administration, scoring and interpretation, and documentation—along with suggestions for practice. These issues are not covered in detail in the present chapter, which instead focuses on construct validity.

Ascertaining Construct Validity

Construct validity is paramount in the application of instruments that assess daily functioning. If our goal is to determine the level of specific functional abilities, say, for vocational placement, then we would be interested in knowing whether a person has the requisite skills in an absolute sense. In such a case, cultural differences are not of interest. For example, does the person have sufficient manual dexterity and visuospatial skills to work in an assembly line? The criterion for what constitutes sufficient ability will be indexed by the specific requirements of the job and (ideally) by the minimum level of ability of others already performing that job successfully. On the other hand, if we are interested in understanding whether someone with an acquired injury or cognitive deficits is suffering declines in their ability to live independently, then we need methods for capturing everyday functioning that are environmentally relevant for that individual.

In their adaptation of the Functional Assessment of Chronic Illness Therapy (FACIT; *www.facit.org/translation-linguistic-validation*), Lent, Hahn, Eremenco, Webster, and Cella (1999) suggested five components of instrument equivalency: (1) *semantic*: the meaning of stimulus items is the same; (2) *content*: the items' relevance to each culture is intact; (3) *concept*: the items measure the same theoretical construct; (4) *criterion*: the adapted and original items show similar properties when compared against a standardized measurement; and (5) *technical*: the method of assessment results in comparable cultural measurement. A variation of this scheme refers to component 4 as "item equivalence" and divides component 5 into "operational equivalence," referring to the comparability of the measurement methods across cultures, and "measurement equivalence," referring to the interpretability of results across cultures (Schmidt & Bullinger, 2003).

In a similar vein, a cross-cultural applicability research (CAR) effort led by the World Health Organization (WHO) and the U.S. National Institutes of Health (NIH) addressed both the cultural relativity of disability constructs and the psychometric requirements for the development of cross-cultural instruments to measure disability and adaptive functioning (Üstün, Kostanjsek, Chatterji, & Rehm, 2010). This group focused on obtaining equivalency in three dimensions for a revision of the WHO International Classification of Impairments, Disabilities, and Handicaps (ICIDH; WHO, 1980), now called the International Classification of Functioning, Disability, and Health (ICF: *www.who.int/classifications/icf/en*; WHO, 2018). The dimensions identified were (1) *functional equivalence*: the degree to which domains of activities can be identified that serve similar functions across different cultures; (2) *conceptual equivalence*: whether concepts of disability are understood similarly across cultures; and (3) *metric equivalence*: the degree to which measured constructs exhibit similar measurement characteristics in different cultures. In order to arrive at these components of cultural applicability, CAR investigators from 15 different countries attempted to identify (1) whether the domains, subdomains, and individual items of the original English-language instrument corresponded to concepts in the local culture; (2) whether the domains, subdomains, and individual items were readily translatable, or whether a new English term needed to be adopted to facilitate translation; (3) whether the instrument's components were applicable across sociodemographic groups within a culture; and (4) whether the instrument fit the needs and practices of institutions in the culture.

Although the language used to describe components of instrument adaptation differ somewhat across authors, all point to ascertaining construct validity by ensuring that instruments applied cross-culturally make sense linguistically, are conceptually understood, and have practical relevance in the culture, starting with whether the assessment procedure itself is comprehended in the culture (e.g., familiarity with ranking the severity of symptoms on a Likert scale, or using multiple-choice format). In large measure, these aspects of instrument construction apply not only when determining equivalency between an existing instrument and its cross-culturally adapted counterpart, but also when attempting to construct new instruments to measure adaptive functioning in a particular cultural context.

Linguistic Appropriateness

One aspect of cultural relevance, and among the first steps in the adaptation process, is accomplishing linguistic appropriateness. At its most basic, linguistic appropriateness requires that the words used in instructions and stimulus items be understandable by the person being evaluated. Making changes such as converting Fahrenheit to Centigrade and using metric system conversions where appropriate are simple examples of such adjustments (Ercikan & Lyons-Thomas, 2013). This requirement obliges those constructing or adapting a measure to be familiar with language use in the target population across educational level, social class, gender, geographic region, or any other stratification that may apply to that group. Ideally, the adaptation process includes the participation of informed "insiders"—members of the target population that can provide the necessary insight about linguistic nuances.

For instance, the meaning of words can vary among Spanish speakers of different national origin. In the United States, Spanish speakers comprise the second largest language group in the country, and in some regions, such as Los Angeles, New York, and South Florida, many different Spanish-speaking nationalities are represented. In following instructions to bake a cake, for example, the translation of "cake" for an Argentine population would be "*torta*," a word that means "sandwich" in Mexico, so for the group in Mexico the translation would have to be "*pastel*." In addition, it is important to be aware of idioms that are specific to a group, as exemplified by Loewenstein and colleagues (Loewenstein, Arguelles, Barker, & Duara, 1993). For instance, the term "*moros y cristianos*" (Moors and Christians) is the name of a traditional Cuban dish of rice and beans. In Spain, however, this term denotes the holiday commemorating the *Reconquista*, or the Moorish occupation of the Iberian Peninsula that began in the 8th century and their eventual ouster by the Christians lasting through the 15th century. Because the names of food and dishes are often regionally bound, it may be challenging to construct a linguistically neutral and generalizable activities of daily living (ADLs) instrument that uses food-related stimuli. This can also apply to names of medical conditions that a patient may be required to report. The case of food and illness names additionally illustrates the possible influences of formal education and life experience within the same country or ethnic group, as it can be expected that individuals with greater education and affluence would be familiar with a broader range of food choices, formal medical terms, and other mainstream experiences. Thus, special care needs to be taken to produce translations and adaptations that are linguistically neutral and generalizable to as many variants of the target population as possible, given that regional, educational, and social class differences in language use typically exist not only between countries but also within the same country. Neglecting to attend to these nuances will likely yield suboptimal information in both research and clinical endeavors. Respondents who find the language use unfamiliar may misinterpret the intent, feel lack of rapport, be less engaged in the task, and perhaps come away with negative perceptions about the competence of the personnel or setting.

Conceptual Equivalence

The other challenge of linguistic appropriateness when adapting existing instruments is achieving conceptual equivalence in the translation. As mentioned, words that correspond to a literal translation from the English often do not convey the intended meaning. As an example, when translating the FACT, Bonomi and colleagues (1996) found that in the item "I am proud of how I am coping with my illness," the expression of pride was viewed negatively by Norwegian respondents. As a result of input from physicians and patients, the phrase "proud of" was instead translated as the more acceptable "satisfied with." Similarly, certain concepts or expressions that are common in English may not have close equivalents in another language; an example is the item "I am full of pep" from the Profile of Mood Scales (POMS; McNair, Lorr, Heuchert, & Droppleman, 1971). The POMS is an especially challenging instrument to translate because its scales are made up of words that convey variations of the same concept (e.g., in the Vigor/Fatigue scale: "worn-out," "listless," "bushed"). Depending on the language, there may not be so many nuanced words to convey the same concept, or the same translated word may be assigned to different original words because they are so close in meaning. For the interested reader, the vicissitudes of achieving conceptual equivalence are demonstrated in the International Quality of Life Assessment project guidelines (Aaronson et al., 1992), which details efforts to adapt the SF-36 (Wagner et al., 1998). The SF-36 is one of the short forms of the Medical Outcomes Study (MOS) Health Survey (Stewart, Ware, Sherbourne, & Wells, 1992), a self-report health symptom inventory that has been adapted for use in more than a dozen countries and in multiple languages, including several European languages (Keller et al., 1998), Vietnamese (Ngo-Metzger, Sorkin, Mangione, Gandek, & Hays, 1998), Nigerian Yoruba (Mbada et al., 2015), and Mongolian (Nakao et al., 2016). During the process of adapting this questionnaire, teams of investigators in each country rated the difficulty of translating every item and offered their final wording for discussion within a panel of SF-36 experts to determine that conceptual equivalence was accomplished. Again, this process is best accomplished with assistance from bicultural insiders.

Ecological Validity

As demonstrated by the WHO adaptation of the ICF (Üstün et al., 2010), conceptual equivalence does not apply only to language use but is also dependent on conceptions of health and illness as well as of mental and physical limitations across cultures. Thus, the construct validity of an instrument is threatened if it requires respondents to make judgments or attributions about their cognitive or physical capacities that they are not accustomed to making. Whether the instrument measures dependence in ADLs by self- or other-report, clinician's observation, or direct assessment of performance, the items being measured need to be representative of individuals' experience in order to be meaningful. Therefore, in addition to the linguistic aspects mentioned, the construct validity of a measure of everyday functioning also depends on its ecological validity.

As an example, in developing an ADL scale for use with Thai older adults with dementia, Senanarong and colleagues (2003) included certain culturally specific items that exemplify ecological validity, such as hiring a taxi-boat, bicycling, and walking to the village. Fillenbaum and colleagues (1999) similarly included culturally relevant components of daily functioning when creating an ADL scale for a rural older adult Indian population, such as the ability to remember important local festivals. Some examples of cultural differences in the relevance of items assessing everyday functioning were encountered by Jitapunkul, Kamolratanakul, and Ebrahim (1994) when they attempted to use the Office of Population Censuses and Surveys (OPCS; United Kingdom) disability scale with an older adult Thai population. They noted that certain subscales of the OPCS resulted in extremely large proportions of disability in this group. In particular, the face validity of certain items such as "feels the need to have someone present all the time" and "sometimes sits for hours doing nothing" could not be interpreted in the same way as with English populations, since these can be normal aspects of Thai life. Additionally, certain items that were meant to assess basic ADLs in Western cultures corresponded to extended ADLs in Thai culture. For instance, "climbing a flight of stairs" is considered a basic ambulation activity in Western scales, but since traditional Thai homes contain difficult-to-navigate ladders instead of stairs, this item needs to be considered an extended ADL.

Ecological or face validity can require attention even when the adaptation is between relatively similar cultures. During the adaptation of the SF-36 International Quality of Life Assessment into Swedish, certain items from the original English-language version had to be changed to improve face validity. These included changing "playing golf" to "walking in the forest or gardening," adapting the notion of "walking a block" to a distance in kilometers for rural populations, and noting that the effort and complexity of dressing oneself differ depending on the climate that is typical for that population (Wagner et al., 1998). To determine the ecological validity of items in measures of adaptive functioning, it is therefore also important to establish the degree of familiarity with the tasks or items to which a person is being asked to respond. This issue is critical when attempting to document declines in ADL independence and their relationship to cognitive functioning, as task familiarity is likely to affect responses independently of acquired neuropsychological impairment. ADL instruments that attempt to measure functioning in areas that are unfamiliar may miss the mark. For example, in certain traditional households, men across the socioeconomic spectrum may be unfamiliar with cooking or grocery shopping. In scoring the Clinician Home-based Interview to Assess Function (CHIF), allowances were made for most Yoruba men's relative inexperience in cooking or shopping, unless they lived alone and engaged in those responsibilities (Hendrie et al., 2006). The same may be true of people of high socioeconomic status (SES) in certain settings, who might have service personnel to perform these tasks. Additionally, modern life amenities may facilitate living as an adult without ever having to master certain skills, such as cooking, driving, or wayfinding. Thus, persons fitting these descriptions might perform more poorly on a laboratory task of everyday functioning that requires preparing a meal, driving a car, or using a map, despite intact cognitive status. Level of education can also influence the frequency of interaction and familiarity with aspects of daily functioning, as evidenced by Tozlu and colleagues' (2017) validation of the Turkish version of the Disability Assessment for Dementia Scale. They found that 75% of the older adults in their sample were not performing the item "adequately organize his or her correspondence with respect to stationery, address, stamps" in the Finance and Correspondence section of their assessment. They attributed this to the low–moderate education level of the sample, leading them to exclude this item from their adaptation of the scale (Tozlu et al., 2017). Similarly, very healthy people may have few opportunities to take medications; thus, sicker people may do better at a medication management task. SES could also influence performance on such a task, as indigent people may have had fewer opportunities to interact with health care professionals or take medications. Generational differences and societal changes over time add to these intersecting influences on familiarity with activities of daily living (e.g., could today's 10-year-old make a call on a rotary phone? Could her grandpa edit a video clip on his smartphone?). As such, ADL instruments need periodic revision to keep up with the changing ecological validity (Lindbergh, Dishman, & Miller, 2016).

Another aspect of ecological validity pertains to familiarity with how responses are to be obtained. A clear example is the inappropriateness of requiring an illiterate person to select a response from written questionnaire items. A less obvious instance is demonstrated by the work Baltussen and colleagues (Baltussen, Sanon, Sommerfeld, & Wurthwein, 2002), who had to adapt a visual analog scale (VAS) to measure burden of disease among low-educated residents in rural Burkina Faso, West Africa, in order to maintain ecological validity. As the metric properties of the traditional VAS were unfamiliar in this population, the authors cleverly adopted a finite number of wooden blocks with which respondents could express their valuation of a number of disease states. Additionally, ways of ranking difficulty should be considered across cultures. As depicted by Choi and colleagues (2003) in their validation of the Korean version of the Bayer activities of Daily Living Scale, elderly Koreans had difficulty with a double negative question (e.g., "Does the person have difficulty with . . . "; response: "never") and were not familiar with scales in which higher scores indicated poorer performance. This resulted in the authors reversing both the item form (e.g., "Does the person do . . . well?") and the response scale to reflect that higher scores indicate better performance.

Finally, after considering linguistic appropriateness, conceptual equivalence, and ecological validity, the resulting instrument needs to be tested with a pilot sample from the target population to ensure that it is understood and received as intended. At this stage, additional adjustments can be made based on feedback from the respondents. Only then should the other psychometric properties of the final instrument be subjected to examination, such as criterion validity, internal consistency, and reliability. Figure 5.1 summarizes the goals and steps required for the successful adaptation of measures for use across diverse cultural or linguistic settings. Table 5.1 lists some of the available performance-based and self/informant report measures of functional assessment by language/culture group, focusing especially on older adults.

Experiences in Adapting Direct Observation Measures of Daily Functioning from English to Spanish

Direct observation of ADL performance requires measuring everyday behaviors in the individual's environment or re-creating common activities in a laboratory or clinic setting. The latter is more amenable to standardization and quantification, making it more useful for research and outcomes-based clinical care. This section illustrates the application of the concepts discussed earlier by showing the process of adaptation of laboratory measures of daily functioning for use with Spanish speakers from the U.S.–Mexico border region.

Faced with the need to evaluate functional status in primarily Spanish-speaking study volunteers with HIV in San Diego, California, our group at the HIV Neurobehavioral Research Center (HNRC) undertook the adaptation of a battery of tests of everyday functioning that has shown relationships to HIV-associated cognitive impairment among English speakers (Heaton et al., 2004; Marcotte et al., 1999). These tests assess a number of instrumental activities of daily living (IADLs) by direct observation in the laboratory and also include reports of everyday functioning outside of the laboratory, ranging from subjective ratings of disability and life quality to verifiable information such as automobile driving records. The direct assessment measures conducted in the laboratory include basic (e.g., identifying currency, making change) and advanced (e.g., paying bills, staying

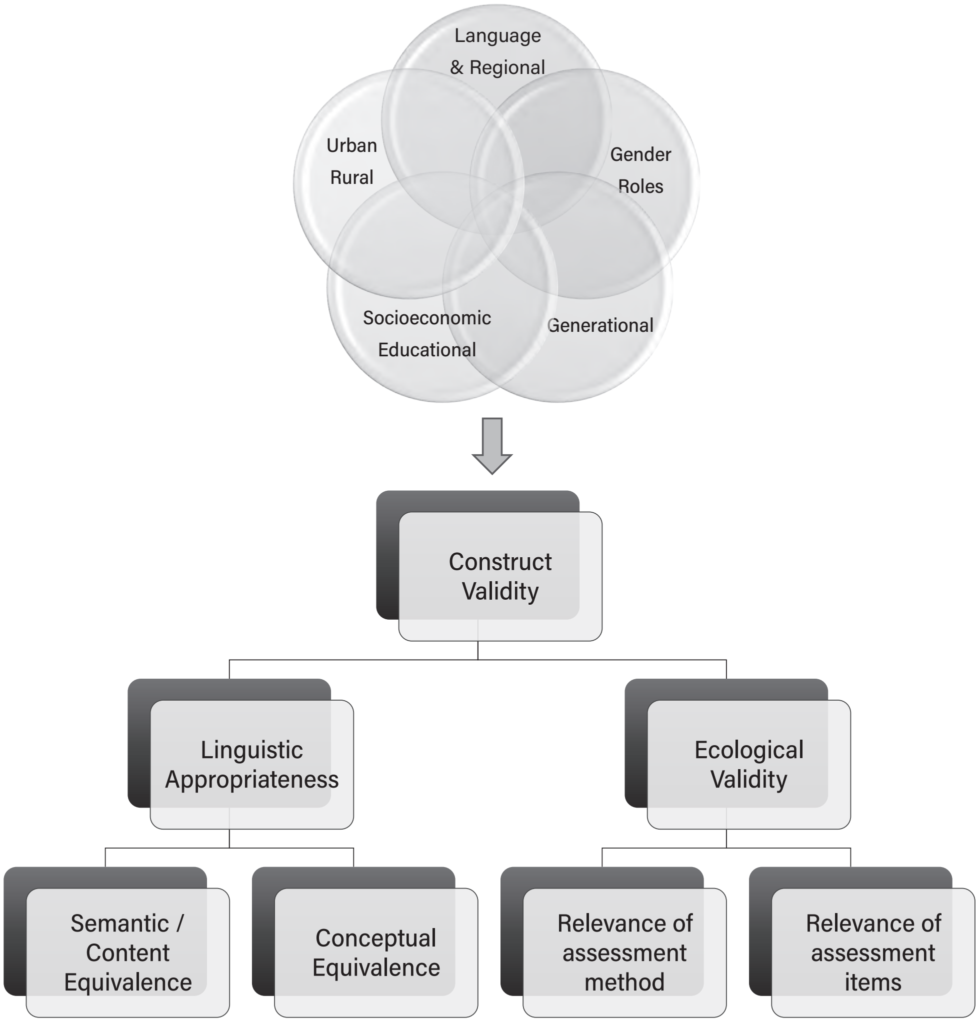

FIGURE 5.1. Schematic of the goals and methods for accomplishing culturally and linguistically appropriate adaptations. The primary goal is to accomplish construct validity by ensuring that adapted instruments are linguistically equivalent and have cultural relevance. Multiple intersecting characteristics of the target respondents can present threats to the validity of the adapted instrument. These can include language use and regional variants, as well as differences in lived experience based on socioeconomic factors, education, generation, gender roles, and urbanicity. The methodology to accomplish a valid adaptation requires initial translation by "insider" experts, with iterative adjustment and harmonization by additional experts, as well as feedback from pilot testing with representatives of the target group. Psychometric properties and equivalence with the original instrument need to be established before the adapted instrument is applied. Normative performance in the population also needs to be determined to interpret level of performance in patient groups.

TABLE 5.1. Selected Scales to Measure Basic and Instrumental ADLs Available in Multiple Languages Denoting the Mode of Administration and Target Population

Test name	ADL areas covered	Languages/culture groups	Format	Target subgroup
Katz Index of Independence in ADLs	Bathing, dressing, toileting, continence, feeding	Arabic[1], Brazilian Portuguese[2], Dutch[3], English[4], Farsi[5], Moroccan-Arabic[6], Spanish[7], Turkish[8,9]	Performance-based	Older adults
UCSD Performance-Based Skills Assessment	Household chores, communication, finance, transportation and planning recreational activities	English[10], Mandarin[11], Portuguese[13], Spanish[13, 14], South Korean[15], Hindi[16], Swedish[17], Danish[18], Japanese[19]	Performance-based	Older adults, severe mental illness
Lawton and Brody IADL Scale	Shopping, cooking, housekeeping, laundry, telephoning, taking medication, making transports, managing money	English[20], Farsi[21], Greek[22], Korean[23], Malay[24], Sinhala[25], Spanish[26]	Self/ Informant report	Older adults
Barthel Index	Feeding, bathing, grooming, dressing, continence, toileting, mobility	English[27], Farsi[28], Spanish[29]	Performance-based	Older adults
Modified Barthel Index	Feeding, bathing, grooming, dressing, continence, toileting, mobility	Hong Kong Chinese[30], Mandarin[31]	Performance-based	Older adults
Bayer Activities of Daily Living Scale	Self-care, orientation, planning	Brazilian Portuguese[32], English[33, 34], German[33], Korean[35], Spanish[33]	Informant report	Older adults with dementia
Direct Assessment of Functional Status	Time orientation, telephone use, financial skills, shopping skills, grooming, eating	Brazilian Portuguese[36], English[37, 38]	Performance-based	Older adults
Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)	Cognitive and functional changes	Arabic[39], Brazilian Portuguese[40], Dutch[41], English[42], French[43], German[44], Italian[45], Korean[46], Mandarin[47], Spanish[48], Thai[49], Turkish[50]	Informant report	Older adults with dementia
Interview for Deterioration of Daily Living in Dementia	Bathing, dressing, toileting, continence, feeding	English[51], Spanish[52]	Informant report	Older adults with dementia

(*continued*)

TABLE 5.1. (*continued*)

Test name	ADL areas covered	Languages/culture groups	Format	Target subgroup
Disability Assessment for Dementia Scale	Financial skills, telephoning, driving, medication management, shopping	English[51], French[53], Italian[54], Korean[55], Mandarin[56], Turkish[57]	Informant report	Older adults with dementia
Klein-Bell ADL Scale	Mobility, telephoning, dressing, toileting, bathing, eating	English[58], Swedish[59]	Performance-based	Older adults
Groningen Frailty Indicator	Mobility, toileting, shopping	English[60], German[61], Mandarin[62], Romanian[63]	Self-report	Older adults
Functional Independence Measure	Self-care, mobility	English[64], Farsi[65], Turkish[66]	Informant report	Adults, stroke rehabilitation
Clinician Home-based Interview to assess Function	Cooking, shopping, finances, medication management, housekeeping	English[64], Yoruba[67]	Informant report	Older adults with dementia
Self-Administration of Medication Tool	Medication management	English[68], Mandarin[69]	Self-report	Adults
Thai ADL Scale	Feeding, bathing, grooming, dressing, continence, toileting, mobility	Thai[70]	Performance-based	Older adults with dementia
Medication Management Instrument for Deficiencies in the Elderly	Medication management	English[71]	Performance-based	Older adults
Medication Management Test	Medication management	English[72]	Performance-based	Older adults
Autonomie Gerontologie Groupes Iso-Resources Scale	Orientation, communication, toileting, dressing, feeding	French[73]	Self-report	Older adults

(*continued*)

Erlangen Test of Activities of Daily Living in Persons with Mild Dementia and Mild Cognitive Impairment	Telephoning, making transports, managing money, self-care, housekeeping	German[74]	Performance-based	Older adults with dementia
Activities of Daily Living Questionnaire	Bathing, dressing, toileting, continence, feeding	Mandarin[75]	Informant report	Older adults
Nottingham Extended Activities of Daily Living Scale	Mobility, cooking, money management, housekeeping	Turkish[76]	Self-report	Older adults

Note. [1]Karam, Khandakji, Sahakian, Dandan, & Karam (2018); [2]Duarte, Andrade, & Lebrão (2007); [3]Reijneveld, Spijker, Dijkshoorn, 2007; [4]Katz, Downs, Cash & Grotz, 1970; [5]Azad, Mohammadinezhad, Taghizadeh & Lajevardi, 2017; [6]Reijneveld, Spijker, Dijkshoorn, 2007; [7]Cabañero-Martínez, Cabrero-García, Richart-Martínez, & Muñoz-Mendoza, 2009; [8]Reijneveld, Spijker, Dijkshoorn, 2007; [9]Arik et al., 2015; [10]Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001; [11]McIntosh et al., 2011; [12]Mantovani et al., 2015; [13]Mausbach, Tiznado, Cardenas, Jeste, & Patterson, 2016; [14]Garcia-Portilla et al., 2014; [15]Kim et al., 2015; [16]Narayanan et al., 2015; [17]Harvey et al., 2013; [18]Vesterager et al., 2012; [19]Sumiyoshi et al., 2016; [20]Lawton & Brody, 1969; [21]Mehraband, Soltanmohamadi, Akbarfahimi, & Taghizadeh, 2014; [22]Mystakidou et al., 2013; [23]Won, Rho, SunWoo, & Lee, 2002; [24]Kadar, Ibrahim, Razaob, Chai, & Harun, 2018; [25]Siriwardhana, Walters, Rait, Bazo-Alvarez, & Weerasinghe, 2018; [26]Vergara et al., 2012; [27]Mahoney & Barthel, 1965; [28]Oveisgharan et al., 2006; [29]Cabañero-Martínez, Cabrero-García, Richart-Martínez, & Muñoz-Mendoza, 2009; [30]Leung, Chan, & Shah, 2007; [31]Min, Yuanyuan, & Yan, 2008; [32]Mapi Research Institute, 1999; [33]Erzigkeit et al., 2001; [34]Hindmarch, Lehfeld, de Jongh, & Erzigkeit, 1998; [35]Choi et al., 2003; [36]Pereira, Oliveira, Diniz, Forlenza, & Yassuda, 2010; [37]Loewenstein et al., 1989; [38]Loewenstein & Bates, 1992; [39]Phung et al., 2015; [40]Sanchez & Lourenço, 2009; [41]de Jonghe, 1997; [42]Jorm & Jacomb, 1989; [43]Law & Wolfson, 1995; [44]Ehrensperger, Berres, Taylor, & Monsch, 2010; [45]Isella, Villa, Frattola, & Appollonio, 2002; [46]Lee et al., 2005; [47]Fuh et al., 1995; [48]Morales, González-Montalvo, Del, & Bermejo, 1992; [49]Senanarong et al., 2001; [50]Ozel-Kizil et al., 2010; [51]Teunisse & Derix, 1997; [52]Böhm et al., 1998; [53]Gélinas, Gauthier, McIntyre, & Gauthier, 1999; [54]De Vreese et al., 2008; [55]Suh, 2003; [56]Mok et al., 2005; [57]Tozlu et al., 2014; [58]Klein & Bell, 1982; [59]Söderback & Guidetti, 1992; [60]Steverink et al., 2001; [61]Braun, Grüneberg, & Thiel, 2018; [62]Luh, Yu, & Yang, 2018; [63]Olaroiu, Ghinescu, Naumov, Brinza, & Heuvel, 2014; [64]Forer & Granger, 1987; [65]Naghdi et al., 2016; [66]Küçükdeveci, Yavuzer, Elhan, Sonel, & Tennant, 2001; [67]Hendrie et al., 2006; [68]Manias, Beanland, Riley, & Hutchinson, 2006; [69]Lin et al., 2018; [70]Jitapunkul, Kamolratanakul, & Ebrahim, 1994; [71]Orwig, Brandt, & Gruber-Baldini, 2006); [72]Gurland et al., 1994; [73]Magnin et al., 2017; [74]Luttenberger, Reppermund, Schmiedeberg-Sohn, Book, & Graessel, 2016; [75]Chu & Chung, 2008; [76]Sahin et al., 2008.

within a budget) financial management, grocery shopping, cooking, ordering and paying for a meal at a restaurant, medication management exercises, and a manualized and computerized assessment of job aptitude. With the exception of tests borrowed from the Direct Assessment of Functional Status (DAFS—Loewenstein & Bates, 1992; Loewenstein, Rubert, Arguelles, & Duara, 1995), which were already available in Spanish, all of our functional measures were first translated into Spanish by a master's level linguist and experienced psychometrist under the supervision of a bilingual neuropsychologist. Then they were back-translated by another bilingual neuropsychologist. Next, the translated measures were circulated among Spanish speakers with neuropsychological experience (psychologists and psychometricians) from five different regions (Argentina, Colombia, Mexico, Puerto Rico, and Spain; these were selected by convenience, but additional input would be sought if the measures were to be used in countries not represented) to elicit refinements in order to make the final measures as linguistically neutral as possible. At this step in the adaptation, we also made certain contextual changes to fit our target population, which, in this case comprised Spanish-speaking immigrants of Mexican origin. As a simple example, for a task that requires ordering a meal at a restaurant, we replaced the English menu items with items listed on the menu of an actual Mexican restaurant in the area. Understanding that our target population likely eats at a variety of restaurants, we made this selection to simplify translation of food items by keeping to one cuisine that was regionally familiar and did not need translation.

The next step in our adaptation process was to pilot the resulting measures with a group of Spanish-speaking study participants to gather feedback about the quality of the translation as well as the ecological validity of the exercises and questionnaires in the battery (Rivera Mindt et al., 2003). Based on this feedback, we made a number of modifications to the original measures in order to make the functional assessments more culturally relevant and appropriate. The modifications were designed to change the cultural context of the task without altering the requisite abilities.

For example, we discovered that few participants used checks or checkbooks in their daily lives; therefore, for a section on financial management, we changed the task such that "utility bills" were paid in cash rather than with checks, and the checkbook balancing task was replaced with having to figure the balance remaining on a phone card (this task is likely now obsolete, given modern international calling plans on mobile phones). For a cooking task, we learned from our pilot participants that few used a microwave oven, as was required in the original English-language exercise. We therefore modified the task to use a hotplate as a stove top, and it had a positive reception. Although the details of the tasks were adapted, the calculations or abilities required to complete each exercise remained the same. Likewise, the scoring schemes and ranges of possible scores for the various measures were unchanged in order to preserve equivalence with the English versions, as much as possible, and facilitate comparisons.

In certain clinical or research settings, it is of interest to identify economic losses associated with unemployment or job changes related to an illness or disability. Among immigrant or displaced populations, factors other than disability may account for changes to lower levels of vocational functioning. These factors might include lack of language proficiency, unavailable documentation pertaining to professional qualifications or permission to work, and barriers to the transfer of professional degrees and licensures obtained abroad. Thus, in our adaptation of a self-report employment questionnaire that includes a complete work history, we made a distinction between highest vocational attainment, earned income, and degree of responsibility at work in the United States *versus* in the country of origin. Additionally, we obtained the participants' own assessments of whether they were employed in accordance with their capabilities, and if not, their perception of reasons why.

Because participants are likely to have different levels of familiarity with certain activities, each task in our battery was followed by a graded 5-point classification of familiarity to determine how frequently the task is encountered in daily life. This information can then be used to examine the influence of familiarity on task performance. Additionally, since our target population was an immigrant sample, we also included a multidimensional acculturation scale to help discern the influence of acculturative factors on task performance. Such information can help to confirm the ecological validity of the battery in a population. In addition to the laboratory tasks, we also included self-report measures of daily functioning, from which we can derive information on concurrent validity.

Implications for Clinical Practice

Clinicians face two main intersecting concerns regarding an intercultural interaction with a patient. One has to do with the psychometric issues that we have discussed so far. That is, are the language and measurement methods appropriate for the patient? Will the results be interpretable? The other concern has to do with ensuring a successful interaction in which a level of rapport and trust is achieved, such that the patient feels respected and motivated to engage in the health care being provided, and that correct information is collected and transmitted. A fairly large literature addresses these considerations, including emerging research in the field of cultural neuroscience, and a number of handbooks focus on concerns in clinical care delivery. Pertinent to issues in neuropsychological assessment, the reader can consult *Conducting a Culturally Informed Neuropsychological Evaluation* (Fujii, 2017), the *International Handbook of Cross-cultural Neuropsychology* (Uzzell, Pontón, & Ardila, 2007), and the *Handbook of Cross-cultural Neuropsychology* (Fletcher-Janzen, Strickland, & Reynolds, 2000).

Referral to a clinician from the same cultural or language group is generally considered ideal. Such clinicians will be better equipped to interact with the patient in a positive way, will have likely researched available questionnaires, tests, and norms, and may have even produced their own translated materials in the absence of published ones. But the option to refer is often not feasible, and clinicians are faced with balancing the ethics of practicing within their sphere of competence versus providing care to all who need it.

To address the first—psychometric—concern in intercultural situations, the clinician who is trying to assess disability in someone with a dissimilar background should attempt to find validated adaptations of the instruments they normally use, or substitute measures of the same constructs that have been validated for use with that patient's population (or the closest approximation). Solutions do not typically abound in this regard, but it is worth scanning the literature for measures that may be available. When language proficiency or literacy are barriers, it is very helpful to have the assistance of a professional medical interpreter to explain procedures, read items, and elicit responses from the patient. If validated instruments are not available, the next best alternative is to employ the professional interpreter to translate, as they are typically better equipped than a lay speaker to convey the intended meaning of health-related questions. However, preparation of the interpreter ahead of time is critical to maintain the fidelity of the assessment, especially when standardization is important, and to ensure that the intended meaning is clear. The interpreter needs to identify issues such as language that is not easily translatable and should be cautioned against filling in details that may be surmised but are not explicitly provided by the patient. Note that in the case of cognitive testing, the use of interpreters is controversial and fraught with threats to the validity of test results. Interpreters may inadvertently "help" the patient in their delivery of instructions, or they may interpret patient responses with some embellishment (Casas et al., 2012). Additional guidance on the use of interpreters can be found in articles by Wright (2014) and Novotney (2020), as well as in professional society guidelines, such as the American Psychological Association (2003, 2010) and the British Psychological Society (2017).

Many hilarious movie scenes have capitalized on intercultural misunderstandings, but in real life the stakes can be high when patients do not receive the competent health care they need. To address the second, broader concern about cultural awareness, cultural humility, and cultural competence (Greene-Moton & Minkler, 2020), health care providers can consider reflecting about the ways in which our background and privilege may influence our assumptions about others, and then follow self-reflection with education. Clinicians ought to do their best to familiarize themselves with the cultures they are likely to encounter with some frequency. It will not be possible to become conversant about every culture's health beliefs or about what constitutes appropriate communication or interactions. Lists of "dos and don'ts" may be useful as general guidelines and may help avoid irreparable offense, but one should guard against stereotyping. There is likely to be considerable variability *within* groups, perhaps as much as that *between* groups, dependent on sociodemographic characteristics that may affect views on gender roles, respect for elders, family hierarchy and involvement, and the importance placed on social status. One should also avoid assuming similarities in customs or belief systems based on broad-stroke ethnic classifications (e.g., "Hispanics" or "Middle Easterners" or "Whites") since these descriptors do not capture the heterogeneity in countries of origin, significance of race, religious beliefs, language, political background, immigration circumstances, generational differences, and other aspects that may influence the interaction with health care providers. For example, black Americans will be highly heterogeneous with regard to a broad range of characteristics, such as experiences of discrimination, degree of trust in institutions, and disparities in education, depending on when and in which region of the country they grew up, their socioeconomic status, and other circumstances. Heterogeneity on many of these dimensions also applies to American whites, to Asian Americans, and so on. Differences in world view, which are not limited to members of "other cultures," can manifest in the conception and description of illness symptoms, the interpretation of questions and instructions, and the patient's comfort with the clinical interaction. For the interested reader, the late neuropsychologist Alfredo Ardila (1946–2021), who wrote extensively about cultural influences on psychometric testing, summarized issues of cultural mismatch in a 2005 article that remains relevant today (Ardila, 2005).

A guiding principle in approaching intercultural clinical interactions is to practice cultural humility. In this context, that means cultivating an interest in understanding the ways in which clinician–patient differences could interfere with effective care delivery. It also means being honest about one's lack of familiarity and respectfully asking questions to understand the patient's world view. For example, rather than assume that a patient shares one's scientific explanation for the problems they are experiencing, the clinician could elicit information about the patient's explanatory systems about health: for example, "What is your understanding about your [condition]? How did it start? Is there anything that makes it better/worse?" As another example, to inform the deployment of interventions, the clinician could inquire about the patient's decision-making process, such as the expected role of family or religious influences: for example, "How do you usually make important decisions? What helps you decide which option you should choose?"

A number of resources are available to help professionals hone their skills in intercultural endeavors. Many professional organizations and institutions such as universities and medical centers will offer workshops in aspects of cultural competence. There are also workshops designed to build awareness about mitigating inequities, such as recognizing implicit bias, antiracism measures, and ally skills training (learning ways to use one's privilege to intervene on behalf of those experiencing discrimination). The U.S. Department of Health and Human Services (HHS) offers a short online course for behavioral health professionals covering principles of cultural competence and cultural humility, ways to learn about a client's cultural identity, how communication styles can differ across cultures, how to elicit a patient's explanatory model, and strategies to reduce bias (*https://thinkculturalhealth.hhs.gov/education/behavioral-health*). HHS also created a blueprint to implement institutional-level changes in this area, called the National Standards for Culturally and Linguistically Appropriate Services (CLAS) in Health and Health Care (*https://thinkculturalhealth.hhs.gov/clas*). Such trainings will not make the clinician a cultural expert, so perhaps this "competence" is aspirational. Nonetheless, they will guide self-reflection about one's biases and ability to provide the requested services, and give tools for communicating more effectively with patients from diverse backgrounds.

Conclusions

The early 20th-century writings of Soviet psychologist Lev Vygotsky (1896–1934) and his student Alexander Luria (1902–1977), who is considered a founding figure in neuropsychology, show that sociocultural influences on human psychology have been contemplated for well over a century. Their thinking is credited with the founding of cultural-historical psychology (Yasnitsky, van der Veer, & Ferrari, 2014). Until relatively recently, however, discussion of culture had been largely absent from clinical psychology education, despite its obvious relevance to patient assessment and care. The challenges of intercultural behavioral assessment have been considered since Luria, although appreciation of how these challenges might reflect or effect inequities, or how to mitigate sociocultural influences on test performance, is a much more recent development in the history of our profession. Awareness of the need for culturally appropriate instruments has blossomed over the past 30 years among the various disciplines that deal with measurement of disability and functional independence. In the United States, this evolution mirrors not only immigration and globalization trends, but also increasing recognition of entrenched and institutionalized inequalities between groups with various identities (and intersections of identities). This development has been punctuated by a time of national reckoning as we enter the third decade of the 21st century, and has elevated equity, diversity, and inclusion as societal values.

In this chapter, we focused primarily on the general principles guiding the adaptation of measures and potential sources of threats to validity. Substantial gains have been made in the development of parameters to guide the adaptation and construction of instruments for use across diverse cultural contexts, all with the aim of creating measures that have sound psychometric properties. A number of widely used instruments, primarily self-report questionnaires that survey ADLs within other aspects of disability and health functioning, have been systematically adapted for use in multiple linguistic and cultural contexts, and their psychometric properties have been investigated. Such work is invaluable because it allows comparison of the functional impact of various health-related states across the world. In order to examine relationships between cognitive status and everyday functioning in diverse populations, not only do the ADL measurements need to be standardized and subjected to psychometric rigor, but also neuropsychological tests need to be appropriately adapted and normed for the groups on which they will be used.

Significant work remains in the area of performance-based assessment of function. This method has intrinsic appeal, as it yields a more proximal and standardizable observation of actual ability (Moore, Palmer, Patterson, & Jeste, 2007), but less has been reported on the applicability of these measurements in diverse populations, either across the world or among ethnocultural groups within the same country. One performance-based battery that has been applied in a number of linguistic and cultural groups is the University of California at San Diego (UCSD) Performance-based Skills Assessment (UPSA; Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001; Becattini-Oliveira et al., 2018). The UPSA has been used primarily in studies of schizophrenia. It has been adapted for use in Brazil (Mantovani, Machado-de-Sousa, & Salgado, 2015), China (Wang et al., 2016), Japan (Sumiyoshi et al., 2016), South Korea (Kim et al., 2015), India (Narayanan, Bhatia, Velligan, Nimgaonkar, & Deshpande, 2015), Denmark (Vesterager et al., 2012), Spain (Garcia-Portilla et al., 2014) and Sweden (Harvey et al., 2009). In the United States, performance on the UPSA was useful in predicting degree of community responsibilities among older Mexican Americans with schizophrenia (Cardenas et al., 2008). In addition, it has shown ability to discriminate between schizophrenia patients and healthy controls among Spanish- and English-speaking Hispanics (Bengoetxea et al., 2014; Mausbach, Tiznado, Cardenas, Jeste, & Patterson, 2016), although performance was also influenced by level of education and acculturation.

With performance-based assessment, it may be challenging to create instruments that are universally equivalent. An additional challenge is posed by rapidly changing technologies for accomplishing activities of daily living (e.g., mobile banking; voice-activated phone calling) that require frequent updating of instruments for use within the same cultural group to avoid obsolescence and decreased ecological validity. There may in fact be few activities of everyday functioning that can be standardized across cultures or sociodemographic groups with vastly different daily living experiences, such as, say, Japanese business executives and indigenous residents of the Orinoco River region. Such cross-group comparisons may need to be restricted to populations with similar ranges of industrialization and literacy, but the challenge is open to tackle the creation of these kinds of measurements. In principle, it should be possible to arrive at conceptual-level categories of daily functioning (e.g., procuring nourishment, maintaining shelter, engaging in commerce) that could be agreed are universally applicable to humans. The WHO

ICF (2001, 2010) is an example of such an attempt; see Chapter 2 for additional details on the WHO ICF.

In sum, the generation of culturally appropriate and equivalent instruments is possible and desirable for the purpose of comparing effects of interest across populations. There will be cases where the human experience is so dissimilar that sufficient equivalence among instruments cannot be accomplished. Conceptually, however, ecologically valid methods can be devised to measure the functional impact of illness and brain dysfunction within a population, even when cross-group comparisons are challenging.

Moreover, we suggest that direct observation of functional abilities in the patient's real world may be the best indicator of cognitive status in persons with little or no formal education, or life experiences that are vastly unfamiliar to us, where our traditional neuropsychological tests and other laboratory instruments may be less informative. Performance-based laboratory measures can serve the same purpose, with the added benefit of standardization, as long as ecologically valid tasks for the individual can be designed.

For clinicians faced with intercultural assessment, we recommend seeking training and guidance from local, national, or international organizations on cultural competence in health care delivery. When possible, clinicians should use assessment instruments that are validated for populations that resemble the patient on important characteristics. Professional interpreters can be useful for conducting interviews and assisting with questionnaires, whereas recruiting bilingual/bicultural family members can help supply details about the patient's history, but family ought not be asked to interpret or translate assessments, except as a last resort if professional resources are not available. In all but the most optimal of situations (i.e., the clinician and patient come from similar cultural groups and validated instruments exist), evaluation results ought to be interpreted and reported with caveats and caution.

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SECTION B

Assessment of Specific Functional Abilities and Assessment Considerations

CHAPTER 6

The Relationship between Instrumental Activities of Daily Living and Neuropsychological Performance

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For individuals to live independently, they must have the ability to take care of themselves and to function autonomously in their environment. Difficulties with independent function as a result of brain impairment often have profound effects on both the physical and psychological well-being of the patient, his or her family as well as significant financial consequences for society as a whole. The ability to accurately assess both higher- and lower-order functional abilities and how they relate to real-world performance is critical to the remediation and management of persons with brain-related impairments.

Functional abilities are typically divided in two specific subgroups conceptualized as basic activities of daily living (BADLs) and instrumental activities of daily living (IADLs). On the one hand, BADLs are those tasks that are related to basic self-care, such as feeding, dressing, self-transfer, toileting, and grooming (see Kane & Kane, 1981; Loewenstein & Mogosky, 1999). On the other hand, IADLs refer to activities of daily living that, as the name implies, are instrumental in allowing the individual to effectively interact with the environment to obtain needed goods and services. IADLs by definition require higher cognitive complexity than BADLs, which involve more rudimentary skills. IADLs are required for independent living at home and within the community, and they allow the individual to cope with the demands of everyday life. These activities include, but are not limited to, shopping, taking medications, cooking and performing other household chores, managing money and personal finances, and using means of communication (e.g., telephone, mail) and transportation (e.g., driving, taking the bus or subway; Kane & Kane, 1981; Lawton & Brody, 1969; Tuokko, 1993; Harvey, Loewenstein, & Czaja, 2013). IADLs are generally distinguished from specific vocational or work-related skills that are necessary for gainful employment. Although IADLs typically refer to activities in the home environment, IADL impairment in areas such as utilizing transportation or using different means of communication may adversely impact work attendance and/or performance.

The interest in assessing the ability to perform activities of daily living has its origins in rehabilitation medicine and occupational therapy (Bennet, 2001; Loewenstein & Mogosky, 1999; Harvey et al., 2013). The primary goal of the functional assessment of activities of daily living is to identify the patient's strengths and weaknesses so that these are incorporated in treatment planning and in rehabilitation and management efforts. Depending on the expertise of the health professional and the clinical setting, he or she may be asked to render an opinion regarding the degree to which an individual is able to carry out BADLs or IADLs both independently and safely. For example, physicians who specialize in physical medicine and rehabilitation, and occupational and physical therapists who work in rehabilitation institutions with individuals with severe head injury or advanced neurological diseases or dementias, are frequently asked to determine the degree to which BADLs may be compromised. In contrast, neuropsychologists working in outpatient settings or nonrehabilitation settings with individuals who have mild brain injury, are more likely to be asked to render an opinion about an individual's cognitive status and its impact on his or her ability to drive, manage finances, self-administer medications, and carry out other IADLs. The opinions of these professionals could lead to changes in the home environment to protect the individual's safety and could have a profound impact on the individual's autonomy, including decisions made about guardianship and living arrangements.

In addition to patient care, the assessment of an individual's ability to carry out IADLs is an essential part of diagnostic procedures that require the identification of functional deficits thought to be present in various psychiatric and neurodegenerative disorders. As an example, the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013) requires deterioration in social and/or occupational functioning as criteria to diagnose major neurocognitive disorder. In fact, one of the primary differences between an individual who meets criteria for dementia, according to the National Institute for Neurological and Communicative Diseases and Stroke—Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann et al., 1984) and an individual with mild cognitive impairment (MCI) is that the individual with dementia requires the presence of functional impairment, whereas the MCI subject requires relatively intact functional abilities, despite the presence of cognitive deficits. This is consistent with the newer National Institute on Aging/Alzheimer's Association (NIA/AA) criteria for dementia and a diagnosis of probable Alzheimer's disease (McKhann et al., 2011).

The discussion that follows examines the ability to perform IADLs from a cognitive standpoint. While a person's functional capacity as measured by performance-based instruments assessed in the clinic often gives important information about the requisite cognitive and functional abilities required to perform everyday activities, we maintain that contextual cues and environmental supports as well as motivational issues may influence performance on specific real-world tasks.

Three key elements need to be considered when assessing the impact of cognitive status on the ability of individuals to perform IADLs: causation, change, and specificity.

The *element of causation* refers to the fact that the loss of the ability to perform an IADL needs to be cognitive in nature and not secondary to physical limitations. As an example, a right-handed patient may be unable to write checks because of the loss of control of the right arm after a left-hemisphere stroke. If the patient is conceptually able to describe all the steps that would be needed to complete the task correctly, including what information needs to be included in the check and where it should be placed, then there has been no cognitive-functional loss in his or her ability to write a check. This point underscores the importance of conducting a thorough medical evaluation to rule out physical factors (e.g., poststroke paresis, loss of vision secondary to diabetes retinopathy) as the main reason for impairments in the performance of an IADL. In cases where physical and cognitive factors coexist in the individual, it is usually difficult to disentangle the relative contribution of each factor in the resulting functional deficit. For example, a young adult who lost motor control of an arm as a result of a traumatic brain injury and an older adult who has limited vision may both have memory problems superimposed upon their physical limitations. Clearly, the interdisciplinary collaboration of physicians, neuropsychologists, occupational therapists, and physical therapists is needed for the comprehensive evaluation and treatment planning of such cases.

The *element of change* refers to the need to compare an individual's current ability to perform an IADL with his or her ability and to carry out the task in the past. For example, if a patient was never able to balance a checkbook or had never engaged in balancing a checkbook and is still unable to do the task, then functional loss in that ability cannot be reliably measured. In other words, the inability of a person to perform a functional task that he or she has never performed or mastered may not constitute actual functional decline. In our work with older adults from heterogeneous backgrounds, we find that many of our patients have never performed banking transactions electronically or developed proficiency with automated menu-driven telephone systems. Thus, the fact that they may not be able to perform this task upon assessment should not be conceptualized as evidence of cognitive-functional decline. The requirement that functional deterioration be present to meet DSM-5 criteria for dementia assumes that the clinician has adequate understanding of a person's premorbid functioning and that deterioration in function parallels decline in cognitive abilities rather than merely reflecting lack of familiarity with a task. In addition, health professionals must be aware that a person who never learned to drive, prepare meals, or manage finances may be suddenly jeopardized by the loss of a significant other who once performed those activities. In these cases, these skills were never learned but may remain important targets for assessment and intervention.

The *element of specificity* can be divided into three types that frequently coincide: task, person, and environment specificity. Different IADLs have different cognitive characteristics and demands. Thus, an individual may be unable to perform a specific IADL but may still be able to perform other IADLs without difficulty. For example, individuals who have amnestic MCI (see Petersen et al., 1999) are more likely to have difficulty with IADLs that have strong episodic memory demands (e.g., remembering to take medications) than with those with more procedural motor demands (e.g., dialing a telephone number). Some tasks have multiple cognitive determinants, any one of which can adversely affect functional performance. For example, paying bills is an important component of the ability to manage finances. However, a component analysis of this task reveals that an individual might not be able to pay a bill after a brain injury because of the inability to understand the bill or because he or she has forgotten that the bill arrived. Provided that the person has intact prospective memory (i.e., the ability to remember to perform an intended action), which would allow him or her to remember the intended action of paying the bill, the person may still be unable to pay the bill because of confusion as to how to write a check or prepare a letter for mailing. There are also instances in which the individual manages to pay a bill but because of difficulties in balancing his or her checkbook, the checking account may have insufficient funds. All of these possible causes for not paying the bill may potentially lead to deleterious consequences (i.e., loss of electricity in one's home, discontinuation of telephone services). Thus, it is not only important to understand functional deficits in terms of task-specific performance but also by gaining an appreciation for specific elements that underlie a particular functional deficit.

Task-specific factors interact with person-specific variables such as cognitive and functional reserve. Given a similar pattern and degree of cerebral dysfunction, an individual who may have worked as an accountant may evidence better performance on functional tasks related to finances relative to someone who recently had to learn this skill because of the death of a spouse. Other person-specific variables may include the individual's ethnocultural/linguistic background, premorbid strengths and weaknesses, compensatory abilities and motivation, amount of practice with certain IADLs, and degree to which a task has been overlearned. Many caregivers of patients with dementia become aware of the patient's functional changes when they observe the difficulties faced by their loved ones when trying to perform IADLs in new circumstances or unfamiliar environments (e.g., preparing a meal in an unfamiliar kitchen). Preparation of a meal requires an interaction between task- and subject-specific characteristics; difficulties encountered in an unfamiliar kitchen reflect environment-specific characteristics. Persons with brain injury or cognitive impairment typically fare better when performing routinized tasks in familiar environments and in the presence of overlearned situational cues.

Assessment of IADLs

To assess an individual's ability to perform IADLs, clinicians typically utilize information from one or more of the following sources: (1) self-report by the individual, (2) information provided by the individual's informant(s) (e.g., relatives, close friends, proxy), or (3) direct observation of the individual's ability to perform tasks that are similar to the functional task in question.

Self-Report and Informant Report

Information about the patient is usually provided by the patient him- or herself and/or by informants. Both the self-report by the individual and the report by the informant(s) are usually elicited in a clinical interview, which may be supplemented by information obtained from questionnaires and/or rating scales.

Although most clinicians seem to agree about the importance of asking the patient about his or her functional status, there are conflicting reports in the literature regarding the extent to which self-reports of functional status should be considered valid. Myers, Holliday, Harvey, and Hutchinson (1993) reported a high correspondence between the self-report of older adults regarding their functional abilities and their actual performance in the home. In contrast, other investigators have shown that, relative to younger adults, old and very old individuals may be less accurate in their judgment of their own functional capacities (Hoeymans, Wouters, Feskens, van den Bos, & Kromhout, 1997; Sinoff & Ore, 1997). Other studies have questioned the relative weight that should be given to the report of patients themselves versus their informants. Various investigations have shown that patients with dementia often overestimate their functional abilities, whereas caregivers may either overestimate or underestimate these abilities (Argüelles, Loewenstein, Eisdorfer, & Argüelles, 2001; Loewenstein et al., 2001; Mangone et al., 1993; Weinberger et al., 1992). While neurologically impaired patients commonly underestimate their deficits because of agnosia, it is also possible that those with significantly depressed mood may complain more about their inability to carry out daily functional activities. For example, Kaye and colleagues (2014) found self-reported disability in PTSD was much greater than actual functional capacity. Furthermore, depressed caregivers may be particularly susceptible to overreporting functional impairment.

There are innumerable self-report measures and informant-based rating scales for assessing patients' ability to perform BADLs and IADLs (Lindeboom, Vermeulen, Holman, & De Haan, 2003). Perhaps the most widely used method of ascertaining a patient's ability to perform IADLs is via informant report by a relative or close friend who has had the opportunity to observe the patient in his or her real-world environment. One of the first measures created using this approach was the Instrumental Activities of Daily Living Scale (IADLS) by Lawton and Brody (1969). This measure taps abilities to engage in activities such as shopping, managing finances, taking medications, preparing food, doing laundry, and using the telephone. Other commonly used IADL scales administered to the patient and/or the informant include the Bayer Activities of Daily Living Scale (BADLS; Erzigkeit et al., 2001), the Disability Assessment for Dementia (DAD; Gelinas, Gauthier, McIntyre, & Gauthier, 1999), the Older Adults Resource Center Scale (OARS; Fillenbaum & Smyer, 1981), and the Functional Activities Questionnaire (FAQ; Pfeffer, Kurosaki, Harrah, Chance, & Filos, 1982).

The Everyday Cognition (ECog) scale is a more novel questionnaire that has gained recent attention. Developed by Farias and colleagues (2008), the ECog is a 39-item rating scale that includes both self- and informant-ratings, measuring different cognitive domains that are linked to everyday real-world functions. Domains such as executive functions (organization, planning, divided attention), language, memory, and visuospatial function are included. Ratings are made on a 4-point scale, and the person is asked to rate cognitive function in these areas relative to how they performed 10 years earlier. The six subscale scores can be combined to create a composite ECog Global score, and the measure has been particularly useful in evaluating older adults who are cognitively unimpaired and with mild MCI. Statistically significant associations between the ECog Memory Domain and hippocampal volumes on MRI have been found in MCI patients (Farias et al., 2013). Additionally, the instrument exhibits good psychometric properties, including factorial validity by confirmatory factor analysis (Farias et al., 2008), and a short-form has been developed (Farias et al., 2011). Among persons who were cognitively normal and those with MCI, everyday memory, planning and everyday visuospatial subtests of the ECog were predictive of future loss of independent function.

Two advantages of utilizing self- and informant-report scales are the ease of administration and scoring and the fact that they can be completed by the patient and/or informant while in the waiting room. A major disadvantage of self-report when evaluating neurologically impaired patients such as those with Alzheimer's disease or specific right-hemisphere cerebral infarctions is that patients may exhibit varying degrees of anosognosia. Given that they may be unaware of their deficits and changes in their functional abilities, self-report measures may overestimate actual functional status. Another disadvantage of the self-report is that even individuals who are aware of their deficits may choose not to report changes in their functional status due to fear of social stigma and/or losing their independence (e.g., especially driving privileges). As it relates to informant-reports, it has been recognized that high-contact informants who know the patient well are better than low-contact informants (Harvey et al., 2013). Sabbag et al. (2011) found that friends of patients with schizophrenia tended to overestimate functional performance in contrast with high-contact clinicians, who were much more accurate in their ratings.

An advantage of informant-based rating scales is that the informant usually rates the patient based on real-world functional performance of IADLs. Thus, informant-based scales tend to be less susceptible to those fluctuations in the patient's cognitive status and motivation that may affect performance and behavior in the clinician's office. In addition, given that the informant is likely to interact with the patient over long periods of time and in many situations, his or her report may serve as an overall estimate of the individual's functional status across settings and time. Specifically, reliable information provided by a knowledgeable informant is helpful to the clinician who is attempting to establish the degree to which an individual has experienced functional deterioration relative to his or her premorbid level of function. On the other hand, an informant may feel uncomfortable reporting changes in the patient's functional ability out of a sense of loyalty or for fear that the family member might lose critical privileges, including driving. The level of stress and depression, marital dynamics, and individual personality styles that involve minimization and denial as well as overexaggeration may further affect the accuracy of the self-report of the spouse and other family members.

Performance-Based Approach

The performance-based approach usually requires the patient to perform the particular activity under the observation of the examiner, who utilizes behaviorally based measures to assess different aspects of functional capacity. Performance-based assessments have the advantage of providing an objective behavioral evaluation of the functional skills required for daily living, such as using the telephone, meal preparation, medication management, writing a check, balancing a checkbook, and making change for a purchase. Such direct assessment is particularly useful in the evaluation of patients who may not have an informant, in cases where there is doubt about the validity of information provided by a sole informant, and in cases where there are discrepant opinions among multiple informants. Direct observation of the individual as he or she carries out the functional tasks can be conducted in the clinic and/or the patient's home.

Various research groups have developed standardized testing protocols so that the assessment of an individual's functional capacity can be objectively assessed and quantified. Such tests have typically been developed for older adults and for those with cognitive impairment; they include some of the measurements described in further detail below.

Performance Test of Activities of Daily Living

The Performance Test of Activities of Daily Living (PADL; Kuriansky, Gurland, & Fleiss, 1976) categorizes patients into one of three levels of functional independence (independent, moderately dependent, or dependent) through the administration of 16 tasks related to basic and independent activities of daily living. Most tasks include the manipulation of props, which can be assembled into a portable kit and administered in remote settings. The PADL includes assessment of grooming, hygiene, eating, dressing, communication, time orientation (e.g., telling time on a clock), and safety awareness (e.g., turning a light switch on and off). The PADL was designed so that tasks could be easily understood and carried out by the patient. Task instructions are simple and direct and facilitate translation of the instrument for use in other languages. The props help convey, nonverbally, what is expected. A trained paraprofessional can administer the PADL in about 20 minutes.

Direct Assessment of Functional Status Scale

The Direct Assessment of Functional Status (DAFS; Loewenstein et al., 1989) scale was originally developed to assess functioning in Alzheimer's disease and related disorders, but researchers have also found it useful with other patient populations, such as those with schizophrenia (Evans et al., 2003; Patterson et al., 1998) and Huntington's disease (Hamilton, 2000). The test measures functional abilities across multiple tasks in both BADL and IADL domains, including time orientation, communication, transportation, financial skills, shopping, grooming, and eating. Two unique features of the DAFS are a memory task in the shopping subscale (recall and recognition of a grocery list) and the optional transportation subscale, which assesses an individual's ability to understand and respond to road signs. Examining functional capacity on the transportation subscale is important for patients who are still driving but for whom driving competence may be a concern. The DAFS has also been translated for use in non-English-speaking populations and takes 30–35 minutes to administer.

Structured Assessment of Independent Living Scales

The Structured Assessment of Independent Living Scales (SAILS; Mahurin, De Bettignes, & Pirozzolo, 1991) divides 50 ADL tasks into 10 subscales: fine motor, gross motor, dressing, eating, expressive language, receptive language, time orientation, money-related skills, instrumental activities, and social interaction (e.g., appropriate responses to social greetings). In addition to the total score, reflective of overall functioning, the SAILS generates a motor score and a cognitive score. Administration and scoring of the SAILS are guided by detailed, behaviorally anchored descriptions and can be used in both clinical and research settings. Overall, the tasks take approximately 60 minutes to complete.

Assessment of Motor and Process Skills

Designed as a tool for occupational therapists, the Assessment of Motor and Process Skills scale (AMPS; Fisher, Leu, Velozo, & Pan, 1992) measures the quality of performance by the effort, efficiency, safety, and level of independence involved in both ADL motor and process skills. Motor skills include actions in which the client moves him- or herself or an object, whereas process skills are actions involving a logical sequence of steps, appropriate tool/material selection, and adaptation to problems as they occur. The AMPS inventory contains 83 standardized ADL tasks, varying in degree of difficulty, and a brief interview is used to help the client choose two tasks that are particularly relevant and familiar. For performance comparisons, the AMPS computer package adjusts scores for task/item difficulty and rater severity. Training to administer and score the AMPS includes a 5-day workshop plus follow-up reliability and tester calibration requirements; however, the test has been standardized cross-culturally and internationally (e.g., the United States, England, Sweden, Japan) on over 100,000 individuals for use in research and clinical practice. Administration typically takes about 45 minutes, but the time required varies by tasks chosen and individual level of functioning.

Cognitive Performance Test

The Cognitive Performance Test (CPT; Burns, Mortimer, & Mechak, 1994) is composed of six common daily tasks: dressing, shopping, toast making, telephone use, washing, and traveling. The assessment focuses on the degree to which an individual's functional abilities and deficits affect performance on these tasks; simple task completion is not the main variable of interest. Performance is classified into one of six ordinal levels of functional disability that range from profoundly disabled to normal functioning (these levels are based on Allan's [1982] cognitive disability theory). During testing, as deficits or competencies appear, the tester changes the task demands according to a standardized procedure, thus tailoring the test for each individual throughout the administration. The degree and type of help required for task completion are then reflected in the rating. For example, an individual whose task performance is organized, efficient, and without error would be rated as a level 6 (normal), whereas a participant who shows a trial-and-error approach and often needs additional specific directions to complete the task is functioning at level 4 (moderate functional decline). Completion of the battery takes approximately 45 minutes.

Kitchen Task Assessment

The Kitchen Task Assessment (KTA; Baum & Edwards, 1993) focuses solely on the ADL task of cooking and analyzes performance in terms of the cognitive processes involved and the subsequent level of cognitive support needed to complete the task. During the KTA, which can be administered in the clinic or the home, the individual is asked to make cooked pudding. The tester evaluates the performance across multiple components, and scoring is based on whether each component was completed independently, with verbal assistance, with physical assistance, or not completed at all. From task observation and the scored results, the tester or clinician can recommend appropriate strategies that caregivers can use to help the impaired individual complete other ADLs. The KTA takes less than 30 minutes to administer and is appropriate for use in both clinical and research settings.

Test of Everyday Functional Ability

The Test of Everyday Functional Ability (TEFA; Weiner, Gehrmann, Hynan, Saine, & Cullum, 2006), which was originally called the Texas Functional Living Scale, was designed as a brief measure of functional competence. This 21-item test includes subscales related to dressing, time, money, instrumental activities (e.g., addressing an envelope, using a telephone), and memory (e.g., remembering to take medications). The TEFA can be administered in about 15 minutes by a bachelor's-level tester.

UCSD Performance-Based Skills Assessment

One widely used direct assessment of functional capacity is the UCSD Performance-Based Skills Assessment (UPSA; Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001), a measure of communication skills, household chores, finances, and planning recreational and other activities. This measure is easy to administer, has demonstrated reliability and validity, and can provide direct and quantifiable information on functional capacity. Since the UPSA and the UPSA-B (a short form of UPSA which includes the Communications and Finances subscales) are performance-based functional measures, they may be preferable to self-reports of patients who often overestimate their abilities or to the reports of questionable informants. It has also been shown to be effective in assessing the functional capacity of persons with depression, schizophrenia, schizoaffective and bipolar disorder (Mausbach et al., 2010, Depp et al., 2012), and mild cognitive impairment in the elderly (Goldberg et al., 2011), and it has been associated with real-world functional outcomes (see Harvey, Loewenstein, & Czaja, 2013). Importantly, it has also been used with many different ethnic and cultural groups. Although correlations with the UPSA and UPSA-B correlate 0.6 or greater with neuropsychological measures, some argue that UPSA measures tap functional behaviors but that the items are more psychometrically similar to cognitive measures. It has also been argued that contextual cues or supports in the individual's actual environment may result in different performance of real-world functional abilities than performance-based functional capacity instruments such as the UPSA or UPSA-B.

Specific Levels of Functioning Scale

The Specific Levels of Functioning Scale (SLOF; Schneider & Struening, 1983) is a 43-item multidimensional behavioral survey administered to an individual or to a high-contact caseworker or a clinician of a patient diagnosed with mental illness, selected on the basis of his or her familiarity with that person. Measures such as the SLOF are most effective when completed by a high-contact clinician who knows the patient well and can weigh informant and patient reports against his or her own clinical judgment. The SLOF assesses the patient's current functioning and observable behavior, and focuses on a person's skills, assets, and abilities rather than deficits that once served as the central paradigm guiding assessment and intervention for persons with disabilities. It comprises six subscales: (1) physical functioning, (2) personal care skills, (3) interpersonal relationships, (4) social acceptability, (5) activities of community living and (6) work skills. While the SLOF has been extensively validated with schizophrenia patients, studies have shown that 64% of patients with bipolar disorder evidence deficits in one or more SLOF domains (Depp et al., 2010).

Functional Skills Assessment and Training Battery

Impairment in IADLs may occur in the early stages of MCI. However, there are few reliable measures of IADL in MCI that have a sufficient range of scores in clinically and cognitively unimpaired elderly. The Functional Skills Assessment and Training battery (FUNSAT; Czaja et al., 2017; Harvey et al., 2021) is a sensitive computerized performance-based measure of everyday functional capacity. The computerized battery of everyday tasks includes simulations of a doctor's visit, medication refill, and financial management tasks. Research on this instrument has shown that older adults with amnestic MCI performed significantly poorer on all three tasks. Performance on these measures was also moderately correlated with standard measures of cognitive abilities and showed good test–retest reliability and feasibility of use among older adults.

Functional assessments have also been developed for use in other clinical populations. The UPSA described earlier (Patterson et al., 2001) was originally designed for persons with schizophrenia or schizoaffective disorder. The ability to manage medications in individuals with schizophrenia can also be assessed employing instruments such as the Medication Management Ability Assessment (MMAA; Patterson et al., 2002). Heaton and colleagues (2004) have described the use of performance-based tasks that tap financial skills, medication management, shopping, and cooking as well as vocation-specific skills in individuals with HIV infection.

Despite the above-mentioned strengths, the performance-based approach has its limitations. Performance on tests of functional capacity may not always capture patient-specific or environment-specific variables that affect real-life performance and that (though present in the testing situation) may not be present in the patient's everyday environment. Some of these variables involve the ability to self-initiate and complete a task, the overall motivation of the patient, and the presence of environmental variables that cue the patient that the task needs to be performed. Moreover, the same task that can be completed in the laboratory under optimal conditions may not be as successfully performed in an environment with multiple cognitive and task demands or with less structure. An illustration of this principle is often seen in acquired brain injury. In a quiet office, a secretary recovering from a brain injury may have the cognitive, motivational, and functional capacity to use the telephone, take a message, and type. However, if placed in a busy office in which attention has to be divided among various distractors (e.g., patients presenting at a reception area, the ringing of the telephone, a letter that is being composed) the individual's functional performance may be severely compromised.

Clinician-Based Evaluations

It has been increasingly recognized that good clinical judgment may depend on data garnered from a wide variety of sources. For example, physicians, occupational therapists, and physical therapists in outpatient rehabilitation settings may rely on their direct observations of performance-based behaviors, staff ratings of the patient's functional ability, and judgments of family members who have a chance to evaluate the patient in his or her real-world environment. In some instances, a wealth of functional information may be derived from home visits conducted by a nurse, occupational therapist, physical therapist, or social worker. Through this interdisciplinary approach, the effects of physical limitations, cognitive limitations, and motivational factors can be weighed when arriving at a diagnostic determination and a comprehensive treatment plan.

The Role of Neuropsychological Assessment in the Assessment of Ability to Perform IADLs

From its earliest days, clinical neuropsychology aspired to understand the impact of brain lesions and diseases on cognitive functioning. Early work with individuals who suffered penetrating brain injury, blunt head trauma, or strokes culminated in a rich understanding of the relationship between the damaged brain structures and the multiple facets of memory and other cognitive processes (e.g., attention, executive function). Our knowledge of the cognitive sequelae of brain injury continues to be enriched by advances in psychometrics, neuroimaging, and cognitive neuroscience.

A long-held assumption in the field of neuropsychology is that cognitive processes involved in memory, language, visuospatial skills, attention, and executive function underlie most IADLs. A logical conclusion of such an assumption is that the measurement of cognitive status should allow the clinician to infer the functional status of the patient (see Loewenstein & Mogosky, 1999). Certainly, those with substantial cognitive impairment will likely have difficulties on many higher-order functional tasks, particularly those that involve multistep cognitive operations or divided attention. It is difficult to imagine an individual with profound generalized neuropsychological impairment managing his or her finances, driving an automobile, or returning to the many functional demands of everyday life. In actual clinical practice, however, persons frequently have only mild or moderate cognitive impairments in specific domains, with some areas evidencing only minimal or no cognitive deficits. Varying strengths and weaknesses and differences in cognitive reserve among individuals (see Scarmeas & Stern, 2004; Whalley, Deary, Appleton, & Starr, 2004) may act as mediating factors between actual brain injury or disease and the individual's ability to function. In our work, we have encountered persons with brain injuries who have significant cognitive impairment but who nevertheless continue to show relatively preserved functional abilities. This suggests that, in addition to cognitive reserve, individuals may also vary in their *functional reserve*. As previously discussed, the ability to perform IADLs is likely related to a combination of person-, task-, and environmental-specific factors. This complexity may explain in part why knowledge of neuropsychological function alone may not provide sufficient information in many cases to make judgments about the person's ability to perform IADLs in real-world settings.

In general, the literature across different patient groups suggests that there is an association between neuropsychological test performance and the ability to perform IADLs. Neuropsychological function, most notably executive ability, has been shown to relate to functional competence in diverse groups such as community-dwelling older adults (Bell-McGinty, Podell, Franzen, Baird, & Williams, 2002; Cahn-Weiner, Boyle, & Malloy, 2002; Cahn-Weiner, Malloy, Boyle, Marran, & Salloway, 2000; Rapp et al., 2005; Royall, Palmer, Chiodo, & Polk, 2005) and in patient populations diagnosed with

Alzheimer's disease (Boyle, Paul, Moser, & Cohen, 2004; Cahn-Weiner, Ready, & Malloy, 2003), cerebrovascular disease (Jefferson, Paul, Ozonoff, & Cohen, 2006), postacute head injury (Farmer & Eakman, 1995; Goverover, 2004), heart transplantation (Putzke, Williams, Daniel, Bourge, & Boll, 2000), schizophrenia (Jeste, Patterson, et al., 2003), and HIV infection (Albert et al., 2003; Heaton et al., 2004).

Early cognitive deficits have been related to an increased risk of functional decline among older adults (McGuire, Ford, & Ajani, 2006) and to increased mortality (McGuire et al., 2006; Schupf et al., 2005). Early functional deficits have also been related to cognitive decline in longitudinal studies of older adults (Plehn, Marcopulos, & McLain, 2004). In addition, there are specific patterns of neuropsychological deficits that may be related to functional performance. Earnst and colleagues (2001) found that performance on neuropsychological tests tapping the executive component of working memory was strongly associated with performance on a test of functional capacity that assessed basic money skills and ability to manage bank statements and a checkbook. In a study of 69 older patients who presented for clinical assessment, Baird, Podell, Lovell, and McGinty (2001) found that in addition to the Dementia Rating Scale, seven out of nine neuropsychological measures entered into regression equations predicting scores on a scale that assesses the ability to carry out IADLs. In another investigation, Hoskin, Jackson, and Crowe (2005) found that neuropsychological performance was related to the capacity of persons with acquired brain injury to manage their personal finances. These investigators compared participants who were handling money independently with those who had been appointed an administrator by the court to help them manage their finances. Results indicated that measures of working memory, impulse control, and cognitive flexibility correctly classified 83.7% of individuals in the correct functional group. Interestingly, measures of memory had no discriminatory power. Woods and colleagues (2006) found that the ability to retrieve words that refer to action (i.e., verbs) was more strongly associated with IADL dependence among HIV-infected individuals, relative to the ability to retrieve words that start with a specific letter or that belong to a particular category, resulting in an overall hit rate of 76%.

In addition, performance on neuropsychological measures such as memory, attention, and conceptual abilities has been related to medication adherence and management (Hinkin et al., 2002; Jeste, Dunn, et al., 2003; Putzke et al., 2000). Cognitive performance has also been associated with performance on driving simulators and on-road driving evaluations (Grace et al., 2005; Lundqvist et al., 1997; Marcotte et al., 2004; Reger et al., 2004; Rizzo, McGehee, Dawson, & Anderson, 2001). A particularly effective predictor of driving performance has been the Useful Field of View (UFOV), a test tapping visual attention (see Clay et al., 2005).

A primary goal of neuropsychological assessment is to determine patterns of cognitive strengths and weaknesses as they relate to important real-world outcomes (Sbordone, 1996). In their review of the literature, Franzen and Wilhelm (1996) and Spooner and Pachana (2006) differentiate between veridicality and verisimilitude in describing the ecological validity of neuropsychological tests. *Veridicality* refers to the extent to which performance on neuropsychological tests relates to measured performance on real-world tasks, whereas *verisimilitude* refers to the degree to which the task demands of a test reflect the actual demands imposed on the person by the real-world environment. Clearly, most studies in the field are concerned with veridicality. It has been increasingly recognized that neuropsychological measures administered in controlled conditions that facilitate optimal performance may not tap the real-world demands of higher-order functional tasks that often must be completed in the presence of many environmental demands. In our laboratory, we have worked on paradigms designed to increase verisimilitude. For example, in our studies of MCI in older adults, we have been developing and refining paradigms that tap time- and event-related prospective memory as well as face–name associations and memory for common, everyday objects. Thus, we have focused on paradigms that more closely tap some of the real-world difficulties reported by subjects with MCI. Although traditional tests of auditory list learning, memory for story passages, and memory for designs are often useful as cognitive tests, their applicability to real-life demands (e.g., remembering to take medications at a specific time, putting a name together with a face) may be more limited. We first developed the DAFS to assess the real-world abilities of persons with mild dementia. More recently, with Sara Czaja, an internationally recognized behavioral scientist with a background in human factors engineering, we developed the computerized performance-based functional outcome measures previously mentioned, the FUNSAT, which was included in a longitudinal study of older adults with mild cognitive impairment (MCI, preMCI, and normal cognition). Performance on these measures was also moderately correlated with standard measures of cognitive abilities.

Limitations of Neuropsychological Studies Based on Correlation Analyses

At face value, the above-mentioned studies point to a significant association between neuropsychological test performance and the ability to carry out IADLs. However, one must be cautious about applying group findings to individual cases and about making causal inferences on data that assess statistical associations. Although most studies demonstrate statistically significant relationships between neuropsychological measures and functional performance, the degree of variability in neuropsychological performance and functional performance frequently does not exceed the unexplained variance associated with the dependent variable (see Loewenstein & Mogosky, 1999; Silver, 2000; Bowie et al., 2010; Harvey, Loewenstein, & Czaja, 2013). Specifically, even if the association between the variables of interest exceeds a healthy correlation of 0.7, more than 50% of the performance variability on functional measures remains unexplained.

In our judgment, more informative methods to determine the utility of neuropsychological measures in predicting actual functional performance include techniques such as logistic regression, discriminant function analysis, and receiver operating characteristic (ROC) curve analysis. These approaches yield estimates of sensitivity and specificity, providing information to the clinician about how many persons with functional impairment are accurately identified as impaired and how many persons without functional impairment are accurately identified as unimpaired by neuropsychological tests. The next step would be to calculate positive and negative predictive values based on the base rates of true levels of impairment in specific settings. Unfortunately, there is a paucity of such studies in the literature. Further, even high levels of sensitivity on a measure may yield low positive predictive power when target conditions or behaviors have a low base rate within the environment.

Many clinicians would feel comfortable concluding that an individual with a normal neuropsychological profile is likely to be able to drive and to manage his or her medications or finances. On the other hand, it is difficult to imagine that a clinician would feel comfortable recommending these activities for an individual scoring below the 1st percentile on a broad array of commonly employed neuropsychological measures of memory, language, attention, executive function, and visuospatial skills. The patients who fall in the mild-to-intermediate impairment ranges in neuropsychological test performance are the ones who often constitute a challenge when trying to make judgments about their degree of functional impairment.

While there is little debate that specific cognitive abilities underlie functional capacity, it should be recognized that neuropsychological measures are not unidimensional but rather tap multiple cognitive functions. More importantly, given that functional performance in real life is often dependent on the complex interaction of person-, task-, and environmental-specific variables, it is not surprising that there is far from a one-to-one correspondence between neuropsychological test results and IADLs. Indeed, in our work on cognitive remediation techniques for those with early Alzheimer's disease, we pay special attention to task specificity. We have found that the use of spaced retrieval (see Camp & Stevens, 1990) and procedural motor memory practice can lead to improvements in performance on functionally relevant tasks in individuals with mild Alzheimer's disease. The concept of spaced retrieval is based on paradigms that require the individual to make associations between two targets (e.g., face–name association) and to gradually lengthen the interval between the presentation of the target and the patient's recall of the association. If the individual fails at a longer interval, the interventionist returns to the last previous shorter interval in which there was success. Procedural learning involves more implicit motor memory subserved by basal ganglia systems and is not as dependent on explicit memory, which is very dependent on the integrity of hippocampal and entorhinal cortex structures. In contrast, we have found that simply training different component cognitive processes (e.g., attention, concentration) thought to underlie task performance has no effect on outcome (Loewenstein & Acevedo, 2006; Loewenstein, Acevedo, Czaja, & Duara, 2004).

Minimizing Errors of Clinical Judgment

In general, functional assessment is most complete when information is obtained from multiple sources. It is important to gather as much information as possible from collateral informants regarding the patient's current and past ability to perform specific IADLs. In addition, an examination of the patient's performance on neuropsychological measures may be helpful when making treatment recommendations and when deciding if referrals or additional assessments (preferably in home) are necessary. For example, an individual, his or her spouse, and their children may insist that the patient is able to drive independently, manage finances, and buy needed goods. However, on direct functional assessment, the patient is unable to count currency, make change for a purchase, write a check, or balance a checkbook. Neuropsychological testing may also evidence severe impairments in memory, attention, visuospatial skills, concept formation, speed of processing, and the ability to shift cognitive sets. Despite the reports of the patient and family members, the patient is likely at risk. In many states across the country, the results of such an evaluation would prompt a report to the state of concerns about the patient's driving ability and a recommendation that an on-road driving test be conducted. The issue is not merely whether the person has the procedural knowledge and motor skills to operate a vehicle but whether he or she has the cognitive capacity to recognize changing environmental conditions, such as watching out for children in a school zone or taking an alternate route if a road is blocked. Additionally, it might be necessary for a nurse or a social worker to perform a home visit to ensure that the person is actually capable of managing his or her finances and medications in the everyday environment. The nature of the patient's neurological status as well as the possible need of serial assessments should also be taken into consideration. For example, an individual with a head injury may have a functional disability that dissipates over time and that will show improvement in subsequent evaluations. Conversely, a person with early Alzheimer's disease may not demonstrate functional impairments at a given time but may evidence these deficits on follow-up assessments.

Recommendations for Clinicians and Future Directions

New empirically based approaches are needed to more fully capture the demands of real-world activities of daily living. Neuropsychologists, occupational therapists, and other allied health professionals have been at the forefront in developing performance-based instruments for older adults. There is also an increasing appreciation of the value of developing new paradigms that integrate information from related fields of cognitive psychology, human factors engineering, behavioral medicine, and computer sciences. The challenge to neuropsychology is to appreciate the richness of alternative approaches developed by allied disciplines and to find ways of incorporating these approaches in our continuing pursuit of scientific knowledge.

Researchers and clinicians recognize that those neuropsychological tests that may be useful for diagnosis may not necessarily be the same measures that are most useful for monitoring cognitive and functional change over time. Similarly, the neuropsychological tests that may be useful for diagnostic purposes may not be the optimal measures to predict real-world functional performance. Real-life situations are usually based on open systems where environmental circumstances are fluid and may be unpredictable. In contrast, strict standardization procedures require the administration of cognitive measures in a controlled testing environment that minimizes distractions and maximizes test performance. A continuing challenge to the field is to develop standardized instruments that adequately capture the multiple demands that are placed simultaneously on the individual's cognitive resources.

Ideally, these more sensitive and ecologically valid neuropsychological measures would allow us to further understand the effects of medications and medical conditions on cognitive test performance, especially among older adults. Emerging technologies using computer microprocessors have enabled the development of more sophisticated performance-based measures to assess attention, cognitive processing speed, and working memory, and to examine the relationship of these cognitive processes to functional test performance. In this regard, information and communication technologies, artificial intelligence, and human factors engineers have made significant contributions to the field by studying how to optimize human–machine interfaces that are used in everyday appliances and systems such as smart phones, telephone and web-based menu navigation systems, and even the automobiles that we drive (Czaja & Sharit, 2003).

Promising technologically enhanced approaches have been developed over the last decade to evaluate everyday functioning such as ecological momentary assessment and computerized functional skills assessment. However, to date, there are no agreed upon standards for which methods are best able to reliably assess change in symptoms over time from normal cognition to a state of functional change that may reflect the onset of underlying neuropathology. Moreover, rather than view these assessment methods as competing, there continues to be important value in considering self-report measures of cognitive status and intraindividual variability across performance on these measures to gain a comprehensive understanding of an individual's real-world capacity (Schmitter-Edgecombe, Sumida, & Cook, 2020).

The limitations of available cognitive tests in the prediction of functional performance in the real world are sometimes not appreciated by neuropsychologists who may be asked to render an opinion about the patient's functional status. The professional opinion offered by a neuropsychologist may be used by physicians, rehabilitation treatment teams, the schools, and the courts to make decisions that may dramatically affect the patient's quality of life, autonomy, and independence. For example, a cognitively normal, older, non-native, English-speaking immigrant with 6 years of education, whose sole work experience has been repetitive manual labor, may score at the impaired level on neuropsychological tests frequently used by neuropsychologists, such as the Rey–Osterrieth Figure Test, the Boston Naming Test, the Trail Making Test, and subtests of the Wechsler Adult Intelligence Scale (e.g., Similarities, Block Design). If the neuropsychologist conceptualizes the test results as a true reflection of the patient's cognitive status without consideration of the limitations of many mainstream neuropsychological tests when used with individuals of different ethnocultural/linguistic backgrounds, he or she may erroneously conclude that the patient's "cognitive impairment" is likely to result in inability to carry out IADLs. Several cross-cultural studies examining the functional status of older adults have had to rely on IADLs that differ from those traditionally assessed in scales used in the United States (see Fillenbaum et al., 1999; Senanarong et al., 2003). In other words, IADLs vary across cultures, and those that may be essential in certain cultural groups may be irrelevant in others.

On the other hand, the neuropsychologist may be evaluating a patient who scores within normal limits on memory for stories on the Wechsler Memory Scales and who exhibits normal expressive and receptive language function on the Boston Diagnostic Aphasia Examination. Unfortunately, normal performance on these measures does not guarantee that the patient will be able to manage and process the welter of discourse material that individuals must manage in their everyday environment. Similarly, normal performance on a list-learning task does not necessarily imply that the person will remember to buy needed grocery items, to pay the electricity bill, or to appropriately respond to environmental cues signaling that the bill should be paid or that it was already paid. The expertise of neuropsychologists in test development and construction places neuropsychology in a unique position to develop tests with verisimilitude. In addition, it allows our field to advance our knowledge of factors, including ethnocultural/linguistic factors, that mediate the relationship between cognition and real-life functioning.

Conclusions

It is increasingly recognized that measures that presumably tap specific cognitive processes rarely tap a unitary cognitive construct and that, rather, performance on widely employed functional assessment instruments frequently tap various cognitive domains (see Gold, 2012). The notion that cognition, as reflected by neuropsychological tests, is the sole requisite for independent real-world function is, at best, misguided and ignores the multifactorial nature of the determinants of many aspects of person-, task-, and environment-specific variables that may affect real-world functioning. Pioneering work by Wilson and colleagues (Wilson, 1993; Wilson, Clare, Baddeley, Watson, & Tate, 1999) and the cogent arguments presented by Spooner and Pachana (2006) underscore the importance of examining the practical aspects of memory (e.g., prospective memory) that are rarely assessed in traditional neuropsychological measures, thus limiting their ecological validity. This laudable goal would be facilitated by an integration of information stemming from allied disciplines such as rehabilitation medicine, occupational therapy, human factors engineering, and behavioral neurology. Already, psychologists in rehabilitation settings are developing sophisticated treatment approaches that go beyond a specific cognitive domain and that directly train the acquisition and maintenance of functional skills (see Loewenstein & Acevedo, 2006).

To enhance clinical utility, future studies should assess the impact of varied neurological conditions on specific IADLs. In addition, empirical studies should utilize techniques such as ROC curves, logistic regression, and discriminant function analysis to examine outcomes of interest (e.g., sensitivity, specificity, positive and negative predictive values) in different clinical populations and in groups of varied ethnocultural/linguistic backgrounds. The identification of factors other than neuropsychological test performance that can augment the prediction of ability to carry out IADLs in real life would further advance our knowledge in this important field.

The complexity that neuropsychologists face in understanding the multifactorial nature of functional performance on different IADLs can appear daunting. The alternative, however, is to refuse to accept the limitations associated with existing practices and the consequences of making inaccurate judgments that can adversely affect the lives of our patients and the fulfillment of our professional obligations.

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CHAPTER 7

The Prediction of Employment Functioning from Neuropsychological Performance

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Neuropsychological tests remain the cornerstone of assessment and expression of brain function in multiple cognitive spheres. Relating findings on neuropsychological tests to “real-world functioning” represents one of the most valued uses of neuropsychological assessment. However, the current array of neuropsychological tests was not designed to predict specific real-world abilities in any but the broadest manner (such as an IQ score predicting general ability to function, overall). Unfortunately, neuropsychological tests do not correlate perfectly with functional outcomes, including employment outcomes in persons with acquired brain disease. Although we do not yet have an array of neuropsychological tests that are known to directly predict specific aspects of real-world functioning, the tests we use today still have a very important role in assessing outcomes. Neuropsychological tests remain the most direct way to assess cognitive and emotional abilities that are important for employment and academic performance.

Conditions that affect a person’s cognitive functioning can have a profound impact on his or her ability to work. Traumatic brain injury (TBI) is the most widely studied condition, with annual estimated costs in lost productivity and medical care around $60 billion in 2000 dollars (still the cited study by the Centers for Disease Control and Prevention [CDC] as of the writing of this chapter), which is $91.6 billion in 2020 dollars (Corso, Finkelstein, Miller, Fiebelkorn, & Zaloshnja, 2006). Other conditions that result in cognitive impairment (e.g., HIV/AIDS, multiple sclerosis [MS], stroke, brain tumors) also result in lost productivity relating to work and other outcomes. Some psychiatric disorders (e.g., posttraumatic stress disorder, bipolar disorder, major depression, and schizophrenia) are associated with cognitive impairment and resulting loss of work productivity or disability.

Measuring Employment: Abilities

It is, of course, unrealistic to expect that every important behavior relevant to performance in any job for each person undergoing a neuropsychological assessment can be assessed by one or more neuropsychological tests. Reviews of the cognitive aptitudes required for occupations are listed in the *Dictionary of Occupational Titles* (DOT; Lees-Haley, 1990); U.S. Department of Labor (*Dictionary of Occupational Titles*, 1991). The updated DOT, called the Occupational Information Network (O*NET; U.S. Department of Labor, *O*NET* 2020), lists 21 possible "cognitive abilities," an additional 10 "psychomotor abilities," and 12 "sensory abilities" that are considered "worker characteristics." These are enduring characteristics that may influence both performance and the capacity to acquire knowledge and skills required for effective work performance (see Table 7.1 for O*NET worker abilities). Neuropsychologists have also traditionally measured many of the abilities (e.g., auditory attention and finger dexterity). Note that the abilities considered important for various job titles were determined by expert panels and not by empirical validation using actual tests.

A brief review of the Mental Measurements Yearbook with Tests in Print (MMY; *The Twentieth Mental Measurements Yearbook*. Lincoln, NE: Buros Center for Testing) using the test category *vocations* and the subfield *ability* yielded 139 assessment tools, including performance-based, interest, and psychological/emotional instruments. These assessments may maximize verisimilitude—the similarity of data collection method to the real-world task—but it is impractical to think that, even if valid, an individual professional could learn to administer and interpret performance on every job-specific performance assessment tool. Therefore, a different approach is required.

One perspective on neuropsychological tests in relation to real-world functioning is that the tests measure meta-abilities that are generally applicable to performance of a broad range of vocations (a global "g" [or general] factor, if you will, of "real-world ability") rather than predicting discrete or specific vocations. A closer inspection of the various descriptions of the vocation-specific measures listed in the MMY reveals that each measure can be classified into one of two groups. One group contains measures that assess a job-specific skill, such as specific clerical or mechanical skills, and the other group contains measures that assess a broader cognitive ability that can be applied in many vocations, such as verbal, computational, or visuospatial abilities. Of the vocation-specific tests we identified, approximately half assess some aspect of cognition such as vocabulary, problem solving, or verbal comprehension. There have been measures that sample broad domains considered important for a wide range of jobs. For example, the General Aptitude Test Battery (Dvorak, 1947) has been in use for decades, with strong evidence for predicting employment performance, such as a meta-analysis that yielded an operational validity of 0.57 in predicting work samples in jobs of medium complexity (Salgado & Moscoso, 2019). However, the limited studies in clinical populations (Taylor, 1963) make it difficult to apply in patient populations. Several other aptitude batteries suffer from the same lack of research in clinical populations, and in general, the few studies in clinical populations suggest that these batteries do not predict employment outcomes as well as they do in healthy populations (Salgado & Moscoso, 2019; Taylor, 1963) or that the predictive validity is independent of disease characteristics (King et al., 2014).

Although no study directly compares the predictive validity of neuropsychological

TABLE 7.1. Abilities—Enduring Attributes of the Individual That Influence Performance

Cognitive abilities	Psychomotor abilities	Sensory abilities
Verbal abilities	*Fine manipulative abilities*	*Visual abilities*
Oral comprehension	Arm–hand steadiness	Near vision
Written comprehension	Manual dexterity	Far vision
Oral expression	Finger dexterity	Visual color discrimination
Written expression		Night vision
	Control movement abilities	Depth perception
Idea generation and reasoning abilities	Control precision	Glare sensitivity
Fluency of ideas	Peripheral vision	
Originality	Multilimb coordination	*Auditory and speech abilities*
Problem sensitivity	Response orientation	Hearing sensitivity
Deductive reasoning	Rate control	Auditory attention
Inductive reasoning		Sound localization
Information ordering	*Reaction time and speed abilities*	Speech recognition
Category flexibility	Reaction time	Speech clarity
	Wrist–finger speed	
Quantitative abilities	Speed of limb movement	
Mathematical reasoning		
Number facility	Physical abilities	
	Physical strength abilities	
Memory	Static strength	
Memorization	Explosive strength	
	Dynamic strength	
Perceptual abilities	Trunk strength	
Speed of closure		
Flexibility of closure	*Endurance*	
Perceptual speed	Stamina	
Spatial abilities	*Flexibility, balance, and coordination*	
Spatial orientation	Extent flexibility	
Visualization	Dynamic flexibility	
	Gross body coordination	
Attentiveness	Gross body equilibrium	
Selective attention		
Time sharing		

Note. From U.S. Department of Labor, National O*NET Consortium. O*NET OnLine (interactive web application). Available at *online.onetcenter.org*.

versus vocation-specific assessments, it seems reasonable to expect that neuropsychological tests perform as well as many of these cognitively themed employment tests in assessing employment performance. Both measure the similar construct of cognitive abilities, and there is ample evidence supporting the predictive validity of both kinds of tests (Guilmette & Kastner, 1996; Kuncel & Beatty, 2013). Neuropsychological tests are an important alternative to the administration of job-specific tests, especially when the issue of brain dysfunction exists. The neuropsychological test can, therefore, assess both the effect of central nervous system dysfunction and aspects of real-world capability.

This chapter reviews recent data on the ability of neuropsychological tests to predict several aspects of employment functioning after acquired brain dysfunction. Here we emphasize the ability of neuropsychological tests to predict employment performance in the context of specific illnesses or conditions. If, for example, future job performance was best predicted in a TBI population by the presence and duration of posttraumatic amnesia, and neuropsychological tests added little or no predictive power beyond this condition, there would be limited utility and rationale for the administration of neuropsychological tests to predict work functioning. Of course, when the details of the TBI are unknown, some sort of testing may be the only basis for predicting future employment performance. And because neuropsychological studies of employment outcomes have not been performed in every disease population, it is necessary to extrapolate findings from the few populations that have been studied (e.g., TBI, HIV/AIDS) to populations that have not been studied as extensively (e.g., brain tumor, neurotoxic substance exposure). In this chapter, we review models of the relationship between neurocognitive abilities, environmental factors, inter/intrapersonal variables, disease characteristics, and employment outcomes. In addition, we review studies of the ability of neuropsychological tests to predict employment outcomes; recent literature on specific neuropsychological abilities, such as executive function and memory, to predict employment outcomes; performance-based assessment of work skills; and rehabilitation for return to work. We conclude with recommendations for future directions for the development and validation of a new generation of neuropsychological tests to relate to employment outcomes.

Measurement of Employment: Outcomes

Employment outcomes can be measured in a variety of ways, and it will be helpful to review some outcome measures to set the stage for the rest of this chapter. Many studies employ outcome as a dichotomous variable: a patient is either employed or is not employed. Table 7.2 contains general categories of outcome measures and example variables, many of which have been used as outcome variables in the neuropsychological literature and a few of which are reviewed next.

Examples of most outcome measurements will be presented throughout the chapter, but a few studies deserve mention for optimal methods. Nybo, Sainio, and Muller (2004)

TABLE 7.2. Measurement of Vocational Outcomes

Employment characteristic	Example variable
Presence of employment	Employed versus unemployed Control for local unemployment rates
Quality of performance	Supervisor ratings Direct observation Objective performance assessment Absences Job satisfaction Supported versus independent employment
Duration of employment	Frequency of job changes Part-time versus full-time
Relationship to predisease functioning	Loss of income Decline in job complexity

measured employment stability in pediatric TBI, with assessments conducted up to 40 years post-injury, one of the longest follow-up periods in the extant literature. Some other studies characterize outcomes as return to work either at premorbid levels or at a "modified" (i.e., reduced) level (Ruffolo, Friedland, Dawson, Colantonio, & Lindsay, 1999). An approach that considers the local circumstances to employment outcomes controls for unemployment rates within the region where patients live (Doctor et al., 2005). These authors devised a predicted employment rate based on current employment statistics and compared a brain-injury unemployment rate versus a predicted rate that accounted for demographic factors. One of the most detailed assessments of employment stability was conducted by Machamer and colleagues (Machamer, Temkin, Fraser, Doctor, & Dikmen, 2005), who assessed job stability 3–5 years post-TBI and defined job stability in several ways, including number of months worked full time, number of full-time jobs, and duration of uninterrupted full-time work. This study represents one of the more sophisticated assessments of job stability in the neuropsychological literature. Fraser, Machamer, Temkin, Dikmen, and Doctor (2006) applied the U.S. Department of Labor's "Reasoning Development" aspect, as well as the amount of preparation required for a job (measured by the Specific Vocational Preparation rating), to job titles in the *Dictionary of Occupational Titles* in a sample of TBI survivors. They observed that those who maintained the more complex jobs had, among other variables, better neuropsychology test scores. Their study also showed that even among those who returned to work, there was a significant decrease in job complexity after the injury. It is obvious that measurement of employment outcomes is complex, with some outcomes being more important in one clinical population versus another (e.g., reduction in hours in MS vs. employed vs. unemployed in TBI).

A final note should be made regarding self-report scales, of which there are a few. Examples include the Vocational Cognitive Rating Scale (Greig et al., 2004), which is an instrument designed to measure cognitive impairment in the workplace for people with chronic mental illness, and the Work Behavior Inventory (WBI; Bryson, Bell, Lysaker, & Zito, 1997), which is a measure of work performance as it relates to social skills, cooperativeness, work habits, work quality, and personal presentation. The validity of these measures probably varies with the degree of insight from each person. While self-report instruments are better than no employment measure, we recommend, when possible, getting objective data especially in clinical populations with cognitive impairment. As a case in point, Baughman, Basso, Sinclair, Combs, and Roper (2015) used the Sinclair Performance Inventory (Sinclair, Tucker, Cullen, & Wright, 2005), which has a parallel instrument for supervisor rating and employee self-rating. Patients who were classified as neurocognitively impaired overrated their work performance compared to supervisor ratings, demonstrating the need to account for sources of bias.

Models of the Relationship between Cognitive Abilities and Employment

Clinical Models

The major models of functional outcome (including employment outcome) in relation to brain dysfunction come from the TBI literature (Kendall & Terry, 1996; Ownsworth & McKenna, 2004). These models are comprehensive and rightly include all factors that impact outcome, of which cognitive abilities are just one. Other noncognitive contributors include premorbid factors such as pre-illness intellectual abilities, demographic factors, substance use history, premorbid employment history, available resources (e.g., socioeconomic status of the patient, social support), situational factors (e.g., status of the job market, the ability of a job to accommodate certain disabilities), and injury factors (e.g., physical impairment).

Kendall and Terry (1996) devised their model because they believed that most studies and clinical decisions assumed that in TBI, neurological factors (e.g., characteristics of the injury, cognitive impairment) explained psychological adjustment and well-being. These authors reviewed the literature on non-neurological factors that influenced adjustment post-TBI and found that multiple factors (e.g., pre-injury factors) can contribute to outcomes. The model has had significant influence on researchers and rehabilitation specialists because it formalized the role of non-neurological factors in determining outcome.

Ownsworth and McKenna (2004) proposed a model that focused on rehabilitation after brain injury, in which they highlight intrapersonal factors such as self-awareness and other metacognitive and emotional factors as they relate to successful rehabilitation. This model was developed based on a systematic review of the empirical literature. It was designed specifically to assess employment outcomes. Intrapersonal factors are among the targets of their rehabilitation approach, such as developing insight and compensation strategies. Other targets for rehabilitation are categorized as environmental factors, such as employer education and training.

With regard to direct empirical support for employment outcome models, Schonberger, Ponsford, Olver, Ponsford, and Wirtz (2011) used structural equation modeling employing clinical and self-report data from a sample of 949 TBI survivors. They found support for contributions to employment outcomes from the following factors: pre-injury (education, mental health, employment, age, sex), injury (posttraumatic amnesia [PTA], spine and limb injuries), and post-injury (mood, cognitive, behavioral changes).

Although the Kendall, Ownsworth, and Schonberger models were designed around TBI, the models are applicable to other etiologies of cognitive impairment as well. These models are neutral regarding what course the disability will take, except that they assume that rehabilitation can change the outcome. This issue is important because the prediction of disability is, of course, complex and multifactorial, considering such factors as premorbid characteristics, current resources, and emotional, behavioral, and environmental factors. The models assume a change in functioning due to a disease, which may not be applicable to psychiatric conditions such as schizophrenia, which develop in early adulthood often before a person has established independent functioning as an adult.

Nonclinical Theoretical Contributions

The field of industrial and organizational (I/O) psychology is oriented around rigor and methods of psychology, as applied to issues of critical relevance to business (and therefore employment functioning), including assessment. I/O psychology has well-developed theories about the assessment of individual abilities as related to workplace performance. Kuncel and Beatty (2013) reviewed the status of cognitive assessment from the I/O psychology perspective. In this nonclinical overview, assessment is broadly characterized in three categories. (1) Ability tests measure a person's behavioral repertoire at any one point in time. The source of the ability is not specified but is assumed to come from both innate capacities (e.g., genes) and acquired capacities (e.g., education). (2) Aptitude tests are ability tests designed to measure the potential to gain from maturation, education, or training. (3) Achievement tests measure the specific change associated with some sort of intervention, such as school or training. In theory, ability and aptitude tests would remain unchanged after a period of maturation or intervention, while achievement tests would improve. In practice, the three categories of tests are not independent and often have few differences. Furthermore, ability tests have a known factor structure, with an overarching factor of "general mental ability" or *g*. The concepts of fluid and crystallized intelligence have application in both I/O psychology and clinical neuropsychology. The I/O model of "investment" posits that fluid intelligence is necessary for the acquisition of crystallized intelligence. Clinical neuropsychology generally believes that fluid intelligence is most affected by neural injury. As applied to employment functioning, neurocognitive impairment reduces fluid intelligence and therefore reduces the capacity for work achievement. What we know from clinical neuropsychological research is that neurocognitive impairment also reduces specific abilities (therefore lowering *g*).

Prior Reviews of Neuropsychology and Employment Functioning

In one of the first manuscripts to focus on neuropsychological tests and employment outcome, Heaton and Pendleton (1981) reviewed neuropsychological predictors of everyday functioning, including employment functioning. In their review, they included studies of both normal and impaired populations and described several studies that established the well-accepted association between employment functioning and IQ. The general finding from all the studies of IQ is that unemployed people have lower IQ scores than employed people and that occupations considered to be of a higher or more challenging level are associated with higher IQ scores. A very important finding is that IQ is known to correlate approximately 0.5 with measures of employment performance, accounting for only 25% of the variance. Heaton and Pendleton also described the few then existing studies of neuropsychological test performance predicting employment functioning. They observed that in studies in which the Halstead–Reitan Battery was used, the average impairment rating was an independent and more powerful predictor of employment than IQ test scores. They also observed, as reported by Heaton, Chelune, and Lehman (1978), that the Minnesota Multiphasic Personality Inventory (MMPI) clinical scales are an additional independent predictor of employment status in a cross-sectional design. Thus, the predictive power of neuropsychological tests was demonstrated more than 40 years ago, but neither IQ nor neuropsychological test scores explain most of the variance in employment status or employment performance. In the light of I/O psychology data and theory, these early studies began to hint at the noncognitive emotional and personality factors that could contribute to predicting employment performance, especially in leadership positions in which emotional and personality characteristics may play a larger role in job performance (McHenry, Hough, Toquam, Hanson, & Ashworth, 1990).

Guilmette and Kastner (1996) reviewed the literature on neuropsychological tests and prediction of vocational functioning and provided 13 conclusions. Among their conclusions: The greater the degree of impairment, the less employable a person was; neuropsychological tests were better at predicting failure than success; neuropsychological tests should be supplemented with psychosocial/psychological tests to improve predictive validity; and future research would benefit from consistent neuropsychological batteries across studies and validation of brief batteries tailored to specific occupational groups. Importantly, these authors observed that because of the limitations of existing studies, the field of neuropsychology lacks consensus on the predictive power of neuropsychological tests on occupational outcome. As will be seen in the rest of this chapter, the problem of varying methods—especially the various ways that employment outcomes are operationalized—persist today. They concluded that neuropsychological assessment can predict vocational performance only modestly until further research provides grounds for stronger predictions.

Sherer and colleagues (2002) conducted a rigorous literature review that assessed 23 studies of the predictive power of neuropsychological tests in TBI by using guidelines established by Division 40 of the American Psychological Association for empirical support of neuropsychological practice (Heaton, Barth, Crosson, & Larrabee, 2002). The authors concluded that the best prediction of reemployment after TBI occurs when neuropsychological testing is performed soon after posttraumatic amnesia resolves. Moreover, they reported that regardless of when neuropsychological testing is performed relative to the injury, the continued presence (i.e., at the time of testing) of neuropsychological impairment is significantly associated with unemployment or decline in quality of employment relative to pre-injury status. In contrast, their review of studies in which neuropsychological testing was performed closer in time to the measurement of employment status (i.e., late in the recovery process or concurrent with measurement of employment status) did not provide clear evidence that neuropsychological testing is useful in predicting employment status. Although the latter studies contained methodological issues (e.g., small sample sizes, excessive number of statistical analyses, inadequate sample description) that possibly clouded interpretability of neuropsychological tests' predictive value, the authors raised the very important issue of the timing of neuropsychological assessment, with the weight of evidence suggesting that in TBI, the earlier neuropsychological testing is conducted, the more value it may have in predicting employment outcome. Since Sherer's 2002 meta-analysis, one study has cast doubt on the value of early neuropsychological evaluation. DiSanto and colleagues (2019), reviewed below, found that post-acute evaluations did not predict employment stability. It may be that the varying methodology and quality of studies explains the mixed findings with regard to the optimal time for a neuropsychological evaluation for employment prognosis.

Kalechstein, Newton, and van Gorp (2003) used a quantitative, analytical approach to reviewing the literature on the ability of neuropsychological tests to discriminate employed versus unemployed status across multiple patient populations (e.g., mixed neurological, epilepsy, TBI, HIV). Although their meta-analysis relied on a small number of studies, all seven studies demonstrated at least small effect sizes when employed versus unemployed patients were compared on neuropsychological test scores. The innovative approach of this meta-analysis is that the authors subdivided the neuropsychological tests from each of the studies into one of eight cognitive domains. Tests in every domain were able to discriminate employed from unemployed persons. The effect sizes were greatest (medium) for the domains of intellectual functioning, executive systems functioning, verbal learning and memory, and nonverbal learning and memory. The smallest effect size was observed for tests of language. The authors reviewed the numerous limitations of this kind of analysis, including the inability to account for job complexity, demographic factors, and so on. Nevertheless, this study made an important contribution in its finding that abilities in specific neuropsychological domains may be better at discriminating employment status than others.

The consideration of non-neuropsychological factors has probably received less attention than it should, as highlighted by Gorman, Foley, Ettenhofer, Hinkin, and van Gorp (2009). While their review focused on HIV-infected persons, the lessons can apply to most neurological populations. The authors discussed non-neuropsychological factors that are barriers to employment, including medical problems (nausea, diarrhea, etc.), social stigma, the role of disability payments, gender issues, and psychiatric issues (especially depression). Studies in HIV-infected persons show that the unemployment/inconsistent employment is associated with intellectual functioning, learning, memory, and executive functioning. Similarly, Von Ah and colleagues (2016) reviewed employment outcomes in breast cancer survivors and found that subjective cognitive symptoms were associated with generally poorer work outcomes, but that the studies using objective neuropsychological tests (n = 3) did not reveal a consistent relationship between neuropsychological scores and outcomes. Poor methodology in this literature limited the conclusions that could be drawn, but subjective cognitive complaints may be associated with non-neurological factors such as depression or other self-perception consequences after breast cancer treatment. Apathy, which does not always manifest as neuropsychological impairment but which is common in a number of neurological and psychiatric conditions, has been studied in at least two populations (Huntington's disease and schizophrenia) and has been found to be a significant predictor of unemployment, hours worked and work behavior problems (Bull et al., 2016; Jacobs, Hart, & Roos, 2018).

Empirical Studies of Neuropsychology and Employment Functioning

Seminal Studies of Neuropsychology and Employment Functioning

Ever since a historic study (Heaton et al., 1978) reported discriminant function analyses that neuropsychological test scores, in combination with MMPI scales, could classify employment status in greater than 80% of their mixed clinical sample, there has been an abundance of research on the association between neuropsychological test scores and employment, as can be seen from the reviews we have described. In this section, we review several studies that were not included in the published reviews to provide an updated summary of the state of the literature.

One of the largest studies came from the TBI Model Systems program. DiSanto and colleagues (2019) analyzed employment outcomes from the TBI Model Systems National Database in 5,683 persons with moderate and severe TBI. A subset of this sample (n = 1,204) had neuropsychological testing approximately 4 weeks after the injury, and the study evaluated predictors of employment stability (without comparing post- to pre-injury employment quality). Stability was defined as paid employment at years 1, 2, and 5 post-injury, with stable employment defined as paid employment at each of the three follow-up times. Even though simple analysis found that the stably employed had higher scores on the neuropsychological tests than the unemployed patients, the neuropsychological variables did not predict employment stability when other factors were included in the regression model (demographic, pre-injury, environmental, and TBI characteristics). This study underscores the complexity of recovery from TBI and the many factors that contribute to a positive employment outcome and forces us to consider that shared variance among neuropsychological test scores and the complex array of other factors may have contributed to outcomes. It is also possible that the assessment one-month post-injury, which is well before the expected plateau of neurocognitive recovery starting around 6 months, may not reflect the optimal time point when assessment is used to prognosticate employment outcome. This is in contrast to the evidence we discussed earlier in the Sherer meta-analysis.

Machamer and colleagues (2005) went beyond the simple prediction of return to work by observing the stability of employment after TBI in a sample of 165 consecutively admitted patients. As noted earlier, they measured employment stability as number of months worked full time, number of full-time jobs held, and maintenance of employment once returned to full-time work. When they categorized patients by percent of time worked during the follow-up period, they found that less time worked was associated with lower Glasgow Coma Scale (GCS) scores, longer time to follow commands post-injury, worse neuropsychological performance, and pre-injury job instability. The model that explained the most variance ($R^2 = .43$) in predicting percent of time worked during the follow-up period included the digit symbol test, pre-injury earnings, and pre-injury arrest record. Maintenance of employment was best predicted by Performance IQ score, arrest record, and pre-injury earnings. The same group (Doctor et al., 2005) presented a novel analysis of TBI employment outcome by comparing 1-year relative risk ratios for a TBI sample and a control sample on failure to return to work. As might be expected, having had a TBI presented more than a fourfold increase in unemployment risk compared to the general population, and lower test scores 1-month post-injury were significantly associated with greater risk for unemployment.

Careful selection of participants contributes to the ability of a study to draw conclusions about predictors of employment outcomes. Cattelani, Tanzi, Lombardi, and Mazzucchi (2002) demonstrated this in their study of patients with severe TBI. The group was selected to rule out premorbid confounding factors to future employment: all were employed or in school and had no predisposing conditions. They divided their eligible participants into demographically matched groups of reemployed and non-reemployed groups, and found that TBI characteristics, including combined posttraumatic amnesia (PTA) and coma duration, distinguished the two groups. They observed that worse early activities of daily living (ADL) problems were associated with lower likelihood of resumption of pre-injury employment. Wechsler Adult Intelligence Scale—Revised (WAIS-R) scores and that lower examiner ratings of neuropsychological abilities also predicted worse outcome. This design provides the best evidence that pre-injury characteristics do not explain all adverse employment outcomes.

While TBI is the most frequently studied population in this topic, several other populations have been studied and have provided empirical support for the predictive validity of neuropsychological testing for employment outcome. In a large sample of HIV-infected persons, where neurocognitive impairment starts more insidiously than TBI, Marquine et al. (2018) showed that the presence of neurocognitive impairment predicted unemployment even when controlling for numerous biomarkers, such as HIV, renal, liver, and other disease-related biomarkers based on the Veterans Aging Cohort Study or VACS Index (Justice et al., 2010). Evidence for the predictive validity of neuropsychological tests in a medical sample (kidney transplant) was presented by Gelb, Shapiro, and Thornton (2010). After kidney transplant, better neurocognitive performance on several measures was associated with working ≥ 20 hours/week employment even when controlling for depressive symptoms. In MS, Honan, Brown, and Batchelor (2015) showed that objectively measured cognitive abilities predicted both postdiagnosis employment status and change in number of hours worked, and test scores were better than self-reported complaints. Morrow and colleagues (2010) provide evidence that, in MS patients, a very small decline in neuropsychological test scores—2-point change in raw CVLT-2 total learning—can predict clinically significant employment decline—3.7 odds ratio for deterioration in employment status. While this finding needs replication, such precise predictive value can be extremely useful in the clinical and medicolegal context. McGurk and colleagues (2013) observed that, in people with schizotypal and paranoid personality disorders, a higher composite neuropsychological test score predicted current employment status, even when controlling for clinician-rated psychiatric symptoms. These studies present ample evidence across a variety of patient populations that neuropsychological test performance is, in general, a predictor of a variety of employment outcomes.

Some studies rely on self-reported cognitive functioning and provide support that subjective ratings also predict employment outcomes. For example, Ruet and colleagues (2019) investigated 8-year employment outcome in a sample of 85 severe TBI survivors. Unemployed persons reported more executive dysfunction in addition to numerous other neurological and functional complaints. Of course, self-reported symptoms usually represent more than true cognitive impairment.

Some studies have been conducted in which neuropsychological test scores do not predict employment outcomes. In an HIV-infected sample taken from volunteers in a vocational rehabilitation program (Chernoff, Martin, Schrock, & Huy, 2010), neuropsychological test scores did not effectively predict employment outcomes. These authors cautioned against the clinical utility of neuropsychological testing in predicting employment outcomes even when studies reveal statistical significance. This study is important because it sampled those most likely to seek services for return to work instead of the more common sample of clinical patients who tend to be more cognitively impaired. And, as might be expected, in *mild* TBI, neuropsychological tests are not associated with return to work, while postconcussive symptoms are (Nolin & Heroux, 2006; Waljas et al., 2014). These studies remind us that neuropsychologists must pay attention to the context of our evaluations and apply the most relevant evidence to our practice.

From these studies and from the summary of previous literature in the review articles we have summarized, it is clear that neuropsychological testing reliably predicts employment status and employment functioning (job stability, number of hours worked) but clearly does not explain all employment outcomes. Subjective complaints, pre-injury factors, other disease factors, and environmental factors all contribute to outcomes. Importantly, large-scale studies have found that neuropsychological tests did not predict employment outcomes, and one study cautioned against the clinical utility of neuropsychological testing. It is also possible that in some patient papulations for whom there is little measurable neuropsychological impairment (e.g., mild TBI), neuropsychological testing is not useful in predicting outcomes. We turn our attention now to the evidence for domain-specific predictive validity of neuropsychological tests.

Global and Summary Scores Are Consistent Predictors

One problem across studies of neuropsychological and employment outcome is the variability in the test batteries administered (Guilmette & Kastner, 1996). One solution is to use a summary score across the entire battery (like a mean *t*-score, global deficit score, or domain summary score) that can be used to predict outcome. The deficit score approach—in which scores at or above a threshold defining normal are not weighted, while those falling in the impaired range are weighted according to the magnitude of impairment—has received support from several studies. Research with HIV-infected adults (Carey et al., 2004) provides evidence that sufficient sensitivity and specificity can be achieved with a global deficit score (Heaton, Miller, Taylor, & Grant, 2004) even when batteries are composed of different tests. This research suggests that the use of summary scores may generalize across batteries and might be an approach to overcome some methodological variability across studies. In another example, Newnan, Heaton, and Lehman (1978) found that a cutoff score of 1.61 on the Russell Average Impairment Rating classified 78% of their subjects as employed or unemployed, with a positive predictive value of 81% and a negative predictive value of 70%. Mahmood and colleagues (2019) found that global deficit scores predicted not only the amount of time spent working but also wages. This study was conducted with unemployed patients with severe mental illness (schizophrenia, bipolar, major depression) who participated in a supported employment treatment program. This line of evidence supports the conclusion reached by Guilmette and Kastner (1996) that neuropsychological tests are better at predicting failure (i.e. by using summary scores emphasize impairment) than success. One possibility regarding this tendency is that tests' predictive strength is better for the more impaired patients, with the implication that brief screening in such populations may be as predictive as longer batteries.

Composite scores that include the full range of performance (as opposed to the deficit score approach) also have proven value in predicting employment outcomes. Gorske, Daley, Yenerall, and Morrow (2006) observed in a nonclinical, welfare-to-work sample that general intelligence as measured by the WAIS-R was the strongest correlate of self-reported work functioning, with a weaker correlation for attention and working memory measures and no significant correlation for drug use, general memory, executive functioning, or mental flexibility. It is noteworthy that a comprehensive regression including all the above variables accounted for less than 10% of the variance in the employment index. In a sample of 229 persons with bipolar I disorder, a summary score (average z-score) from eight neuropsychological test scores was significantly lower (Cohen's d = 0.58) in unemployed versus employed participants. Interestingly, two of the eight test scores did not differ between the groups: letter-number sequencing and Wisconsin Card Sorting Test perseverative errors. In this study, tests of executive functioning do not discriminate employment status, while the global score did. This underscores that summary scores may be a more reliable predictor of employment status than individual domains or test scores. Even a simple cognitive screening test such as the Montreal Cognitive Assessment [MoCA] has been shown to modestly predict return to work after stroke (van der Kemp et al., 2019). As noted earlier, the severity of impairment may affect the predictive validity, and fewer or shorter tests may suffice for adequate prediction of being employed.

As can be seen, substantial evidence exists that deficit scores that give weight to impaired scores as well as summary scores that capture the full range of performance

(IQ, average normative scores) consistently predict outcomes. The evidence for individual domains and tests is much more variable and is reviewed next.

Specific Neuropsychological Abilities That Predict Employment Outcome

There are some good reasons why neuropsychologists do not administer the same battery to every patient. First, a neurological problem may have unique neuropsychological ability deficits, and these disease-specific deficits may explain employment problems. For example, in TBI, memory and attention were significant predictors of employment outcome (Brooks, McKinlay, Symington, Beattie, & Campsie, 1987), whereas in intellectual disabilities, motor and vocabulary predicted better functional independence (Blackwell, Dial, Chan, & McCollum, 1985). In MS, unemployment is best predicted by verbal memory, numerical reasoning, and verbal fluency (Benedict et al., 2006; Fraser et al., 2009), whereas in HIV, verbal learning (California Verbal Learning Test, total trials 1–5) was the strongest predictor of return to work (van Gorp et al., 2019).

Second, psychosocial and behavioral factors such as those measured by the MMPI-2, Beck Depression Inventory (BDI), or the various frontal system questionnaires (Malloy & Grace, 2005; Wilson, Evans, Emslie, Alderman, & Burgess, 1998) can add to or even replace predictive validity of neuropsychological performance. Again, disease-specific factors may dictate the tools that provide the best predictive validity.

Third, the length of time to administer a long fixed battery is not practical in the current environment of limited reimbursement and higher clinical workload. Since our clinical practice is unlikely to see uniform test batteries, it is important to understand the predictive validities of specific domains and instruments when assessing employment concerns.

Executive Functions

Many neuropsychologists contend that executive functioning is the most important domain when considering complex behavior such as that required for employment. Studies of disorders in which executive functioning is a prominent deficit inform us about the importance of executive functions. In schizophrenia, the evidence is mixed regarding whether executive functioning is a primary predictor of work problems. McGurk, Mueser, Harvey, La Puglia, and Marder (2003) have reported that intact executive functioning and verbal learning predict more wages earned and more hours worked over a 2-year follow-up period. Over a 4-year follow-up period, total hours of competitive work and total wages earned during that period were best predicted by executive functioning, working memory, and speed of information processing. Other studies have partially replicated these results in other patient populations (Church, Seewald, Clark, Jak, & Twamley, 2019). When work performance *quality* is rated by an independent observer, verbal learning and delayed recall predict better performance 4 months later in a schizophrenia vocational rehabilitation sample (Evans et al., 2004). Interestingly, executive functioning (Wisconsin Card Sorting Test [WCST] and Trail Making Test Part B) was not associated with outcome in this study. Papathanasiou, Messinis, Zampakis, and Papathanasopoulos (2017) found that processing speed and memory, but not executive functioning, predicted unemployment in their sample of 30 progressive MS patients. Several studies have raised the possibility that executive functioning is not a core deficit or that the executive functioning domain is a complex construct better explained by core components such as learning or executive subcomponents such as complex problem solving (Morse, Schultheis, McKeever, & Leist, 2013).

Other studies provide supportive evidence for the role of executive functions in predicting employment functioning, although often in combination with other cognitive domains (Gorman et al., 2009; Weber et al., 2012). Van Gorp and colleagues (2019) found that those who experienced deterioration in employment status over a 2-year period (27 of the 124 participants reported subsequent unemployment or reduced work hours) had lower executive functioning scores at baseline (from the Minimal Assessment of Cognitive Functioning in MS). When controlling for other baseline differences between the groups, executive functioning remained a significant predictor of employment deterioration (as well as physical disability) controlling for attention and self-reported depression/fatigue/cognitive complaints.

We must recognize the complexity of the domain of executive functioning and acknowledge the many tests used to assess this domain. The above studies used various tests to measure executive functioning, and although this domain remains a centerpiece of neuropsychological assessment and conceptual thinking, it may be too heterogeneous to yield an empirical basis for the broad construct of executive functioning to predict employment outcome.

Memory

Unlike the complex array of executive functions, memory is a more straightforward ability that is relatively easy to measure in clinical practice. Many studies have found memory abilities to significantly predict employment functioning (Abi-Saab, Fiszdon, Bryson, & Bell, 2005; Mackin, Horner, Harvey, & Stevens, 2005; van Gorp et al., 2007), but see Church et al. (2019). Abi-Saab and colleagues (2005) used the cortical/subcortical memory profile to determine whether specific types of memory deficits predicted outcomes in their work rehabilitation study. They found that the normal and subcortical profiles benefited most from rehabilitation in that these groups increased their work hours more than the cortical group. However, the "cortical" group's memory profile seemed to be more impaired overall, with significantly worse recognition memory in addition to impaired recall. Memory is also a predictor of employment outcomes in persons with substance abuse problems (Mackin et al., 2005; Weber et al., 2012), HIV infection (van Gorp et al., 2007), and TBI (Novack, Bush, Meythaler, & Canupp, 2001). In most of these studies, memory was not the sole predictor of employment outcome; other domains such as executive functioning, working memory, or visuospatial also predicted employment outcomes. Indeed, Giugiario et al. (2012) found that psychopathology mediated the relationship between verbal memory and employment outcomes. In first-episode psychosis, Karambelas, Cotton, Farhall, Killackey, and Allott (2019) found that neuropsychological test scores did not predict employment status 18 months later when controlling for age, gender, premorbid IQ, negative symptoms, participation in an employment treatment program, and baseline employment status, although higher scores on verbal memory did (weakly) predict more hours worked for the sample (semipartial $r = .17$). Similarly, neurocognitive summary score did not predict employment status in a sample of 143 persons infected with HIV in a regression that controlled for a novel executive test (modified

Tower of London, which correlated only modestly with the neuropsychological test scores), while AIDS status and the novel executive test did predict unemployment (Cattie et al., 2012).

As with the review of executive functioning above, memory does not appear to be a unique predictor of employment outcomes. However, there seems to be evidence across a number of clinical populations that memory may be the more consistent predictor of employment functioning than executive functions.

When the body of research on specific neurocognitive domains is considered as a whole, no single domain can be considered the "best predictor" of employment outcomes, even in diseases where one domain is the primary deficit, such as executive functioning in schizophrenia. This partially explains why studies that use global scores of cognitive functioning consistently find global scores as significant predictors of employment outcomes. The inherent higher reliability of summary scores (versus the usually lower reliability of their individual component scores) may explain the more consistent findings that summary scores better predict employment outcomes.

Performance-Based Assessment of Employment Functioning

If there is such variability in neuropsychological tests as predictors of work functioning, why not develop a set of performance-based measures of work functioning that directly measure the abilities important for various jobs? As described at the beginning of this chapter, there are many performance-based assessments for career planning, applicant screening, and job placement purposes used primarily by persons involved in employment and career planning outside a clinical context, but there are few performance-based assessments of employment functioning specifically designed for rehabilitation of clinical populations. The Behavioral Assessment of Vocational Skills (Butler, Anderson, Furst, Namerow, & Satz, 1989) is one such test, and it consists of a standardized measurement of a person's ability to assemble a wheelbarrow using printed instructions. Trained examiners rate patients on their ability to follow directions, maintain their attention, and tolerate frustration, as well as on several other variables in the face of preplanned interruptions and criticisms by the examiner. In their sample of 20 participants with brain injury, this test predicted ratings of employment performance during a 3-month trial work placement, independent of neuropsychological test scores. There have been no studies of this instrument since this initial publication, perhaps reflecting limited interest in a test with such limited content validity. Commercially developed employment assessment instruments have been studied in persons with HIV infection (Heaton et al., 1994, 2004). The instrument, called the COMPASS (Valpar International Corporation, Tucson, AZ) purports to assess work skills, although in reality it is weighted toward general cognitive and motor skills (e.g., reasoning, arithmetic, language comprehension, immediate memory) that are then scored along dimensions deemed important work-related skills and abilities by the *Dictionary of Occupational Titles* (1991). While this performance-based battery is correlated with neuropsychological test performance, there is little data to support the idea that it is empirically better than neuropsychological tests in predicting employment outcomes. One can also use expert ratings of actual or simulated job performance (LeBlanc, Hayden, & Paulman, 2000). Consistent with other research, such ratings have been associated with global scores (e.g., WAIS-R) but less consistently with individual domains or tests. Leblanc and colleagues reported correlations between specific job performance ratings and specific neuropsychological tests, but the rater was not blind to test performance, indicating that the findings need replication with blind raters.

In summary, there is little research in clinical populations on performance-based testing that was designed to assess work-related abilities. Because "employment functioning" encompasses such a broad domain that includes physical as well as cognitive abilities, and because it is impossible to design a single test or series of tests to measure the myriad complex work skills required in today's occupations, it is not surprising that research in this area is scant. It is also not surprising, given the complexity of measuring employment outcomes, that little is known about the cut points or thresholds at which performance on a test predicts success or failure in work functioning.

Fitness for Duty Evaluations

Because this chapter is devoted specifically to neuropsychology and neurocognitive domains, we will not undertake a review of the broader issue of fitness for duty evaluations. However, a few issues specific to neuropsychology deserve mention here. First, some evaluations are mandated by regulatory bodies that include neuropsychological tests, such as the Federal Aviation Administration's specifications for aviation psychological evaluations (FAA, 2020). Second, it is not uncommon for neuropsychologists to be asked to give an opinion about fitness for duty for professionals whose work affects public safety, such as doctors and nurses (Pitkanen, Hurn, & Kopelman, 2008; Polles, Williams, Phalin, Teitelbaum, & Merlo, 2020), military personnel(Kelly, Mulligan, & Monahan, 2010), astronauts (Kane, Short, Sipes, & Flynn, 2005), and even other psychologists, especially when a brain disease is present and could impair neurocognitive abilities. Of course, the above discussion of empirical evidence for neuropsychological data in predicting work performance applies just as well to fitness for duty evaluations, although additional expertise is needed about rights of workers with disabilities, human resources policies, and any laws that apply to impaired professionals.

Remediation of Cognitive Deficits to Improve Employment Functioning

Many excellent books and reviews are available on rehabilitation of cognitive deficits with the goal of employment (Johnstone & Stonnington, 2009; Noggle, Dean, & Barisa, 2013; Tyerman & King, 2008). Approaches to vocational rehabilitation vary widely and depend on the nature of the disease (Noggle et al., 2013). Interventions that can apply across patient populations include supported work in which a job coach or vocational rehabilitation specialist provides regular support as the person returns to work, pharmacotherapy for treatment of problematic symptoms, and cognitive remediation.

Cognitive remediation has received support as an effective treatment in helping patients return to work. McGurk and colleagues (2016) succinctly characterized studied treatments as "drill-and-practice" exercises and other more problem-solving approaches (coaching, self-management, etc.). Programs such as Neurocognitive Enhancement Therapy (NET; Bell, Bryson, Greig, Fiszdon, & Wexler, 2005), Thinking Skills for Work (TSW; McGurk, Mueser, DeRosa, & Wolfe, 2009), and Cognitive Symptom Management and Rehabilitation Therapy (CogSMART; Twamley, Vella, Burton, Heaton, & Jeste, 2012) have all been studied as treatments to improve vocational functioning. Most of these treatments have produced measurable benefit, though some of them have shown larger effect sizes (NET, TSW) than others (CogSMART). Tan (2009) proposed some creative approaches in applying neuropsychological findings to vocational rehabilitation in schizophrenia, such as exploiting errorless learning in this patient group that has largely intact procedural memory but impaired episodic memory. Fraser, Strand, Johnson, and Johnson (2012) provided a helpful guide for the application of neuropsychological evaluations in vocational rehabilitation, although the study's reliance on the cognitive strengths and weaknesses in the neuropsychological profile does not yet have a solid evidence base, especially given the complexities of vocational rehabilitation goals (e.g., whether employment is feasible for an individual, whether the individual should return to previous employment or seek a different vocation, whether a job coach or other support is needed).

Technological solutions in the rehabilitation of cognitive impairment have long been a topic of discussion (Lynch, 2002) but have led to few empirical studies. Several attempts have been made to devise computerized cognitive retraining treatment, but only a few studies have found them to generalize beyond improvement in the computer task itself (Lundqvist, Grundstrom, Samuelsson, & Ronnberg, 2010). The meta-analysis by Chan, Hirai, and Tsoi (2015) of computer-assisted cognitive rehabilitation (in which computerized training is part of a broader rehabilitation strategy, including other interpersonal therapy such as groups or supported employment) found significant gains in employment outcomes. However, this review did not isolate the computer training as a primary mechanism for change. Indeed, there is still a paucity of studies that support computer training as an effective mechanism of action to improve employment outcomes. However, a growing number of studies of computer-assisted rehabilitation show some generalization of skills (Matsuoka et al., 2019), and we look forward to future studies that will shed light on whether computerized cognitive rehabilitation can enhance employability.

Technology has more commonly been used in the role of a "cognitive prosthetic." By now most clinicians have witnessed (and probably themselves adopted) the use of mobile devices (phones, tablet computers) equipped with reminder software to overcome memory and planning deficits. In 2015, we saw the publication of an entire volume devoted to the use of assistive technology in cognitive rehabilitation (O'Neill & Gillespie, 2015). This book reviewed existing technology as well as the promising future for compensation for memory, attention, affect, visuospatial and executive functions, and language. A key principle regarding technological devices (and any external cognitive prosthetic) is the notion of "scaffolding," or providing some external structure to assist or even replace the damaged cognitive ability.

Recommendations for Clinicians

Neuropsychologists will need to go beyond identification of deficits and venture into recommendations that can directly apply to a patient's vocational rehabilitation. This effort represents a challenge when there is scant empirical support for neuropsychological profiles—especially the lack of data about the clinical usefulness of the strength/weakness classical profile interpretation (Barisa & Barisa, 2001). Perhaps the most useful starting place is consideration of treatment goals in the context of objectively measured abilities. West (1995) observed that "[j]ob retention is enhanced by assisting individuals to find jobs that are worth keeping" (p. 310). Based on the review in the present chapter, the following suggestions are made for clinical application of neuropsychological assessment for employment treatment planning:

1. Always first consider the purpose of the evaluation. Is the question about whether a person should return to work? Type of job? Full-time or part-time? Then tailor the battery to the referral question.
2. Global/summary scores are the most reliable predictors of employment functioning, and batteries should be designed to yield such scores when employment is part of the referral question.
3. Be careful not to overinterpret performance in specific domains or on individual tests for treatment planning and prognostication, since there is inconsistent evidence about domain and test predictive validity.
4. Base your recommendations in the context of the required abilities, with Department of Labor abilities and individual job descriptions as a guide.
5. Use knowledge of disease characteristics to guide recommendations, including disease course and typical cognitive deficits for the diagnosis.
6. Apply existing models of employment outcome to guide conceptualization and recommendations. Most importantly, consider premorbid work functioning as a sort of "upper limit" on likely employment outcomes after brain injury or disease.
7. Base treatment recommendations on empirically supported treatments.
8. If a vocational rehabilitation specialist is involved, communicate with that provider to create the most useful, person-specific recommendations.

Focus of Future Research to Improve Predictive Validity

On one hand, this review of the neuropsychological factors that predict employment functioning reveals a pattern of research that is largely disease-based. The fields of I/O psychology, social psychology, and human factors research, on the other hand, contain theoretical models that can provide new perspectives that may help clinical researchers focus their questions. If neuropsychological research is ever to advance theoretically beyond the "disease and domain" doldrums, we could draw from the I/O theoretical models such as the three-factor model of intellectual abilities (verbal, perceptual, and image rotation; Johnson & Bouchard, 2005); or more complex models that include broad cognitive measures like IQ as well as educational attainment, individual personality characteristics, and social influences; or even the possible primary role of working memory capacity in intelligence (Ackerman, Beier, & Boyle, 2005).

From the practical side of neuropsychological/vocation research, several future directions can be drawn from this review. First, the empirical basis of our practice will be improved when studies go beyond simple statistical group difference and utilize predictive and classification statistics such as discriminant function, odds ratios, and positive and negative predictive values. Future studies could be held to a standard requiring such classification statistics, which, while idealistic, would require investigators, funding agencies, and peer reviewers to regularly implement classification methods in these studies. The utility of neuropsychological evaluations in predicting employment outcomes would then have a strong empirical basis and justify the role of neuropsychological assessment in many different treatment settings. Furthermore, controlling for disease-specific variables (e.g., PTA and loss of consciousness in TBI, AIDS status in HIV, or lesion location and volume in stroke) and demographic/premorbid variables will allow us to have a strong foundation for the predictive validity of our test scores.

Second, the often-stated claim that neuropsychological profiles can provide a "map" of cognitive strengths and weaknesses that can then guide rehabilitation is a largely unsubstantiated claim, even if it is ultimately proven to be true. Although the studies reviewed here have found associations between baseline cognitive abilities and later employment outcomes, no studies to our knowledge have assessed whether individualized treatment plans based on neuropsychological profiles improve employment outcomes. While such research is methodologically difficult, requiring quantifying neuropsychological profiles in large samples and then predicting outcomes, this research is necessary to have an empirically based practice for the application of individual profile interpretation to individual employment outcomes.

A third focus of future research is for researchers to use the same measures of employment outcome across studies. One option is the development of task-independent standardized rating scales that would formally rate work behaviors that are directly observed. This will improve the quality of data for employment outcome end points. The first step in this direction has been developed by LeBlanc and colleagues (2000) and is called a "situational vocational evaluation" (SEval). In its current form, as described above, a certified vocational evaluator has the subject perform simulated work activities and then rates his or her performance on 16 indices in one of three general categories (visual processing, memory, and executive functioning). The main problems requiring further research with this approach include developing standardized rating criteria that would result in sufficient interrater reliability and ensuring that all relative domains were assessed. If such a generalized rating system could be developed, then the clinician would have a standard instrument (much like the Functional Independence Measure [FIM] that is widely used in physical and occupational therapy outcome studies) that could be applied regardless of the specific vocation. A related recommendation is that studies should attempt to obtain data from the employer or supervisor, also circumventing inaccuracies related to self-report.

A fourth recommendation is that studies use more consistent methods. A primary problem in this field of research is not the lack of empirical data (as seen above, there are many studies in many patient populations) but the fact that the methods are so variable that it is difficult to make recommendations for evidence-based practice when the studies do not reflect clinical practice. Especially regarding the breadth of the test batteries, omission of important domains such as verbal memory, processing speed, or executive functioning allows one to conclude that some tests are only sensitive, while specificity remains undetermined. To conduct a study of neuropsychological predictors of employment, one should include the primary domains of attention, verbal and spatial memory, processing speed, executive functioning, and visuospatial functioning. This will increase the generalizability of the study.

This review supports many of the conclusions made by Sbordone (2001), including the following: (1) Individual predictions of employment abilities need to be weighted by the fact that no neuropsychological test score can accurately predict employment performance and that neuropsychological testing as a predictor of employment ability should be interpreted with caution since the procedure is not an actual measure of employment performance and since the testing situation is rarely similar to the actual employment environment; and (2) many factors other than neuropsychological test scores need to be considered when predicting employment abilities, such as pre-injury work performance and job stability, past or current substance abuse, psychological disorders and stressors, and any medical, neurological, or developmental disorders. The more these issues can be addressed with an empirical approach, the less guesswork will be required, and the less uncertainty will result from neuropsychological assessment and treatment of individuals with acquired brain disorders.

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CHAPTER 8

Medication Management

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Medication adherence is broadly defined as the accurate use of medication as prescribed and refers to proper administration of medicine in the correct dosage, at the appropriate time, at the prescribed frequency, and in accordance with any special instructions (Kröger et al., 2017). Proper medication adherence can prevent or delay the deleterious effects of many chronic illnesses and is generally associated with improved health over a longer period of time. For example, it has been demonstrated that consistent antihypertensive therapy is associated with a 35–40% lower incidence of stroke, a 20–25% reduction in myocardial infarction, and a more than 50% reduction in heart failure (Neal, MacMahon, & Chapman, 2000). Despite the many benefits associated with adequate medication adherence, existing literature suggests that compliance with medication regimens is at best moderate and tends to decline over time in almost all chronic conditions (Dunbar-Jacob, 2002; Krousel-Wood et al., 2011). In fact, despite the critical impact of medication adherence, rates of compliance are lower than 50% in most studies (for review, see Dunbar-Jacob et al., 2000; Haynes, McDonald, Garg, & Montague, 2003).

Inadequate compliance with medication regimens has been shown to be associated with a host of untoward consequences, including declines in overall health and increased risk of hospitalization (Ascher-Svanum et al., 2006; Ho et al., 2008), increased morbidity and mortality (Conn & Ruppar, 2017; Faught, Duh, Weiner, Guerin, & Cunnington, 2008; Rasmussen, Chong, & Alter, 2007), and higher health care costs (Gilmer et al., 2004; Kane & Shaya, 2008; Perreault et al., 2012; Sokol, McGuigan, Verbrugge, & Epstein, 2005). It has been estimated that medication nonadherence alone may have a direct economic cost of at least $100 billion annually (Aitken & Valkova, 2013).

Research on medication adherence has expanded greatly over the past 20 years. Early work demonstrated that nonadherence is a complex, multidimensional problem. Previous studies have found poor medication adherence to be associated with a host of factors, including neurocognitive dysfunction, insight and judgment, alcohol and drug use, psychiatric disturbance, the class of prescribed medication, regimen complexity, drug efficacy, the route of administration, occurrence of negative side effects, type and chronicity of disease/illness, human factors (e.g., packaging and labeling of medication bottles, grade level at which health-related materials are written), physician interaction and communication style, financial resources, level of daily activity, degree of social isolation, family support, beliefs and attitudes regarding one's health, and level of health literacy. Whereas the majority of early studies focused on single constructs as possible determinants of poor adherence, subsequent investigations have incorporated broader, multifactorial models of medication-taking behavior. Recent studies have also focused on novel technological advances in the measurement of adherence, as well as specific factors and interventions that could help to improve medication-taking behavior.

This chapter presents a broad overview of current knowledge regarding the complex nature of adherence to medication regimens and those factors most clearly associated with individuals' medication-taking behavior. In doing so, we begin with a critical review of medication adherence methodologies and measurement techniques, including clinician ratings, self-report measures, pill counts, pharmacy records, electronic monitoring, physiological measurements such as blood tests, and laboratory-based analog measures. An examination of medication adherence behaviors in select neurocognitive disorders then follows, with special attention paid to research conducted in the areas of normal aging, dementia, HIV/AIDS, and psychiatric illness. These disorders were chosen because they represent well the varied literature in the field and illustrate many of the common problems associated with medication nonadherence in those with impaired cognitive abilities. Also included is a brief review of the major psychosocial models that have been used to explain adherence behavior, including theories related to autonomy and self-efficacy, treatment expectancies, the health beliefs model, the theory of reasoned action, and social action theory. The chapter concludes with an evaluation of various medication management interventions, discussion of future directions in medication adherence research, and recommendations for clinicians.

Lest the reader underestimate the personal and public health impact of these issues, and instead view medication adherence and compliance with provider/public health directives as only applicable to our patients, and not to one and all, and before delving into the wider issues introduced above, a brief discussion of two topics of inestimable current import is not only timely but of enduring import. Adherence to physician instructions and, on a broader level, adherence to public health directives are at the very core of medication adherence. As we write this chapter, the world is in the throes of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2; better known as COVID-19) pandemic, which is superimposed on an emerging wider awareness of the long-standing existence of structural, systemic racism that includes health disparities affecting medication access/adherence among its innumerable ills. In the United States millions of individuals are not adhering to physician/public health directives with regard to protective actions that can reduce the risk of viral transmission. Studies have already begun to emerge on this topic. An Internet-based survey study of 8,317 adults drawn from 70 countries examined COVID-19 compliance from the perspective of the Heath Beliefs model (Clark et al., 2020). They found that *perceived efficacy* of the following guidelines regarding distancing and mask use predicted better compliance, whereas *perceived risk* of contracting COVID-19, or *perceived severity* of the virus, was unrelated to whether individuals hewed to protective guidelines. In other words, whether or not a person feels personally at risk for COVID-19, if they don't think masks or distancing works, then why bother? Does the same thought process apply to medications/preventive actions for other diseases?

Park, Russell, et al. (2020) surveyed 1,015 adults and found that adherence levels varied based on the protective action in question. Whereas 95% of participants avoided going to bars and 87% attempted to maintain social distancing, only 50% complied with instructions to wear a mask in public. In general, they found men and younger adults were less adherent, whereas older age and financial security were predictive of better adherence. The United States has also seen that adherence to COVID-19 public health directives can greatly differ as a function of political affiliation. Additional study of this peculiarity is clearly needed, especially if it begins to extend to other aspects of medical compliance in other diseases.

The work of Shiau, Krause, Valera, Swaminathan, and Halkitis (2020) on the nexus of COVID-19, HIV, and structural racism on medication adherence provides a compelling lens through which to view the impact of three scourges affecting the United States and the world. They employ the term *syndemic* to capture the effects of two or more epidemics interacting synergistically. For example, they point out that a disproportionate number of ethnic minorities are among the ranks of the HIV-infected populace as well as those who have been infected with COVID-19. Health disparities affecting minority populations have resulted in higher rates of comorbid disease (a risk factor for more severe COVID-19 illness) and differential access to health care. One cannot adhere to a health care provider's advice if barriers prevent receiving that advice in the first place.

The need to shelter in place, avoid mass transit, and reduce in-person clinic visits due to COVID-19 can also be expected to impact medication adherence to other diseases. Treatment interruptions due to an inability to see one's provider or fill a prescription may have negligible effects for some conditions but can pose dire consequences for others, such as people with HIV who can rather quickly develop medication-resistant viral mutations. Work conducted by Halkitis and colleagues in the aftermath of the 9/11 crisis found that medication adherence levels significantly declined among persons living with HIV (Halkitis, Kutnick, Rosof, Slater, & Parsons, 2003). Halkitis and colleagues rightly fear that history is again repeating itself and that similar mistakes are now being made in addressing COVID-19.

Adherence Methodologies and Measurement Techniques

A number of techniques have been used to measure medication adherence, all of which are characterized by unique strengths and weaknesses. These techniques provide objective measures, such as plasma drug levels and electronic measuring devices; subjective information, such as patient self-report or clinician ratings; and indirect measures, such as pharmacy refill records and clinic appointment attendance.

Biological Markers

Blood levels provide precise quantification of adherence to medications with a long half-life. For example, blood tests are an excellent means by which to ascertain lithium levels and, by extension, to determine whether patients with bipolar disorder are taking their lithium carbonate as prescribed. In contrast, blood tests are not as useful for evaluating adherence rates to medications that are rapidly metabolized. In such cases, blood levels can detect whether patients have recently taken their medication but cannot assist in determining whether patients typically take their medication as prescribed. In other cases, blood tests/assays for specific drugs do not exist, can be cost prohibitive, or cutoffs regarding what levels constitute adherence versus nonadherence may not be adequately defined.

Metabolic tracers offer a promising approach to address these challenges. An inert substance easily detected and measured in urine, saliva, or blood is compounded with an active drug (or placebo in the case of clinical trials) and used to quantify adherence. Ideal tracers are safe and inactive, and have a half-life consistent with the dosing schedule of the prescription medication. Examples of tracers used with some success in past studies include riboflavin (Herron et al., 2013) and quinine (Babalonis, Hampson, Lofwall, Nuzzo, & Walsh, 2015). Babalonis and colleagues have demonstrated, for example, that low-dose quinine can be successfully used to track patient adherence to oxycodone. The authors suggest the inert substance may be a good candidate for further development as a medication tracer, as it is cost effective and easily detected in both blood and urine using standard laboratory procedures; demonstrates a suitable half-life of about 10 hours in blood and 16 hours in urine; is unlikely to interact with active drug; and is seemingly safe and well tolerated.

Pill Counts

Pill counting is another technique that has been used to measure adherence rates. The technique is relatively straightforward. If one knows how many pills a patient initially possessed and how many pills should have been ingested in the intervening time period, it is easy to calculate the number of pills that should remain at the end of the study period. Excess doses are considered to reflect doses not taken as prescribed. For example, consider a patient on a 3 pills/day regimen who begins with 100 pills and returns to clinic 30 days later. If 10 pills remain, this would be interpreted as perfect adherence (100 – (30 × 3) = 10). While this system is easy for the researcher/clinician to calculate, a decided drawback is that it is easy for patients to calculate as well. Accordingly, prior to their return to clinic, patients may remove extra doses from their pill bottle and thus appear more adherent than they actually are.

An innovative approach to overcome this limitation was introduced by David Bangsberg and colleagues at the University of California San Francisco (UCSF; Bangsberg, Hecht, Charlebois, Chesney, & Moss, 2001). They conducted "unannounced pill counts," appearing at the residences of HIV+ study participants without warning. They found this approach to correlate well with biological outcomes (e.g., HIV viral load, or the amount of virus circulating in the blood). Although this methodology may work well in a dense urban community such as San Francisco or New York City, it may be excessively cumbersome and resource intensive in a sparsely populated rural setting or a sprawling metropolis. A compromise may be unannounced telephone-based pill counts in which participants are asked to quickly count their pills. This process, which is increasingly practiced, minimizes the reporter's ability to quickly calculate the "correct" number of pills.

Self-Report

Self-report is another widely used methodology. The strengths of this method include its negligible cost and ease of data collection. Conversely, a significant weakness of self-report measures is that, for a multitude of reasons, many patients may overstate their actual adherence rates (Garber, Nau, Erickson, Aikens, & Lawrence, 2004). For example, studies of HIV-infected adults have revealed that patient self-report, relative to electronic monitoring techniques, tends to be accurate among patients who candidly admit to poor adherence but may overestimate actual adherence rates by approximately 10–20% among the large subset of patients who claims perfect or near-perfect adherence (Arnsten et al., 2001; Levine et al., 2005).

Pharmacy Refill Records

Pharmacy refill records have also proven to be a cost-effective proxy for direct measurement of medication adherence. This technique rests on the assumption that if patients are refilling their medication prescriptions in a timely fashion, they are more likely to be taking their medication as prescribed as compared to individuals who are late in refilling their prescriptions. This approach works best in settings where pharmacy records are centralized and can be easily obtained (e.g., Veterans Administration Medical Centers). The most obvious limitation of this adherence tracking method is that pharmacy records cannot reveal when dosing errors have occurred or the precise time at which a patient may discontinue treatment (Halpern et al., 2006).

Electronic Measuring Devices

The fallibility of self-report may be particularly salient when dealing with individuals who are cognitively impaired. Individuals with a dementing disorder may encounter considerable difficulty remembering whether or not they took their medication as prescribed. This inability is particularly pronounced when self-reported adherence is queried for more distal time periods. For this reason, the utilization of electronic monitoring devices (e.g., Medication Event Monitoring System [MEMS], Aprex Corp, Union City, California; Wisepill device, Wisepill Technologies, Somerset West, South Africa) may better estimate actual adherence. MEMS embeds a computer chip in the cap of a pill bottle that automatically records the date, time, and duration of pill-bottle opening. The drawbacks of this method include the bulky nature of the MEMS cap bottle, which precludes inconspicuous transportation of one's medications. This can lead to pocket-dosing behavior in which patients remove an extra dose from their pill bottle to consume at a later time rather than carry their pill bottle with them. Wisepill is an electronic pillbox that sends a cellular signal to a web-based server upon opening. An individual's adherence can be monitored in real time, and an intervention can be triggered (e.g., patient contact via phone, text message, etc.) in the event a compartment is not opened at the prescribed time. Initial investigation suggests this type of technology is easy for patients to use and may eventually be a relatively low-cost method for monitoring and promoting adherence (Pellowski et al., 2014). Although electronic monitoring devices are not a perfect measure of medication compliance, numerous studies show they may be more accurate than pill counts or self-report (Daniels et al., 2011; McClintock, BeKampis, Hartmann, & Bogner, 2020).

As the technology embedded within electronic monitoring devices becomes smaller, less intrusive, and more affordable, alternative approaches to track adherence will increasingly be available to both researchers and consumers. For example, several companies are combining wearable technology with ingestible sensors to monitor and confirm the exact date and time of pill dosing. An early prototype developed by Proteus Digital Health, Inc. uses a small patch attached to the body to detect ingestion of a tiny 1 mm by 1 mm sensor that can be affixed to most oral medication. In an initial study by Belknap et al. (2013), the device correctly identified the presence of ingestible sensors with 100% accuracy across more than 1,000 ingestion events. Subsequent investigations suggest the system is well accepted, highly accurate, has the potential to confirm adherence on a dose-by-dose level, and poses low risk to users (Lui et al., 2020; Bonacini et al., 2020). Similar ingestible sensors have since been used successfully to measure adherence to a wide variety of drugs, including statin and antihypertensive agents (Thompson et al., 2017), diabetic treatments (Browne, Behzadi, & Littlewort, 2015), and medications prescribed following organ transplant (Eisenberger et al., 2013).

Performance-Based Laboratory Measures

In addition to attempts to assess real-world medication adherence, several investigators have created laboratory-based measures thought to reflect individuals' ability to adhere to medical recommendations (Albert et al., 1999; Gurland, Cross, Chen, & Wilder, 1994; Heaton et al., 2004; Patterson et al., 2002). Work by these groups has found that, as expected, cognitive disorder is associated with poorer performance on these analog tests of medication management.

To better characterize possible medication management problems faced by individuals suffering from schizophrenia, Patterson and colleagues modified an existing measure to better mimic interactions between patients and prescribing physicians (Medication Management Ability Assessment [MMAA]; Patterson et al., 2002). Performance on the MMAA has been associated with memory and executive abilities of participants with schizophrenia (Jeste et al., 2003; Patterson et al., 2002). Interestingly, the MMAA has also been studied in relationship to a virtual reality (VR) task designed to simulate the medication-taking environment (Baker, Kurtz, & Astur, 2006). Like the MMAA, the experimental VR task correlated with memory and executive functioning, but it also showed a significant relationship with sustained attention. Finally, direct observation has also been used (e.g., in tuberculosis programs), but it is prohibitively expensive in all but select cases.

Review of Medication Adherence in Select Neurocognitive Disorders

Normal Aging

Older adults experience more chronic illness and consume more medications than any other age group (see Ball et al., Chapter 10, this volume; Catlin, Cowan, Hartman, Hefler, & NHEAT, 2008; Huang et al., 2002; Williams & Kim, 2005). Over 87% of older adults regularly take some form of medication and 29–39% use at least five prescription medications concurrently (Charlesworth, Smit, Lee, Alradhan, & Odden, 2015; Qato, Wilder, Schumm, Gillet, & Alexander, 2016). The number of drugs taken increases when patients become institutionalized or enter residential care. Between 67 and 80% of non-institutionalized ambulatory older adults may receive drugs but, in nursing homes, the consumption rate can be as high as 97% (Ray, Federspiel, & Schaffner, 1980). Unfortunately, considerably higher rates of noncompliance have been reported among older patients. Estimates have ranged from 26% to as high as 75% (Iuga & McGuire, 2014; Ostrum, Hammarlund, Christensen, Plein, & Kethley, 1985; van Eijken, Tsang, Wensing, de Smet, & Grol, 2003; Yazdanpanah, Saleh Moghadam, Maxlom, Haji Ali Beigloo, & Hohajer, 2019), and adherence seems to be particularly problematic for commonly prescribed agents such as those used to control hypertension, hyperlipidemia, and arthritis. As many as 10% of older adults take drugs prescribed for other people, and more than 20% may take medications not currently prescribed and commit drug administration errors that could have serious clinical consequences (Lamy, Salzman, & Nevis-Olesen, 1992). Similarly, inappropriate drug discontinuation or restriction may occur up to 43% of the time in this population (Jackson, Ramsdell, Renvall, Smart, & Ward, 1984; Steinman, Sands, & Covinsky, 2001; Wimmer et al., 2017).

Older adults can experience age-related declines in the cognitive processes necessary for successful medication adherence (Raz, 2000) and therefore may be at higher risk for neglecting to take medications as prescribed. One of the most prominent causes of non-adherence in this group is forgetfulness related to medication administration (Campbell et al., 2012). In an early adherence study among older adults, Col, Fanale, and Kronholm (1990) reported that poor recall had a seven-fold stronger relationship to treatment nonadherence than did any other predictor. Memory failure leading to poor medication adherence likely takes two forms. As elaborated by Morell, Park, and Poon (1990), patients must (1) remember the correct way to take a medication (retrospective memory); and (2) must remember to do so at the proper time (prospective memory). Morell and colleagues have found that (1) older adults have poorer recall of drug instructions than do younger controls; (2) both younger and older individuals have more difficulty recalling medication regimens as they became more complex; and (3) even when given unlimited time to learn medication instructions, older adults often do not study drug instructions sufficiently well to recall them (i.e., they appear to be more prone to metamemory failures).

Comprehension problems have also been shown to be associated with poor adherence to medication instructions among older adults, including comprehension of labels on pill bottles and instructions orally related by the patient's physician (Diehl, Willis, & Schaie, 1995; Oliffe et al., 2019). For example, Kendrick and Bayne (1982) reported older adults had difficulty translating the instruction "Take every 6 hours" into a specific plan. Similarly, Morrell, Park, and Poon (1989, 1990) found that about 25% of information in a medication plan was misunderstood by older adults when they were presented with an array of prescription labels and asked to develop a dosing schedule based on the instructions. Lower health literacy in this group has also been implicated in poor comprehension of medication instructions and therefore worse overall adherence (Mayo-Gamble & Mouton 2018; Morrow et al., 2006). These studies suggest that, as a result of age-related declines in comprehension and memory, older adults have less information available to them, relative to younger individuals, following exposure to instructions.

In addition to age-related decrements in memory and comprehension, declines in sensorimotor function, attention, working memory, processing speed, and executive functioning have long been shown to be associated with adherence to medication regimens (Austin, Klein, Mattek, & Kaye, 2017; Conn, Taylor, & Miller, 1994; Isaac, Tablyn, & McGill–Calgary Drug Research Team, 1993; Smith et al., 2017). Declines in perceptual acuity can interfere with patient discrimination of basic medication information, such as medication tablet color (Skomrock & Richardson, 2010). Impaired motor function is related to problems opening medication bottles and cutting pills (Isaac et al., 1993). With regard to attention, Zacks and Hasher (1997) found older adults are deficient in their ability to both direct and inhibit attention to irrelevant information as well as cope with increased cognitive load under time constraints. For example, dosage errors in one study increased 15-fold among older patients when the number of drugs prescribed was increased from one to four (Parkin, Henney, Quirk, & Crooks, 1986). Similarly, noncompliance was found to be 3.6 times more prevalent among older patients using two or more pharmacies to fill their prescriptions than among those using only one (Col, Fanale, & Kronholm, 1990).

Medication adherence also involves working memory, processing speed, and numeric abilities. Considerable empirical evidence has demonstrated that working memory and speed of cognitive processing decline with age and therefore may negatively impact medication-taking behaviors. Decrements in processing speed are thought to compromise adherence by interfering with the complete processing and comprehension of information. For example, if mental operations regarding a medication regimen are performed too slowly, early information may be lost during the subsequent planning process. Finally, declines in numeric ability, observed as early as age 50 (Reyna, Nelson, Han, & Dieckmann, 2009; Schaie, 1996), are hypothesized to inhibit correct dosage interpretation and to contribute to medication noncompliance.

Although older adults may be more likely to have cognitive deficits that negatively impact adherence, there are, of course, many other factors predictive of treatment compliance in this population (Gellad, Grenard, & Marcum, 2011). Stronger adherence can be observed among those with better stability in lifestyle, more structured schedules/routines, less drug and alcohol abuse, and greater familiarity with medication taking and the establishment of routines and regimens to do so successfully. Other predictors include financial status (i.e., can the older patient afford their medication?), disease-related knowledge, the patient–provider relationship, untoward side effects (e.g., patients often unilaterally discontinue medications that produce intolerable side effects), health beliefs (e.g., increased internal locus of control and greater fatalism regarding health issues), health literacy, degree of social integration versus isolation, and availability of family members and others who can provide reminders and direct support when needed.

Dementia

Older individuals with dementia often have exceptionally low levels of medication adherence. A recent systematic review of the literature by El-Saifi, Moyle, and Tuffaha (2018) showed that adherence in this group ranged from only 17 to 42% and that frequency of premature medication discontinuation ranged from 37 to 80%. Equally notable is the finding that nonadherence was associated with an increased risk of hospitalization or death in this population. Not surprisingly, studies have confirmed that patients with dementing conditions such as Alzheimer's disease typically have difficulty not only remembering which medications they are taking, but also the reason for their use, secondary to disruptions in short-term memory, judgment, and insight (Smith et al., 2017). More interesting, however, are findings regarding the association between executive deficits and poor medication adherence in this population. Results from such studies have implications for work with a variety of other populations, including those with traumatic brain injury (TBI) and schizophrenia, for whom impairments in executive functions are also common. Studies have found that executively impaired patients are more likely to resist care and are less likely to comply with medication regimens (Allen, Jain, Ragab, & Malik, 2003; Hinkin et al., 2002).

Adhering to medication regimens requires involvement of executive functions because taking medicines involves developing and implementing a consistent plan to adhere; remembering to adhere, which typically requires time-based (e.g., at 5:00 P.M.) or event-based (e.g., with food) prospective memory; and remembering whether the medicine was taken as desired (described as "source monitoring"). Importantly, prospective memory difficulties are associated with neurological compromise (e.g., HIV-1 infection, Woods et al., 2006; TBI, Schmitter-Edgecombe & Wright, 2004). Source monitoring is also likely to become more difficult when the action is repetitive (Einstein, McDaniel, Smith, & Shaw, 1998). Recall of an isolated event (e.g., whether or not a dose of medication was taken before bed) can be hampered by the fact that similar events have occurred many times in the past and therefore, as a whole, tend to blur together in memory due to repetition and reduction in novelty.

Persons with executive dysfunction may fail to organize their schedule in a manner necessary to accommodate medication taking. On the other hand, such individuals may perseverate on medication taking and unintentionally overdose. Moreover, executive deficits may contribute to faulty reasoning such that medications are not necessary or that alternative doses or modified regimens are acceptable.

In addition to executive dysfunction, several other important factors have been identified as unique barriers to adherence among older adults with cognitive impairment. For example, Campbell and colleagues (2012) performed a systematic evidence-based review of the literature and note that difficulties understanding new dosage instructions, trouble coordinating medication use into one's daily routine, neuropsychiatric symptoms (e.g., uncooperative behavior), and living alone are additional challenges among this population. They suggest frequent person-to-person prompts are more likely to improve adherence in this group than "nonhuman" reminders. Other research has shown that caregiver factors also have a unique and significant impact on medication adherence among individuals with dementia. Notably, adherence in this group is negatively impacted when caregivers have lower levels of education, less robust cognitive functioning, lower self-efficacy, poorer health knowledge, and a greater number of medical problems (El-Saifi, Moyle, Jones, & Alston-Knox, 2019). The most efficacious strategies for improving adherence among individuals with dementia remains a topic of debate in the literature (for a systematic review of interventions, see Kröger et al., 2017).

HIV/AIDS

The introduction of highly active antiretroviral therapy (HAART) in the mid-late 1990s resulted in improved virological, immunological, and clinical outcomes, including improvement in neuropsychological functioning, in HIV-infected adults. Unfortunately, a number of studies have demonstrated that unless adherence rates are sufficiently high, this can lead to increased viral replication and the development of drug-resistant HIV strains, with obvious adverse personal and public health consequences. At the same time, memory impairment, motor and psychomotor slowing, attentional disruption, and executive dysfunction are common among HIV-positive individuals.

Our group measured medication adherence among 137 HIV-infected adults who completed a comprehensive battery of neuropsychological tests (Hinkin et al., 2002). Only 34% were classified as good adherers (e.g., taking at least 95% of doses as prescribed). The mean adherence rate for subjects with cognitive impairment was only 70%, whereas cognitively normal individuals had a mean adherence rate of 82%. Subjects with neuropsychological deficits were twice as likely to be classified as poor adherers, and it was executive dysfunction and working memory impairment that drove this relationship. A follow-up longitudinal study of 215 HIV+ adults demonstrated that cognitive decline over a six-month interval between baseline and follow-up was likewise associated with deterioration in adherence (Becker, Thames, Woo, Castellon, & Hiunkin, 2011).

Neuropsychological Dysfunction, Regimen Complexity, and Medication Adherence

Although considerable progress has been made in simplifying HIV medication regimens, many patients are still prescribed a number of different medications to be taken at varying points throughout the day. Using the above data set, we explored the relationship between neuropsychological dysfunction, regimen complexity, and adherence. As can be seen in Figure 8.1, not only does regimen complexity adversely affect medication adherence, but this effect is particularly pronounced among the cognitively impaired, who were able to successfully adhere to only a little over half of their prescribed doses. Complex medication regimens were not nearly as problematic for the neuropsychologically normal participants.

Aging, Neuropsychological Impairment, and Adherence

A number of studies have found older HIV-infected adults to be at greater risk for neuropsychological compromise. Because of this heightened risk of cognitive impairment, we posited that older participants (defined here as those over the age of 50) would be less adherent than younger participants. Contrary to our expectations, we found older participants were actually far more adherent than younger subjects. In fact, 53% of older participants were classified as good adherers, whereas only 26% of younger subjects were able to attain a 95% adherence rate. It may be that taking medication requires fewer lifestyle modifications for older cohorts or that such adjustments are less burdensome for this group, who may more easily incorporate pill taking into their daily activities. Older individuals are also more likely to have prior experiences taking daily medications for other age-related illnesses.

A different picture emerges when we look at the interaction between advancing age and neurocognitive compromise. We grouped the above participants as a function of medication adherence (using the 95% adherence cutpoint) and age (using 50 as a cut point) and then compared these groups' performances on neuropsychological testing. Results showed little difference in cognitive functioning between the two younger groups and the older good adherers. In decided contrast, older participants who were poor adherers performed far worse on neuropsychological testing. Further, while deficits in encoding have

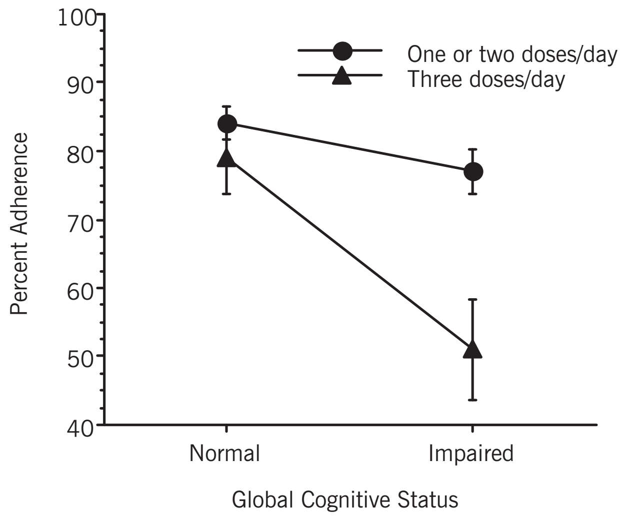

FIGURE 8.1. Relationship between cognitive status, regimen complexity, and medication adherence among HIV-infected adults. ● = One or two doses per day; ▲ = three doses per day. Reproduced with permission from Hinkin et al. (2002).

been found in participants who demonstrate either good or poor adherence, only those with poor medication compliance were found to also have deficits in memory retrieval (Wright et al., 2011). Additionally, prospective memory—"remembering to remember"—may be a stronger predictor of medication adherence than traditional neurocognitive domains (e.g., attention, verbal memory). Zogg and colleagues found prospective memory to predict self-reported medication management more strongly than several other factors, including performance on routine neuropsychological tasks, mood disorder or psychosocial factors (Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012).

While we have conceptualized cognitive dysfunction as causing poor adherence in this population, it is equally plausible that poor adherence results in a number of untoward clinical outcomes, including neuropsychological impairment. In all likelihood, a bidirectional relationship exists, with cognitive impairment adversely affecting patients' ability to adhere to their medication regimen, which in turn results in further disease progression and a worsening of cognitive function. Figure 8.2 depicts the relationship between medication adherence and specific neurocognitive domains among HIV-infected adults. This latent/structural modeling analysis demonstrated that neurocognitive impairment was associated with poor medication adherence in older, but not younger, HIV+ patients (Ettenhoffer et al., 2009). Among older HIV+ participants, processing speed, motor skills and executive functioning were strongly related to poor medication adherence. A longitudinal follow-up study showed intraindividual variability (dispersion) in cognitive function was associated with worse antiretroviral medication adherence (Thaler et al., 2015). Given that dispersion in cognitive performance has been shown to occur prior to conversion from normal cognition to mild or major neurocognitive disorder, it is possible that dispersion could be used to improve early detection and intervention of poor adherence.

Further, another longitudinal study (Ettenhoffer, Foley, Castellon, & Hinkin, 2010) following 91 HIV+ patients over time found that change in global cognition from baseline testing to follow-up was significantly mediated by medication adherence (Figure 8.3).

Drug Use/Abuse and Medication Adherence

Drug use or abuse may also adversely affect medication adherence via several potential mechanisms. Multiple studies have found substance abuse to be a risk factor for development of neuropsychological impairment. Drug use can also give rise to new-onset psychiatric dysfunction or exacerbate a preexisting condition. Disruptions to sleep and eating patterns and increased psychosocial instability may also contribute to poorer adherence.

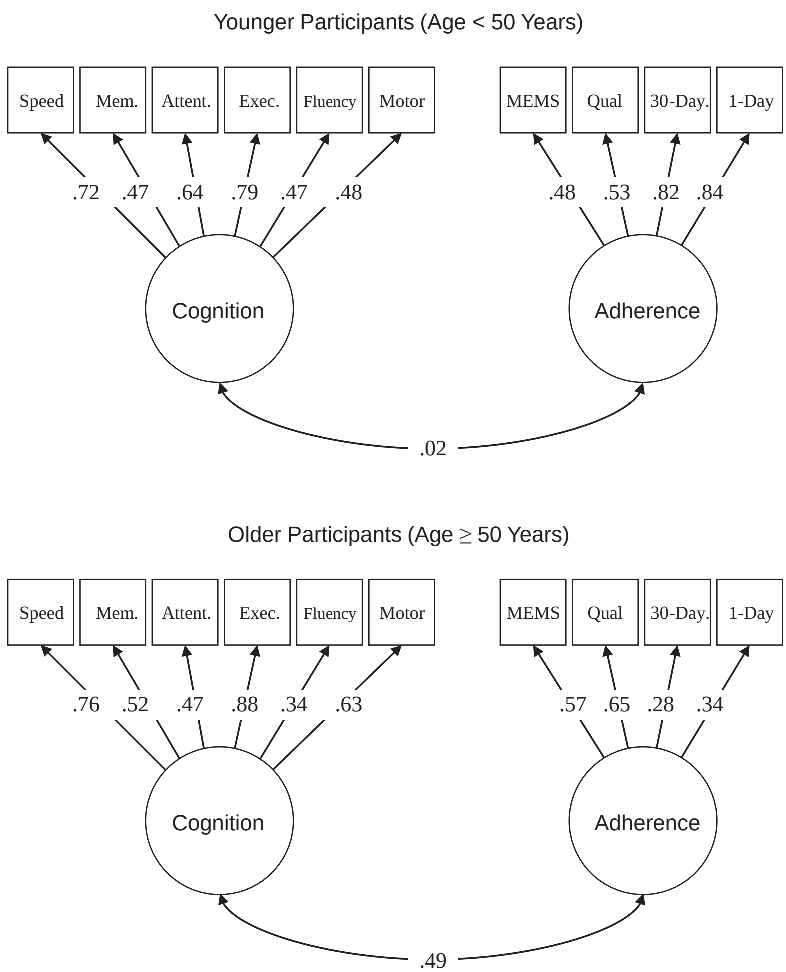

FIGURE 8.2. Latent model of cognition and medication adherence among younger and older HIV+ adults. From Ettenhoffer et al. (2009).

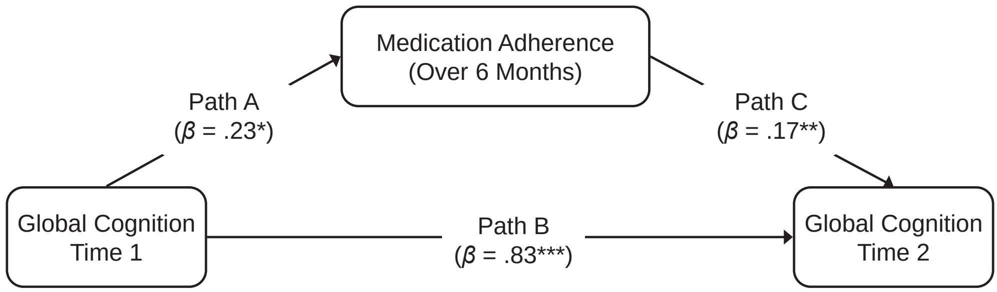

FIGURE 8.3. Model of longitudinal path analysis of global cognition and medication adherence. From Ettenhoffer et al. (2010).

In a longitudinal study funded by the National Institute on Drug Abuse (NIDA), we examined the impact of drug use/abuse on medication adherence among 150 HIV-infected individuals, 102 of whom tested urinalysis positive for recent illicit drug use. Medication adherence was tracked over a 6-month period using an electronic monitoring device (MEMS caps). We found individuals who were urine-positive for illicit/recreational drugs demonstrated significantly worse medication adherence than did drug-negative participants (63 vs. 79%, respectively). Logistic regression revealed that drug use was associated with over a four-fold greater risk of adherence failure. The use of stimulants (i.e., cocaine or methamphetamine) proved to be particularly disruptive to adherence in this sample. Participants who tested positive for stimulants were seven times more likely to be poor adherers than those who tested negative. The association between cocaine use, poor neurocognitive function, and poor medication adherence has been replicated by other groups (Meade, Conn, Skalski, & Safren, 2011).

Interestingly, we were able to compare adherence rates for time periods when subjects were not using stimulants to time periods when those same subjects were using stimulants. We computed 3-day adherence rates for visits at which participants tested stimulant positive, as well as adherence rates for visits at which the same participants tested stimulant negative. The 3-day mean adherence rate for subjects who tested positive for recent stimulant use was 51.3% compared to a 3-day mean adherence rate of 71.7% for the same individuals when they had not recently used stimulants (Figure 8.4). As such, the deleterious impact of drug use on adherence may be more a function of *state* than of *trait*.

A meta-analysis found consistent associations between alcohol use disorders, antiretroviral nonadherence, and poor outcomes of HIV treatment (Azar, Springer, Meyer, & Altice, 2010). Another study assessed the alcohol drinking behaviors and medication adherence of 272 HIV+ men and women (Parsons, Rosof, & Mustanski, 2008). These authors found patients were nine times more likely to be nonadherent on days during which they consumed alcohol. Further, the probability a patient would be nonadherent on a day of alcohol use increased 20% with each alcoholic beverage they drank. Patients with more experience consuming alcohol were found to be at less risk for the negative medication adherence. Nevertheless, more complex medication regimens put subjects at increased risk for nonadherence during days they consumed alcohol.

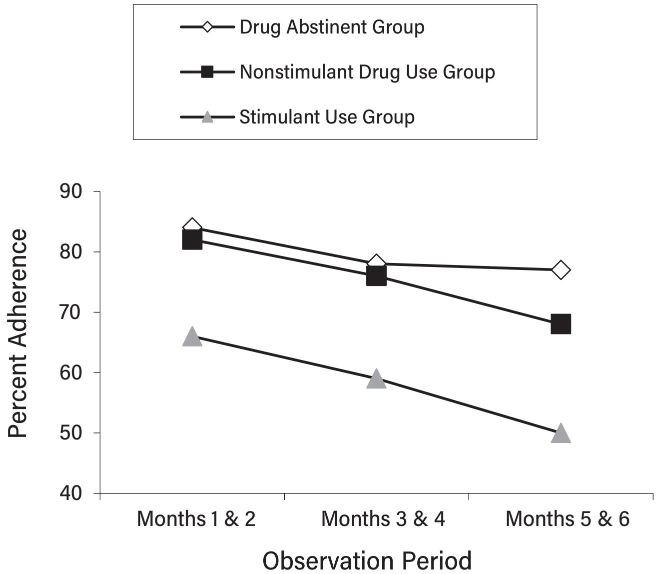

FIGURE 8.4. Medication adherence rates among stimulant using, nonstimulant drug using, and drug-abstinent HIV-infected participants over a 6-month period. Adapted from Hinkin et al. (2007).

Psychiatric Status

Personality characteristics and temperament can influence medication adherence. Across a number of medical conditions, agreeableness and conscientiousness are associated with better adherence (Axelsson, Brink, Lundgren, & Lötvall, 2011; Axelsson, Cliffordson, Lundbäck, & Lötvall, 2013; Lima, Machado, & Irigaray, 2018), while neuroticism and irritability correlate with poorer adherence (Jerant, Chapman, Duberstein, Robbins, & Franks, 2011; Axelsson et al., 2013; Lima et al., 2018). However, the relationship between personality/temperament and medical adherence is not as simple as it might seem on first blush. Adherence has been predicted by intricate configurations of personality/temperament characteristics that would seem to run counter to our understanding if we only took into account the contributions of individual characteristics. For example, persons with *high conscientiousness* and high neuroticism tend to be less adherent, as do those with *high agreeableness,* low conscientiousness, and high openness to experience (Axelsson et al., 2011). Additionally, those with a Type D personality, individuals with a propensity for negative affectivity (e.g., irritability and worry, pessimism, low self-confidence) and avoidance of social interactions (e.g., emotional reticence, fear of social rejection/disapproval), also often demonstrate poor medical adherence (Li et al., 2016; Wu & Moser, 2014).

Psychiatric disorder (e.g., depression, anxiety, psychosis) is associated with poor compliance with medical treatments as well (Edinger, Carwille, Miller, Hope, & Mayti, 1994; Hinkin et al., 2000; McAuley et al., 2015). Psychiatric populations have been found to have especially low rates of adherence to psychotropics (e.g., 26–73%; Drake, Osher, & Wallach, 1989; Razali & Yahya, 1995). Also, psychiatric conditions are associated with poorer adherence to medications for general medical conditions (Ciechanowski, Katon, & Russo, 2000; Wang et al., 2002; Banta et al., 2009). In addition, substance abuse and dependence, which are common in many psychiatric groups, exact a yet greater toll on medication adherence (Colizzi et al., 2016; Foglia, Schoeler, Klamerus, Morgan, & Bhattacharyya, 2017; Daneault et al., 2019). With regard to psychiatric status and medication adherence, mood disorders and psychosis have been studied more than other conditions.

Mood Disorders

A meta-analytic review suggests depressed individuals are about two times more likely to be noncompliant with medication and behavioral treatment regimens (Grenard et al., 2011). In unipolar depression, 1-year relapse rates can be as high as 80% in those not taking antidepressants compared to 30% for those who are adherent to antidepressants (Myers & Brainthwaite, 1992). Patients with major depressive disorder tend to show significant, stepwise decreases in adherence over time (Demyttenaere et al., 2008); it is estimated that about 20–60% of depressed individuals are nonadherent to antidepressants; this number tends to increase over time in individuals without private insurance (Roberson et al., 2016; Myers & Brainthwaite, 1992). A large-scale study (n = 3,606) conducted in Spain demonstrated that lower antidepressant doses were associated with better adherence, as were prescriptions consisting of selective serotonin reuptake inhibitors (SSRIs) alone versus SSRIs in addition to noradrenaline reuptake inhibitors (Roca et al., 2011). Further, a meta-analysis of studies that collectively followed 12,243 patients with HIV/AIDS and comorbid depression/psychological distress found that undergoing treatment for depression increased a patient's odds of successfully adhering to their prescribed medication by 83% (Sin & DiMatteo, 2014).

With regard to bipolar depression, data from 1,341 participants who served in the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) study evidenced a nonadherence rate of nearly 24% over a 21-month period (Hong, Reed, Novick, Haro, & Aguado, 2011). Lower adherence was associated with poorer social function, worse mood, alcohol or cannabis abuse, and longer manic or mixed episodes prior to the baseline visit. These findings are consistent with several other more recent studies (Bauer et al., 2013, 2019). Additionally, data suggests that poor medication adherence is related to a greater number of medications and pill burden, younger age (under 30), lower educational attainment, being single, being male, cognitive deficits and problems with planning, poor insight, negative attitudes toward treatment, poor understanding of bipolar illness and its treatment, lower life satisfaction, and poor occupational functioning (Bauer et al., 2013, 2019). In the EMBLEM study, individuals with bipolar disorder who were less adherent sustained double the treatment-related expenses compared to those who were more adherent; the increased cost was primarily due to inpatient stays (Hong et al., 2011). Moreover, others have demonstrated that about 60% of individuals admitted with mania fail to adhere to prescribed medication regimens in the month prior to hospitalization (Keck et al., 1996).

A review of controlled treatment studies suggested individually tailored treatment plans involving family or significant others that provide greater psychoeducation seem to be key components for improving adherence in bipolar disorder (Sajatovic, Davies, & Hrouda, 2004). Similarly, increased monitoring of medication use (Sajatovic et al., 2015), a positive attitude toward treatment (De las Cuevas, Peñate, Wenceslao, & Sanz, 2014; Arvilommi et al., 2014; Edgcomb & Zima, 2018), and insight into the condition under treatment (Edgcomb & Zima, 2018) are associated with better medication compliance. That said, adherence to one medication is not necessarily predictive of adherence to other medications (Arvilommi et al., 2014).

Psychosis

Poor adherence is especially problematic for patients with psychotic spectrum disorders. For example, one study suggested individuals with schizophrenia demonstrated nearly a 60% nonadherence rate over an 8-week period (Yang et al., 2012). Such findings are disconcerting, as antipsychotic nonadherence is a major barrier to effective treatment in this population (Dolder et al., 2004). Several studies have shown that approximately two-thirds of individuals with schizophrenia are noncompliant. This is particularly the case among younger adults during their first-episode, half of whom are partially compliant and the other half completely noncompliant (Buchanan, 1992; Fleischhacker, Meise, Gunther, & Kurz, 1994; Hickling, Kouvaras, Nterian, & Perez-Iglesias, 2018; Weiden, Shaw, & Mann, 1995). Additionally, 55% of those with schizophrenia who are nonadherent to antipsychotics tend to relapse over the course of a year, compared to only 14% of those who comply with their medication regimen (Stephenson, Rowe, Haynes, Macharia, & Leon, 1993). Poor medication adherence among patients with schizophrenia is associated with a variety of negative outcomes, including hospital readmission, worsening of symptoms, and homelessness (Marder, 1998; Moore, Sellwood, & Stirling, 2000; Olfson et al., 2000).

Medication adherence in psychosis is negatively associated with younger age (Hui et al., 2013; Hickling et al., 2018), comorbid substance abuse (Kampman & Lehtinen, 1999; Daneault et al., 2019), presence of medication side effects (Leclerc, Noto, Bressan, & Brietzke, 2015; Hickling et al., 2018), depressive symptoms (Fenton, Bllyler, & Heinssen, 1997; Kampman & Lehtinen, 1999), positive symptoms[1] (Moritz et al., 2013; Leclerc et al., 2015; Hui et al., 2016), absence of social support from family or friends (Leclerc et al., 2015; Alston, Bennett, & Rochani, 2019), practical barriers (e.g., inability to afford medications, unemployment, lower educational attainment, physical abuse; Fenton et al., 1997; Kampman & Lehtinen, 1999; Leclerc et al., 2015), violence/abuse and/or legal history (Leclerc et al., 2015; Spidel, Greaves, Yuille, & Lecomte, 2015), lack of insight (Fenton et al., 1997; Kampman & Lehtinen, 1999; Hui et al., 2016), poor attitude toward treatment (Richardson, McCabe, & Priebe, 2013), and neurocognitive dysfunction (Fenton et al., 1997; Kampman & Lehtinen, 1999; Hui et al., 2016). Regarding cognition, while this population often exhibits cognitive impairment (Heinrichs & Zakzanis, 1998; Schwartz, Rosse, Veazey, & Deutsch, 1996), this seems to pose less of a barrier to their medication adherence than a lack of insight (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002). While poor insight along with other cognitive deficits may decrease patients' ability to adhere to their treatment regimens (Green, 1996; Green, Kern, Braff, & Mintz,

[1] Moritz et al. (2013) found that 28% of their sample reported poor antipsychotic adherence due to not wanting to lessen positive symptoms.

2000), the relationship between insight and adherence in psychosis is complex. Specifically, poor insight only appears to impact the adherence of individuals with schizophrenia who have intact memory function, not those with memory deficits (Yang et al., 2012).

Individuals with psychosis tend to have high rates of substance use/abuse prior to and after the onset of clinical symptoms (37–65% and 45–66%, respectively; Colizzi et al., 2016). Interestingly, nicotine, alcohol, and cannabis have been shown to be particularly detrimental to antipsychotic medication adherence (Hui et al., 2013; Leclerc et al., 2015; Colizzi et al., 2016; Foglia et al., 2017; Daneault et al., 2019). It is unclear if these three drugs are particularly detrimental to adherence in individuals with psychosis because they are as easy to obtain as they are legal (in most states), have specific neurocognitive effects related to poor adherence (e.g., reduced attention, memory, and executive ability), intensify psychotic symptoms, or are a combination of these influences. What is clear, however, is that substance abuse is related to nonadherence and often a worsening of symptoms in persons with psychosis (Werner & Covenas, 2017).

Other Factors

While neurocognitive deficits have been routinely observed in bipolar disorder and schizophrenia, such deficits have only been variably associated with poor medication adherence in these populations (see Depp & Lebowitz, 2007; Lepage, Bodnar, Joober, & Malla, 2010; Jerant et al., 2011). Though somewhat perplexing, these mixed findings could be due to several factors. For example, it is possible that persons with greater psychiatric difficulties and cognitive impairment receive more medication management support from caregivers; have motivational and/or emotional disturbances that interfere with adherence to a greater degree than cognitive difficulties; spend more time in supervised care where their medication use is supervised; and/or fail to enroll or stay enrolled in studies of treatment adherence.

Ethnicity and/or socioeconomic status, as well as attitudes and beliefs about psychotropic medication, may also play a role in adherence among individuals with psychiatric disorders (Garrido & Boockvar, 2014; Tan et al., 2019). For example, in a large study ($n = 2,000$), 78% reported they felt antidepressants were addictive, less than half thought antidepressants were effective, and only 16% believed antidepressants should be given to those with depression (Priest, Vize, Roberts, Roberts, & Tylee, 1996). With regard to ethnicity, individuals from ethnic minority groups have been shown to be less adherent to psychotropic medications than nonminority individuals (Fleck, Hendricks, Del Bello, & Strakowski, 2002; Sleath, Rubin, & Huston, 2003). Poor adherence in these groups may be due to health inequities, prohibitive cost, beliefs about depression or other psychiatric illnesses, distrust of the true intention of the prescribing provider, concerns about psychotropics, treatment preferences, and/or stigma related to psychiatric care (Bultman & Svarstad, 2000; Maidment, Livingston, & Katona, 2002; Sirey et al., 2001). Interestingly, Garrido and Boockvar (2014) found Latinx individuals were more likely to take psychotropics if they believed they were prescribed for a physical condition rather than emotional/mental difficulties.

Research on medication adherence for comorbid medical conditions (e.g., epilepsy, diabetes, breast cancer) indicates that socioeconomic status has a small but significant impact (Alsabbagh et al., 2014; Billimek & August, 2014; Caccavale, Weaver, Chen, Streisand, & Holmes, 2015; Loiselle, Rausch, & Modi, 2015; Smith, Mara, & Modi, 2018); this effect persists even if cost barriers are removed (Alsabbagh et al., 2014; Zhang & Baik, 2014). These findings emphasize the importance of educating patients and the general public about the importance, safety, and efficacy of psychotropic agents and other medical treatments.

Psychosocial Models of Adherence

While this chapter focuses primarily on the impact of cognitive abilities on medication adherence, medication adherence is multifactorial in nature (Remien et al., 2003). Studies suggest that it may also be influenced by side effects, self-efficacy, lifestyle factors and self-identity, illness ideology, affect and psychiatric disturbances, patient perceptions, and medication burden (Christensen, Wiebe, Edwards, Michels, & Lawton, 1996; Reynolds, 2003; Williams, Rodin, Ryan, Grolnick, & Deci, 1998; Carrick, Mitchell, Powell, & Lloyd, 2004; Remien et al., 2003; Wilson, Hutchinson, & Holzemer, 2002). Theories developed to explain health-related behaviors have been applied to the study of medication adherence and are reviewed next.

Health Beliefs Model

One model that has received the most traction with regard to medical adherence is the health beliefs model (HBM; Rosenstock, 1974). This model posits that health behaviors depend on the desire to avoid illness and the belief that certain actions will prevent or alleviate illness. The model consists of four dimensions: (1) Perceived susceptibility to illness; (2) perceived illness severity; (3) perceived benefits of treatment; (4) and perceived barriers to treatment compliance. HBM theory predicts individuals are more likely to comply with treatment if they believe themselves to be vulnerable to the illness, perceive the consequences of illness as severe, are convinced of the efficacy of a treatment regimen, and see relatively few costs associated with adherence (Budd, Hughes, & Smith, 1996; Smith, Ley, Seale, & Shaw, 1987).

In addition to these four dimensions, the HBM further suggests that demographic, psychosocial, and psychological variables may influence individuals' perceptions and thereby indirectly impact health-related behaviors. Moreover, the HBM suggests individuals may need a prompt (e.g., a reminder of the threat of illness, necessary actions to reduce the impact of an illness) before they will engage in positive health-related behaviors (Weinstein, 1988). These "cues to action" may be internal (e.g., perception of pain or other physical or cognitive symptoms) or external (e.g., comments made by trusted others). The HBM has been shown to explain variation in medical adherence behavior in patients with a variety of diseases and disorders, such as HIV/AIDS (Barclay et al., 2007), hypertension and heart disease (Mirotznik, Feldman, & Stein, 1995; Brown & Segal, 1996; Mendoza, Munoz, Merino, & Barriga, 2006), diabetes (Harris, Skyler, Linn, Pollack, & Tewksbury, 1982), epilepsy (Green & Simons-Morton, 1988), renal disease (Cummings, Becker, Kirscht, & Levin, 1982), other medical conditions (Yue, Li, Weilin, & Bin, 2015; Dempster, Wildman, Masterson, & Omlor, 2018), as well as psychiatric symptoms and illnesses (Adams & Scott, 2000; Cohen, Parikh, & Kennedy, 2000; Clatworthy, Bowskill, Rank, Parham, & Horne, 2007; Patel, de Zoysa, Bernadt, & David, 2008; Willis, 2018). Additional support for the HBM comes from a meta-analysis of

116 adherence studies across a range of medical conditions. This analysis showed that perceived susceptibility (threat) to illness and perceived illness severity were among the strongest predictors of medication adherence (Diamatteo, Haskard, & Williams, 2007).

Autonomy, Self-Efficacy, and the Patient Health Engagement Model

Medication adherence has also been discussed in terms of social determination frameworks, in which autonomous (volitional) and controlled (nonvolitional) behavior regulation are distinguished. Here, "self-efficacy" refers to the belief in one's ability to *organize* and *execute* an action, and "autonomy" relates to one's *regulation* of actions. This theory received partial support in a study with a mixed sample of patients required to adhere to fairly simple medication regimens (Williams et al., 1998). They found that a sense of autonomy with regard to health care management accounted for 68% of the variance in adherence. In addition, perceived physician support of autonomous health care management was found to significantly mediate this relationship. Interestingly, perceived barriers did not predict adherence, although these were negatively correlated with autonomy and perceived autonomy support, suggesting autonomy may mediate the relationship between perceived barriers and adherence. It is also possible that increased autonomy facilitates self-efficacy, thereby reducing perceived barriers. In either case, this study suggests personal engagement, control, and social support are important to adherence.

The Patient Health Engagement model (PHE model; Graffigna, Barello, Bonanonmi, & Lozza, 2015) and the PHE scale (Graffigna, Barello, & Triberti, 2016) were developed to describe and assess the health care engagement of patients. The PHE model and scale were created in response to the realization that greater patient engagement was important for medical adherence and to the need for tools to help clinicians better facilitate engagement in their patients. The model reflects a continuum of engagement in the domains of cognition, feeling, and action, each of which must be worked through to successfully traverse each stage of the model. (For additional detail, see Graffigna et al., 2015, 2016.)

Graffigna, Barello, and Bonanomi (2017) used structural equation modeling to determine the role of patient activation in self-reported medication adherence in a sample of 352 Italians suffering from a range of chronic medical conditions (e.g., asthma, type II diabetes, lupus, hepatitis). As hypothesized, they found that patient activation predicted self-reported medication adherence. Additionally, they reported that the patient–clinician relationship, emotional status, and PHE impacted patient activation. Moreover, PHE mediated the relationship between patient–clinician and emotional status on the level of patient activation.

Theory of Reasoned Action

The theory of reasoned action (Ajzen & Fishbein, 1980) states that the *intention* to adhere is the best predictor of adherence. It views intentions as a function of patients' beliefs and expectations, their values, and the pressures exerted by their social referent group. Noting that the best intentions can be thwarted if the requisite abilities or opportunities are lacking, Ajzen (1985), in his theory of planned behavior, incorporated locus of control into the previous model. Research has shown that although both models have reasonable predictive utility, the theory of planned behavior (which takes into account attitudes, subjective norms, perceived control, and intention) may be more appropriate for health care and for conditions that are not entirely under the patient's perceived control (e.g., cancer, epilepsy; Millstein, 1996; Lorish, Richards, & Brown, 1990).

Additional Psychosocial Models

Social support has been shown to impact adherence and has been built into numerous models; it is often theorized to interact with various external (e.g., environmental, cultural) and internal factors (e.g., biological variables; Ewart, 1991; Dimatteo, 2004; Simoni, Frick, & Huang, 2006). Social support can be divided into structural and functional components. Structural components include marital status, living arrangement, and the density of one's social network, whereas functional components are practical support, emotional support, and family cohesion. Meta-analytic studies have shown functional support, particularly practical support (e.g., support that makes a given behavior easier to execute), which is highly predictive of medication adherence (Dimatteo, 2004; Lanouette, Folsom, Sciolla, & Jeste, 2009). Emotional support and family cohesiveness have also been found to be associated with adherence (Dimatteo, 2004; Lanouette et al., 2009), while family conflict is negatively related to compliance (Dimatteo, 2004). Similarly, others have shown that medication adherence suffers when caregivers are overburdened (Perlick et al., 2004). Among structural supports, marital status and living with someone are modestly related to adherence (Dimatteo, 2004; Lanouette et al., 2009). Barclay et al. (2007) found poor adherence in young HIV+ individuals was predicted by low self-efficacy and lack of perceived utility of treatment, whereas neurocognitive deficits was the sole predictor of poor adherence in older HIV+ adults.

In sum, many theories have been advanced to explain medication adherence across a wide range of patient populations. Findings generated by these theories have shown that sociodemographic factors (e.g., SES, drug use, ethnic/racial minority status), treatment expectancies, health beliefs/attitudes, self-efficacy and engagement, a sense of autonomy, social support, cohesive and positive support networks, emotional functioning, and coping styles all seem to play a part in medication adherence. Additionally, many investigators have begun to examine how these factors interact and influence adherence. That said, little is known about how these factors interact with neurocognitive deficits. Beyond their direct effects on medication adherence, cognitive difficulties may moderate or mediate the influence of variables such as treatment expectancies, health beliefs, autonomous health care management, coping styles, and social support. Indeed, the impact of neurocognitive deficits on the myriad factors contributing to medication adherence is an important topic requiring significant additional investigation.

Medication Adherence Interventions

Given the potential deleterious effects of poor medication adherence, there is a great need for effective interventions for improving medication-taking behavior. One simple method to improve adherence is to present medication information in a systemic, organized, and accessible format (Morrow, Leirer, Altieri, & Tanke, 1991; Morrow, Leirer, Andrassy, Tanke, & Stine-Morrow, 1996). For example, use of larger font sizes, conventional font styles, and unjustified text may be more appropriate for older adults and for those with vision or cognitive impairments (Drummond, Drummond, & Dutton, 2004). Instructions may also be improved by adding icons that highlight important information (Wickens, 1992), using relatively short paragraphs, and relying more heavily on summaries, headings, and bullet points. Other studies recommend employing active rather than passive voice and avoiding double negatives.

Given the frequency of polypharmacy reviewing and possibly reducing the number of medications may help to improve adherence. Some researchers have suggested that the timing of medication taking should be matched to patients' daily schedules whenever feasible, because if regimens interfere with normal everyday activities, poor adherence is more likely to occur. Despite the wealth of information that has come from studies in the human factors literature, the health care industry has yet to implement many of these findings to enhance the comprehension of medical information among patients. For example, the packaging and labeling of prescription medications has changed very little over the years; most patients filling prescriptions receive standard orange containers with minimal instructions printed in small font across a curved and glossy white sticker. Clearly, much work is needed to translate research findings into everyday, practical enhancements for medication comprehension and compliance.

Interventions incorporating education (Zullig, McCant, Melnyk, Danus, & Bosworth, 2014), social and care provider support (Kalichman et al., 2011; Palacio et al., 2015), and/or motivational interviewing and cognitive-behavioral therapy (Kalichman et al., 2011) have been shown to be effective in improving medication adherence. Interventions that incorporate a multiple of the aforementioned components are also likely to be more successful than those focused on just one (Haynes et al., 2003).

Another intervention, the Disease Management Assistance System (DMAS), has been developed targeting HIV+ patients with cognitive impairment. Combined with monthly adherence counseling, DMAS provides patients with verbal reminders to take their HAART medications at prespecified times throughout the day. Using electronic drug exposure monitor (eDEM) caps to track patient adherence over 24 weeks, Andrade et al. (2005) demonstrated that DMAS improved adherence for patients with preexisting memory impairments.

Despite the promise of many interventions in increasing medication compliance, most do not result in sustained improvements (see Koenig et al., 2008). It is possible that cognitive impairment and/or motivational issues may be responsible for reductions in adherence overtime. Certainly, cognitive deficits can introduce additional barriers that are likely to impact adherence (Wright et al., 2011) even if generally effective interventions are utilized. For this reason, focusing on cognitive remediation and on ways to apply such interventions to medication management may be of benefit.

There are two primary approaches to cognitive rehabilitation: restorative (e.g., practice drills to improve memory function) or compensatory interventions (e.g., use of a daily planner; (Wilson, 1999). Rehabilitation strategies may target specific deficits (e.g., memory impairment, executive dysfunction) individually or in combination. Targeting isolated cognitive deficits is most beneficial for individuals who suffer from solitary impairments. However, this approach may still provide benefit to those with multiple/overlapping cognitive deficits.

Despite the potential benefits of restorative approaches, compensatory interventions are likely to be most efficacious for medication adherence. Studies have demonstrated the effectiveness of external aids such as pillboxes and pill bottle alarms (Mackowiak et al., 1994), voicemail and pager-based reminders (Simoni et al., 2009), and organizational charts and calendars (Zullig et al., 2014) for improving adherence. Smartphones of course execute many of the aforementioned aid functions. While most smartphones contain preloaded reminder applications/software that can be used to improve medication compliance, more robust applications, such as Google Keep and Evernote, can be downloaded to further simplify and enhance adherence. Smartphone users have rated MyMedSchedule, MyMeds, and RxmindMe to be among the best standalone medication management applications for their ease of use and functionality (Dayer, Heldenbrand, Anderson, Gubbins, & Martin, 2013). These applications, of course, can be easily coupled with calendar, task management (e.g., to-do lists) and health care apps (e.g., Kaiser). While automated medication reminders can be helpful, these do not always improve adherence. In a study of text message reminders for blood pressure medication, text messages were well tolerated and appreciated, but seemingly were rarely heeded (Buis et al., 2014). In fact, no differences were found between treatment and control groups. As with other medication adherence interventions, external aids are likely to fall short if patients are not motivated to be adherent.

Emerging technologies may hold the key to improving adherence in persons with cognitive impairment, even if they are unmotivated. For example, while text message reminders are generally well received (e.g., Buis et al., 2014), the effectiveness of text message reminders can be improved if they better match the client's issues with adherence (e.g., memory problems, health beliefs, beliefs about medication). Research has shown that reinforcement learning algorithms can help to determine which type of text message reminder is the best match for given patients and can help improve their adherence rate by 5–14% (Piette et al., 2015). However, even with a perfect reminder message, some clients may fail to adhere to their prescribed medication regimen. In such cases, real-time monitoring and feedback can be useful. Data from Wisepill, the electronic medication box that sends cellular signals to a web-based server regarding compartment opening (Pellowski et al., 2014) can be viewed in real time by care providers and can be used to provide interventions (e.g., medication reminder calls) on the fly. Participants have endorsed the utility and ease of using Wisepill, while others have expressed concern about their medication adherence being monitored by others. It is possible these latter individuals did not want to be accountable for their medication adherence. However, such accountability is likely to improve adherence, as evidenced in previous work (e.g., home visits by nurses and community workers have been shown to increase adherence to antiretroviral therapy (ART) in persons with HIV/AIDS; Williams et al., 2006). Also, while devices like Wisepill may be help improve medication adherence, ingestible sensors provide more direct, real-time monitoring of adherence (Belknap et al., 2013).

Future Directions

Most early research on medication-taking behaviors focused on single constructs as possible determinants of poor adherence, such as the patient's demographic features (e.g., age, race, gender) or aspects of the therapeutic regimen (e.g., number of medications). However, as this chapter shows, medication adherence is an extremely complex behavior, and it is likely that no single variable can account for the rates of poor compliance that have been consistently observed across various health conditions and patient populations.

Continued research that considers multiple explanatory factors is greatly needed. Only by examining complex models of adherence behavior that take into account demographic, medication, disease, psychosocial, and neurocognitive variables will the most important predictors of adherence be identified and appropriate interventions be developed.

Considering the limited effectiveness and efficacy of most available medication adherence interventions, greater emphasis should be placed on finding effective techniques to improve medication compliance and clinical outcomes. Interventions are needed to enhance patient education, increase patients' health literacy, encourage the use of automatized drug delivery systems, improve monitoring of medication use, and enhance communication about adherence between providers and patients. Because the factors influencing adherence are many and varied, multifaceted, tailored interventions will likely be necessary to improve self-administration of medications in most populations. Finally, because physicians frequently underestimate subtle cognitive impairment in their patients (Zasler & Martelli, 2003), clear-cut practice guidelines and suitable methods of measuring cognitive, motor, and sensory functions required for accurate drug administration are essential for ultimate preventive management.

Highlights and Recommendations for Clinicians

- Rates of medication adherence are lower than 50% in most studies.
- Measurement methodologies can be divided into techniques providing objective data (plasma drug levels and electronic measuring devices), subjective information (patient self-report or clinician ratings), and indirect data (pharmacy refill records and clinic appointment attendance).
- Older adults experience more chronic illness and consume more medication than any other age group. Unfortunately, considerably higher rates of noncompliance have been reported in this population, with estimates ranging from 26% to as high as 75%.
- Older individuals and those with medical illness can experience decline in the cognitive functions necessary for successful medication compliance.
- Strong medication adherence requires adequate comprehension, processing speed, attention, working memory, learning, memory, and numeric abilities.
- Mild and major neurocognitive disorders place patients at significantly increased risk for poor medication adherence.
- Cognitive impairment adversely affects patients' ability to adhere to their medication regimens, and poor adherence in turn results in further disease progression and worsening cognitive function.
- Factors contributing to increased medication adherence may include:
  - Stability of lifestyle, less drug and alcohol use, greater familiarity with medication taking, and the establishment of routines and regimens to do so successfully.
  - Financial status and degree of social integration versus isolation.
  - Disease knowledge, health literacy, the patient–provider relationship, side effects and health beliefs.
- Drug use or abuse also adversely affects medication adherence via several mechanisms including:

- increased risk for cognitive impairment and new-onset psychiatric illness.
- disruption of eating and sleeping patterns.
- increased psychosocial instability.

- Psychiatric illness increases the likelihood patients will be noncompliant with treatment.
  - Individuals with major depressive disorder, for example, tend to show significant, stepwise decreases in medication adherence over time.
  - Poor adherence is especially problematic for patients with psychotic spectrum disorders.
- Intervention methods include the following:
  - Present medication information in a systematic, organized, and accessible format (large font, bullet points, simple language).
  - Match the timing of medication to patients' daily schedules whenever feasible.
  - Incorporate education and support for caregivers.
  - Use techniques from motivational interviewing and cognitive-behavioral therapy.
  - Combine monthly adherence counseling with verbal reminders to take medications at prespecified times throughout the day.
  - Engage patients in rehabilitation services to target specific cognitive deficits (e.g., memory impairment, executive dysfunction) and build compensatory strategies.
  - Recommend pillboxes (analog or electronic), prepackaged dosing, use of calendars and organizational charts, as well as traditional, voicemail, or text alarms.
- Take note of the health literacy level of your patients and educate accordingly.
- Future research is needed on interventions to improve patient education, increase health literacy, enhance use of automatized drug delivery systems, simplify monitoring of medication use, and promote stronger communication between providers and patients regarding adherence patterns.

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CHAPTER 9

The Brain on the Road

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Automobile driving is an indispensable activity of daily life, yet vehicle crashes are common. In the United States more than 6 million crashes occur annually, injuring or killing millions (National Highway Traffic Safety Administration, 2019). Trends are similar worldwide (World Health Organization, 2020). Crashes are a preventable global public health disaster that must be urgently addressed. Crash risk is often elevated in cognitively impaired driver populations. Cognitive impairments can affect drivers who are healthy, aging, or have disease. Risk extends beyond injury or fatality and can lead to greater rates of driving curtailment and cessation—increasing risk of social isolation, loss of independence, depression, and reduced quality of life.

This chapter examines relationships between cognition and driver behavior, including tools for discriminating between safe and unsafe drivers and linking driver behavior to driver cognition and health. Studies of cognitively unimpaired and impaired drivers in driving simulators and in the field (i.e., in controlled on-road and naturalistic settings using instrumented vehicles) reveal valuable information on the coordinated activities of neural systems (e.g., attentional, visuomotor, and decision making) that are needed for safe driving. Results link back to improving assessments of driver cognitive impairment in real-world contexts. The results can inform public policy and help guide the development of in-vehicle safety countermeasures and semiautomated vehicle systems to avert real-world car crashes, injuries, and death.

Cognitive impairment is ubiquitous in the medical and aging populations and can also affect otherwise young, healthy drivers. Myriad disorders and factors can produce cognitive impairment and affect driving ability, including neurologic (e.g., Alzheimer's disease, Parkinson's disease), physiological (e.g., diabetes), sleep (e.g., obstructive sleep apnea), psychiatric (e.g., personality disorders, depression), aging, and medication-induced (licit and illicit) causes. This chapter outlines a conceptual framework and general principles for studying driving in these populations rather than a specific approach to each disorder.

Conceptual Framework

Extensive findings support a theory- and evidence-based framework for evaluating driver behavior based on evaluating cognitive domains that are critical for safe driving (Rizzo, 2011). In this framework, cognitive abilities and impairments determine specific driver behaviors and safety errors, which predict crashes. In turn, driver behaviors index cognitive abilities, which may link back to underlying disease pathology. Observing how humans interact with complex machines and systems, like the vehicle, may provide a more sensitive index of underlying impairment than standard clinical tests (e.g., neuropsychological exams), resulting in improved ability to detect disease, even in preclinical or prodromal stages.

Some factors that produce driver errors can be prevented or controlled (Runyan, 1998). Interventions for injury prevention can operate before, during, or after a crash at the levels of driver capacity, vehicle and road design, and public policy (Michon, 1979). Relationships between driver behavior and safety errors can be represented by an imaginary triangle (Heinrich, Petersen, & Roos, 1980). Visible "above the water line" events are safety errors that produce car crashes resulting in fatality, injury, or (most frequently) property damage. Submerged "below the water line" events are behaviors that are related to crashes and occur more frequently.

Safety errors are driver behaviors that depend on context. For example, changes in driver lane position variability (an aberrant driver behavior) may index drugged or impaired driving (U. S. Food and Drug Administration, 2017). Greater lane position variability in the context of marked lane markers may index lane-crossing errors. Not all driver behaviors that link to cognitive impairment are errors, and some behavior patterns may be adaptive and not amount to errors, yet reveal driver cognitive abilities and state. Safety errors range from relatively innocuous errors, such as failing to check the rearview mirror on a deserted highway, to more serious errors such as choosing to drive while drowsy or distracted. Safety errors that occur in specific contexts, such as deviating from the traffic lane while a vehicle is in the opposing traffic lane, can produce near crashes (a.k.a., "near misses") or crashes. Although crashes produce an overwhelming public health burden, they are statistically infrequent events and tend to follow a Poisson distribution (i.e., a discrete probability distribution expressing the probability of a number of events occurring in a fixed period of time if these events occur with a known average rate and are independent of the time since the last event; e.g., Siskind, 1996, and Thomas, 1996).

A key strategy for research on determining crash risk in the real world is to discover the relationships between high-frequency–low-severity events that produce errors or near misses but not crashes, and low-frequency–high-severity events that lead to reported crashes in states' epidemiological records. High-frequency–low-severity events can be thought of as "crash surrogates." Crash surrogates are typically aberrant driver behaviors like patterns (e.g., slow deceleration at a stop sign) or errors (e.g., failure to stop at a stop sign). Crash surrogates happen more frequently than crashes (improving ability to collect and analyze data), can illuminate the behaviors that occurred before and after a crash, and can predict the likelihood a driver will have a crash. Determining the cognitive impairments (and how they map to driver health or disease) that produce aberrant driver behaviors and how these are affected by context (e.g., vehicle design, in-vehicle distraction) or environmental demands (e.g., weather, roadway) elucidates the mapping of cognitive mechanisms to behavior. Analyses of driver behavior in demanding environments (e.g., poor weather, intersections), which challenge impaired drivers, can further elucidate the interplay between driver cognition and behavior by improving ability to discriminate between impaired (even mildly) and unimpaired drivers (Rizzo et al., 2005).

Driver cognitive impairment is mediated by several driver-level factors that can be monitored contemporaneously with driver behavior. Key factors include driver physiology, sleep, and mobility behaviors. Abnormal driver physiology (e.g., glucose fluctuations in diabetes) can cause cognitive impairment that affects driver behaviors. Sleep and mobility impairments, common in disease or aging, can predict cognitive impairment (Tolea, Morris, & Galvin, 2016) and decline. Disrupted sleep impairs drivers acutely and chronically, affecting decision making, memory, and attention (Sternberg, Ballard, Hardy, Katz, Doraiswamy, & Scanlon, 2013). Wearable sensors, like actigraphy (Tippin, Aksan, Dawson, Anderson, & Rizzo, 2016), now make it possible to monitor these factors to improve predictions of driver health and safety.

Figure 9.1 depicts a simple information-processing model for understanding driver errors that may lead to vehicle crashes and shows where different impairments may interrupt different stages in the model. The driver (1) perceives and attends to the stimulus and interprets the situation on the road; (2) formulates a plan based on the particular driving situation and relevant previous experience or memory; (3) executes an action (e.g., by applying the accelerator, brake, or steering controls); and (4) monitors the outcome of the behavior as a source of potential feedback for subsequent corrective actions. The driver's behavior is either safe or unsafe as a result of errors at one or more of these stages in the driving task.

The risk of driver errors increases with deficits in attention, perception, response selection (which depends on memory and decision making), response implementation (a.k.a., executive functions), and awareness of cognitive and behavioral performance (a.k.a., metacognition). The individual's emotional state, level of arousal (or sleepiness), psychomotor factors, and general mobility (e.g., Marottoli, Cooney, Wagner, Doucette, & Tinetti, 1994; Uc et al., 2006) are also relevant. Individuals with impairments in

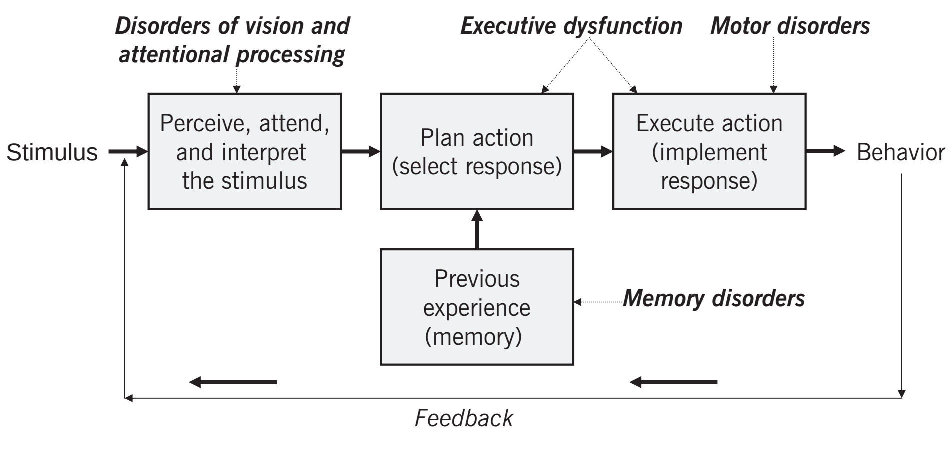

FIGURE 9.1. Information-processing model for understanding driver errors.

these domains are more likely than unimpaired drivers to commit errors that lead to motor vehicle crashes. Some errors can be detected because drivers normally self-monitor their performance. When feedback on driving performance fails to match expectations, the discrepancy is often identified "online" and drivers can take corrective action. Drivers typically self-monitor performance and correct errors. Cognitive impairment reduces driver ability to self-monitor, correct, and realize their impaired status, producing aberrant driver behaviors like errors that can be quantified and tracked to predict driver cognitive abilities.

Overview of Cognitive Impairment and Driving

Cognitive impairment has been robustly linked to impaired driver behavior and safety across a variety of test modalities (e.g., simulator, controlled on-road, and naturalistic driving studies). Typically, state licensure exams do not explicitly test for cognitive impairment but may have general restrictions for certain diseases that have a greater risk for cognitive impairment (e.g., diabetes, dementia). The fairness of these restrictions and evidence to support them are a matter of debate (Graveling & Frier, 2015). Generally, drivers with cognitive impairment exhibit aberrant driver behaviors, like impaired vehicle control (Merickel, High, Dawson, & Rizzo, 2019) and increased speed variability (Thompson et al., 2012), that are linked to increased rates of safety errors and crashes (Anderson et al., 2012). Cognitive impairment is also linked to driving curtailment and cessation (Connors, Ames, Woodward, & Brodaty, 2017), which may reduce mobility and quality of life, resulting in loss of independence, social isolation, and caregiver burden. Driving environment factors that challenge drivers (e.g., reduced visibility, intersections, and higher speed limit) link to greater crash risk in populations where cognitive decline is common (e.g., older drivers). We detail below specific mechanisms between cognitive abilities and driving.

Sensation and Perception

Automobile driving requires selective processing of a large volume of continuous and often competing sensory and perceptual cues from vision, hearing, vestibular, and somatosensory (tactile or haptic and vibratory) sources. Visual cues are especially important to driving because they convey long-range information about driver self-trajectory (egomotion), changes in the terrain, and the trajectories of other objects on a potential collision course with the driver.

Static and dynamic visual cues provide indispensable information on the structure, distance, and time to contact other objects that may arise unexpectedly across the panorama. We survey the world with binocular visual fields that normally span about 180 degrees. The fovea has the highest acuity and spans about 3 degrees around fixation; the macula spans about 10 degrees and participates in detail-oriented tasks such as map reading and sign localization. The peripheral visual fields have low visual acuity but good temporal resolution and movement detection.

Visual loss creates risk for drivers and can correspond to several underlying causes, such as aging, disease, and lesions in visual pathways. Visual sensory abilities can be measured with a variety of tests (e.g., visual acuity [static or dynamic], contrast sensitivity, visual field loss, glare recovery). State licensure tests typically incorporate limited visual assessments, most commonly far visual acuity and visual field tests, but do not incorporate more sensitive measures of visual sensory function. Drivers who pass these licensure tests may still have visual impairments that increase driving risk (Owsley & McGwin, 2010). Visual loss is linked to increased safety errors (Aksan et al., 2012) and crash risk (Ball, Owsley, Sloane, & Roenker, 1993). Visually impaired drivers can have impaired vehicle control (Merickel et al., 2019), which may be related to difficulty perceiving road signs or hazards resulting in sudden vehicle control maneuvers (Owsley & McGwin, 2010), and reduced driving exposure and driving cessation rates (Freeman, Munoz, Turano, & West, 2006).

Common eye disorders cause visual sensitivity loss and visual field impairments that can impair driver safety. For example, cataracts are a risk factor for car crashes (Owsley, Stalvey, Wells, Sloane, & McGwin, 2001) and are treatable with surgery. Cataracts are ubiquitous in aging eyes, causing a reduction in acuity and distracting reflections (e.g., halos around lights) or glare. Glaucoma can affect driving by producing both visual impairments (e.g., contrast sensitivity, acuity) and visual field loss (e.g., hemianopsia, scotimata). Macular degeneration affects areas of high-detail vision around the fixation point. Retinitis pigmentosa, an inherited condition that tends to affect younger drivers, constricts the peripheral visual fields, causing inability to detect objects approaching from the side. Even glasses may cause trouble while driving due to reflections, distortions, or discontinuities. Glare is a disabling effect of intense light and reflections off object surfaces or ocular media that can veil our perception of critical environmental targets (Stiles & Crawford, 1937). Glare from the headlights of oncoming traffic can mask terrain changes and nearby vehicle locations.

Drivers with lesions of visual areas in the occipital lobe and adjacent temporal and parietal lobes have various visual field defects (e.g., homonymous hemianopia or quadrantanopia) and may fail to perceive objects or events in the defective fields (Rizzo & Barton, 2005). Search strategies to compensate for the visual defect may create extra work that distracts from the driving task. Lesions in the occipital and parietal lobes (in the dorsal or "where" pathway) may have greater effects on driver behavior than lesions in the occipital and temporal lobes (in the ventral or "what" pathway). Dorsally located lesions produce visual loss in the ventral or lower visual fields that may obscure the view of the vehicle controls and much of the road ahead of the driver. Dorsal visual pathway lesions can impair processing of movement cues, as in cerebral akinetopsia (cerebral motion blindness), and reduce visuospatial processing and attention abilities. Some patients with these lesions have impairments in visual search and the useful field of view (UFOV; i.e., the visual area that can be acquired without moving the eyes or head) and are unfit to drive. One example is the hemineglect syndrome, which results in failure to orient to targets in the left visual hemifields in patients with right parietal lobe lesions (Rizzo & Barton, 2005). Another is Bálint's syndrome (simultanagnosia/spatial disorientation, optic ataxia, and ocular apraxia), which generally involves bilateral dorsal visual pathway lesions.

Ventrally located lesions produce upper-visual-field defects that may impair driving less than other lesions; however, they may cause impairments in (1) object recognition (visual agnosia), affecting interpretation of roadway targets, (2) reading (pure alexia), affecting roadway sign and map reading, and (3) color perception (cerebral achromatopsia), impeding use of color cues in decoding traffic signals and road signs and detection of roadway boundaries and objects defined by hue contrast (Rizzo & Barton, 2005).

Drivers with cerebral lesions may have various deficits that affect perception of structure and depth and are not measured by standard clinical tests. The brain employs multiple cues to determine object structure and depth because this information is so critical for interacting with moving objects and obstacles (Palmer, 1999). Binocular stereopsis (stereo vision) and motion parallax provide unambiguous cues to relative depth. For motion parallax, moving the head along the interaural axis produces relative movement of objects. The orderly relationship between relative velocities of images across the retina and relative distances of objects in the scene provides cues to structure and depth. Motion parallax impairments may contribute to vehicle crashes when impaired drivers must make quick judgments with inaccurate or missing perceptual information on the location of surrounding obstacles (Nawrot, 2001).

Detecting and avoiding potential collisions require information on approaching objects and the driver's vehicle. Objects set to collide with the driver stay at a fixed location in the driver's field of view, whereas "safe" objects move to the left or right. Time to contact (TTC) is estimated from the expanding retinal image of the approaching object. Older drivers are less accurate than younger drivers at detecting an impending collision during braking and judging if an approaching object will crash into them (Andersen, Cisneros, Saidpour, & Atchley, 2000). Performance is worse for longer TTC conditions, possibly due to a greater difficulty in detecting the motion of small objects in the road scene ahead of the driver.

Displacement of images across the retina during travel produces optic flow patterns (Gibson, 1979) that can specify the trajectory of self-motion (egomotion) with accuracy. Perception of heading from optical flow patterns is optimal in a limited part of the flow field surrounding the future direction of travel (Mestre, 2001). On curved roads, drivers tend to fixate the information flowing from the inside edge of the road where the curve changes direction (Land & Lee, 1994). The findings are relevant to detection of collisions, design of roads, and positioning of traffic warnings within a driver's dynamic visual environment and may be interpreted in terms of a dynamic UFOV (see the section on attention and driving below).

Perception of structure from motion (SFM; also known as "kinetic depth perception"), whereby subjects see the three-dimensional structure of an object defined by motion cues, is a likely real-world use of motion cues that may fail in drivers with cerebral lesions. SFM can be measured using a task in which subjects perceive shapes defined by random dot elements that move among varying amounts of random dot noise; this ability is impaired in akinetopsia and early Alzheimer's disease (Rizzo & Nawrot, 1998). SFM deficits have been associated with greater risk for safety errors and car crashes in driving simulation scenarios (Rizzo, 2001).

Executive Functions and Driver Behavior

Executive functions provide control over information processing and are a key determinant of driver strategies, tactics, and safety. These functions include decision making, impulse control, judgment, task switching, and planning (e.g., Damasio, 1999; Rolls, 1999). Executive functions strongly interact with working memory and attention, which operates on the contents of working memory (Norman & Shallice, 1986). The mapping between executive functions measured in laboratory settings and real-life driver behavior can be addressed using a set of theoretically motivated tasks. Table 9.1 shows hypothesized relationships between off-road cognitive (executive function) tests and specific driver behaviors.

Decision Making

Decision making requires the evaluation of immediate and long-term consequences of planned actions. Impaired decision making appears to be a critical factor in driver errors that lead to vehicle crashes. Causes of impaired decision making include acquired brain

TABLE 9.1. Hypothesized Relationships between Tests of Executive Function and Driving Behaviors

Test name	Ability measured	Driving behavior	Reference
Iowa Gambling Task	Decision making	Traffic violation (e.g., speeding); engaging in behavior extraneous to driving	Bechara et al. (1994)
Go/No-Go	Decision making and response inhibition	Running red light; timing of left turn across traffic; engaging in behavior extraneous to driving; stopping at or continuing through a yellow light	Podsiadlo & Richardson (1991)
Tower of Hanoi	Planning and execution of multistep tasks	Sudden brake application; swerving across lanes; running car near empty; viewing a map while driving (extraneous behavior)	Lezak (1995)
Wisconsin Card Sorting Test	Response to changing contingencies	Failure to adjust speed or following distance in response to changing road conditions	Lezak (1995)
Trail Making Tests A and B	Response alternation	Failure to alternate eye gaze appropriately between road, mirrors, and gauges	Lezak (1995)
Stroop Color and Word Test	Response inhibition, impulse control	Glances of > 2 seconds off road; e.g., with passenger present or while eating; failing to pull over for emergency vehicle or making inappropriate maneuver for emergency vehicle; speeding up to prevent another driver from merging	Lezak (1995)
AX-Continuous Processing Task	Working memory, response inhibition, impulse control	Running red light; following lead car through intersection; following familiar routes even though intending to deviate	Beck et al. (1956)
Controlled Oral Word Association	Cognitive fluency and flexibility (verbal)	Slowed processing of verbal traffic signs; failure to adjust to altered driving conditions (e.g., slowing in response to construction signs)	Lezak (1995)
Design Fluency	Cognitive fluency and flexibility (nonverbal)	Slowed processing of symbolic or pictorial traffic signs; failure to adjust driving in response to such signage	Lezak (1995)

lesions affecting prefrontal areas (due to stroke, trauma, or neurodegenerative impairment), antisocial personality disorder, effects of drugs and alcohol (Rizzo, Sheffield, & Stierman, 2003), and fatigue (Paul, Boyle, Rizzo, & Tippin, 2005). Driving outcomes of impaired decision making could include traffic law violations (e.g., speeding), unsafe vehicle maneuvers, extraneous and unsafe behavior while driving, and, in some cases, crashes.

Go/No-Go Decision Making

Driver strategies include deciding on a sequence of trips or stops (for gas, food, directions, or naps), evaluating traffic and weather risks, and making go/no-go decisions regarding whether to take a trip. Driving outcomes of go/no-go decisions could include adapting to speed changes near a school, choosing to switch on the headlights at twilight or in rain, changing gears on a hill, and deciding whether and when to overtake another vehicle, change lanes in traffic, or pass through intersections and traffic signals.

Abstract virtual environments can be used to assess go/no-go decision-making behavior in a driving-like task. Using a personal computer equipped with a steering wheel and pedals, cognitively unimpaired ($N = 22$) and impaired ($N = 28$) subjects drove through intersections that had gates that opened and closed (Rizzo, Severson, Cremer, & Price, 2003; Rizzo, Sheffield, et al., 2003). A green "Go" or red "Stop" signal appeared at the bottom of the display as the subject approached the gate, and a gate-closing trigger point was computed. Cognitively impaired drivers who had frontal lobe damage had more crashes into closed gates, more failures to go open gates, and longer times to complete the task. These findings suggest a failure of response selection criteria based on prior experience, as previously reported in individuals with decision-making impairments on a gambling-related task (e.g., Bechara, Damasio, Tranel, & Damasio, 1997). Drivers who had lesions in areas that did not produce executive dysfunction performed well on the go/no-go task, supporting the specificity of this task in localizing decision-making impairments in a driving-like task.

Surveillance of Driver Decisions at Traffic Intersections

Real-world patterns of driver go/no-go decision making can be evaluated from experimental observations of many drivers as they pass through traffic intersections. Wierwille, Hanowski, and Hankey (2002) used video surveillance to assess driver errors at intersections with stop signs or traffic lights during high-volume traffic, providing an evaluation of real-world driver go/no-go decision making. The analyses resulted in the development of probability taxonomies that provide a framework (decision tree) for analyzing critical incidents in large volumes of data. For every 10,000 drivers entering the intersection, 3.3% made some sort of driver error: 1.5% during left turns, 0.5% during right turns, 0.4% going forward, and 0.9% during other activities; 41/10,000 drivers ran through red lights—31 on left turns, 8 going forward, and 2 on right turns. For intersections with stop signs, there was a 3.0% overall probability of a driver-error critical incident of any type. Most occurred during left turns (1.5%), followed by going forward (0.7%), right turns (0.2%), and other scenarios (0.6%). The overall rate of running the stop sign was 19/10,000 vehicles, and the rate for a rolling stop was similar, at 15/10,000 vehicles, for a total stop sign violation rate of 34/10,000 vehicles. Wierwille et al. (2002) showed that red-light-running events are also common critical incidents, occurring at a rate of about 3%. However, these observations of general traffic do not provide specific insight into the causal mechanisms or the precipitating or contributing factors in impaired drivers. Greater insight is needed into specific decision-making mechanisms in these situations to identify possible intervention strategies.

Impulse Control/Response Inhibition

Drivers with impaired decision making may also show impairments in impulse control and response inhibition. Impulse control is related to decision making but does not involve evaluation of immediate and long-term consequences (Evenden, 1999). "Impulsiveness" can be perceptual, cognitive, or motor. Motor impulsiveness may be "nonaffective," as on the Stroop (1935) test, in which subjects must identify the color of ink used to print a conflicting color name by inhibiting automatic reading of the color name. Affective motor impulsiveness occurs when a person cannot inhibit a habit of responding to a stimulus that predicts a reward with affective value, as when a driver impulsively speeds up to prevent another car from merging ahead. In perceptual impulsiveness, failure of inhibition occurs at the level of working memory, before a response can be readied and executed. Observers may have more trouble identifying a visual target among distracters if the distracters are familiar. For instance, a driver traveling in a stable convoy of vehicles may follow the convoy through an intersection without noticing that the signal has turned red. Cognitive impulsiveness reflects inability to evaluate the outcome of a planned action and may give the appearance of failure to perceive or evaluate risk. For example, a driver may embark on a long road trip despite poor weather conditions or an unsound vehicle.

Perceptual impulsiveness resembles "lapses" in the Reason taxonomy (Reason, 1984) of error. Lapses represent failure to carry out an action rather than commission of an incorrect action. Lapses may be caused by the interruption of an ongoing sequence by another task, and they give the appearance of forgetfulness. For example, a driver returning home from work may begin talking on a cell phone and miss ("forget" to take) a highway exit. Disinhibition failures in executive dysfunction may contribute to "slips," errors in which an intention is incorrectly executed because the intended action sequence departs slightly from routine. Slips may resemble inappropriate but more frequent actions and are relatively automated (Norman, 1981). In this case, behavior is guided by a contextually appropriate strong habit due to lack of close monitoring by attention. A driver whose destination requires deviation from a familiar route may make a wrong turn toward a more habitual destination. A driver approaching a tollbooth may be distracted by an onboard warning light, fail to decelerate, and strike a slower lead car.

Drivers with executive dysfunction may commit rule-based errors when they believe they understand a situation and formulate a plan by "if–then" rules, but the "if" conditions are not met, a "bad" rule is applied, or the "then" part of the rule is poorly chosen (e.g., failing to service their vehicle, resulting in their vehicle breaking down in traffic).

Decision-making impairment can occur independently of memory impairment, but memory impairment can compromise a driver's decision-making ability because the driver cannot learn or recall all the situational contingencies required to make optimal decisions. Knowledge-based errors signify inappropriate decision making and planning due to failure to comprehend (e.g., a driver who is overwhelmed by traffic complexity and lacks information to interpret it correctly).

In practice, it is often difficult to determine unambiguously whether an error leading to a critical incident was due to a driver lapse, slip, rule-based, or knowledge-based error. Accordingly, we use a set of specific operational definitions for detecting critical incidents and empirically derived “decision tree” tools for classifying these unsafe incidents and identifying their likely causes. Such empirically derived tools and models provide taxonomic frameworks for organizing and interpreting data on driver error and for identifying common causes and mitigation strategies from seemingly unrelated instances.

Attention and Working Memory

A critical executive function related to driving is the continuous direction of attention to relevant features of the driving environment. We remember and act upon attended stimuli, not unattended items. There is increasing evidence that specific regions of the prefrontal cortex are essential in directing cognitive resources toward accomplishing tasks with a wide range of memory demands (Nyberg et al., 2003). Defects of attention clearly impair driver decisions (e.g., Ball et al., 1993; Owsley, Ball, Sloane, Roenker, & Bruni, 1991) and affect a variety of processes. Automatic attention processes are fast and involuntary and should contribute to subconscious corrections during driving, including control of the steering wheel or accelerator pedal position during uneventful driving on mundane highway segments (McGehee, Lee, Rizzo, Dawson, & Bateman, 2004). Controlled attention processes are slow and operate during capacity-demanding tasks and conscious decision making. Examples include glancing between the road and rearview mirror while maneuvering in and out of a traffic convoy, or the deliberate surveillance of a busy intersection with changing traffic signals, using head and eye movements. This is a “dilemma zone” where critical go/no-go decisions (see above) must be made (Mahelel, Zaidel, & Klein, 1985). The decision to accelerate or brake depends on driving speed and the time for which the green or yellow signal is visible.

Owsley and colleagues (1991) and Ball and colleagues (1993) linked driving impairment with reduction in the UFOV, the visual area from which information can be acquired without moving the eyes or head (Ball, Beard, Roenker, Miller, & Griggs, 1988). Performance on the UFOV task depends on speed of processing and divided and selective attention. UFOV performance begins to deteriorate by age 20. This deterioration may reveal itself as a shrinking of the field of view or a decrease in efficiency with which drivers extract information from a cluttered scene (Sekuler, Bennett, & Mamelak, 2000). Diminished efficiency is worse when attention is divided between central and peripheral visual tasks. Driver behavior may also change when attention is divided between the road and an onboard task.

Focused Attention

Executive functions control the focus of attention (Vecera & Luck, 2003). Without focused attention, we may be unaware of marked changes in an object or a scene made during a saccade, flicker, blink, or movie cut. This is known as “change blindness” (Rensink, O’Regan, & Clark, 2000). Traces of retinal images in visual working memory fade without being consciously perceived or remembered (“inattentional amnesia”). The very act of perceiving one item in a rapid series of images briefly inhibits ability to perceive another image, the “attentional blink” (Rizzo, Akutsu, & Dawson, 2001). Focused attention is thought to permit consolidation of information temporarily stored in visual working memory. Perceptual errors are likely if working memory is still occupied by one item when another item arrives, due to interference or limitations in capacity, which at a bottleneck stage admits only one item at a time.

Failure to detect roadway events increases when information load is high, as at complex traffic intersections with high traffic and visual clutter (Batchelder et al., 2003). Driver errors occur when attention is focused away from a critical roadway event in which vehicles, traffic signals, and signs are seen but not acted upon, or are missed altogether (Treat, 1980). Sometimes eye gaze is captured by irrelevant distracters (Kramer, Cassavaugh, Irwin, Peterson, & Hahn, 2001), such as "mudsplashes" on a windscreen that prevent a driver from seeing a critical event (e.g., an incurring vehicle or a child chasing a ball). Drivers with cerebral lesions are liable to be "looking but not seeing," even under conditions of low information load (Rizzo et al., 2001) and resembling the effects observed in air-traffic controllers during prolonged, intensive monitoring of radar displays.

Shifting Attention

Safe driving requires executive control to shift the focus of attention among critical tasks such as tracking the road terrain; monitoring the changing locations of neighboring vehicles; reading signs, maps, traffic signals, and dashboard displays; and checking the mirrors (Owsley et al., 1991). These tasks require an ability to shift attention between disparate spatial locations, local and global object details, and different visual tasks. Drivers must also shift attention between modalities when they drive while conversing with other occupants, listening to the radio or tapes, using a cell phone, or interacting with in-vehicle devices. These attentional abilities can fail in drivers with visual processing impairments caused by cerebral lesions.

Functional neuroimaging studies show changes in frontal lobe activity with driver speed control (Calhoun et al., 2002; Peres, van de Moortele, Lehericy, LeBihan, & Guezennez, 2000) and with alcohol-impaired driving (Calhoun, Pekar, & Pearlson, 2004). These studies suggest that conversation distracts the brain from processing information in a visually demanding task such as driving, and vice versa (Just et al., 2001). Cell phone conversation disrupts driving performance by diverting attention to an engaging cognitive context other than the one immediately associated with driving (Strayer & Johnston, 2001). Other modern "infotainment" devices also take cognitive resources away from the driving task (Ehret, Gray, & Kirschenbaum, 2000). Interference occurs at the level of central processes that can be disrupted by cerebral lesions. Relevant interactions in aging and brain injury can be measured by administering a controlled auditory verbal processing load during driving tasks (Boer, 2001).

Metacognition

Metacognition is the awareness of one's own thought processes and efficacy. This self-awareness of cognitive processes can include specific contexts and strategies to enhance understanding (e.g., "My brain works best before lunchtime"; "I should keep lists") (Fernandez-Duque, Baird, & Posner, 2000). Metacognition has been linked with executive functions by cognitive, developmental, and educational psychologists studying control of cognition, the developing awareness of the mind in children, and effects of awareness on learning and academic success (Mazzoni & Nelson, 1998). Some neuropsychologists and cognitive scientists study the anatomy of self-awareness (Fernandez-Duque et al., 2000; Mazzoni & Nelson, 1998) and awareness of impairments in neurological and psychiatric patients (e.g., with Korsakoff's amnesia, aphasia, schizophrenia, neglect syndrome; McGlynn, 1998), in patients with prefrontal lesions (Stuss & Knight, 2002), and in those with alcohol and drug effects or fatigue and sleep deprivation. Metacognition depends on the coordinated activity of multiple brain areas (McGlynn, 1998) and is relevant to driver safety in terms of awareness of (1) cognitive functions, (2) driver behavior; (3) vehicle performance, (4) road conditions, (5) rules of the road, (6) self-impairment, and (7) compensatory strategies to mitigate the effects of impairment. Lack of awareness of impairments (anosognosia) may exacerbate the consequences of impairments in other aspects of cognition (Anderson & Tranel, 1989). Drivers who lack awareness of their impaired cognition and behavior are liable to place themselves and others in harm's way while driving because they fail to take steps that might compensate for their impairments.

Predictions of driver safety may fail because drivers may behave differently in the real world than might be expected based on tests in the clinical laboratory (Reger et al., 2004). The relationships between disease status, clinical measures of cognition and awareness, and driver behavior may help clinicians working with patients and families to improve or rehabilitate cognitively impaired drivers (Eby, Molnar, Shope, Vivoda, & Fordyce, 2003). Natural and naturalistic studies in the field (see below) can help describe more accurately how cognitive dysfunction affects everyday behaviors, including automobile driving (Rizzo, Robinson, & Neale, 2006).

Emotions and Personality

Driving a motor vehicle can be a major source of annoyance, especially for aggressive drivers (Sivak, 1983) who may curse, shout, gesticulate, speed, flash their lights, ignore traffic signals, fail to signal, tailgate, drive under the influence of drugs and alcohol, or even use their car to block or strike another car or a pedestrian. "Road rage" is a media-coined term used to describe extremely aggressive and often criminal events (Brewer, 2000). Aggressive drivers are more likely to be young, male, and single, use alcohol or drugs, have a premorbid personality disorder, and experience increased levels of stress at home, work, and in a car (DiFranza, Winters, Goldberg, Cirillo, & Biliouris, 1986; Holzapfel, 1995). Car-related stresses may include crowded roadways, vehicle breakdowns, getting lost, and slow drivers ahead. Stressful life events, such as disruption of personal relationships, may precede some car crashes. Having a gun in the car is a marker for dangerous and aggressive driver behavior (Miller, Azrael, Hemenway, & Solop, 2002). Personality factors associated with aggressive driver crash involvement are thrill seeking, impulsiveness, hostility/aggression, and emotional instability (Beirness, 1993; Schwebel, Severson, Ball, & Rizzo, 2006). Psychiatric disorders are associated with several factors that may impair driving, including cognitive impairments (e.g., attention, memory, decision making), abnormal arousal or emotional states (e.g., depression), substance abuse, fatigue due to sleep disruption, medication effects, and psychosis (Tsuang, Boor, & Fleming, 1985). A driver with depression may fail to focus attention adequately on the road. A driver with schizophrenia may be distracted by pathological thoughts or hallucinations.

Antipsychotic, antidepressant, and anxiolytic medications may slow driver reaction times and decrease driver arousal. Effects of medication may vary with acute or chronic usage. The impacts of personality and personality disorders, aggression, risk taking, psychiatric disorders, and drugs on driver safety and crash risk require further study.

Arousal, Alertness, and Fatigue

Attention, perception, memory, and executive functions that are crucial to the driving task are acutely and chronically affected by impaired sleep (Dinges, 2000). Sleep impairments can be related to work factors (e.g., night shift), lifestyle, medication, and underlying disease. Chronic sleep impairment is associated with cognitive decline over the lifespan (Altena, Ramautar, Van Der Werf, & Van Someren, 2010). Many vehicle crashes are caused by sleepy drivers (Leger, 1994; Lyznicki, Doege, Davis, & Williams, 1998), including busy health care personnel (Barger et al., 2005). Sleep deprivation may cause neurologically normal, high-performing young adult airline pilots to perform as if they have visual constriction or simultanagnosia, as in Bálint's syndrome (Russo, Thorne, & Thomas, 1999; Thorne, Thomas, & Russo, 1999).

Drivers with sleep disorders such as obstructive sleep apnea syndrome (OSAS), are at particular risk for a crash (Horstmann, Hess, Bassetti, Gugger, & Mathis, 2000). They may fail to recognize or minimize their level of sleepiness (Engleman, Hirst, & Douglas, 1997) and subsequent awareness of impaired driving. Some drivers in sleep-related crashes deny having felt tired beforehand (Jones, Kelly, & Johnson, 1979). OSAS is common in commercial truck drivers (Brittle, Fiedler, Cotterman, & Palmer, 2014), and sleep-deprived truck drivers often underestimate their fatigue (Arnold et al., 1997). Symptom minimization may be intentional or due to unawareness of sleepiness (Stutts, Wilkins, & Vaughn, 1999), possibly due to an altered frame of reference for fatigue.

Sleep disturbances may accompany the hallmark motor, cognitive, psychiatric, and autonomic disturbances in Parkinson's disease (PD), due to varied involvement of noradrenergic, cholinergic, and serotoninergic systems (Wallace et al., 2020). Excessive daytime sleepiness or "sleep attacks" have been reported secondary to the use of dopaminergic medications for treatment of PD (Ferreira, Galitzky, & Brefel-Courbon, 2000; Hauser, Gauger, Anderson, & Zesiewicz, 2000). The reported lack of warning before falling asleep might actually point to amnesia or lack of awareness for the prodrome of sleepiness (Olanow, Schapira, & Roth, 2000).

The border between wakefulness and sleep is indistinct, and falling asleep can be viewed as a process characterized by decreasing arousal, lengthening response time, and intermittent response failure (Ogilvie, Wilkinson, & Allison, 1989). Gastaut and Broughton (1965) found that 2–4 minutes of electroencephalograph (EEG)-defined sleep must elapse before more than half of subjects recognize that they had actually been sleeping. The EEG may show progression from wakefulness to Stages I and II sleep, or it may be preceded by "microsleeps" in which the EEG shows 5 or more seconds of alpha dropout and an increase in theta activity (Harrison & Horne, 1996). These periods of approaching sleep onset have been correlated with subjective sleepiness among long-haul truck drivers (Kecklund & Akerstedt, 1993) and healthy, sleep-deprived drivers, as well as with deteriorating driving simulator performance in healthy, sleep-deprived drivers (Reyner & Horne, 1998) and OSAS patients (Paul et al., 2005).

Further research is needed to address how cognitive errors in the driving task increase as a function of severity of sleep disturbances, measured by polysonography (PSG) and the Multiple Sleep Latency Test (MSLT). Continuous positive airway pressure (CPAP) therapy in drivers with OSAS should lead to improvement in cognitive function, driving performance, and awareness of impairment. It is an area for further research.

Observed drowsiness can be quantified through physiological and cognitive performance measures. Self-reported estimates of acute drowsiness can be obtained using the Stanford Sleepiness Scale (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973) and those of chronic drowsiness using the Epworth Sleepiness Scale (Johns, 1991). Physiological indices of impending sleep can be measured aboard a vehicle, using a variety of techniques. These include EEG (e.g., of drowsiness or microsleep), decreased galvanic skin response (GSR), increased respiratory rate, increased heart rate variability, reduced electromyograph (EMG) activity (e.g., cervical paraspinous muscles), and percent eyelid closure (PERCLOS). PERCLOS scores of 80% or greater are highly correlated with falling asleep (Dinges, 2000). The lid closure can be used to trigger auditory or haptic warning (e.g., vibrating seats in a long-haul truck), which may prevent sleep- or drowsiness-related crashes.

Drug Effects

Certain medications have been associated with greater relative risk of automobile crashes in the epidemiological record (e.g., Ray, Thapa, & Shorr, 1993). Antidepressants, pain medications, antihistamines, anticonvulsants, antihypertensives, antilipemics, hypoglycemic agents, sedatives, and hypnotics have all been implicated. Aside from general drowsiness, the specific mechanisms whereby these medications impair driver behavior remain unclear. Drug use, including use of prescription medications, may cause as many fatal accidents as alcohol consumption (Centers for Disease Control and Prevention, 2006). Alcohol and illicit drugs such as marijuana (e.g., Lamers & Ramaekers, 2001) and methylenedioxy-*N*-methylamphetamine (MDMA; e.g., Logan & Couper, 2001) also pose serious driving safety risks. One study examining the effects of alcohol alone, marijuana alone, and their combined effects reported significant impairment in driving ability following administration of alcohol or marijuana alone, whereas combining the two substances resulted in "dramatic" impairments in such driving-related phenomena as time driven out of lane and standard deviation of lateral position (Ramaekers, Robbe, & O'Hanlon, 2000). Likelihood of impaired driving is typically quantified by legal cutoffs for sobriety (usually 0.8–1.0 mg/dl of ethanol in the United States and 0.5 mg/dl in Europe).

Deleterious effects of drugs on driving seem likely to depend partly on neurotransmitter systems involved in "executive functions" that are known to be critical for driving: decision making and working memory. According to a "somatic marker hypothesis" (Damasio, 1994), decision making is largely guided by somatic (emotional) signals linked to prior experiences with reward and punishment. Somatic state generation is linked to a neural system that includes the ventromedial (VM) prefrontal cortex, amygdala, and somatosensory cortices (SI, SII, and insula). Working memory defects result from dysfunction in a neural system in which the dorsolateral prefrontal cortex is a critical region (see above). Elucidation of the chemical substrates (e.g., serotonin, dopamine, acetylcholine) that modulate frontal lobe functions in at-risk older drivers may help guide development of pharmacological interventions that improve cognitive performance in the driving task. Studies of the effects of pharmacological agents on driving performance can be conducted most safely in a driving simulator (Lamers, Bechara, Rizzo, & Ramaekers, 2006).

Assessment of Driver Behavior

Road Tests

States generally consider a road test, conducted under the direct observation of a trained expert, to be the "gold standard" of driver fitness. The expert grades driver behavior on several driving tasks to calculate a cutoff score in order to classify a driver as safe or unsafe for licensure. However: (1) Road tests were developed to test novice drivers; (2) road testing carries the risk inherent in the real-world road environment; (3) road test conditions can vary depending on environmental factors and course selection; (4) driving experts may have grading biases; and (5) few data show that road tests results correlate with crashes. Several attempts have been made to develop empirically based reliable and valid road tests (e.g., Hunt et al., 1997).

State Records

The main data that transportation researchers have on actual collisions and contributing factors are collected post hoc (in forensic or epidemiological research). These data are highly dependent on eyewitness testimony, driver memory, and police reports, all of which have serious limitations. The best information regarding near collisions generally comes from anecdotal reports by driving evaluators and instructors (usually testing novice drivers) and police reports of moving violations. Most of these potential crash precursors, if they are even recognized, are known only to the involved parties and are never available for further study and subsequent dissemination of safety lessons. In some cases, crash and citations records can be linked with other databases, like those on prescription medication use, to provide further insight into possible driver health or medication factors that may have influenced a crash (Treager et al., 2007).

Driving Simulators

Driving simulators have been applied to (1) quantify driver behavior in cognitively impaired drivers, (2) study basic aspects of cognition in drivers with brain lesions, (3) probe the effects of information-processing overload on driver safety, and (4) optimize the ergonomics of vehicle design. Driving simulation offers advantages over the use of road tests or driving records in assessments of driver fitness (Figure 9.2). Simulator studies provide the only means to exactly replicate the experimental road conditions under which driving comparisons are made; simulations are safe, with no risks associated with real roads or test tracks. Simulation has been successfully applied to assess behavior profiles in drivers who are at risk for a crash due to a variety of different conditions, including sleep apnea, drowsiness, alcohol and other drug effects, aging, Alzheimer's disease, Parkinson's disease, HIV, glaucoma, cancer, rheumatoid arthritis, orthopedic surgery, diabetes, traumatic brain injury, and other conditions (Dalury, Tucker, & Kelley, 2011; Marcotte et al., 2006; Merickel et al., 2019). There are several different types of simulators (e.g., film, noninteractive, interactive, fixed vs. motion based, desktop, full cab; cf. Milgram, 1994). Simulators may be combined with devices aimed at detecting driver states, like attention (e.g., eye-tracker), brain activity (e.g., EEG), and physiology (e.g., BIOPACs and similar equipment).

Figure 9.3a shows how driving simulation can be applied to study drivers with mild-to-moderate cognitive impairment due to Alzheimer's disease (AD). In this simulation, subjects drive on a virtual highway passing an emergency vehicle (a police car) stopped by the shoulder of the highway. To minimize the chance of contact with the vehicle or nearby pedestrian, the driver must perceive, attend to, and interpret the roadway situation, formulate an evasive plan, and then exert appropriate action upon the accelerator, brake, or steering controls, all under pressure of time. Figure 9.3b shows the typical response of a normal individual—that is, slowing and steering around the parked police vehicle.

A relative drawback to simulation research is simulator adaptation syndrome (SAS), which is characterized by autonomic symptoms including nausea and sweating (Stanney, 2002). The discomfort is thought to be due to a mismatch between visual cues of movement, which are plentiful, and inertial cues, which are lacking or imperfect, even in simulators with a motion base (Rizzo, Sheffield, et al., 2003). In our experience, SAS is more likely with crowded displays (as in simulated urban traffic), advanced age, female gender, increased braking and accelerating (e.g., intersections), longer simulated drives, and history of migraine or motion sickness. SAS may also result from conflicts between visual cues that are represented with differing success in modern computer displays. SAS can increase subject dropout in simulator experiments and limit the experimenter's ability to repeatedly test a subject's response over an extended drive, particularly when the

FIGURE 9.2. An older driver in a high-fidelity simulator at the University of Nebraska Medical Center's Mind & Brain Health Labs.

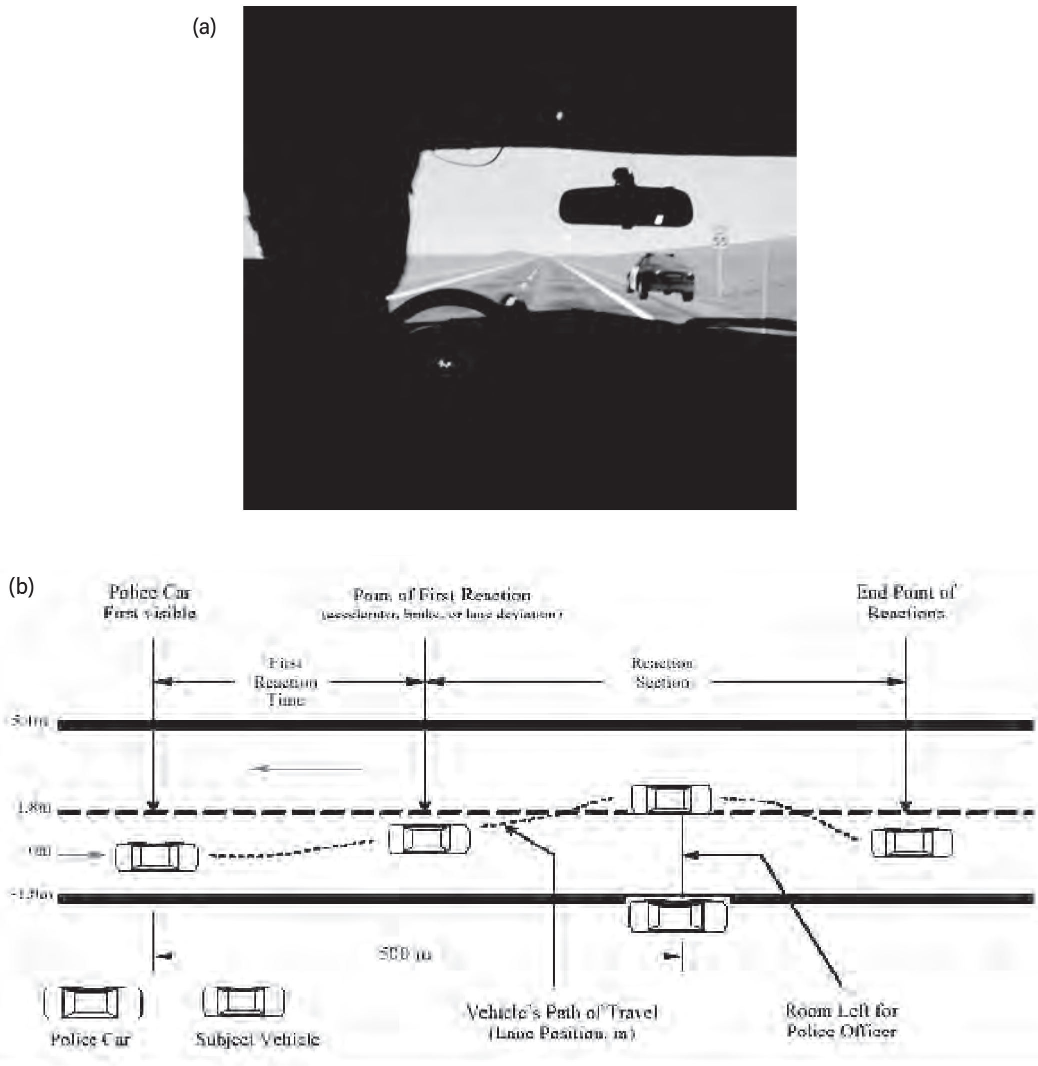

FIGURE 9.3. (a) Driving simulation requiring avoidance of a stopped police car. (b) Avoidance maneuver of an unimpaired simulator driver.

response involves rapid braking or other behaviors that increase risk of SAS. Choice of equipment and scenario design (e.g., avoiding braking) can minimize SAS.

Another issue in simulator-based research is the need to test the validity of the simulation (e.g., Marcotte et al., 2004). This may involve detailed comparisons of driver behavior in a simulator with performance in an instrumented vehicle and with state records of crashes and moving violations in each population of drivers being studied. The apparent face validity of the simulation—that is, that the driver appears to be driving a car and is immersed in the task—does not guarantee lifelike performance. Drivers may behave differently in a simulator due to a variety of factors—lack of familiarity with the simulator vehicle, SAS, low-fidelity graphical displays, observation awareness (Hawthorne effect), lack of fear of injury—compared to real-life driving situations in which life, limb, and licensure are at stake. They may even perform differently when the same scenario is implemented on different simulator platforms, motivating the need for development of standard scenarios.

Efforts to improve driving simulators have often focused on making the simulations more "lifelike"; yet the added cost (e.g., of a mechanical motion base) might not translate to better assessments of driver safety. Abstract versions of reality that enhance some critical environmental cues (e.g., dynamic texture or shading) and minimize others might provide more effective tests (of "functional reality") that correlate even better with actual driver behavior (see the description of the go/no-go scenario above). Advances in understanding the role and representations of key visual cues from the environment in dynamic graphical displays should improve the acceptance and measurement characteristics of driving simulator tools.

The future application of driving simulation to study drivers with medical impairments will benefit from a standardized approach to scenario design, certification standards for ecological validity of simulator graphics and vehicle dynamics, uniform definitions of measures of system performance, and cost-effective methods for geospecific visual database development (Rizzo, Severson, et al., 2003).

Instrumented Vehicles: Controlled, On-Road Drives

Instrumented vehicles (IVs) permit quantitative assessments of driver behavior in the field, in a real car (including the driver's own car), under actual road conditions. These naturalistic measurements are not subject to the type of human bias that affects inter-rater reliability on a standard road test. For these reasons, several groups have developed multipurpose field research vehicles (see Figure 9.4 for an example of an instrumented vehicle). These vehicles are designed to examine objective indices of driver behavior in normal and potentially unfit drivers and to assess the safety and usability of prototype automotive technologies, including on-road tests of human–machine interactions with semiautomated vehicle systems. Each consists of a midsized vehicle with extensive instrumentation and sensors hidden within its infrastructure.

Internal networks of modern vehicles allow for the continuous communication of detailed information from the driver's own car (Rizzo, Jermeland, & Severson, 2002). Modern vehicles report variables relevant to speed, emissions controls, and vehicle performance, and some vehicles allow more detailed reporting options (e.g., on seatbelt and headlight use, climate and traction control, wheel speed, and antilock brake system activation). Standard, on-board vehicle sensors can be enhanced with supplemental sensors. Radar systems in the vehicle can gather information on the proximity, following distance, and lane-merging behavior of the driver, and other neighboring vehicles on the road. Global positioning systems (GPSs) can show where and when a driver drives, takes risks, and commits errors. Wireless systems can check the instrumentation and send performance data to remote locations. These developments can provide direct, real-time information on driver strategy, vehicle usage, upkeep, drive lengths, route choices, and decisions to drive during inclement weather and high traffic.

The driving assessment in an IV can incorporate segments of "baseline" driving to

(a)

(b)

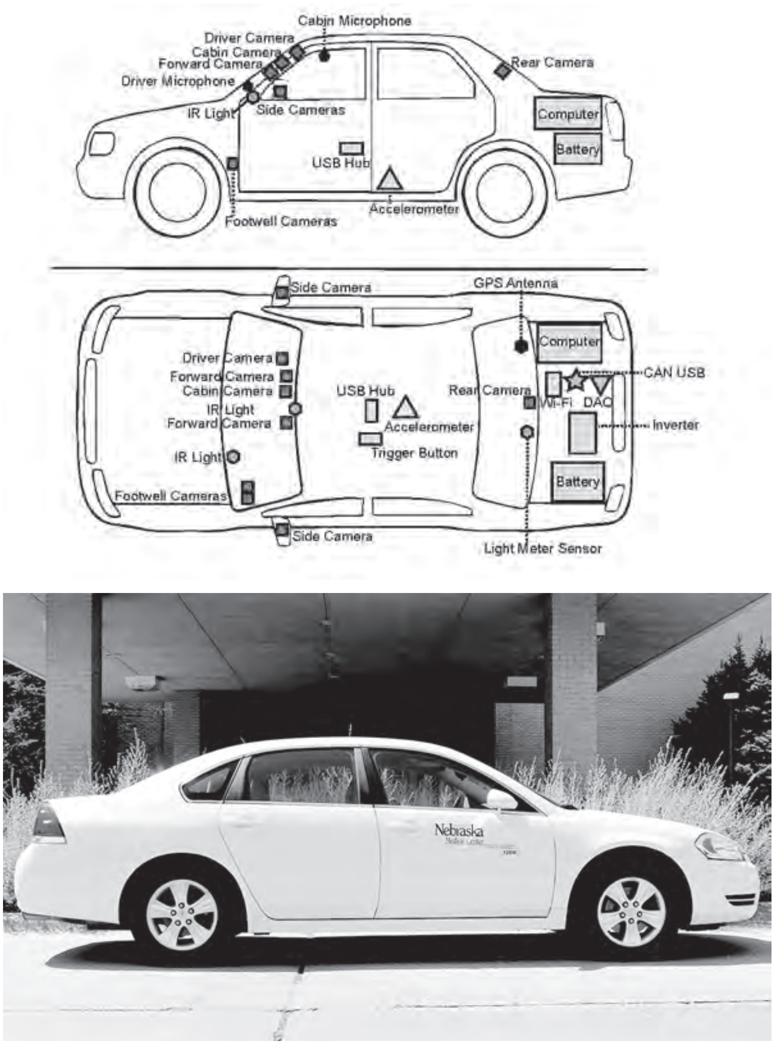

FIGURE 9.4. Example systems diagram (a) showing in-vehicle sensors, cameras, and in-trunk computer system for a lab-owned instrumented. Instrumentation systems take advantage of manufacturer-installed sensors and supplemental instrumentation installed post-purchase. While instrumentation is extensive, it is unobtrusively installed (b).

assess vehicle control on uneventful segments of highway under conditions of low-cognitive loading. The drives can also incorporate essential maneuvers such as left turns, right turns, stopping at a stop sign, and maintaining vehicle control. Kinematic measures of driver control during vehicle maneuvers include speed, lateral and longitudinal acceleration, yaw, and others (Figure 9.5). For example, large lateral accelerations indicate when a driver has swerved to miss an obstacle, whereas large longitudinal accelerations occur when a driver either braked hard or accelerated hard to avoid an obstacle (Merickel,

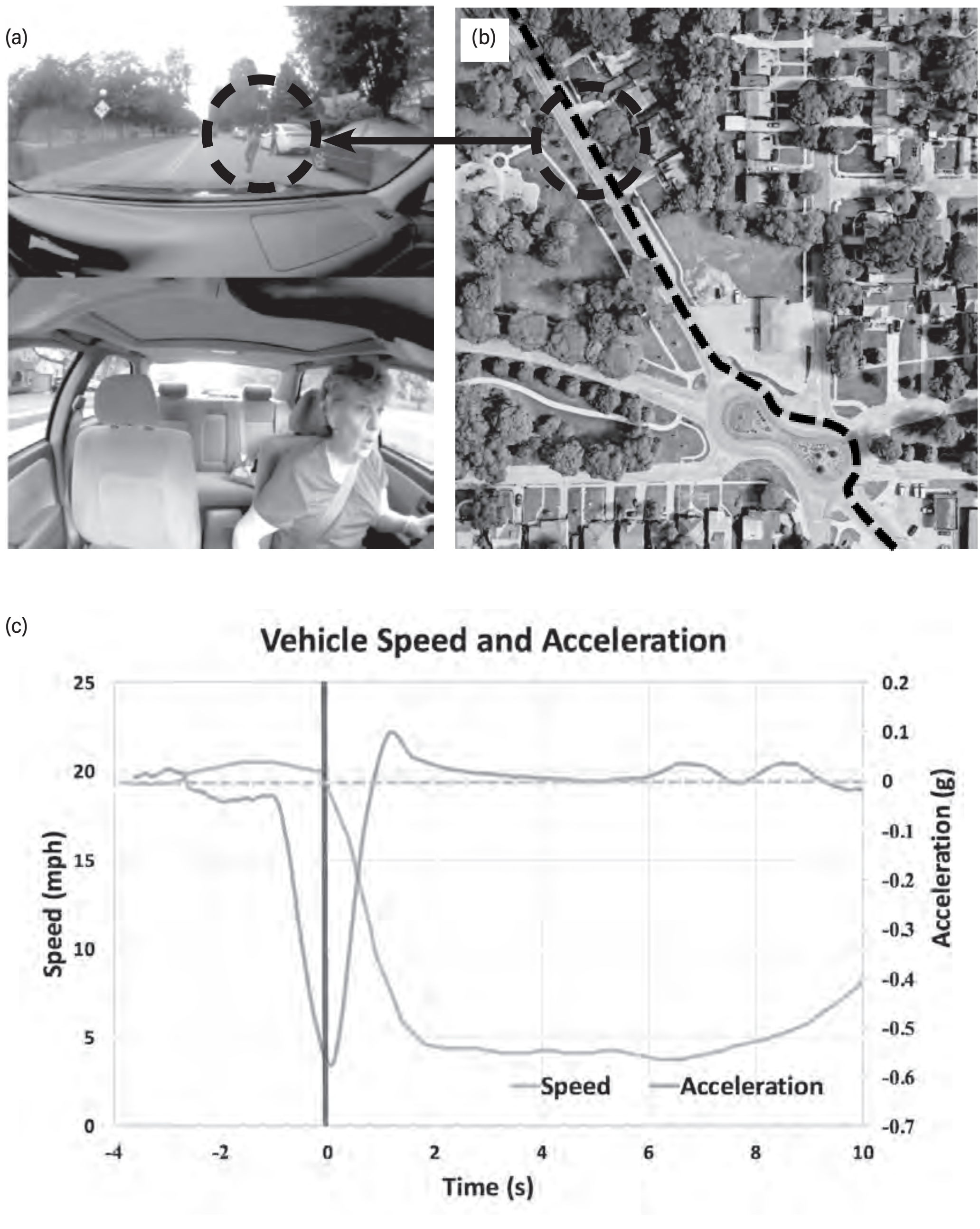

FIGURE 9.5. A driver of an IV rapidly brakes to avoid hitting a child (a). Vehicle sensors capture the vehicle's rapid deceleration (c, speed) and increase in forward g force (c, acceleration). GPS data (b) capture the vehicle's location.

High, Dawson, & Rizzo, 2019). High yaw rate can indicate if a driver has swerved or is rapidly turning the steering wheel.

In addition, standardized challenges can be introduced that stress critical cognitive abilities during the driving task. These tasks are comparable to scenarios implemented in driving simulators and include route-finding tasks (Uc, Rizzo, Anderson, Shi, & Dawson, 2005), sign identification (Uc et al., 2006), and multitasking (i.e., driving while performing distracter tasks, as holding a conversation or using in-vehicle devices such as cell phones and navigation equipment; Rizzo et al., 2004).

The advantage of using IVs to study patients with relatively specific cognitive impairments is exemplified in preserved procedural knowledge for driving skills in drivers with relatively circumscribed and dense amnesia following bilateral hippocampal and parahippocampal lesions caused by herpes simplex encephalitis. Radar-equipped IVs have also provided insights on traffic entry judgments in older drivers with attention impairments (Pietras, Shi, Lee, & Rizzo, 2006). Drivers pressed a button to indicate the last possible moment they could safely cross a road in front of an oncoming vehicle. The speed and distance of the oncoming vehicles were measured, and time to contact was calculated. Each driver's time to cross the roadway was independently measured. Compared to unimpaired drivers, attention-impaired drivers accepted shorter TTC values, took longer to cross the roadway, and showed shorter safety cushions (the difference of time to contact and time to cross the roadway). A Monte Carlo simulation analysis was used to model how potential differences between the attention-impaired and nonimpaired groups might influence traffic dynamics and the potential for crashes. It showed that these performance differences increased the crash risk of the impaired group by up to 17.9 times that of the nonimpaired group. IVs can also be used to assess excessive risk taking in younger drivers (Boyce & Geller, 2002).

Olsen, Lee, and Wierwille (2002) combined IV video and radar data to study lane change decisions in neurologically normal adult drivers. Of 8,667 lane changes, 304 (3.5%) were unsafe because the driver initiated the lane change while a vehicle was nearby in the adjacent lane (e.g., in the blind spot) or was forced to make an evasive maneuver to avoid a crash. Continuous monitoring of radar and video information from the IVs of drivers with a range of cognitive abilities could provide additional insight into mechanisms of error that lead to such critical incidents that car crashes may result ("naturalistic driving").

Instrumented Vehicles: Naturalistic Driving

A driver's personal vehicle may also be instrumented as an IV by installing unobtrusive, passive, in-vehicle sensor instrumentation (Figure 9.6; e.g., Chakraborty et al., 2019; Dingus, Neale, & Garness, 2002; Merickel, High, Dawson, et al., 2019; Rizzo, Stierman, et al., 2004). Controlled, on-road drives are limited by brief observation periods (30–45 min) in which drivers navigate standardized routes that may not reflect their usual driving patterns in an unfamiliar vehicle (Anderson et al., 2012; Uc, Rizzo, Johnson, Dastrup, Anderson, & Dawson, 2009). These drives are accompanied by a researcher, which may affect driver behavior and alertness (Hawthorne effect). Studies are limited by small sample sizes, which do not capture the interindividual variability present in drivers. Lack of repeated observation prevents identification of driver safety changes due to comorbid factors such as daytime sleepiness, medication dosing, and physiology (Drincic, Rizzo, Desouza, & Merickel, 2020). These factors can be characterized in naturalistic studies with continuous, repeated observations. A person driving his or her own IV is exposed to the usual risk of the real-world road environment without the psychological pressure that may be present when a driving evaluator is in the car. Road test conditions can vary depending on the weather, daylight, traffic, and driving course. However, this is an advantage in naturalistic studies because repeated observations in varying real-life settings can provide rich information regarding driver risk acceptance, safety countermeasures and adaptive behaviors, and unique insights on the ranging relationships between low-frequency–high-severity driving errors and high-frequency–low-severity driver errors. Driver behavior data can be linked with in-laboratory assessments of driver health and functional abilities and state crash and citation records to establish objective driver safety. Data collected in naturalistic studies is typically immense and presents challenges to traditional analytic techniques such as human review, often necessitating machine learning and computer vision techniques (Figure 9.7) to reduce and analyze data (Ozcan et al., 2020).

Such “brain-in-the-wild” relationships (Rizzo et al., 2006) were explored in detail in a study of naturalistic driver behavior and safety errors in 100 neurologically normal individuals, driving 100 total driver years (Dingus et al., 2005; Neale, Dingus, Klauer, Sudweeks, & Goodman, 2005). All enrolled drivers allowed installation of an instrumentation package into their vehicle (78 cars) or drove a new model-year IV provided for their

FIGURE 9.6. An example instrumentation system that can be installed easily and unobtrusively in a driver’s own vehicle. The white computer box (a) connects to vehicle power, coordinating the system and storing data. The black sensor package (b) contains sensors to record driver behavior. Additional sensor data is pulled from the vehicle’s on board diagnostic port (OBD) using a commercially available OBD device (c). Sunglasses are shown for size reference.

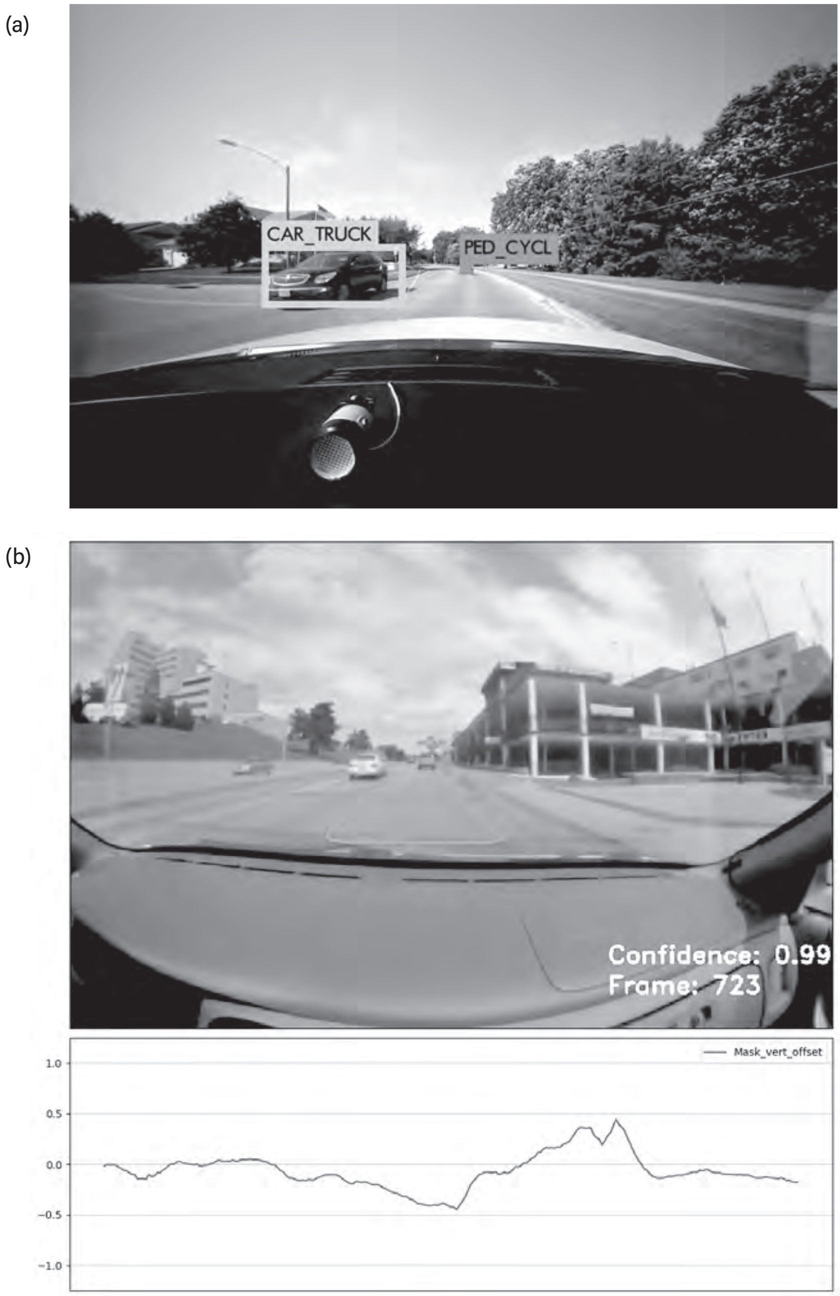

FIGURE 9.7. Computer vision algorithms can automatically process video data from thousands of miles of naturalistic driving data collection. Algorithms are trained on annotated data sets. (a) An example of detecting objects in the forward roadway, here a cyclist (PED_CYCL); the IV is following and a car (CAR_TRUCK) is in the opposing traffic lane. (b) An example of lane tracking. The outlined polygon in the forward roadway view shows the detected lane area, and the graph shows the vehicle's detected lane position over time.

use. Data collection provided almost 43,000 hours of actual driving data, over 2 million vehicle miles. There were 69 crashes, 761 near crashes, and 7,479 other relevant incidents (including 5,568 driver errors) for which data could be completely reduced. Crash severity varied, with 75% being mild impacts, such as when tires strike curbs or other obstacles. Using taxonomy tools to classify all relevant incidents, researchers reported that the majority could be described as “lead vehicle” incidents. However, several other conflict types (adjacent vehicle, following vehicle, single vehicle, object/obstacle) occurred at least 100 times each. Driver inattention was deemed to be a factor in most of these incidents. In summary, IVs can gather continuous data over long periods of time in naturalistic studies of driver behavior. These studies, which hitherto relied on questionnaires completed by individuals who may have unreliable memory and cognition, can offer unique insights into vehicle usage by at-risk drivers.

My Car, the Doctor

Converging evidence maps driver behavior to age-related functional decline (Carr & Ott, 2010), abnormal physiology (Merickel et al., 2019), and other disease states such as visual decline (Owsley & McGwin, 2010)—supporting the feasibility and utility of the vehicle as a diagnostic tool to screen, index, and monitor driver health, including indexing diagnosis, disease severity, disease progression, and objective measurements of disease impact (e.g., reduced mobility and quality of life, loss of independence). Emerging evidence suggests that older drivers who have AD pathology (amyloid plaque) but no measurable cognitive decline show deficits in controlled, on-road driving studies (Roe et al., 2017). This evidence is bolstered by findings that early signs of cognitive decline, even in older drivers without AD diagnoses, impact vehicle control (Merickel et al., 2019) and other driver behaviors like driving frequency (Molnar, Eby, Bogard, Leblanc, & Zakrajsek, 2018). This finding suggests that the vehicle may be used to improve screening and detecting early AD, even before the driver is aware of or seeks clinical care for their decline. In drivers with type 1 diabetes, real-time vehicle data have been successfully combined with wearable sensor data from continuous glucose monitors to quantify real-time, at-risk driver behaviors due to acute abnormal glucose states (e.g., hypoglycemia) that impair cognitive function (Chakraborty et al., 2019; Drincic et al., 2020). These data suggest that driver behavior patterns may index acute abnormal physiology, suggesting that vehicle data could inform screening of undiagnosed diabetes or objective assessments of diabetes severity (Drincic et al., 2020).

This ultimately supports the use of the vehicle to track health disease “in the wild,” inform patient care, and support development of personalized medicine programs and interventions. While patients drive their vehicles almost daily, many see their doctor only a few times a year. The patient’s vehicle provides rich, continuous data on health that may be combined with personal devices (e.g., phones) to improve patient health assessment. Passive monitoring of patient behavior that links back to health and disease may also overcome health care barriers such as a lack of providers, geographic hurdles, health disparities across groups and regions, and the desire of many patients to age at home. Data can also inform fair guidelines for fitness to drive assessments that preserve safety while concomitantly minimizing mobility loss. Applications of this framework anticipate vehicles as health care tools for detecting, screening, and responding to drivers who are aging or have medical disorders; connected to sensors at home, work, and on the driver; and linked to clinical trials, electronic medical records, and health care networks. Applications include advancing clinical and translational research on disease outcomes and progression.

Countermeasures

Cognitive impairment is an important risk factor for vehicle crashes in older adults. Adverse outcomes include side impact collisions at traffic intersections, inaccurate time-to-contact estimates leading to unsafe traffic entry decisions and rear-end collisions with lead vehicles and run-off-the-road crashes on curved roads. Cognitive interventions with speed of processing and attention training may help mitigate crash risk in some drivers (see the work of Ball and colleagues, e.g., Ball et al., 1988). Another promising intervention strategy is to develop on-board driver assist and collision warning devices to mitigate the risk of crashes in drivers with cognitive impairments.

Our group has conducted research aimed at determining an optimal set of signals for alerting drivers to unsafe behavior and impending traffic conflicts using a driving simulator and then an IV, and estimating the benefits of the proposed safety interventions across the United States in terms of crashes averted. A key aspect of this research is to develop collision warning algorithms and display parameters. Effective warning systems must promote a timely and appropriate driver response and minimize annoyance from nuisance warnings (Bliss & Acton, 2003; Kiefer et al., 1999). The system's success depends on how well the algorithm and driver interface match driver capabilities and preferences (Brown, Lee, & McGehee, 2001; Burgett, Carter, Miller, Najm, & Smith, 1998; Lee, McGehee, Brown, & Reyes, 2002; Tijerina, Jackson, Pomerleau, Romano, & Peterson, 1995). Algorithms are calculated to signal when to issue warnings and have strong effects on the safety benefit of collision warning systems. Driver interface is also important because it influences how quickly the driver responds and whether the driver will accept the system. A loud auditory warning might generate a quick response, but frequent loud warnings could undermine driver acceptance by distracting and annoying drivers. Another key interface characteristic that could affect driver behavior and acceptance is the warning modality. Several studies have found that haptic displays (e.g., a vibrating seat, pedals, or steering wheel) improve driver reactions to collision situations (Janssen & Nilsson, 1993; Raby, McGehee, Lee, & Norse, 2000; Tijerina et al., 2000).

Driver alerting systems must communicate urgency and minimize annoyance. To express the immediacy of attention required by the situation and to minimize confusion, the alert urgency should map systematically to the degree of hazard (Edworthy & Adams, 1996). Different sounds communicate urgency levels. Perceived urgency of sounds changes predictably with fundamental frequency, amplitude envelope, harmonics, interpulse speed, rhythm, repetition, speed change, pitch range, pitch contour, and musical structure (Edworthy, Loxley, & Dennis, 1991), with interpulse speed having the strongest influence. People perceive atonal bursts as more urgent. Increasing the number of burst repetitions will crease alert urgency, but also irritation. Annoying alerts may attract attention but lead a driver to ignore or disable them.

Annoyance, like urgency, can be assessed psychophysically and physiologically (Loeb, 1986). Annoyance may signify a reaction to a sound based on its physical nature, emotional content, novelty, or the situation being judged (Fucci, Petrosino, McColl, Wyatt,

& Wilcox, 1997). Annoyance depends on sound loudness, noisiness, sharpness, roughness, harmony, and tonality (Khan, Johansson, & Sundback, 1997). Noisiness increases with sound level, duration, frequency, spectrum, complexity, and abruptness of increase. Increasing loudness slowly and decreasing it rapidly is more annoying than increasing it rapidly and decreasing slowly.

Existing studies have focused on visual or auditory cues in operators with normal or corrected-to-normal vision and cognition without considering how response patterns might change for impaired observers. Complementing visual cues with cues in another sensory mode speeds reaction time (Nickerson, 1973). Haptic cues may speed response and reduce annoyance and offer a promising cue for alerting drivers to critical events in information-rich domains. Haptic warnings have proved more effective than visual cues in alerting pilots to mode changes in cockpit automation (83 vs. 100%), but the warnings did impede concurrent visual tasks (Sklar & Sarter, 1999). One type of haptic cue (torque-based kinesthetic) reduced reaction times more than auditory cues (Gielen, Schnidt, & Van den Heuvel, 1983), and another type (vibrotactile) enhanced reaction time to visual cues (Diederich, 1995). Older drivers may rely more on alert signals because of reduced self-confidence (Lee & See, 2004) and may use sound and vibration alerts more effectively than visual alerts if they have visual-processing impairments.

Automation

Manufacturers are currently deploying vehicles with automated systems that are capable of partial vehicle operation—extending beyond alerting and warning systems. Impaired drivers have tremendous potential to benefit from semi- to fully automated vehicles (Classen, Jeghers, Morgan-Daniel, Winter, King, & Struckmeyer, 2019). On-road safety risk could be mitigated by effective transfers of control between vehicle and driver when unsafe driver states are detected (e.g., an inattentive driver) or even fully operating the vehicle for a driver who would otherwise be too impaired to drive (e.g., Alzheimer's disease), preserving safety and mobility (Knoefel, Wallace, Goubran, Sabra, & Marshall, 2019). While fully automated systems have begun entering the roadway, they are decades away from widespread deployment. Current systems rely on a safe driver (e.g., attentive, alert, and unimpaired) to supervise system performance and take over control when the system turns off or fails (Merat, Jamson, Lai, Daly, & Carsten, 2014). Drivers with cognitive impairment may be ineffective system monitors, have impaired awareness of system function, misinterpret system capabilities, and be further taxed by additional cognitive load during the driving task due to monitoring and interacting with semiautomated systems (Neubauer, Matthews, Langheim, & Saxby, 2011). The prevalence of on-road driver impairment underscores manufacturer need to develop semiautomated vehicle systems while considering interaction with impaired drivers.

Limited research exists assessing impaired driver ability to interact safely with semiautomated vehicle system. These knowledge gaps—combined with the promise of improving driver safety, mobility, and independence in impaired populations—provide a rich area for research aimed at developing design principles for semiautomated vehicle system design in impaired drivers. Simulator-based research programs show potential to address these questions but raise issues related to fidelity, artificialness of system design, and ability to monitor changes in driver impairments overtime (e.g., sleep, physiology, medication wear-off). Controlled on-road drives permit testing on real vehicle systems in real driving conditions but may introduce ethical limitations such as inability to study system interaction with an acutely impaired driver (e.g., sleepy, distracted) and need to mitigate unsafe driving situations where systems may be most likely to engage or have the most relevance for safety assessments (e.g., failing to brake when approaching a vehicle). Naturalistic driving experiments have the potential to overcome these limitations by observing a driver's typical behavior and system interactions over time. At the same time, these experiments pose challenges related to recruitment (many people do not own vehicles with these systems, and systems are not standardized across manufacturers). Additional considerations are the "moving target" nature of real-vehicle systems due to software updates (also affecting controlled-on road drives); the difficulty of determining when the system was on or off due to proprietary restrictions and "silent" system failures (e.g., failure to detect a lane marker); and the difficulty of overtly assessing driver knowledge of the system in real time (e.g., asking the driver if they were aware the system was on). Despite these challenges, research in this area shows promise for reducing disease impact in impaired drivers.

Practical Assessment and Public Policy

Demographic and health factors may impact driving ability. Relevant factors are age, education, gender, general health, cognitive status, vision status, mobility, and driving frequency. Frequency of driving can be assessed using a Driving Habits Questionnaire (Ball et al., 1998). Health status information can be obtained using a checklist of medical conditions (e.g., heart disease, cancer) and noting when they occurred. Certain medical factors (e.g., use of some medications, a history of falls, back pain, kidney disease, heart disease, diabetes, stroke, bursitis, visual impairment, sleep apnea) are associated with increased risk of driving errors (see Hu, Trumble, Foley, Eberhard, & Wallace, 1998).

The psychological state of drivers can be collected using the General Health Questionnaire (GHQ; Goldberg, 1972). Medication use can be assessed by asking drivers to bring all prescription and over-the-counter medication to the clinic. A driver's chronic sleep disturbance can be assessed from the driver's self-report on the Epworth Sleepiness Scale.

A relevant visual assessment can include tests of letter acuity, contrast sensitivity, and visual field sensitivity (which is often assessed using automated perimetry). UFOV reduction in patients who have normal visual fields can be demonstrated using visual tasks under differing attention loads (Ball et al., 1993). Overall visual health can be assessed with the National Eye Institute Visual Function Questionnaire–25 (Mangione et al., 2001).

Several standardized tasks can be used to assess cognitive abilities that are essential to the driving task (see below). Impaired performance on some of these tasks (e.g., Rey Complex Figure Test [CFT], Trail Making Test Part B) may be especially predictive of driving safety risk. Of note, neuropsychological test scores are often corrected (e.g., scaled for age and education) to improve the ability to detect deviations from normative reference groups. However, what matters on the road is pure ability, regardless of demographic characteristics. For example, if a driver exhibits slowed processing speed, it is relevant that they are slow compared to all other drivers who might be on the road, not just compared to other drivers in the same demographic group. Studies that aim to correlate neuropsychological performance with driver behavior and to generate predictions of safety in individual drivers should use raw (i.e., not corrected for age, education, or gender) neuropsychological test scores. Alternatively, uncorrected scaled scores could allow for placement of the measures on a common metric and assist in normalizing the distribution. Importantly, although some large normative groups make this approach potentially attractive, evidence suggests that the use of norms from different groups results in significantly different standard scores (Anderson et al., 2007). No single test is sufficiently reliable to base judgments on fitness to drive, and a variety of sources and approaches are needed (Reger et al., 2004).

Briefly, Judgment of Line Orientation (JLO) assesses visuospatial perception. Visuoconstructional ability is tested using the Rey–Osterreith Complex Figure Test copy version (CFT-copy) and the block design subtest (Blocks) from the Wechsler Adult Intelligence Scale—Revised (WAIS-R). The CFT-recall version and the Benton Visual Retention Test (BVRT) assess nonverbal memory, while the Rey Auditory Verbal Learning Test (AVLT) indexes anterograde verbal memory. The Trail Making Test Part B (TMT-B) and Controlled Oral Word Association (COWA) test aspects of executive function. These tasks are described in detail elsewhere (e.g., Lezak, 1995). Several approaches have been developed to derive an overall estimate of neuropsychological functioning—for example, the global deficit score, which emphasizes number and severity of deficits by assigning more weight to below-average performances (Marcotte et al., 2004). We have also found it useful to calculate a composite measure of cognitive impairment (Adstat; Cogstat) by assigning standard *T*-scores (mean = 50, *SD* = 10) to each test from the neuropsychological assessment battery (Rizzo, Anderson, Dawson, & Nawrot, 2000; Uc et al., 2005). Mobility can be assessed using functional reach task and the get-up-and-go task (e.g., Podsiadlo & Richardson, 1991). Of course, many other potentially useful tests of vision, cognition, and mobility, as well as of personality and driving habits to consider, can be considered, depending on the questions being asked and the resources, expertise, and time available for testing.

Special concerns are often raised about fitness to drive with Alzheimer's disease (AD), the most common cause of abnormal cognitive decline in older adults (Alzheimer's Association, 2018). Johansson and Lundberg (1997) raised the important concerns that the first manifestation of AD may sometimes be a fatal crash and that preclinical AD raises the risk of a crash several fold. Brain autopsies showed neuropathological evidence of possible or probable AD in over half of 98 older drivers who perished in vehicle crashes, yet none had a diagnosis of AD (Lundberg, Hakamies-Blomqvist, Almkvist, & Johansson, 1998).

The Swedish Road Administration (Vägverket) proposed operational guidelines for assessing fitness to drive in motorists with dementia, based on screening measures such as the Clinical Dementia Rating (CDR) and the Mini-Mental State Examination (MMSE). Generally, patients with moderate to severe dementia (e.g., cutoffs: MMSE $\leq$ 17; CDR $\geq$ 2) should not drive. The American Academy of Neurology (AAN) supports the use of regular testing and optional reporting of cases involving dementia. Several national organizations (e.g., Association/National Highway Traffic Safety Administration, American Academy of Ophthalmology, American Association of Motor Vehicle Administrators, American Diabetes Association, and the Federal Motor Carrier Safety Administration) have formulated their own guidelines for at-risk drivers with visual, cognitive, or medical impairments, based on the best available current peer-reviewed evidence. In these policy-making efforts, it is critical to consider individual driver risk factors (e.g., disease severity, co-morbid conditions, awareness), the relationship of driver safety assessments and outcomes (e.g., a crash), risk to the public, and potential risk to the driver due to driving restrictions (e.g., loss of independence) (Table 9.2).

The AAN has sought to create fair, comprehensive, and accurate guidelines for advising drivers with neurological disease or cognitive impairments as to whether they should continue to drive (Iverson et al., 2010). These guidelines are based on results from well-designed, controlled studies of driving in patients with dementia from any cause or mild cognitive impairment. The results suggested that a patient's clinical dementia rating (CDR) score and the caregiver's rating of the patient's driving ability presented the strongest evidence for determining fitness to drive. Drivers with mild dementia (CDR of 1) had a substantially higher risk for unsafe driving and were recommended strongly to discontinue driving. Other recommended forms of risk management were encouraging family support for alternate transportation and referral to a driving specialist for evaluation. A patient with dementia's self-rating of driving ability was considered unreliable for determining driver safety. While it was beyond the scope of their review, the AAN acknowledged that visual and mobility factors may mediate risk from dementia. They have recommended that mildly demented drivers be retested at 6-month intervals. Foley, Masaki, Ross, and White (2000) studied driving cessation in older men with incident dementia in the Honolulu Asia Driving Study (HAAS), a population-based longitudinal study of AD and other dementias of over 3-year durations. Only 22% of the participants in incident cases of diagnosed AD or other dementia with a CDR of 1 were still driving at time of evaluation, versus 46% of those with a CDR of 0.5 (30% overall).

Foley, Masaki, White, Ross, and Eberhard (2001) took issue with the AAN. Whereas the AAN recommended that patients with AD and CDR of 1 should not drive and that their families should be informed of this clinical recommendation, Foley and colleagues (2001) suggested that patients may not accept the physician's advice and family members may have trouble complying with this recommendation. The AAN recommended

TABLE 9.2. Driving End Points and Their Prediction of Unsafe Driving

End point	Comment
Reported at-fault accident above baseline rate	Valid, insensitive
Reported at-fault accident without comparison to baseline rate	Less valid, insensitive
License revocation by statute	Valid factor, insensitive
Driving privileges revoked by family member	Probably valid, insensitive
Self-surrender of license	Probably valid, very insensitive
Failed on-road driving test by blinded professional examiner using statutory criteria	Valid factor, sensitive, probably the gold standard
Failed on-road driving test by blinded professional examiner using validated research criteria	Valid, sensitive

referring patients for a driving evaluation to determine which patients with AD and a CDR of 0.5 were “appropriate” to continue driving, but Foley and colleagues countered that this assessment assumed that this service was readily available and ideally covered by a patient’s health insurance policy. In reality, there are few qualified examiners in the United States, and the charge for an evaluation may not be covered by a typical Medicare-linked supplemental insurance. Given population aging trends (Administration for Community Living, Administration of Aging, & U.S. Department of Health and Human Services, 2018), demand for driver evaluation services and insurance coverage will increase. The AAN acknowledged that it is difficult to enforce cessation of driving and that adequate testing facilities are lacking. They asserted that the AAN guidelines were developed for health care professionals to point out potential problems associated with allowing even mildly cognitively impaired individuals to drive but were not designed to recommend legislation. State and federal governments are responsible for legislation and enforcement of driving restrictions.

Duchek and colleagues (2003) showed that many drivers with CDR scores of 1 or greater are unsafe to drive within a year of their road tests. However, mandatory reporting of drivers with health complaints is controversial because it may inhibit drivers with treatable conditions from seeking required medical attention. The American Medical Association (AMA) recommended that physicians report their patients’ medical conditions when the condition poses a threat and the patient is apparently disregarding the physician’s advice not to drive—with liability protections for good-faith reporting.

The AAN supports the development of better evaluation tools to assess driver safety, to help physicians recognize when a driver should be referred for evaluation, and to help state officials conduct such an evaluation. Critically, state agencies are not equipped to perform complex assessments of behavior in drivers with flagged medical conditions for determination of driving safety. Training and diagnostic tools can be developed in collaborations between state transportation officials and other medical groups. Stricter driving and reporting standards may be needed for drivers who provide public transportation or transport hazardous material. State and federal efforts are needed to provide transportation resources for individuals unable to transport themselves. Health care personnel should review the driving laws in their area and be prepared to discuss and document their medical recommendations in light of these regulations (American Academy of Neurology, 2006).

Conclusions

Safe driving requires the coordination of attention, perception, memory, motor and executive functions (including decision making), and self-awareness or metacognition. These abilities may be impaired by fatigue; overwork; illicit drugs and alcohol; advancing age; medical, neurological, personality, or psychiatric disorders; and prescription drug effects. Because age or medical diagnosis alone is often an unreliable criterion for licensure, decisions on fitness to drive should be based on empirical observations of behavior, preferably under conditions of optimal stimulus and response control in environments that are challenging, yet safe. Real-life crashes are sporadic, uncontrolled events during which few objective observations can be made. Personal accounts and even state crash records may be incomplete, and crashes are underreported. In most cases, state road tests are designed to test if novice drivers know and can apply the rules of the road, not to predict crash involvement in veteran drivers who may now be impaired. Linkages between cognitive abilities measured by neuropsychological tasks and driver behavior assessed using driving simulators and natural and naturalistic observations in IVs can help standardize the assessment of fitness to drive. By understanding the patterns of driver safety errors that cause crashes, it may be possible to design interventions to reduce these errors and injuries and increase mobility. These interventions include driver behavior monitoring devices, collision alerting and warning systems, road design, and graded licensure strategies.

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CHAPTER 10

Naturalistic Assessment

Everyday Environments and Emerging Technologies

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Understanding the potential impact of changes in cognition on the everyday functioning of individuals with cognitive impairment is an important area of study in neuropsychology. Neuropsychologists are increasingly being asked to answer referral questions about how a patient's compromised cognitive abilities will impact their everyday functioning, including capacity to manage medications, work, or handle finances (Marcotte, Scott, Kamat, & Heaton, 2010). Several comprehensive reviews of the literature conducted with varying patient populations (e.g., mild cognitive impairment, mixed geriatric, neuropsychiatric, and rehabilitation) have consistently concluded that cognitive predictors account for about 20–25% of the total variance in functional status (McAlister, Schmitter-Edgecombe, & Lamb, 2016; Royall et al., 2007; Tucker-Drob, 2011). Functional status is typically measured in studies by self- or informant-report questionnaires or performance-based measures, which serve as proxies for real-world functioning. These methods have both advantages and disadvantages (e.g., reporter bias; Moore, Palmer, Patterson, & Jeste, 2007; Sikkes et al., 2009), do not always correlate well with each other (e.g., Burton, Strauss, Bunce, Hunter, & Hultsch, 2009; Finlayson, Havens, Holm, & Van Denend, 2003; Loewenstein et al., 2001; Tabert et al., 2002), and may capture different aspects of everyday functioning (e.g., Schmitter-Edgecombe, Parsey, & Cook, 2011).

One important challenge for assessment of everyday functioning when measured with methods commonly used in the clinic or laboratory is demonstrating that the administered tests are ecologically valid (i.e., correspond to functioning in real-world settings; Sbordone, 1996). An individual's performance in a time-limited, specific testing situation may not necessarily relate to behaviors that occur over longer periods of time across varying everyday environments and situations (Donovan et al., 2011). Moreover, administration of a test that resembles an everyday task does not necessarily mean that the test is ecologically valid (Ziemnik & Suchy, 2019). For example, finding that an individual is unable to write out a check in the laboratory environment may tell one little about the individual's capacity to pay bills if the person banks online. In addition, compensatory strategies used in the real world, such as a grocery list or reminder alarm, may help support an individual's ability to complete a task despite poor cognitive abilities (Weakley, Weakley, & Schmitter-Edgecombe, 2019). Alternately, finding that an individual can complete a deductive problem-solving task in a highly structured laboratory environment may not necessarily generalize to what the individual is able to do when more complex, open-ended problems arise in an unstructured everyday environment. Furthermore, noncognitive factors, including physical, neuropsychiatric, behavioral, and environmental (e.g., frailty, fatigue) factors, may markedly affect an individual's ability to function in the everyday environment despite adequate performance in the laboratory (Harvey, 2011; Stika et al., 2020).

It has been argued that naturalistic observation of individuals in everyday environments would provide the most valid determination of "real-world" outcomes (Marcotte et al., 2010). The field of naturalistic assessment is evolving as advances in technology now allow for the collection of large amounts of data over extended periods of time in real-world settings. In this chapter, we discuss assessment in naturalistic settings and highlight the strengths and challenges of the varying approaches. We focus on naturalistic assessment methods conducted within the home environment, when driving, and within the community.

Naturalistic Assessment: Home-Based Tasks

Many everyday tasks take place within the home, including cooking, grooming, and managing finances. Identifying the cognitive correlates that may contribute to functional impairment in specific everyday activities has been limited by the need to rely on proxy measures for assessment (i.e., laboratory questionnaires and performance-based tests). Many performance-based measures simulate real-world tasks (e.g., write out a check) and are scored based on elements of task accuracy. More recently, researchers have begun to code activity completion for detailed error types based on observing how individuals complete the complex activities of daily living (e.g., making toast and coffee, preparing for a day out) in the laboratory or a real-world environment (e.g., Giovannetti et al., 2008; Schmitter-Edgecombe & Parsey, 2014a). In addition, advances in smart technologies are beginning to allow for continuous, unobtrusive assessment of everyday activities within the home environment. These studies are informing understanding of the underlying everyday functional difficulties and may lead to the development of better everyday compensatory strategies and interventions for functional limitations.

Naturalistic Direct Observation

Naturalistic tasks refer to tasks developed to mimic everyday activities in either laboratory or real-world settings that allow for direct observation of task performance and completion (Robertson & Schmitter-Edgecombe, 2017). Example naturalistic direct observation tasks are listed in Table 10.1. The Naturalistic Action Test (NAT; Schwartz, Buxbaum, Ferraro, Veramonti, & Segal, 2003) is performed within the laboratory environment.

Participants are seated at a semicircular table that contains everyday objects and are required to complete multistep naturalistic actions to achieve a goal (e.g., make toast and coffee, pack a lunchbox). Activity completion is coded for a variety of error types, including commission (i.e., performing task steps inaccurately) and omission (i.e., not completing a task step) errors. Similarly, the Multiple Object Test (MOT) requires individuals to complete five different routine tasks, such as lighting a candle and preparing a letter to mail, and performance is based on number and type of errors, as well as total time (Beyle et al., 2018). The eight Instrumental Activities of Daily Living (8 IADLs; Schmitter-Edgecombe et al., 2011), Day Out Task (DOT; Schmitter-Edgecombe, McAlister, & Weakley, 2012), and Apartment Map Task (Amap; Sanders & Schmitter-Edgecombe, 2012) are all performed within a university campus apartment and require participants to complete individually scripted IADLs (e.g., water plants, fill medication dispenser) or more open-ended, complex activities that require multitasking and planning to be executed efficiently (e.g., DOT, Amap). Performance is coded on a variety of dimensions, including execution accuracy and efficiency, task sequencing, and task error types (e.g., omissions, inefficiencies, substitutions, irrelevant actions). Similarly, Chevignard and colleagues' (2008) cooking task requires that individuals bake a cake and cook an omelet for two people in a kitchen setting, and scoring is based on error classifications. The Rabideau Kitchen Evaluation- Revised (RKE-R; Neistadt, 1992) requires patients to prepare a cold sandwich with two fillings and a hot instant beverage in a kitchen setting. The task is broken down into 40 subcomponents that are scored based on the amount of examiner assistance needed.

These naturalistic, direct observation, performance-based tasks allow for assessment to go beyond a measure of general completion of everyday activities to evaluate the underlying nature of the difficulties. For example, the RKE-R allows for assessment of the amount of support needed for task completion (Yantz, Johnson-Greene, Higginson, & Emmerson, 2010). In individuals with Alzheimer's disease (AD), studies with the NAT

TABLE 10.1. Example Performance-Based Naturalistic Direct Observation Tasks

Scale	Author
Multiple Errands Task (MET)	Shallice & Burgess (1991)
Rabideau Kitchen Evaluation- Revised (RKE-R)	Neistadt (1992)
Test of Grocery Shopping Skills (TOGSS)	Hamera & Brown (2000)
Naturalistic Action Test (NAT)	Schwartz et al. (2003)
Functional Cognitive Assessment Scale (FUCAS)	Kounti et al. (2006)
Complex Task Performance Assessment (CTPA)	Wolf et al. (2008)
Assessment of Motor and Process Skills scale (AMPS)	Fisher & Bray Jones (2010)
Executive Secretarial Task (EST)	Lamberts et al. (2010)
Day Out Task (DOT)	Schmitter-Edgecombe et al. (2012)
Apartment Map Task (Amap)	Sanders & Schmitter-Edgecombe (2012)
Night Out Task (NOT)	Schmitter-Edgecombe & Cunningham (2020)
Multiple Object Test (MOT)	Beyle et al. (2018)

revealed difficulties with omission errors, which were associated with episodic memory loss and reduced volume in the hippocampus and medial temporal lobe (Bailey, Kurby, Giovannetti, & Zacks, 2013; Giovannetti et al., 2008; Seidel et al., 2013). These naturalistic direct observation measures have objective and reliable coding systems with good interrater reliability (e.g., Schwartz et al., 2003), and some have demonstrated convergent validity with both performance-based and self- and informant-report measures of functional status (e.g., Schmitter-Edgecombe et al., 2011). Despite these strengths, the tests are typically administered at a single evaluation point, and poor motivation could lead to lower scores. Testing and scoring can also be costly in terms of supplies and are time intensive. In addition, although naturalistic, the tests are not administered in the person's own home where performance could be supported by the familiar home environment (Park, Fisher, & Velozo, 1994; Toneman, Brayshaw, Lange, & Trimboli, 2010).

The Assessment of Motor and Process Skills scale (AMPS; Fisher, 1993; Fisher & Jones, 2010) has been widely used by occupational therapists to assess everyday activities in the home. The examinee is asked to choose at least two everyday tasks that they perform on a regular basis from the AMPS manual, which has over 80 calibrated tasks (Fisher et al., 2012). The person sets up and performs the task in their home. Performance on motor (e.g., observable physical actions) and process (e.g., sequencing and task adjustment) skills are scored based on effort, efficiency, and safety. Scores are then entered into a computer program that uses a many-faceted Rasch analysis to adjust scores for skill item difficulty, task challenge, and individual evaluator effects (Fisher, 1993). Qualitative data, such as the evaluator's direct observation of why a specific everyday task is difficult for an individual to perform, can also be used for clinical purposes (Park et al., 1994). The AMPS has been found to be a reliable and valid assessment instrument in multiple populations (e.g., traumatic brain injury [TBI], stroke, dementia; Bouwens et al., 2008; Kizony & Katz, 2002; Lange, Spagnolo, & Fowler, 2009; Lindén, Boshcian, Eker, Schalén, & Nordström, 2005). The AMPS must, however, be administered by an occupational therapist who has received extensive training in AMPS administration procedures and has been calibrated as a reliable and valid AMPS rater. In addition, the occupational therapist has to travel to the person's home, which can sometimes be time consuming and cumbersome. People may also be more anxious or careful when completing the tasks as their performance is being closely watched and coded by the examiner. In addition, given that the person choses a task with which they are familiar, the task may be overlearned, which, though helpful in understanding performance on routine tasks, may not capture how well the person might do if they need to learn a new task or make adjustments in a routine.

Smart Homes

The creation of smart environment testbeds (e.g., Helal et al., 2005; Intille et al., 2006) has laid the groundwork for continuous, unobtrusive assessment of everyday activities within the home. Several types of sensors can be used in a smart home environment to gather information about everyday activities. As examples, infrared sensors (i.e., motion sensors) provide information about the location of an individual within the home; magnetic door sensors indicate when a particular door or cabinet is shut or open; vibration and pressure sensors attached to particular items (e.g., bed, medicine dispenser) can indicate when the item is in use; and light sensors report ambient light levels. One advantage of employing ambient sensors is that the smart home can gather information without the resident wearing anything or performing activities in any particular manner for data collection. The sensors are also unobtrusive and do not require any video-based data. In the following paragraphs, we describe research from our group (i.e., Center for Advanced Studies in Adaptive Systems [CASAS], Washington State University [WSU]) and others which suggests the possibility of using smart home-based sensor data and machine learning techniques to provide insights on functional status.

Activity Recognition

Sensor-recorded event states (e.g., on/off for motion sensors) can be transformed into a vocabulary of activity information (e.g., work, eat) that can then be used to describe and assess behavior. Examples of everyday activities that have been recognized using methods such as machine learning include clean house, prepare meals, take medicine, sleep, bathe, and exercise (Bulling, Ward, & Gellersen, 2012; Cook, 2012). Most approaches recognize activities offline after the sensor event features have been extracted and labeled by an expert human analyst who can identify what was occurring when the sensor patterns emerged (e.g., exercise, cook). This process is time consuming and prone to human error, with interrater reliability often low for activities that do not occur frequently. Our group's approach identifies activities as they occur in real time and learns a model that generalizes to new homes, reducing the burden of users needing to label collected data (see Krishnan & Cook, 2014). The derived information about a person's activities is then used along with other sensor-derived features (e.g., sleep duration, time outside home) to inform understanding of a person's everyday functioning.

Functional Status Assessment

As a first step toward examining whether sensor-derived data could provide information about the quality of everyday activity performance, we completed cross-sectional studies in a smart home testbed at WSU. We had younger adults, healthy older adults, individuals with mild cognitive impairment (MCI) and with dementia complete scripted IADLs (e.g., water plants, cook oatmeal; Schmitter-Edgecombe & Parsey, 2014a) and a complex, multitasking activity (i.e., Day Out Task; Schmitter-Edgecombe, McAlister, & Weakley, 2012). As participants completed activities, ground truth labels were provided, and the behavioral quality of task performances was coded. We found poorer performance as a function of age and cognitive impairment in time to complete the everyday tasks, and in task accuracy, efficiency, and the types of errors being committed (e.g., inefficiencies, omissions, off-task behaviors; Schmitter-Edgecombe et al., 2011; Schmitter-Edgecombe & Parsey, 2014a, 2014b; McAlister & Schmitter-Edgecombe, 2013). Having established clinically observable differences in functional abilities across groups, we then evaluated whether sensor-derived features (e.g., time spent on the entire activity, time spent on each step of the activity, triggered sensor events, unusual sensor events triggered) could be used to capture these differences. We found that machine learning algorithms applied to the sensor data could be used to distinguish between diagnostic groups (e.g., cognitively healthy, MCI, or dementia) and automatically predicted the quality of scripted IADLs and more complex, multitasking performance (Dawadi, Cook, & Schmitter-Edgecombe, 2013; Dawadi, Cook, Schmitter-Edgecombe, & Parsey, 2013).

The smart apartment testbed presents a unique opportunity to collect direct behavioral observation data within a naturalistic environment and to provide ground truth for sensor labeling. However, these experimental testbeds differ from participants' own homes, and repeated measurements of the same everyday activities are not examined, which may result in missed trends such as when an indicator might be fluctuating (Haimowitz & Kohane, 1993). Continuous unobtrusive monitoring has been used to evaluate behaviors such as pillbox use, overall activity level in the home, gait, time out of the home, computer use, sleep, and sleep quality (e.g., Galambos, Skubic, Wang, & Rantz, 2013; Kaye, 2008; Paavilainen et al., 2005). A study by Hayes and colleagues (2008) revealed that, in comparison to controls, variability on measures of walking speed and day-to-day activities was associated with a diagnosis of MCI. One recent study that holistically tracked the behaviors of individuals living in smart homes using a variety of sensor types (e.g., motion, bed, pill) found that, in comparison to healthy controls, individuals with MCI were less active, had more sleep interruptions, and forgot their medications more times per month (Rawtaer et al., 2020). This work illustrates how sensors can feasibly be used within the real-world environment to collect continuous data and detect differences in behaviors between individuals with impaired and intact cognition.

Sensor measurements of sleep patterns, gait, activity rhythms, and indoor activities have also been found to correlate with everyday functioning and cognitive status. For example, Robben and Krose (2013) found that the location and transition patterns of an individual's indoor mobility behavior correlated strongly with the AMPS, while Paavilainen and colleagues (2005) found a significant relationship between sensor observed time spent in bed and self-reported functional ability and objective measures of cognitive status. Using sensor data collected over a 2-year period from older residents (age 73+) living in their own homes (single-dwelling) that were turned into smart homes, we introduced machine learning methods to quantify and track changes in everyday activities (i.e., sleep, IADLs: cook, eat, relax, grooming, out of home) and in mobility. In this approach we correlated sensor-derived changes in an individual's everyday activities and mobility with changes in standardized clinical scores of cognition (i.e., Repeatable Battery for the Assessment of Neuropsychological Status; Randolph, Tierney, Mohr, & Chase, 1998), mobility (Timed Up and Go; Podsiadlo & Richardson, 1991), and self-reported functional status (IADL-Compensation; Schmitter-Edgecombe, Parsey, & Lamb, 2014) and mood (Geriatric Depression Scale; Sheikh & Yesavage, 1986) collected at six-month intervals (Dawadi, Cook, & Schmitter-Edgecombe, 2016a). We also evaluated methods for predicting an individual's clinical scores by using automatically recognized activity parameters, as well as sleep and mobility parameters, to model the resident's daily behavior (Dawadi, Cook, & Schmitter-Edgecombe, 2016b). We found that we were able to detect cognitive and functional changes relative to baseline and between consecutive assessment points using several different modeling techniques (e.g., Dawadi, Cook, & Schmitter-Edgecombe, 2016b; Alberdi et al., 2018a, 2018b). The data also revealed the largest correlations between specific behavior features (e.g., outing patterns, daily routine) and mobility, followed by cognition and then by mood (Alberdi et al., 2018b). Although much more research is needed to improve the algorithmic solutions and to ensure generalization to different homes and populations, this preliminary work indicates that smart home technologies have the potential to assess, track, and predict the cognitive, physical, and functional health of patients.

In addition to modeling progressive change in everyday functioning, as might occur in a neurodegenerative disease, it is also important to develop algorithms that may signal more acute, abrupt changes in everyday functioning. One challenge to such work is deriving methodologies that will automatically identify anomalous or rare events that may indicate a cause for concern. In machine learning, anomaly detection is less thoroughly understood than recognizing instances of well-defined concepts. Clinical translation of this work will also require that developed activity recognition and health algorithms (e.g., sleep quality, functional status) are demonstrated to be reliable and valid measures of everyday activities and health-related parameters. In addition, research is needed to better understand the types of health information that clinicians will find useful for clinical decision making, and to show that the sensor-derived data provides improved value to the clinical decision-making process. Health care providers have expressed concerns about information overload, including the potential that irrelevant information could detract from patient care (Kang et al., 2010). A related issue is how to visualize collected data and health events in a way that can be easily digested by those who need to use the data, including users, caregivers, and professionals. For smart environment technologies to be successfully adopted and used in everyday life, users must continuously be involved in the development, evaluation, and validation process.

Additional technological challenges relate to sensor longevity. Battery life for many sensors (e.g., item sensors) that could be used to monitor behavioral health is one week or, in some cases, days. Ongoing research is investigating alternative energy sources (e.g., solar radiation, thermal gradients, and kinetic energy). Large amounts of continuous data can also produce challenges when analyzing and interpreting the data; advances in methodologies that can quickly process large amounts of data and classify targeted activities will be needed. In addition, interdevice communication remains a challenge. Other issues that must be addressed include privacy, confidentiality and security of the personal information collected from smart environments (Beringer, Sixsmith, Campo, Brown, & McCloskey, 2011; Courtney, Demiris, & Hensel, 2007). Approaches to privacy that give individuals control over when and where information is gathered and that can flexibly modify who has access to the data (e.g., make privacy notifications a prominent and accessible feature) are being investigated (Babbitt, 2006; Moncrieff, Venkatesh, & West, 2008; Zheng, Apthorpe, Chetty, & Feamster, 2018). Although research has shown that people are willing to risk privacy in order to maintain autonomy (Courtney, Demiris, Rantz, & Skubic, 2008; Townsend, Knoefel, & Goubran, 2011), situations are likely to arise where family members want to use monitoring technologies for safety concerns, but obtaining informed consent from the individual may be difficult due to dementia or other concerns about the technology. As a society, we will need to address ethical concerns that are sure to be raised about in-home monitoring technologies.

Naturalistic Assessment: Driving

Driving, a complex everyday task carried out in a continually changing environment, involves motor skills, multisensory perception, and numerous cognitive abilities (Apolinario et al., 2009). Cognitive impairment has been identified as one factor that can impact a person's ability to drive a motor vehicle (Lafont, Laumon, Helmer, Dartigues, & Fabrigoule, 2008). On-road tests and driving simulators are most commonly used as measures of driving outcome in studies evaluating neuropsychological factors that predict driving ability, and these methods are reviewed in Chapter 9, this volume. Despite the link between cognition and driving safety, data also suggest that not all persons with cognitive deficits are incompetent drivers (Cox, Quillian, & Thorndike, 1998; Rizzo, McGehee, Dawson, & Andersen, 2001), making it important to identify the types of factors that contribute to driving impairment.

Naturalistic Driving Studies

As also described in Chapter 9, advances in vehicle instrumentation techniques have made it possible to examine real-world driving situations through the collection of continuous kinematic, global positioning system (GPS) radar and video data (Guo & Fang, 2013). In these naturalistic driving studies, vehicles are fitted with video cameras that continuously record the road ahead of the vehicle, the driver's face, and possibly an over-the-shoulder view of the driver's hands during driving (Carsten, Kircher, & Jamson, 2013). Potential obstacles on the roadway or roadside and proximity to other vehicles can be recorded with radar. In addition, other on-board sensors can record vehicle accelerations in three dimensions and rotational motion along the same axes (Wu, Aguero-Valverde, & Jovanis, 2014). The instrumentation is installed as unobtrusively as possible to prevent the driver and other drivers who may see the equipment from changing their driving behaviors (Carsten et al., 2013). Drivers are asked to drive in their daily lives, just as usual, and all data is recorded and stored on an on-board data acquisition system. To reduce the amount of data, some systems may only save data gathered around a triggered event (e.g., sudden deceleration).

In the first large-scale naturalistic driving study in the United States, the 100-Car Naturalistic Driving Study (Dingus et al., 2006), driving data were collected continuously for 12 months from > 100 primary drivers in northern Virginia. More recently, the Strategic Highway Research Program (SHRP2) study collected data from > 3,400 volunteer drivers, ages 16–80, from six different regions in the United States. The vehicles were heavily instrumented (e.g., video of driver, forward radar, vehicle location, vehicle control positions), and data was collected continuously for trips taken over a 2-year period. This resulted in nearly 50 million travel miles and 2 petabytes of data (Transportation Research Board, 2014). The collected data can be linked with a database that includes detailed roadway information (i.e., Roadway Information Database, [RID]) on approximately 12,000 centerline miles of highway in and around the study sites as well as with other information such as work zones, cell phone records (post hoc), traffic, and weather conditions. A subset of SHRP2 data, created for crash and near-crash events, includes secondary task engagement as a potential contributing factor (i.e., Naturalistic Engagement in Secondary Tasks [NEST]) through frame-by-frame video coding of these events (Owens, Angell, Hankey, Foley, & Ebe, 2015). To learn more about SHRP2 data access, see *https://insight.shrp2nds.us*.

One of the primary purposes of naturalistic driving studies is to collect pre-crash data so that variables that lead to actual crashes in the real world can be determined. Using data from the 100 Car Naturalistic Driving Study, Guo and Fang (2013) found that crash and near-crash risk was associated with age, personality, and critical incident rate (defined as conflicts less severe than the near-crash). Studies have also begun to classify driving behaviors that are indicative of driver distraction (Kuo, Koppel, Charlton, & Rudin-Brown, 2014). Data from the SHRP2 study suggests that behaviors such as off-road glances can be dangerous in situations where a driver gets exposed to a rapidly changing situation and has not adopted sufficient safety margins to protect against a rear-end collision (Victor et al., 2015; Lee, Lee, Bargman, Lee, & Reimer, 2018). Furthermore, in stop-and-go critical driving situations, drivers were found to require more time to recognize the nature and significance of external stimuli as compared to other types of driving situations, such as a vehicle ahead changing lanes or decelerating (Wu & Lin, 2019). This work has demonstrated the feasibility of using vehicle instrumentation techniques to investigate questions related to the role of driver performance and behavior in traffic safety.

To date, naturalistic driving studies have primarily been applied to drivers from the regular driving population. Several recent pilot studies have been conducted with individuals along the continuum from MCI to early-stage AD (e.g., Babulal et al., 2019; Seelye et al., 2017). These studies demonstrated that the driving sensors were feasible to use, well accepted by the older adult populations, and able to identify clinically meaningful changes in daily driving. For example, individuals with MCI were found to drive fewer miles and spend less time on the highway than cognitively intact participants (Seelye et al., 2017). In another pilot study, individuals with early-stage AD exhibited lower tactical self-regulation behaviors, reflecting a poorer capacity to ensure safe distances, adapt driving speed, change lanes, and appropriately anticipate or plan actions (Paire-Ficout et al., 2018).

These in-car continuous data collection systems have a high degree of external validity, as they allow researchers to objectively capture aspects of everyday driving over an extended time period. While some aspects of driving events will remain unobserved (e.g., actions of drivers in other vehicles), the large amount of data gathered offers possibilities to explore a broad range of research questions, including those related to the impact of changing cognition (e.g., progression to dementia) or impaired cognition on driving behaviors. This information could lead to the development of new or targeted training strategies that may assist individuals with cognitive impairment in remaining safe drivers. The efficacy of such interventions could also be evaluated objectively with real-world driving data.

Similar to smart home data collection, the collection of large amounts of continuous driving data leads to both logistical and inferential limitations as well as concerns related to the privacy and security of data (Knoefel, Wallace, Goubran, & Marshall, 2018). For example, in the 100-car study, hard disks had to be exchanged regularly in the vehicles due to limited storage capability without disturbing the driver's natural use of the car (Carsten et al., 2013). Human analysts must also manually process the collected data to classify the occurrence of driving behaviors. This process itself is inherently error-prone, and as the hours of video footage grow, this processing becomes both time and labor intensive. Several approaches have been applied to reduce the data to selected subsets of importance (e.g., near crashes), including various statistical sampling methods (Stutts et al., 2005; Koppel, Charlton, Kopinathan, & Taranto, 2011), video triggers such as vehicle performance data (Klauer, Dingus, Neale, Sudweeks, & Ramsey, 2006), and machine learning and computer vision solutions (Kuo et al., 2014). Application of some of these techniques, such as the creation of algorithms to recognize safety critical events, also require video preprocessing to improve the quality of video and reduce potential confounding situations (e.g., image flickering, changing light conditions; Dozza & Gonzalez, 2013). All current methods have pros and cons, and continued advancements in methodologies for processing large amounts of data quickly while also correctly classifying target behaviors will be needed.

Naturalistic Assessment: Community Tasks

In addition to driving, other important everyday activities like work and shopping are performed within the community environment. Although lab-based measures aim to mimic real-world performance, the quiet lab setting is typically much different from noisier and distracting real-world community settings. Tasks created for community settings are characteristically less structured and allow individuals to complete the task in a more naturalistic manner (Robertson & Schmitter-Edgecombe, 2017). Advances in wearable technologies have also provided additional methods for collecting continuous (e.g., activity level) and momentary data (e.g., fatigue) about psychological, environmental (e.g., distraction) and health variables that may influence everyday performance within the community setting. These measures are providing new ways to examine the impact of both cognitive and noncognitive contextual determinants on everyday functioning.

Naturalistic Direct Observation

Shopping is an everyday task that utilizes organizational skills, multitasking abilities, decision making, and memory (Manee, 2005). In addition, distractors and irrelevant stimuli must be appropriately filtered. The Multiple Errands Test (MET; Shallice & Burgess, 1991) and Test of Grocery Shopping Skills (TOGSS; Brown, Rempfer, & Hamera, 2009; Hamera & Brown, 2000) were created to assess executive dysfunction in an ecologically valid manner. Both tasks require participants to gather specific items in real-world environments (i.e., shopping mall, grocery store). The MET also requires participants to arrive at a destination at a given time, to collect four pieces of specified information, and to follow rules during task completion (e.g., amount of money to use). Performance is scored for task efficiency and accuracy. Both the MET and TOGSS have proven useful in understanding real-world functional deficits (e.g., rule breaks) that occur with a variety of neurological disorders (e.g., TBI, schizophrenia; Cuberos-Urbano et al., 2013; Faith & Rempfer, 2018; Manee, 2005; Rotenberg et al., 2020). Numerous versions of the MET have been created, including virtual reality (e.g., Rand et al., 2009) and simplified hospital (Dawson et al., 2009; Knight, Alderman, & Burgess, 2002) versions, which reduce the time and burden associated with traveling to a grocery store or shopping mall. Studies with the MET have demonstrated associations with functional outcomes, including self-report measures and IADLs (e.g., Dawson, 2009; Maeir, Krauss, & Katz, 2011). Nevertheless, a recent review examining the MET's measurement properties cautions that despite good evidence of interrater and group reliability, other psychometric properties are not well supported, and the use of real-world environments that vary pose challenges for multisite research use (Rotenberg et al., 2020).

Several work-simulated tasks have been developed to predict a person's level of functioning in daily life. These tasks are conducted in an office environment, which allows for easy replication in many settings. The Complex Task Performance Assessment (CTPA; Wolf, Morrison, & Matheson, 2008) presents participants with a primary task (bookkeeping of inventory), secondary task (phone messages), delayed intentions (tell time, give examiner message), and rules. Performance is determined by task completion, phone message completion, number of executive decisions, and inventory control percent complete. Similarly, the Executive Secretarial Task (EST; Lamberts, Evans, & Spikman, 2010; Spikman, Boelen, Lamberts, Brouwer, & Fasotti, 2010) is a 3-hour job assessment procedure that requires individuals to complete several secretarial assignments that include prioritization, delayed intentions, deadlines, and interruptions. Three task scores are derived: initiative, prospective, and executive. Bottari and colleagues (Bottari, Gosselin, Guillemette, Lamoureux, & Pitto, 2011) developed an open-ended budgeting task. Unlike the CTPA and EST, the budgeting task allows the examiner to offer assistance using a hierarchical cueing system. This procedure enables the examiner to obtain scores about the level of assistance necessary to complete the task, which helps to understand the underlying nature of the functional deficits as well as inform clinical decisions about level of care needed. Each of these work-simulated tasks was also found to be a sensitive measure for assessing higher-level cognitive processing deficits, which otherwise might have been difficult to detect with more traditional tasks (Bottari et al., 2011; Lamberts et al., 2010; Wolf et al., 2008).

During the past several decades, rehabilitation hospitals have incorporated naturalistic environments into their facilities (Srinivasan, 1994; Hudson, 1995). These naturalistic environments are often simulated modules, where facsimiles of grocery stores, restaurants, bus stations, cross walks, and recreational venues can help patients make a direct connection to real-life challenges. It has been suggested that the contextually relevant simulated environment provides a unique assessment opportunity to observe patients' habits and better predict functional deficits that exist before the patient transitions into the community (Lawlor & Cada, 1993; Richardson, Law, Wishart, & Guyatt, 2000). Nonetheless, few studies have used these simulated environments to conduct assessment (Robertson & Schmitter-Edgecombe, 2017). The Community Shopping Task (CST), in which individuals are asked to create a grocery list, go shopping for the items, and navigate to a bus in a simulated environment, has demonstrated that individuals with a variety of neurological conditions (i.e., TBI, MS, spinal cord injury, and stroke) require more prompting and time to complete the task compared to cognitively healthy adults. Furthermore, the CST was shown to have higher ecological validity compared to traditional paper–pencil neuropsychological tests (Robertson, Schmitter-Edgecombe, Weeks, & Pimentel, 2018). In another study examining fall risk, Means (1996) created an obstacle course that included many situations known to increase fall risk in older adults (e.g., different textures of flooring). Preliminary results suggested that aspects of both the qualitative and quantitative data could be useful in evaluating fall risk, especially the time to complete the course; however, further validation of the task is required.

Despite the sparse literature evaluating the efficacy of simulated community environments (e.g., Hecox et al., 1994; Richardson et al., 2000), such environments offer possibilities for conducting naturalistic assessment. Simulating a community environment inside the safe confines of a hospital setting creates a desirable in-between of traditional and real-world assessment (Fulper, 1989; Simmons, 1989). Because simulated environments have the added benefit of being in a controllable real-world environment, researchers can modify a number of factors (e.g., number of distractors, open-endedness of tasks) and create hierarchical assessments with differing levels of difficulty. Although work-simulated assessments can often provide this flexibility, simulated environments have the advantage of not taxing a person's imagination or ability to abstractly conceptualize tasks. Furthermore, motivation and effort are important to accurate assessment. As simulated environments are created to have a high degree of face validity, patients may be more motivated to engage with the task (McClusky, 2008).

Drawbacks include issues of accessibility, as it is not always possible to take patients to a real grocery store or to have access to a simulated community environment. Furthermore, because many of these assessment measures are designed for a specific environment (e.g., specific hospital), adoption of such measures will require new standardization for each specific environment (Dawson et al., 2009). Furthermore, many of the tests are lengthy (e.g., EST) and may be considered too cumbersome for efficient assessment, even if the measure offers a higher degree of ecological validity (Rempfer & Brown, 2005). In addition, the open-ended nature of the majority of these tasks can make rating and coding of performance difficult and time consuming. Test–retest reliability can also be problematic. Finally, even though some of these tasks are performed in the real community or a simulated community or represent a work-simulated task, this may not be the environment that the person lives in or will be returning to, which may impact the generalizability of performance.

Bromley and colleagues (Bromley, Adams, & Brekke, 2012a; Bromley, Mikesell, Mates, Smith, & Brekke, 2012b) have applied video ethnography to understand how neurocognitive deficits impact a person's functional abilities in their current environment. Video ethnography is "a nondirective method that allows the researcher to document subjects' behavior while accompanying them in everyday settings" (Bromley et al., 2012b, p. 982). A video recorder and microphone are used to follow the person around. The videos are then watched and four domains of everyday behaviors are coded: behavioral activity level, problem solving, social interaction, and goal pursuit. Pilot data indicate that video ethnography can provide detailed and ecologically valid information about a person's performance in the real world that is associated with neurocognition (Bromley et al., 2012a, 2012b). A strong advantage of this approach is that functional performance is equivalent to behaviors that constitute day-to-day functioning. Moreover, this type of direct observation can provide information about how a participant typically approaches daily tasks, such as whether or not they use compensatory strategies, ask for assistance when needed, or make decisions that might compromise safety. Disadvantages include the time and labor involved in videotaping and coding the data, as well as possible alterations in participant performance due to the observer effect. Furthermore, this assessment cannot easily be applied in hospital populations as a predictive measure to assess functional outcomes.

Wearable Sensors

Recent advances in technology have allowed wearable sensors to become reliable and affordable devices that are feasible measurement tools to use in everyday assessment. Examples of wearable sensors include accelerometers, actigraphs, heart rate monitors, pressure sensors (e.g., for shoe insoles), and smart watches. Wearable sensors allow researchers and clinicians to capture either momentary or continuous data about a person, including variables that represent health, stress, mood, habits, movement, whereabouts, sleep, and activity level (Dunn, Runge, & Snyder, 2018). Many of these measurement devices are relatively unobtrusive and have the capability to improve current naturalistic assessment efforts by capturing typical functioning as opposed to functional abilities under optimized laboratory conditions. However, the limitations of these devices should be considered. Examples include the need to charge the device or replace its batteries, which can put stress on the user (Marschollek et al., 2012); forgetting to wear the device (Devor, Wang, Renvall, Feigal, & Ramsdell, 1994); questions about where to best place the device on the body (Migueles et al., 2017); data security issues (Marschollek et al., 2012); and difficulty obtaining reliable ground truth labels for everyday activities and analyzing large amounts of data. More detailed information about wearable devices can be found in Chapter 11, this volume.

Ecological momentary assessment (EMA) is also a useful tool for naturalistic assessment because of its ability to obtain more reliable subjective data than retrospective questionnaires. EMA administers questionnaires through a device (often a cell phone or tablet) across various time points throughout a person's day. This helps reduce response biases, such as recency effects, and avoids aggregation that can occur when a person is asked to fill out a questionnaire in a traditional laboratory or clinic setting (Augustine & Larsen, 2012; Shiffman, Stone, & Hufford, 2008). In addition, the data is collected while the person is in their natural environment, which increases ecological validity. Researchers have used EMA to objectively assess cognition (e.g., Diehl, Hooker, & Sliwinski, 2015; Schmitter-Edgecombe, Sumida, & Cook, 2020) as well as assess mood (Courvoisier, Eid, Lischetzke, & Schreiber, 2010), drug craving and/or use (Freedman, Lester, McNamara, Milby, & Schumacher, 2006; Phillips, Phillips, Lalonde, & Dykema, 2014), medication adherence (Mulvaney et al., 2012), and real-time associations between fluctuations in cognition and symptom expression (e.g., side effects of medication; Frings et al., 2008). EMA has a few drawbacks. Compliance can be a concern because users have to respond to the questionnaires either via text, phone call, or online; although compliance rates are higher than 75% in most cases (Courvoisier et al., 2010; Phillips et al., 2014). The type and amount of questions and/or cognitive tests used are also limited and must be kept brief in order to increase adherence. Moreover, for some studies, delayed responses can make interpretation difficult, especially when it is unclear as to why the person was not responding at the time of the prompt. Additional information related to the use of EMA to gather information about cognitive status can be found in, this volume.

Conclusions and Clinical Implications

Information about everyday functional status is typically gathered in the laboratory and clinic using either performance-based measures or self- or informant-report questionnaires. While these measures are considered proxies for real-world functioning, they do not always correlate well with each other and may not necessarily represent an individual's functional abilities in real-world environments. In this chapter, we reviewed a variety of naturalistic assessment methods that have been used to gather information about everyday functioning. These methods range from open-ended tasks being performed in the laboratory or a real-world environment to smart and wearable technologies that capture continuous data in home and community settings. Some of these newer technologies offer neuropsychologists novel opportunities to unobtrusively study human behavior within the everyday environment. Such technologies can capture more ecologically valid, impartial, and frequent measures of change, as well as contribute to understanding of contextual determinants (e.g., stress, distraction). These technologies will undoubtedly contribute to our understanding of the relationship between cognition and everyday functioning.

As described in detail in this chapter, all methods have advantages and disadvantages. Added challenges related to the emerging technologies range from battery life limits to techniques for conducting big data analysis. Despite the challenges, these naturalistic methods offer opportunities to enhance understanding of behaviors that comprise everyday functioning within real-world settings. For example, sensor-based technologies could provide an opportunity to observe the natural history of change in everyday behaviors such as driving or home management as individuals age or progress from MCI to dementia. These naturalistic methods may also aid in understanding the types of everyday compensatory strategies that individuals utilize to support and maintain everyday independence. Furthermore, noncognitive factors that may influence everyday functioning, including sleep, mood, and health factors, can be better explored. Such information can then contribute to producing better clinical assessment methods and to shaping interventions that could promote independent functioning.

When integrated with more traditional assessment methods, the opportunities for using naturalistic methods to predict everyday performances and improve health care are significant. With a few exceptions (e.g., AMPS), most of the reviewed naturalistic tests are being used primarily as research tools. Many of the current naturalistic tasks are time consuming and may be expensive to implement, require specific environments, and lack standardization, which make the tasks difficult to execute in clinical settings (Robertson & Schmitter-Edgecombe, 2017). However, several research groups are currently working to develop and validate more open-ended, naturalistic tests that could be used for clinical purposes. As an example, The Night Out Task (NOT; Schmitter-Edgecombe, Cunningham, McAlister, Arrotta, & Weakley, 2021) is administered with props in the laboratory environment and requires participants to multitask and efficiently complete eight activities in preparation for a night out (e.g., compute and gather necessary money; prepare thermos of tea). It also utilizes a tablet-based interface, which allows for numerous process variables (e.g., self-corrections, double-checking) to be coded (Schmitter-Edgecombe et al., 2021). Such tests may eventually provide clinicians with a more ecologically valid way to evaluate and predict everyday functioning.

In the meantime, the current research on naturalistic assessments can continue to inform clinical practice by providing information on how everyday functioning is typically impacted in a variety of neurocognitive disorders. Assessing cognition and function through traditional methods may be insufficient, and additional information gathered through naturalistic assessment methods (e.g., compensatory strategy use, task efficiency, number and types of errors) may provide a wealth of important information. For example, consider a 22-year-old male with a history of severe TBI. He underwent a neuropsychological evaluation 5 years post-injury and demonstrated impairment on most traditional paper–pencil neuropsychological tests administered. However, his performance on the CST, the aforementioned naturalistic assessment performed in a simulated community environment, was intact, and he required little to no help with completing the task, despite his profound cognitive impairment. In contrast, a 40-year-old female with a 10-year history of MS had much more difficulty completing the CST, even though she demonstrated a lesser degree of cognitive impairment, with generally intact attention/processing speed, memory, language, and set-shifting abilities. The difficulties she demonstrated on the CST were not related to physical limitations; rather, she required significant assistance with task initiation, organization, and ability to adjust strategy. These examples illustrate how clinical impressions and recommendations might be influenced by the opportunity to obtain naturalistic assessment data, especially if the referral question is related to the patient's need for assistance or ability to live independently.

Technologies are also increasingly being used in the health care arena. The commercial availability and popularity of wearables has dramatically increased the clinical feasibility of real time monitoring. Many of these technologies can now be integrated into popular electronic medical record platforms, such as the integration between Applehealthkit and Epic, and some have FDA approval for clinical use (Dunn et al., 2018). These advances have the potential to revolutionize health care operations, and neuropsychologists are well positioned to help develop these technologies to improve functional assessment. Sensor-based technologies deployed in naturalistic settings have the potential to enrich a client's clinical picture (e.g., show variability and trends in function), augmenting self- and informant-report and clinical assessment data collected in the office to improve test interpretation and diagnostic decision making. Treatment needs could potentially be identified before functional limitations deteriorated to the point of limited everyday independence and appropriate interventions or preventative strategies initiated. Increased understanding of how compensatory strategies, such as routines and external aids, are utilized by individuals in real-world settings to support independent living could lead to the development of more efficacious interventions. In addition, the data gathered using more naturalistic assessment methods could improve understanding of the relationship between cognition and everyday functioning, as well as inform development of new performance-based and questionnaire measures that may more accurately predict real-world functioning.

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CHAPTER 11

Wearable Sensors, Ambulation, and Health

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Functional capacity, the ability "under controlled conditions, to perform tasks and activities necessary or desirable in" life (Patterson & Mausbach, 2010, p. 139), is an essential component of independent living and diagnostic criteria for mental health and neuropsychological disorders (American Psychiatric Association, 2013). Consequently, assessment, prevention, and intervention health research aims to maintain or improve a person's basic activities of daily living (ADLs; e.g., ambulating, dressing, and toileting) and instrumental activities of daily living (IADLs; e.g., home maintenance and managing medications; Edemekong, Bomgaars, Sukumaran, & Levy, 2020). While the current state of functional capacity research relies heavily on self-report measures, sensors and technology represent powerful measurement tools that remain relatively unused (Garcia-Ceja et al., 2018; Parsey & Schmitter-Edgecombe, 2013).

Sensors and technology have the potential to collect immense amounts of real-world ADL/IADL data. Examples of data (i.e., physical parameters) include biophysical data (e.g., heart rate and body temperature; Al-Eidan, Al-Khalifa, & Al-Salman, 2018; Ray et al., 2019; Wang, Lou, Jiang, & Shen, 2019), routine movement within a home (e.g., at 7 a.m. participant moves from bedroom to bathroom; Cook, Crandall, Thomas, & Krishnan, 2013), routine interaction with home objects (e.g., coffee machine and medication box; Hayes, Hunt, Adami, & Kaye, 2006) and movement outside a home (e.g., distance walked or driven to work; Difrancesco et al., 2016). If such data is translated into an accessible and interpretable format, it could provide a window into a patient's daily functional experiences and behaviors, and serve as a useful tool to many health care workers, including medical doctors, neuropsychologists, nurses, physical therapists, and social workers. On a larger scale, these methods could innovatively respond to significant ADL/IADL-related public health problems if approached through interdisciplinary methods (e.g., engineering, computer and health scientists collaborating, integrating, adapting, and optimizing their research methods; National Science Foundation, n.d.).

To support scientists or community members interested in interdisciplinary health research, we review current and novel inertial (i.e., acceleration-based movement) sensor methodology as an example of how sensors can be used to examine health and everyday functioning. Additionally, in hopes of pushing the field forward, we also review specific methodological problems and research gaps requiring a collaborative interdisciplinary approach to answering relevant public health problems. Special attention is given to important unexplored health disparity and technology research questions, ethical considerations, and necessary training.

Sensors and Technologies

Sensors and Activity Recognition

As scientific advancements continue to miniaturize sensor technology (Kanoun & Trankler, 2004), more sensors are integrated into daily items (e.g., cell phones and watches), providing accessible research tools for collecting physical parameters. For example, sensors embedded in smart phones are frequently used to measure motion (physical parameter), which is examined with algorithms to detect steps (i.e., a sensor event; Mourcou, Fleury, Franco, Klopcic, & Vuillerme, 2015). Once an activity can be reliably and accurately detected (Vrigkas, Nikou, & Kakadiaris, 2015), researchers examine these events for event patterns denoting more complex activities.

When data from different sensors are collected over time, the resulting database can inform researchers about their target population's functional experiences (Cook, Schmitter-Edgecombe, Jonsson, & Morant, 2019). Many technologies, such as mobile phones, include a package of sensors. Fusing data from multiple sensor sources can improve the accuracy of behavior modeling and assessment (Nweke, Teh, Mujtaba, & Al-garadi, 2019; Fotouhi-Ghazvini & Abbaspour, 2020). Consequently, most related research uses multiple sensors and physical parameters.

Wearable and Ambient Sensors

Sensor methodology is typically divided into wearable and ambient, which measures human activity by placing sensors on the body or within a physical environment, respectively (Chen & Nugent, 2019). Consider accelerometer sensors (i.e., frequently found in phones and watches), a motion sensor many people use to measure daily step counts. Specifically, algorithms are used to examine accelerometer data for specific patterns of velocity change that are closely associated with a step movement. Therefore, algorithms can be used to examine mobile accelerometer data for characteristics such as gait and falls (Broadley, Klenk, Thies, Kenney, & Granat, 2018; Sprager & Juric, 2015). Alternatively, accelerometers can be placed on a movable object, like a door, to monitor its use. In this way, a sensor traditionally used as a wearable sensor can also play the role of an ambient sensor. Most of this chapter focuses solely on wearable technology. However, to highlight the flexibility of sensor methods, we also demonstrate how accelerometers can be used within an ambient environment.

Inertial Sensors

Types of Inertial Sensors

Sensors that detect movement are known as inertial sensors and include accelerometers and gyroscopes. Inertial sensors measure acceleration and angular velocity along three dimensions. These sensors are appealing due to their small size and weight, low power consumption, and low cost (Sprager & Juric, 2015). An accelerometer captures changes in velocity along the *x*-, *y*-, and *z*-axes (see Figure 11.1). For example, imagine yourself walking from your front door into your home; an accelerometer would capture the speed at which you moved across the *x*- and *z*-axes, and your body's subtle movements up and down the *y*-axis with each step. The inclusion of a gyroscope sensor can provide additional measures of orientation on the *x*-, *y*-, and *z*-axes known as yaw, pitch, and roll; (see Figure 11.2). For example, imagine a ballerina perfectly twirling on pointe with her body aligned to the *y*-axis. As she twirls, her changing oscillation around the vertical axis would be a yaw measurement.

Samples are collected over multiple time points at a frequency (e.g., sampling every second) referred to as the sensor *sampling rate*. These sensors are commonly embedded in everyday items like mobile phones and watches. When numerous readings are collected, accelerometer data can shed light on movements such as standing, sitting, walking, running, climbing, and hand gesturing (Hong, You, Wei, Zhang, & Guo, 2016; Xiao et al., 2016). Accelerometers and gyroscopes are frequently combined to strengthen movement detection and improve identification of movement types (Yang & Hsu, 2010).

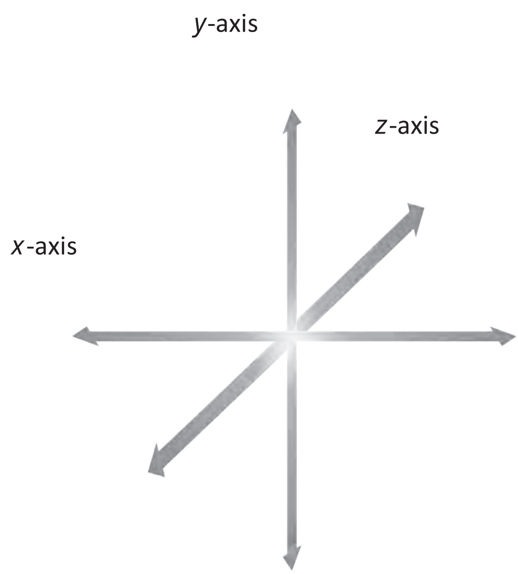

FIGURE 11.1. Three-axis accelerometer.

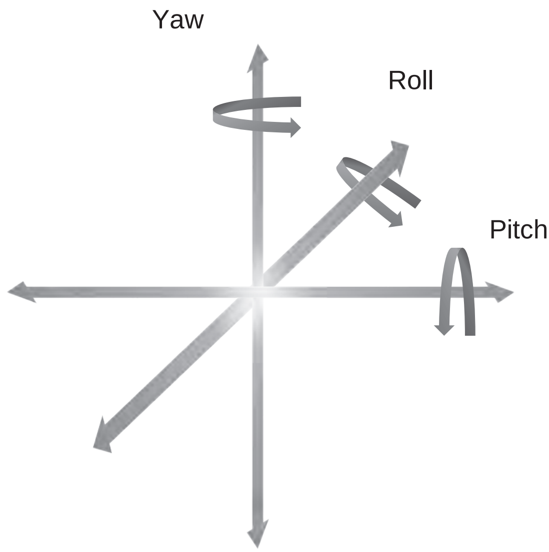

FIGURE 11.2. Three-axis gyroscope.

Inertial Sensors and Physical Activity Measurement

Measuring physical activity is important due to its intimate relationship with health outcomes (Câmara et al., 2020; Hanson & Jones, 2015; Oja et al., 2018; Sheehan & Li, 2020; Manini et al., 2017; Simoes et al., 2006) and functional independence, especially ambulation (Cook et al., 2019; Edemekong et al., 2020; Sylvia, Bernstein, Hubbard, Keating, & Anderson, 2014). Self-report, clinician observations, and accelerometer readings make up some of the different physical activity measurement tools available. Self-report measures of physical activity can be, at first, more convenient and less time intensive, but they are also impacted by social desirability and recall bias (Ryan et al., 2018; Taber et al., 2009). Objective nonsensor physical activity measures include standardized clinic-based mobility tests like the timed up-and-go test (TUG; Podsiadlo & Richardson, 1991). While clinic-based tests like these can be more accurate, they also require a clinician to be present to observe and time the task. Unlike these measures, objective sensor-based measures of physical activity can enhance assessments like the TUG by collecting continuous time-stamped measurements of velocity and orientation (Higashi, Yamakoshi, Fujimoto, Sekine, & Tamura, 2008) and facilitate assessment within home environments without a clinician present (Saporito et al., 2019). Huisingh-Scheetz et al. (2016) examined the independent contribution of accelerometer and self-reported physical activity in predicting older adult disabilities. While weak correlations were reported between accelerometer and self-reported physical activity, both measures were significant predictors of ADL and IADLs when entered into the same model. This suggests that self-report and objective activity measures provide insight in understanding functional impairment.

Inertial sensors are used to examine a range of physical activity research, from basic questions like measuring step counts to mixed methods examining biological, psychological, and social predictors of physical activity behaviors (Alinia et al., 2017). Notably, accelerometers can examine specific facilitators and barriers to physical activity (Bassett, Toth, LaMunion, & Crouter, 2017). For example, factors relating to older adults engaging in physical activity include level of engagement in IADLs (Ando et al., 2019), caring and socializing with pets (Peacock, Netto, Yeung, McVeigh, & Hill, 2020), seasons (Nakashima et al., 2019), and hospitalization (Wanigatunga et al., 2019). Environmental attributes, such as access to public transportation and the presence of sidewalks, have also been examined in relation to physical activity in stroke patients (Kanai et al., 2019). Sociocultural factors have been linked to physical activity too. For example, Japanese older adult women with higher levels of *sekentei,* a sociocultural norm relating to "social appearance or sensitivity about one's reputation," were less likely to engage in physical activities (Murayama, Amagasa, Inoue, Fujiwara, & Shobugawa, 2019, p. 2). Additionally, German older adults were found to walk significantly less on Sundays but not on Saturdays, which may be due to shops, hairdressers, banks, and other stores being typically closed in Germany (Klenk et al., 2019). Together, these inertial sensor studies provide examples of the many avenues researchers can explore with mixed-methods research.

Inertial Sensors: Gait Analysis

An individual's ability to walk reflects an intricate interaction of biological (i.e., nervous, musculoskeletal, and cardiorespiratory system), psychological (e.g., mood and cognition), and social factors (e.g., clinic vs. home environment settings; see Pirker & Katzenschlager, 2017). While analyzing gait is challenging, it serves as a strong predictor of self-reported ADL and IADL dependence (Donoghue, Savva, Cronin, Kenny, & Horgan, 2014; Potter, Evans, & Duncan, 1995), future falls (Mignardot et al., 2014), dependence on a caregiver (Montero-Odasso et al., 2005), cognitive ability (Chou et al., 2019; Sui et al., 2020), diagnosis of dementia (Beauchet et al., 2016), and mortality (Studenski, 2011). These relationships can be also bidirectional. For example, on one hand, gait speed was significantly slower in functionally independent older adults following a hospitalization event (Duan-Porter et al., 2019). On the other hand, gait speed remained a significant predictor of functional decline when combined with age, handgrip strength, chair stands, body mass index, depression symptoms, and physical health conditions within a pooled population sample (i.e., Germany, United Kingdom, Italy, and Netherlands cohort samples), demonstrating the significance of ambulation for functional independence (Jonkman et al., 2019).

Gait measurement tools include traditional nonwearable gait measures like motion capture systems and clinician observations (Hyodo et al., 2020; Sprager & Juric, 2015) and wearable technologies, like inertial sensors. Gait research methodology can also be split into tasks and environments. When gait is examined using tasks reflecting more real-world environments, gait measurements appear to be more predictive of home environment gait. For example, Hillel et al. (2019) examined the accelerometer gait measurements of participants walking within their home (30-second bouts) in relation to laboratory-based walking with and without a dual-task condition. Results indicated only the dual-task laboratory-based walking sample significantly related to the home-based walking sample. Additionally, participants' gait within their home were significantly poorer compared to laboratory gait measurements. Mancini et al. (2016) reported similar findings when they examined turning mobility using inertial measurements. Specifically, turning mobility characteristics obtained from in-home data, but not laboratory measures, differentiated older adults with and without falling history. Similar findings were also reported in children with cerebral palsy whose gait pace and variability measurements within the home were significantly poorer than clinic measurements. Together these findings demonstrate the differences in gait between laboratory and home environments, and they also speak to the clinical utility of inertia sensors, especially when deployed in naturalistic environments (Muro-de-la-Herran, Garcia-Zapirain, & Mendez-Zorrilla, 2014; Sprager & Juric, 2015; Godfrey, Del Din, Barry, Mathers, & Rochester, 2015).

Moving beyond step counts and ambulation duration, we find that the next "step" forward in wearable gait assessments within naturalistic settings is to identify more clinically relevant ambulation characteristics. Gait measurements can be decomposed into more precise variables to highlight detailed components of ambulation like turning angle variability (Mancini et al., 2016). In a separate in-home study, older adults with a fall history were more likely to demonstrate greater step variability on the vertical axis, indicating poorer balance control and reduced variability on the mediolateral axis, which suggested "a reduced ability to adapt to changing environmental conditions" (Weiss et al., 2013, p. 749). The authors noted that, unlike the step counts, these descriptive variables significantly predicted prior and future falls, demonstrating how more nuanced gait variables within naturalistic settings may be better indicators of ambulatory functional problems. Inertial sensors have also been used to better understand targeted diseases. In a sample of patients with Parkinson's disease, tremors and bradykinesia were continuously monitored by measuring gait cadence unique to these clinical symptoms (Darnall et al., 2013; Mahadevan et al., 2020). These measurements were found to have good to strong agreement with clinician ratings of motor symptoms, providing objective measures of symptom severity. A barrier to examining such complex variables for technical teams may be a lack of clinical knowledge to interpret the variables. At the same time, clinical teams may not possess the skills to capture and process complex parameters from inertial data.

Another notable relationship to consider is cognition and gait (Yogev-Seligmann, Hausdorff, & Giladi, 2008). While previously believed to be mostly automatic, research has demonstrated that executive functioning and attention processes are pulled upon while walking (Sunderaraman et al., 2019), and executive functioning and verbal memory can predict decline in gait (Yogev-Seligmann et al., 2008). Notably, within a cognitively intact community-living older adult sample, poorer executive functioning and dual-task gait variability performance significantly predicted future falls within the next 2 years (Herman, Mirelman, Giladi, Schweiger, & Hausdorff, 2010). Within this study, executive functioning was examined using an index made up of response inhibition measures like a go/no-go task, and researchers hypothesized that executive functioning was potentially serving as a cognitive resource to compensate for physical demands of "multitasking and navigating in complex [real-world] environments" (Herman et al., 2010, p. 1090). The literature examining the effectiveness of multifactorial fall interventions focusing on "medication review, strength and balance training, visual and hearing correction and environmental modifications" consistently demonstrates inconsistent findings in samples with poorer cognitive abilities, suggesting that contributing factors of falls may be different in those with and without cognitive impairments (Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012, p. 5). Additionally, while physical interventions with and without a cognitive component in older adults can improve dual-task gait speed, there is little evidence that these interventions improve dual-task costs (i.e., [dual-task gait speed—single-task gait speed]/single-task gait speed) or other gait measures, as well as their effectiveness in improving gait within real-world environments (Plummer, Zukowski, Giuliani, Hall, & Zurakowski, 2015). Moreover, there is a substantial need for interdisciplinary teams to identify or develop sensitive sensor gait parameters mediated by executive functioning and to examine the predictive validity of these measures for future falls. Such measures could support development of gait and fall interventions relating to changes in executive functioning.

As demonstrated, gait is a proxy for biopsychosocial factors impacting mobility. For example, a slow pace could reflect low energy, weak muscles, muscle mass loss, balance issues, poor flexibility at various joints, psychological changes (e.g., depression and cognitive states) (Pirker & Katzenschlager, 2017), cultural background (e.g., city vs. rural occupant gait speed; Ebersbach, Sojer, Muller, Heijmenberg, & Poewe, 2000), or combinations of these factors (Barak, Wagenaar, & Holt, 2006; Kuo & Donelan, 2010). To better capture nuanced gait measures, it is important to include health providers, like physical therapists and health researchers knowledgeable in the population sample. These individuals can provide clinical expertise and assist with identifying specific gait variables, while appropriately interpreting the results with cultural sensitivity. Other methodological topics like sensor body placement (e.g., trunk, shank, or ankle), number of sensors, and sampling frequency would also benefit from collaborations between health scientists and engineering teams.

Inertial Sensors: Fall Detection

Falls are significantly tied to disability (Axmon, Ahlström, & Sandberg, 2019; Eagen, Teshale, Herrera-Venson, Ordway, & Caldwell, 2019). A large portion of inertial sensor research focuses on improving sensor placement and algorithms in order to better detect falls (Ahn, Kim, Koo, & Kim, 2019; Alves, Silva, Grifo, Resende, & Sousa, 2019; Aziz, Musngi, Park, Mori, & Robinovitch, 2017; Scheurer et al., 2019). A significant gap within fall detection research is the lack of real-world fall data (Bagalà et al., 2012). Because of their concerns about harming participants (Poh & Shorey, 2020), researchers use samples of young adults, stunt individuals, and gymnasts, who simulate falling onto soft surfaces (Bagalà et al., 2012; Broadley et al., 2018; Stack, 2017). Although such research reports strong relationships between inertial sensor parameters and detecting laboratory samples of simulated falls, these parameters are less sensitive to real-world falls (Broadley et al., 2018; Stack, 2017). Stack (2017) argues that researchers would benefit from operationally defining a fall and replace simulation data with real-world sensor fall data combined with self-reported falls. Such research is possible within a multidisciplinary setting, where health care providers can identify participants at risk of falling and physical and occupational therapists can assist with sensor placement and data interpretation.

Inertial Sensors: Thinking beyond Wearable Methods

While researchers primarily use wearable inertial sensors to examine health and function, ambient sensor analysis can also be incorporated within home environments to capture daily functioning. Specifically, accelerometers can be placed on objects used routinely (Figure 11.3) to capture the user's behavioral patterns. For example, our research team asked participants to self-report the time and pattern of routine behaviors they believed were part of a typical morning. One of our research participants reported that their morning routine is to wake up, use the restroom, make coffee with cream, take their morning medications, and work on a crossword puzzle using a dictionary (Sumida, Weakley, Schmitter-Edgecombe, & Cook, 2020). Accelerometer sensors (i.e., Estimote Stickers) were placed on the bathroom door, coffee machine, refrigerator door, creamer, medication box, and dictionary. Trial data was obtained by asking the participant to pretend to complete a morning routine, providing an estimate of expected object movement times, durations, and patterns (e.g., bedroom door, then bathroom door, then coffee machine). Accelerometer data was then collected from these objects for three weeks, providing a sample of real-world routine behavior. The trial and real-world routine behavior samples are compared to identify medication non-adherence events. Table 11.1 provides an example of this process, where Days 10 and 12 are consistent with the participant's reported routine and their pillbox moved for 6 seconds each day. However, on Day 11, while the participant's coffee creamer and dictionary sensor data were consistent with their reported routine, their medication box did not move, indicating the participant may have forgotten to take their medication. This methodology provides insight on participant activity patterns without requiring participants to charge and wear devices, a requirement that can be inhibitive for some populations. While piloting currently focused on cognitively intact individuals who could recall their medication adherence, our aim was to capture medication adherence in individuals with cognitive impairment.

FIGURE 11.3. Examples of Estimote sticker sensors placed on objects.

TABLE 11.1. Sensor Data Sample for a Pilot Participant

	Object with Estimate		
	Coffee creamer	Pillbox	Dictionary
Day 10	6:46 a.m.	6:50 a.m.	6:58 a.m.
Day 11	7:08 a.m.	No movement recorded	7:11 a.m.
Day 12	7:12 a.m.	7:51 a.m.	7:34 a.m.

Sensor-Based Private Health Information

Geolocation data are the approximate or specific geographical location of an object. Most commonly associated with GPS (i.e., global positioning system data), geolocation data can also be collected using technologies such as internet protocol (IP) addresses, cell tower triangulation, Wi-Fi signals, radio frequency identification (RFID), and global system for mobile communication (GSM). Since health research requires data to be unidentifiable and comply with the Health Insurance Portability and Accountability Act of 1996, geolocation data will require special management. With ever-increasing smart devices and applications (apps) that utilize location sensors, the possibility for a data breach grows. Therefore, it is important to examine the chain of location data collection and management to prevent such a breach.

Wearable devices typically sync to a particular application or program. Therefore, any wearable device and the associated application or program should be examined for privacy concerns. Data may be collected automatically, like data analytics supporting apps and cloud services. Careful attention should be given to IP addresses, which are used to identify devices like computers or mobile phones as they send and receive information over the internet. If an application is linked to a home or work Wi-Fi, these IP addresses are time-stamped and can identify an individual location up to a street level and arguably to an individual home in more rural areas. If the device connects to several IP addresses, such that a routine of locations can be detected, an individual becomes more identifiable, and therefore these data may deidentify other health-related data to an intended recipient or to a third party such as a service provider. These security risks can be lessened by carefully examining data collection and transmission methods.

Methodological Points to Consider

Methodological Design

Regarding the different research aims between engineering (e.g., creating and evaluating sensors and systems) and health research (e.g., identifying contributors to health), there are many methodological differences to consider when conducting interdisciplinary research. For example, the purpose of pilot testing may be very different between these scientific branches. On the one hand, engineering and computer scientists may pilot-test a sensor with a small participant pool to ensure the reliability of the system components. On the other hand, health researchers may pilot-test patients with varying severity levels or different types of impairment to ensure the reliability of data collection across these clinical factors. Therefore, investing time in operationally defining methodological terms and planning how to integrate methodologies (e.g., sample sizes and adequate iterative pilot testing) can improve the usefulness of the results. Additionally, novel approaches to methodology could be attained by learning about and taking part in the other discipline's tool development and use as well as data collection and processing. For example, engineers and computer scientists could join health researchers while collecting health data in the field, which can give them a sense of the vast variability of behaviors contributing to sensor data collection within more real-world environments such as participant homes. Alternatively, health researchers could learn about the basic mechanics of selected sensors and how to process data, which will improve their understanding of how to maximize the benefit of a sensor's data collection.

Data Processing

There are many different data processing options to consider, including cutoff points and algorithms. By diving into the data, health researchers can assist engineers in accurately selecting the proper data processing method and associated parameter choices for a clinical population. For example, Thralls et al. (2019) demonstrated that significant predictors of health outcomes included vertical axis cutpoint, 15-second vector magnitude cutpoint, 1-second vector magnitude algorithm and machine-learned walking algorithm, but not an individualized cutoff point technique (i.e., based on a 400-meter walk), suggesting that selection of accelerometry processing methods is important. Health researchers may be helpful in identifying the best processing method a priori, given their knowledge of the clinical population.

Pilot, Validity, and Reliability Testing in Targeted Clinical Population

Conducting pilot, validity, and reliability testing within a population of interest is necessary. Falck and colleagues (2019) demonstrated the need to identify specific cutoff points for physical activity for patients with various stroke levels. Specifically, the authors demonstrated individuals with a mild versus moderate-to-severe stroke required different levels of movement (accelerometer) to reach a moderate to vigorous physical activity level (calorimeter). Therefore, cutoff points for acceleration would need to be calibrated by level of stroke severity to accurately calculate expended energy. These findings demonstrate preset cutoff points for different levels of functioning may need alterations to be valid for the population of interest. If systematically conducted, these alterations can be explored and developed during pilot testing.

When conducting pilot, validity, and reliability studies on wearable devices in more naturalistic settings, pilot testing should allow the target population to hold or carry naturalistic daily items (e.g., walkers, backpacks, purses, dog leashes). For example, the reliability and validity of step counts by multiple Fitbit trackers were assessed across different conditions (Alinia et al., 2017). In this study, Fitbit trackers were most accurate while participants (i.e., 15 healthy adults 21–31 years old) walked on a treadmill (i.e., controlled environment); however, error rates increased up to 95.6% when the participant used a walker. Tedesco et al. (2019) reported all tested wrist-worn activity trackers were more error prone when participants used a rollator (i.e., walking aid). Similarly, Chen and Nugent (2016) reported step counts to be significantly underestimated when participants pushed a stroller. Such examples emphasize the need to observe and conduct pilot and reliability testing with target populations within natural environments and conditions using numerous wearable devices across different body locations.

Adherence incentives and barriers for wearable devices should also be explored during pilot testing. For example, Sirard and Slater (2009) examined four adherence strategies in a sample of high school students: control condition, phone calls, daily journaling, and financial compensation for the number of completed days of data. Compensation results indicated young adults were most adherent under the financial compensation condition. In the National Health and Nutrition Examination Survey, 75% of participants were categorized as nonadherent (i.e., less than 7 days of data) and reported "discomfort or inconvenience of wearing a device on the hip over time, and forgetting to put the monitor back on after taking it off at night" (Troiano, McClain, Brychta, & Chen, 2014, p. 6). Within our own studies, older adult participants frequently reported forgetting as a barrier. To mitigate this barrier, two Apple watches, a white and a black watch for the day and night, respectively, were provided to each participant (Cook, Strickland, & Schmitter-Edgecombe, 2020). To identify the best location for charging the Apple watches, we interviewed participants to collaboratively select a location where they completed a daily routine behavior (e.g., bathroom counter where they brush their teeth), which would support remembering to switch the watches. We also assisted them with developing memory strategies, like writing post-it note reminders or setting up alarms. Additional considerations included the comfort and fit of the wearable, participant dexterity versus wearable device dexterity requirements (e.g., maneuvering a watch band buckle), other worn devices (e.g., personal watch), and barriers that participants identify before data collection.

Mixed Methods

A powerful methodological design technique is the combination of wearable inertial sensors and ecological momentary assessment (EMA), a real-time assessment technique used to probe for a participant's current experience, mood, or behavior (see Chapter 10, this volume, for additional details; Burke et al., 2017). By assessing real-time self-reported experiences via EMA while simultaneously collecting physical activity via inertial sensors, valuable information regarding contextually rich, self-reported barriers and facilitators of physical activity can be collected (Liao, Chou, Huh, Leventhal, & Dunton, 2017). In a sample of inactive adults, Liao et al. (2017) collected self-reported affective states using a mobile EMA app and physical activity data using an accelerometer. During baseline, participants who reported experiencing feeling more energetic while completing a physical activity (e.g., jogging) were more likely to sustain physical activity behaviors at 6 and 12 months. Additionally, participants who reported negative affective states during baseline physical activity engaged in less physical activity at 12 months. Because of physical activity's effect on affective states across an exercise event, especially postexercise, the power of combining EMA with wearables is the real-time collection of objective physical activity data and subjective affective states at the start, during and postexercise within their daily environment.

Researchers could push the field further with the use of learning algorithms to predict when a person is exercising to target EMAs more precisely and examine important psychological, social, and environmental variables, like physical (e.g., temperature, facility) and social environment (e.g., alone, with friends or in group), exercise type (e.g., cardio vs. weights), multiple emotional states (e.g., feeling enjoyment and anxiety in learning a new exercise), and safety concerns (e.g., concerns with being harmed; Meyer, Castro-Schilo, & Aguilar-Gaxiola, 2014). A qualitative methodology, like diary entries, could also yield contextual-rich details of internal experiences prior to, during, and following exercises, which are unique to the targeted population. Together, such methodological combinations could be useful in (1) understanding in-the-moment psychosocial–environmental variables, which facilitate or deter physical activity, and (2) deploy interventions during optimal psychosocial states to promote sustained long-term physical activity behaviors.

Future of Wearables

Wearable methodologies are quickly moving to flexible sensor technologies (for a review see Wang et al., 2020). The biomedical world currently is using wearable sensors in non-invasive paper-thin sticker blood pressure monitors (Huang, Tan, Wang, & Yang, 2019), an implantable artificial pancreas (Signore et al., 2019), and flexible artificial electronic skin (Low et al., 2020). The benefits of these technologies include reduction of noise in the data (i.e., reducing the environmental factors impacting data) and increasing adherence. Engineers are continually designing novel, specialized sensing modalities. However, as health research begins to transition to these new technologies, similar methodological considerations need to be conducted. Additionally, extensive community-based participatory research would need to be conducted, especially when samples may include individuals with more severe mental health (i.e., delusions of thought) and low education or technology knowledge.

Wearable Sensors and Health Disparities

Physical and Functional Health Disparities between Racial/Ethnic Groups

Of all the social factors that interdisciplinary research teams need to tackle, examining race and ethnic differences in physical and functional health is paramount. In 2013, the Centers for Disease Control and Prevention reported that obesity was higher in non-Hispanic Black women (51%) compared to non-Hispanic White women (31%); diabetes prevalence was highest among non-Hispanic Blacks, mixed-race individuals, and Hispanics; stroke-related death rates adjusted by age among non-Hispanic Blacks were the highest compared to any other racial/ethnic group; and premature death rates (< 75 years old) from stroke and coronary heart disease were highest amongst non-Hispanic Blacks compared to Whites (Centers for Disease Control and Prevention, 2013). Additionally, American Indians/Alaska Native adults were more likely to meet criteria of obesity, hypertension, coronary heart disease, stroke, and diabetes as well as to die from diabetes compared to non-Hispanic White adults (U.S. Department of Health and Human Services Office of Minority Health, n.d.). When subgroups are examined, hidden differences are further identified. For example, compared to other Asian subgroups and non-Hispanic Whites, Asian Indians and Filipinos have higher coronary heart disease rates (Abesamis, Fruh, Hall, Lemley, & Zlomke, 2016; Palaniappan, Wang, & Fortmann, 2004). Compared to non-Hispanic Whites, Chinese, Filipino, and Japanese American adults are at greater risk of experiencing a stroke (Holland, Wong, Lauderdale, & Palaniappan, 2011; Wild, Laws, Fortmann, Varady, & Byrne, 1995), and Filipinos have higher rates of hypertension (Zhao et al., 2015).

Chronic health conditions have significant consequences for an individual's daily activities. In 2008, the predicted years of life without any functional limitations due to chronic conditions was approximately 6 years greater in Whites (67.0 years) compared to Blacks (61.1 years; Centers for Disease Control and Prevention, 2013). Freedman and Spillman (2016) reported similar findings, but identified older Black women to be at the greatest disadvantage. When functioning was separated into ADL and IADLs, non-Hispanic Black older adults reported the highest prevalence of mobility and ADL limitations compared to non-Hispanic Whites (Vasquez, Binns, & Anderson, 2018). Furthermore, Mendes de Leon and colleagues (2005) reported that differences between Black and White older adults on a performance-based disability test already existed at 65 years of age (i.e., the cusp of the "older adult" category), and differences were greater in women. (For a more comprehensive review on health disparities, see Committee on Community-Based Solutions to Promote Health Equity in the United States, Board on Population Health and Public Health Practice, Health and Medicine Division, & National Academies of Sciences, Engineering, and Medicine, 2017.)

These substantial physical and functional health differences are known as health disparities. Specifically, they are "avoidable, unnecessary and unjust" (Braveman, 2014, p. 7; Whitehead, 1992) differences in health amongst "groups of people who have systematically experienced greater social or economic obstacles to health based on their racial or ethnic group, religion, socioeconomic-status, gender, age, or mental health; cognitive, sensory, or physical disability; sexual orientation or gender identity; geographic location; or other characteristics historically linked to discrimination or exclusion" (HealthyPeople.gov, n.d.).

As demonstrated thus far, interdisciplinary health and wearable sensor-based research can provide a powerful tool to target these health disparities. Consistently, the National Institute on Minority Health and Health Disparities identified "big data," which includes wearables, as part of the next research opportunity in reducing health disparities (Breen et al., 2019; Jones, Breen, Das, Farhat, & Palmer, 2019). However, there is a substantial lack of physical activity research with wearable technology and Black, Indigenous, and People of Color (BIPOC) samples (Thomas et al., 2017; Whitt-Glover et al., 2014).

Health Disparities, Wearable Sensors, and Interdisciplinary Teams

Wearable technologies, especially when combined with EMA, have the power to capture complex relationships between psychosocial factors and physical activity within BIPOC communities. Specifically, race is not a fixed categorical variable but instead is a rich multidimensional, fluid construct (James, 2001). In other words, constructs like perceived safety or neighborhood socioeconomic status do not provide the richness of data to capture the momentary "lived experience" of underserved marginalized communities and their physical activity decisions (Neubauer, Witkop, & Varpio, 2019).

Sensors and technology have the potential to dive into these momentary physical activity events and explore these psychosocial and physical activity relationships further.

For example, Prochnow and colleagues (2020) examined physical activity behaviors in Mexican-heritage fathers from rural *colonia* areas of the South Texas border. The authors reported fathers, who identified more family members within their social networks, engaged in longer periods of moderate to vigorous physical activity. These results indicate that physical activity interventions targeted toward these communities may be most effective and sustainable if developed with the whole family in mind rather than individuals. Therefore, a potential research methodological shift could be examining multiple family member physical activity behaviors and how each family member may impact the other. Alternatively, EMA data could collect information on all family members physical activity behaviors and then prompt one member during an optimum physical activity time for another family member (e.g., "your father typically exercises 30 minutes from now, you may enjoy joining him today").

Mobile wearable technologies were also examined with regard to intervention preferences among African American women (Ceasar et al., 2019; Sillice et al., 2019). For example, Ceasar and colleagues (2019, p. 7) used community-based participatory research methods to interview African American women about a physical activity app. In addition to improving automation, participants reported that the app needed more relatable photos (e.g., "Have a person that's heavier than these people. They look like they're already fit") and removal of emoticons. These qualitative results indicate that digital platforms delivering interventions, especially the interface, may have intrinsic bias by the developer, impacting the user's experience and interest in engaging in the product and intervention.

African American women also reported wanting more health information (i.e., regarding diet and nutrition, stretching and sleep hygiene) and resources for local safe areas to exercise and exercise groups (Ceasar et al., 2019). Concerning safety, Claudel et al. (2019) examined self-reported neighborhood perception in African American and White samples and reported no interactions between groups and neighborhood perception in physical activity, but a noted limitation was that the physical activity location was not collected. Wearable EMA with inertial sensors could provide a solution by capturing physical activity behaviors and prompt for a location or use GPS. Alternatively, Ahuja et al. (2018) reported that African American participants' neighborhood perception predicted sedentary time only in low-median-income areas and discussed how participants perception likely represents a number of unexamined psychosocial factors (e.g., stress or prior neighborhood experiences). Taking a combined wearable and EMA data collection approach, researchers could investigate intraindividual and community-level safety concerns as well as identify individual, group- and community-level interventions. For example, Ray (2017) reported Black males, who perceived their neighborhoods to be predominantly White, were less physically active. While Ray (2017) discussed these findings in the context of racist criminalization of Black men, to the author's best knowledge, physical activity has yet to be examined in relation to proportionate rates of Black male arrests within their neighborhood or participants' fear of being perceived as a criminal. If these psychosocial factors are found to be significant predictors of lower physical activity in Black men, physical activity interventions (e.g., walking programs) may deter participation, be ineffective, or cause iatrogenic effects. Notably, these psychosocial variables may be even more important following Ahmaud Arbery's murder in 2020 (Bowman, 2021). If conducted within community-based participatory research, wearable sensors and EMA could be deployed to examine these relationships and identify facilitators for exercise within marginalized communities experiencing these real-world fears (Brown & Hargrove, 2018).

Viewing race as a rich multidimensional and fluid construct can be accomplished through practicing cultural humility, defined by Yeager and Bauer-Wu as "the lifelong process of self-reflection and self-critique whereby the individual not only learns about another's culture, but one starts with an examination of her/his own beliefs and cultural identities" such that they "step back to understand one's own assumptions, biases and values" (Kumagai & Lypson, 2009; Tervalon & Murray-García, 1998; Yeager & Bauer-Wu, 2013, p. 2). While cultural humility does not replace cultural competence, this attitude and perspective switch can be invaluable in adjusting the methodological approach in culturally sensitive and relevant ways. For example, physical activity wearable research is dominated by step research (Henriksen et al., 2018). However, an unexamined research question is whether steps are the best measurement and intervention for physical activity within different BIPOC communities. Currently, culturally relevant dance is being used to promote physical activity within African American (Lukach et al., 2016; Murrock & Gary, 2008) and Native Hawaiians (Kaholokula et al., 2017) samples. However, if these interventions were to include wearable technologies to measure physical activity, it is uncertain whether current physical activity algorithms could accurately detect dance movement, especially across different cultural dance styles, or categorize dance movement into mild, moderate, and vigorous physical activity levels (energy expenditure).

Questioning one's world and cultural perspective provides opportunities like these to consider how personal perspectives may inaccurately navigate research questions and approaches. Such a perspective switch could be the fuel needed to yield diverse wearable big data resources that the National Institute on Minority Health and Health Disparities hopes will reduce health disparities. Such questioning can also lead to the design of novel methods for detecting bias and fairness in models created by machine learning algorithms. As a result, the downstream impact could be interdisciplinary methodological approaches (e.g., combinations of inertial sensors, machine learning, EMA, diary entries, and interviews), which provide meaningful physical activity data to support the development of culturally relevant and efficacious interventions for marginalized communities.

Data Collection, Processing, and Interpretation: A Consideration of Structural Racism

While sensors and technology can provide more "objective" data compared to self-reporting, sensor design and data collection, processing, and interpretation are all susceptible to human bias. As mentioned previously, an example of biased data was outlined in the fall research section, which discussed how this research is substantially biased due to the development of fall detection algorithms using samples from young healthy actors pretending to fall.

Similarly, research using sensors and technology can have systematic racial bias from data collection through interpretation. An example of sensor design with an unintentional bias is photoplethysmography sensor's lower accuracy in measuring heart rate for individuals with more melanin in their skin (Bent, Goldstein, Kibbe, & Dunn, 2020). Since market wearables frequently combine inertial sensors with photoplethysmography technology to simultaneously capture physical activity and heart rate, researchers using these products would need to carefully process, examine, and interpret heart rate data from participants or groups with darker skin tones. Obermeyer, Powers, Vogeli, and Mullainathan (2019) reported findings of an unintentional bias within a commercial health prediction algorithm, thus demonstrating how systematic racial bias can even directly contribute to health disparities. Specifically, these researchers examined a commercial prediction health algorithm, which used medical expenditures to identify patient's health care needs, and reported finding health disparities but no disparity in health care costs between Black and White patients. Therefore, since the algorithm was trained on health care financial costs, the algorithm indicated that Black and White patient's health care needs were the same, despite Black patients having substantially more chronic health conditions. The researchers discussed how health but not cost disparity was caused by using medical expenditures as training data because (1) medical expenditures are generated differently between Black (e.g., emergency visits and dialysis) and White patients (e.g., inpatient surgical and outpatient specialist costs) and (2) Black patients have less access to health care due to higher rates of poverty and discrimination. Ultimately, the selection of medical expenditures has contributed nationally to structural inequalities. Benjamin (2019) framed these inequalities as the "New Jim Code" and explained how Obermeyer and colleagues (2019) findings are just one example of how "automated systems hide, speed and deepen racial discrimination behind a veneer of technical neutrality" (Benjamin, 2019, p. 421). Such findings underline the need for all sciences to invest in learning about structural racism and discussing how their work impacts marginalized communities, because the responsibility in developing and conducting ethically sound technology and research lies in the humans who are making them (Benjamin, 2019).

As discussed earlier, inertial sensors' raw data represent acceleration and rotational velocity around the *x*-, *y*-, and *z*-axes, which are then run through algorithms to detect and label different types of movements (e.g., walking vs. running). Researchers using market-wearable products are likely using the labeled and not the raw data in their analyses. Consequently, to reduce bias, it is important to understand how sensors work and to conduct pilot, reliability, and validity testing with products to ensure that the labeled movement is accurate, especially when the target sample is substantially different from the sample used to train algorithms. An example of this mentioned previously is how inertial sensors are inaccurate in detecting steps when walking aids like rollators are used because algorithms were trained using data from individuals without disabilities (Tedesco et al., 2019). Conducting multiple community-based participatory research with stakeholders across the study development, data collection and interpretation can also bring to light unknown biases.

Conclusion

This chapter highlights work that has been conducted to date and suggests future paths for examining ADL/IADL-related public health problems, especially ambulation, using wearable technology, particularly inertial sensors. This chapter also describes challenges that must be addressed, including balancing multidisciplinary expertise, maintaining the privacy of individuals represented by sensed data, and identifying and addressing health disparity and bias. As researchers move toward interdisciplinary teams, the power to investigate significant ADL/IADL-related public health problems with sensors and technology increases in feasibility. This chapter provides researchers with initial steps toward achieving this goal.

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CHAPTER 12

Ambulatory Assessment

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A*mbulatory assessment* (AA) includes a wide range of assessment methods aimed at evaluating people in their natural environments, outside constrained clinical settings or artificial laboratory environments (Carpenter, Wycoff, & Trull, 2016). In this chapter, we initially present a broad overview of AA, including the evolution over time, advantages, and challenges. The remainder of the chapter focuses primarily on *ecological momentary assessment* (EMA) as a specific example of AA, given the popularity of this approach and the direct applications of this methodology for better understanding everyday cognitive functioning. Literature on smartphone-based EMA of cognition and the advantages of this approach for researchers and clinicians is reviewed. We discuss how EMA can be used to advance our understanding of *everyday cognition* in both research and clinical contexts, and the importance of measuring *secondary and environmental influences on cognition*. Finally, we present examples of research and clinical use of AA: (1) research utilizing EMA to investigate the relationship between cognition and fluctuations in blood glucose in adults with type 1 diabetes and (2) a proposed clinical practice model for integrating AA in the assessment of older adults. We conclude with suggestions for future directions for both research and clinical practice, and the main take-aways from the chapter.

Ambulatory Assessment

AA was originally focused on real-time self-reports of symptoms in everyday environments, while ambulatory collection of physiological, cognitive and behavioral data has become more common with advances in technology. AA can range from a single assessment (e.g., survey completed at home) to intensive longitudinal designs with a large number of repeated measurements of several different variables and can include a wide range of different data collection approaches. Example data collection approaches include continuous/passive monitoring of physiological states, self-report, behavioral and cognitive performance, electronic diaries, and environmental data capture (i.e., geospatial data, temperature sensors), among other possibilities. Although AA has been used for over 20 years (Fahrenberg & Myrtek, 1996), there has been a significant qualitative leap in the past decade with the use of smartphones and other novel data collection technologies. Gathering information not only on the event of interest, but also on environmental characteristics, such as time and place of occurrence, allows AA to capture important variations in the phenomenon being studied and how it interacts with other environmental factors. In this chapter, we use AA to denote an umbrella term that includes other, more specific forms of "in-the-moment" assessment in everyday environments, such as ecological momentary assessment (see the next section), experience sampling, daily diary studies, and passive physiological monitoring.

The Society for Ambulatory Assessment was launched in 2008 (*http://ambulatory-assessment.org*). For those interested in the history of AA, the book *Ambulatory Assessment* (Fahrenberg & Myrtek, 1996) is devoted to this topic, although given recent advances in technology, many of the approaches used are now obsolete.

Ecological Momentary Assessment

EMA is a methodology used to study dynamic processes via *repeated* assessment of cognition, self-reported symptoms, and physiological processes during daily regular activity using electronic devices (including smartphones; Ebner-Priemer & Trull, 2009). While EMA is often used synonymously with AA (Carpenter et al., 2016), it is more accurately described as a subtype of AA, as it is technically possible to use AA at a single point in time (e.g., TeleNeuropsychology). A core foundation of EMA methodology is that many constructs of interest show variation over time within people in normal everyday environments. This variation may be either a key feature of the underlying construct (e.g., so called state variables such as alertness) or due to the influence of "confounding" variables on the construct of interest (e.g., the effect of fatigue on cognitive performance). EMA allows investigation of data that were previously unavailable or impractical given the limitations of traditional study designs and available technology. For the remainder of this chapter, we generally focus on the use of AA within an EMA framework (i.e., repeated assessments over time), as this approach can provide important insights into everyday functioning. Examples of AA outside of an EMA context (i.e., single assessment in an individual's everyday environment) are discussed throughout the book.

Advantages

Ebner-Priemer and Trull identified six major benefits of EMA: (1) real-time assessment increases accuracy and reduces retrospective bias; (2) repeated assessments allow the study of dynamic processes; (3) multimodal assessments can integrate psychological, behavioral, and physiological information; (4) context-specific relationships can be revealed; (5) real-time interactive feedback can be provided; and (6) ecological assessment enhances generalizability (Ebner-Priemer & Trull, 2009).

The ability to gather information in real time, rather than relying on retrospective self-report, results in improved accuracy of data collection. This advantage is particularly important for subjective symptoms that the respondent may not be able to accurately recall at a later time. Asking what a person is feeling at that precise moment is thought to be more accurate and less influenced by subsequent events compared to asking what a person felt the day or week before. Traditional retrospective self-report measures typically require respondents to average their symptoms over a 1- to 2-week period. Low mood when completing the questionnaire may result in reporting lower “average” mood over the past 2 weeks due to state-dependent memory, or a single stressful or positive event may unduly influence retrospective ratings. Relatedly, repeated assessment within individuals allows for precise measurement of variation in symptoms and performance across time and situations, which is critical to fully understand these constructs, such as mood, substance use, and craving that have high intraindividual variability (Carpenter et al., 2016).

EMA also takes advantage of recent technological advances, such as the widespread availability of smartphones and the vast possibilities for passive contextual data collected via these devices, ranging from exact location, ambient noise, temperature, and environmental air quality (Cartwright, 2016). This contextual data, paired with repeated measurements, can provide insights into previously undetected environmental influences on behavior. For example, emerging evidence using geolocation and EMA has linked exposure to urban greenspace and reduced stress (Mennis, Mason, & Ambrus, 2018). Likewise, physiological data can be measured in conjunction with psychological and/or behavioral assessments to determine associations with internal states. In such a study, the link between socioeconomic status and endocrine function (assessed via ambulatory salivary cortisol) was mediated by variations in EMA-assessed social activities (Zilioli, Fritz, Tarraf, Lawrence, & Cutchin, 2019).

Another promising potential for EMA is its use in conjunction with behavioral interventions, often referred to as an ecological momentary intervention. Real-time interventions can be particularly important when dealing with patients with impulsive traits, substance abuse problems, suicide risk, and other time-sensitive behavioral interventions. One such trial, focused on substance use in adolescents, will provide automated feedback based on responses to the EMA (Wright et al., 2020). Finally, EMA promises to provide results with enhanced real-world applicability, given that the assessments occur in the individual’s typical environment.

Challenges

A concern in the use of EMA is related to the frequency and duration of assessments that result in adequate data capture without causing undue burden. In populations with a long history of using EMA study designs, such as substance use, meta-analysis has found a pooled compliance rate of 75%, with no association between completion rates and assessment frequency or duration (Jones et al., 2019). Similarly, a meta-analysis of EMA studies in children and adolescents found a pooled compliance rate of 78%, with no association between compliance and study duration, no difference between clinical and nonclinical samples, and no difference in studies requiring wearable devices and those without (Wen, Schneider, Stone, & Spruijt-Metz, 2017). This meta-analysis also found a complex interaction between assessment frequency and sample type, with high sampling frequency (6+/day) being associated with better compliance in clinical samples, but lower compliance in nonclinical samples. Thus, key elements of the study design can be difficult to determine without pilot data in the population of interest, particularly in populations that have not been adequately studied with EMA designs.

A second challenge relates to the complexity of data analysis and management, particularly when collecting both active and passive sensor data and high-frequency assessments. For context, a relatively simple EMA study with a sample size of 100, five assessments/per day consisting of 20 discrete variables, collected for 21 days would yield 210,000 data points. Adding continuous passive physiological or geospatial data complicates matters further. Choosing the right instruments, assessment schedules and analyses to measure real-life performance can be a challenging aspect of study design and subsequent data analysis.

Ethical challenges of EMA are primarily focused on data security and confidentiality, which are common to many forms of potentially sensitive electronic data capture. GPS, medical, and other sensitive data collection can raise concerns about privacy (e.g., GPS data could identify where participants live) and require appropriate protections (e.g., encryption and aggregation of data). While real-time data capture allows for timely interventions, there may be associated risks of not recognizing if an individual is at imminent risk for harm. For example, repeated assessment of suicidal ideation must be accompanied by protocols for monitoring this data and associated prompts for staff to protect the safety of individuals who are not physically in the same space.

EMA of Cognition

Although there are some early examples of EMA study designs incorporating cognitive assessment (Cox et al., 2005), the focus was primarily on very simple cognitive constructs due to limitations in available technology (e.g., reaction time, mental math). The current widespread availability of smartphones with large, high-resolution displays has made comprehensive cognitive assessment possible. Among the greatest benefits of EMA for neuropsychology are: the opportunity to measure cognitive performance in real-world settings; the ability to increase measurement precision with the use of digital technology; the reduction of assessment costs and logistical barriers; and the increase in neuropsychological evaluation accessibility (Germine, Reinecke, & Chaytor, 2019). In addition, intensive longitudinal or “measurement burst” study designs dramatically increase reliability when repeated assessments are averaged (Sliwinski, Hoffman, & Hofer, 2010). Further, the ability to economically assess cognition longitudinally has the potential for improving detection of cognitive change over time, within both research and clinical contexts. Lastly, there is increasing evidence that cognitive variability itself is an important marker for brain dysfunction, rather than a source of measurement error (Anderson et al., 2016; Gleason et al., 2018). Temporal variation in executive functioning performance may also be critical for accurate assessment and characterization of this construct (McKinney, Euler, & Butner, 2019).

While not unique to AA, computerized administration of speeded tests is more precise than examiner-administered pencil-and-paper tests and can capture individual trial reaction time variability. Furthermore, AA can mitigate logistical challenges related to traditional in-person test administration, such as the costs (personnel time, clinic/lab space, physical assessment materials), and health risks (Covid-19, immune compromised patients) associated with face-to-face testing, difficulties traveling to a clinic/lab location for those with mobility limitations or who live in rural/remote areas, training required for the examiner, and complex scoring procedures. As such, AA may promote the inclusion of more representative research samples, as well as better study recruitment and retention, and may allow for more complete clinical follow-up.

There are also unique challenges that need to be considered when using AA to measure cognition, including the need for standardization and validation of new assessments (in terms of both the task itself and the device it will be completed on). The need for specific operating systems (e.g., Apple vs. Android), operating system updates, screen size, battery life, internet speed/reliability, and operating system speed variation are some of the technological issues that may limit research and widespread clinical use of AA of cognition (Germine et al., 2019). These factors create significant challenges for normative data collection and necessitate processes for quickly updating or correcting normative data to account for changes in technology. A related concern involves the test stimuli themselves and the inability to measure certain cognitive constructs or response modalities via a given electronic device (e.g., visual motor construction and manipulation). Further, due to the repeated nature of EMA designs, practice effects must be explicitly addressed. Practice effects in cognitive EMA designs tend to show exponential effects over the first few assessments, before such effects rapidly plateau. Any practice effects that are detected should be explicitly modeled or excluded from data analyses when appropriate (e.g., allowing for task practice effects to plateau before including data in analyses). Additionally, alternative forms can be created to minimize practice for the specific stimuli used but must be evaluated for equivalence, and practice effects may still occur for the test procedure itself.

Clinicians may also be concerned about the inability to directly observe test-taking behaviors or assist more impaired patients with task instructions, although single AA sessions can be used in conjunction with a telemedicine visit when necessary. This issue is of critical importance when evaluating populations with moderate-to-severe cognitive impairments who may become confused with task instructions or during assessments. Without visual/auditory observation, it is also possible that important environmental influences will not be appreciated, such as other people in the room, physical limitations (e.g., tremor), and other potential unmeasured distractions (e.g., email notifications). Further, while passive data collection can provide insights into the test-taking context, these must be specified ahead of time. Some data may lack sufficient precision. For example, while GPS may provide information related to the participant's location or movement during testing, it may not be able to determine if a participant is inside a restaurant or just standing on the street in front of one.

For additional information on the use of digital technologies in neuropsychological assessment, see Germine et al. (2019) and Parsons, McMahan, and Kane (2018).

Everyday Cognition

Ecological validity, or the ability of neuropsychological tests to reflect cognitive performance in the real world, is an important consideration in neuropsychology (Chaytor & Schmitter-Edgecombe, 2003). Traditional approaches to cognitive assessment involve environments that are precisely controlled and protected from distractions (i.e., a clinical or laboratory setting that is very different from the demands of an individual's day-to-day life). While this may be ideal for capturing optimal performance, it may not reflect cognitive performance in real-world settings. In addition, it has been demonstrated that single-occasion testing can be influenced by random and systematic within-person variability such as stress, sleep quality, and food intake (Sliwinski et al., 2018) that may not reflect the individual's typical performance. EMA approaches that collect cognitive performance repeatedly over time, either alone or in tandem with environmental and psychological factors, may be able to better characterize everyday cognitive performance (McKinney et al., 2019). This knowledge may enable more accurate prediction of everyday functioning and provide insights into how to modify environments to maximize cognitive performance for individuals. Thus, AA has the potential to increase the ecological validity of neuropsychological assessment. However, this must be tempered with the threats to internal validity inherent when testing is occurring in an uncontrolled environment (e.g., other people completing assessments, using substances, multitasking, talking to other people or watching TV while completing assessments) that may not reflect meaningful variation in cognitive performance. This matter is of particular importance when using these approaches in clinical settings.

The reliability and validity of self-administered mobile cognitive assessments have been evaluated in a number of clinical and nonclinical samples across a variety of cognitive domains (Bouvard et al., 2018; Brouillette et al., 2013; Daniëls et al., 2019; Hansen, Haferstrom, Brunner, Lehn, & Haberg, 2015; Hung et al., 2016; Lee, Williams, & Evans, 2018; Morrison et al., 2018; Schuster, Mermelstein, & Hedeker, 2015; Schweitzer et al., 2017; Sliwinski et al., 2018; Timmers et al., 2014; Wong, Fong, Mok, Leung, & Tong, 2017). A recent review of mobile cognitive assessment studies ($N = 12$) concluded that the majority of studies found good test–retest and internal reliability, as well as good convergent and divergent validity compared to lab-based assessments, although most studies reviewed were in nonclinical populations (Moore, Swendsen, & Depp, 2017). It is important to note that establishing the psychometric properties of AA measures is complex, and gold standards for what constitutes adequate reliability and validity for EMA measures are lacking. A recent effort to establish uniform reporting standards for EMA studies, which includes reporting of the psychometric properties of the items (between and within person), is encouraging, though focused on psychopathology research (Trull & Ebner-Priemer, 2020). A related issue centers on how to establish the validity of new EMA cognitive tests, given that many EMA measures do not have directly analogous traditional neuropsychological measures or have been modified substantially. An alternative approach would be to validate EMA cognitive measures as completely new tests (rather than considering traditional neuropsychological testing methods as the gold standard). An added complexity includes whether the methodology itself (i.e., self-administered mobile assessment in natural environments) can be validated independently of the specific cognitive measures and stimuli used (e.g., digit symbol coding), and whether independent psychometric evaluation is needed for every new clinical population, age range, and device.

Studies involving the assessment of cognition in participants' everyday natural environment initially focused on simple cognitive constructs, such as reaction time (RT) and the ability to perceive, process, and respond to a stimulus (Hakim et al., 2018; Owens et al., 2000; Salthouse & Berish, 2005; Thomson, Nimmo, Tiplady, & Glen, 2009). Working memory has also been the focus of AA cognitive assessment research (Kennedy et al., 2011; Neubauer, Dirk, & Schmiedek, 2019; Riediger et al., 2014; Schulze, Bürkner, Bohländer, & Zetsche, 2018; Schuster et al., 2016; Sliwinski et al., 2018; Veasey, Haskell-Ramsay, Kennedy, Tiplady, & Stevenson, 2015), likely due to its inherently volatile nature. EMA study designs permit modeling of the dynamic interactions of short-term variability (over hours-days) in cognitive performance and patient reported data (Sliwinski, 2010, 2011; Steinerman, Hall, Sliwinski, & Lipton, 2010). EMA can produce reliable estimates of performance and capture short-term changes in cognition (Sliwinski et al., 2018). Many studies have incorporated cognitive assessment in EMA studies of compulsive behaviors and substance use disorders in order to evaluate the effects of abstinence or substance use on cognitive performance (Keenan, Tiplady, Priestley, & Rogers, 2014; Marhe, Waters, van de Wetering, & Franken, 2013; Shiffman et al., 2006; Suffoletto, Goyal, Puyana, & Chung, 2017; Tiplady, Oshinowo, Thomson, & Drummond, 2009; Waters & Li, 2008; Waters, Marhe, & Franken, 2012). See Table 12.1 for a description of studies using an EMA study design to assess cognition.

Time sampling and practice effects can also pose a challenge in cognitive EMA studies. Limitations on EMA frequency, test duration, and number of administered items can negatively affect measurements of within-person change (Calamia, 2019). Guidelines for the optimal frequency and duration of cognitive tests depend not only on the phenomenon being investigated, but also on individual burden and on the impact of practice on the cognitive tests in question. While in theory higher frequency and duration may increase accuracy, possible reductions in compliance, particularly if not random, may result in overall poorer data quality. Thus, the frequency of data collection should be appropriate to the population and question being investigated, taking into consideration the time scale of expected variation in the cognitive domain (i.e., hourly, daily, weekly), minimization of participant burden, and clinical/ research feasibility. For example, a study focused on assessing the association between inhibition and drinking behavior would need to include relatively frequent assessments in the evening to capture cognition during the timeframe when most people drink alcohol. In addition to decisions regarding EMA duration and frequency, practice effects can be a confounder in EMA studies. One possible solution is to ensure that asymptote task performance has been achieved prior to including assessments in data analysis. For example, a recent study using EMA to evaluate the relationship between cognition and functional status in middle-aged and older adults included an initial period where participants repeated testing until they reached asymptote performance prior to beginning EMA data collection (Schmitter-Edgecombe, Sumida, & Cook, 2020). Optimally, researchers will conduct pilot testing to determine these parameters in the target population prior to launching fully powered studies.

Secondary and Environmental Influences on Cognition

It has long been recognized that cognitive performance is impacted by many factors that are either secondary to underlying brain dysfunction or features of the environment, such as emotional distress, fatigue, pain, physiological states, recent stressful experiences, and environmental conditions (temperature, noise; Arnett, 2012). Clinicians routinely administer psychological symptom inventories and gather detailed historical information to better understand these possible influences on cognitive performance. These approaches, however, lack precision and temporal association with cognitive measurement, limiting the ability to determine if cognition is, in fact, adversely impacted in

TABLE 12.1. Description of Selected Cognitive EMA Studies

Cognitive domain/ construct	Example measure	Description of task with administration time	Population	First author (year)
Executive functioning	Stroop	Traditional Stroop interference paradigm requiring participants to name the color of ink for 16 color words. Administration: Smartphone, 5 EMAs per day every 3 hours; each cognitive EMA took < 2 minutes. 14 versions of each test given, counterbalanced for time of day.	34 adults with substance use disorders (*M* age = 41.9 years) and 27 healthy controls (*M* age = 34.8 years)	Bouvard et al. (2018)
Reaction time	Psychomotor Vigilance Test (PVT)	Standard 10-minute PVT. Visual stimuli presented at variable intervals, respond by pressing right or left button on device. Administration: Handheld, self-contained system used for repetitive measurements during preoperative holding room.	Children, 6–11 years. Obstructive sleep apnea group (*N* = 46) and control (*N* = 26)	Hakim, et al. (2018)
Working memory	Spatial working memory	Between 2 and 4 4 × 4 grids, with each grid containing a random display of five dots, were presented. Participant should re-create the pattern of dots from the last grid. Administration: One week of random data capture 5–7 times a day. Each assessment took 230 seconds. Handheld computers used.	Young adults with substance use history, mean age 21.3, *SD* 0.8 (*N* = 287)	Schuster, Mermelstein, & Hedeker (2016)
Processing speed	Digit-symbol substitution	Participants should identify visually presented symbols by touching corresponding digit provided in a reference key. Administration: Mobile assessment. Four consecutive Fridays and Saturdays, every hour from 8 P.M. to 12 A.M. Each assessment was 45 seconds.	Young adults with hazardous drinking, 21–26 years (*N* = 10)	Suffoletto et al. (2017)
Attention	Letter Span task	A sequence of letters was presented one at a time in the center of the screen. After the sequence is completed, participants select the letter sequence from a keyboard display. After two correct sequences, a longer sequence is presented. Administration: Android smartphone, four 15-minute assessments on a single day	Young adults mean age 23.12 years, *SD* 3.02 (*N* = 26)	Timmers et al. (2014)

a given individual patient by a given secondary factor. Emotional distress, fatigue, and pain can vary considerably over days or even hours, making them particularly well suited to EMA data collection strategies. This methodology can provide important information on associations between emotional symptoms, daily experiences, physiological states, environmental conditions, and cognitive performance. As mentioned earlier, real-time assessment minimizes retrospective recall biases and can uncover important associations that would otherwise be contaminated by inaccurate self-appraisals or generalizations over an extended period of time (i.e., how anxious have you been over the past two weeks?). As an example of unique insights that can be gained by this approach, Kahneman and colleagues found that, although baseline assessments of life satisfaction were higher for participants with above-average income compared to those with below-average incomes, daily EMA revealed that mood was actually poorer (with less time spent in pleasurable activities) in those with higher incomes (Kahneman, Krueger, Schkade, Schwarz, & Stone, 2006).

AA can also uncover important temporal relationships between emotional states, environmental stressors, and physiological metrics. For example, studies using EMA to investigate the relationship between day-to-day positive and negative emotional states and salivary cortisol level found that prior-day emotional symptoms were associated with next-day waking cortisol (Adam, Hawkley, Kudielka, & Cacioppo, 2006) that would not have been discovered with other study designs. Further, EMA can be used to understand complex relationships between external events (e.g., stressors), internal emotional states (e.g., negative affect), and cognitive performance, resulting in a more complete understanding of performance in real-world environments. For example, EMA study designs have been used to detect associations between environmental stress (noise exposure), increased arousal, and poorer cognitive performance (Wass et al., 2019). EMA can be used to understand the immediate influence of a stressful event on cognition and how emotional states may mediate this association even when the individual being studied is not aware of these influences. Studies using this methodology point to a correlation between stress and cognitive failure or distractibility (Hyun, Sliwinski, & Smyth, 2019; Lange & Süß, 2014), as well as associations between situational context (e.g., being alone; geographical location), mood, and cognitive function (von Stumm, 2018).

Additional Reading

AA/EMA has a long tradition in the assessment of emotional, behavioral, and substance use disorders. The interested reader is referred to the following additional sources:

- *Compulsive eating* (binge-eating disorder) (Haedt-Matt & Keel, 2011; Smith et al., 2019);
- *Anxiety disorders* (Walz, Nauta, & aan Het Rot, 2014);
- *Mood disorders and dysregulation* (aan het Rot, Hogenelst, & Schoevers, 2012; Ebner-Priemer & Trull, 2009);
- *Borderline personality disorder* (Santangelo, Bohus, & Ebner-Priemer, 201; Trull, 2018);
- *Substance use disorders and other addictive behavior* (Serre, Fatseas, Swendsen, & Auriacombe, 2015; Vinci, Haslam, Lam, Kumar, & Wetter, 2018);
- *General psychiatry* (Raugh, Chapman, Bartolomeo, Gonzalez, & Strauss, 2019);

- *Stress* (Bellido, Ruisoto, Beltran-Velasco, & Clemente-Suarez, 2018);
- Challenges of AA related to *mobile devices* (Carpenter et al., 2016);
- AA *mood* scale validation (Wilhelm & Schoebi, 2007).

EMA Research Example

While the possible research applications of EMA of cognition are numerous and varied, we will provide a specific example from our research group in order to illustrate some of the key logistical issues that need to be considered when using this methodology for cognitive assessment. The following study utilizes EMA of cognitive and psychological symptoms, continuous physiological assessment, and contextual factors. This project is a collaboration between our group at Washington State University and Laura Germine, PhD, director of the Laboratory for Brain and Cognitive Health Technology at McLean Hospital. Dr. Germine is the founder of *www.TestMyBrain.org,* a not-for-profit web-based platform for AA of cognition. The following is a description of our R01 funded by NIH National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), entitled “Glucose Excursions and Cognitive Status in Adults with Type 1 Diabetes” (GuCog). Type 1 diabetes (T1D) is characterized by a requirement to administer exogenous insulin multiple times per day, which typically results in marked fluctuations in blood glucose across hours and days. Hypo- and hyperglycemic clamp studies conducted in laboratory settings have demonstrated that acute changes in blood glucose can result in reversible cognitive dysfunction. Such findings are consistent for moderate to severe hypoglycemia (Allen et al., 2015; Ewing, Deary, McCrimmon, Strachan, & Frier, 1998; McAulay, Deary, Ferguson, & Frier, 2001; McAulay, Deary, Sommerfield, Matthews, & Frier, 2006; Schachinger, Cox, Linder, Brody, & Keller, 2003; Sommerfield, Deary, & Frier, 2004; Sommerfield, Deary, McAulay, & Frier, 2003; Wright, Frier, & Deary, 2009), with mixed findings for mild hypoglycemia and hyperglycemia (Cox et al., 2005; Gonder-Frederick et al., 2009; Sommerfield et al., 2004). These mixed findings lead to important unanswered questions:

1. What factors determine whether mild hypoglycemia and/or hyperglycemia impact short-term cognitive status?
2. Are there real-world glycemic, psychological, or diabetes-related factors that make an individual *more* likely to experience short-term cognitive impairments in everyday environments?

Currently, the short-term effects of blood glucose excursions in everyday environments are unknown and represent a significant gap in our knowledge that is important for patient safety and for the design of new and better diabetes management strategies. This study uses EMA of cognition via self-administered mobile cognitive assessments, coupled with continuous glucose monitoring (CGM), in order to evaluate the relationship between glycemic excursions and cognitive status under naturalistic conditions in adults with T1D. The commercial CGM device (Dexcom© G6) used in this study consists of a subcutaneous sensor and transmitter that is attached via adhesive to the abdomen and a Bluetooth receiver that stores glucose readings. Glucose is measured every 5 minutes for 10 days of continuous wear, with the ability to blind glucose readings from study participants in order to reduce the possibility that knowledge of glucose values at the time of EMA assessment could bias self-reported symptoms and cognitive test results.

Our research design consists of an initial in-person or virtual enrollment visit to explain the study, collect medical record data, train the participant in use of the CGM, and download the study EMA assessment application. Within the next 24 hours, the participant completes an online baseline cognitive and psychosocial assessment battery on any available device, followed by an EMA onboarding training session via the smartphone application. The next morning, the participant begins receiving text alerts to complete assessments consisting of ~5 minutes of cognitive testing and ~2 minutes of questions about current emotional and environmental states (stress, fatigue, mood, anxiety, social context, alcohol/substance use, and interruptions) multiple times per day (Figure 12.1). Because the optimal EMA frequency for adequately sampling the full range of blood glucose values is not currently known, this project includes an optimization phase ($N = 20$) with a 3/day and 6/day EMA schedule. This data is currently being analyzed to determine which schedule (1) includes a wider range of blood glucose values at the time of EMA assessment and (2) is associated with fewer missing data. GPS data is passively collected via the app, as well as information about the device type used and duration of the assessment. After ~20 days (two CGM sensors), a second clinic or virtual visit is completed in order to download CGM data and provide compensation based on the number of assessments completed.

The battery of EMA cognitive tasks includes measures of processing speed, working memory, and cognitive control (see Table 12.2). These tests were selected based on sensitivity to cognitive variability and validation for use in a diverse range of settings, populations, technology platforms, and study types, with psychometric characteristics and data quality comparable to traditional testing methods (Germine et al., 2012), including large samples of adults across the lifespan (Fortenbaugh et al., 2015; Germine, Duchaine, & Nakayama, 2011; Halberda, Ly, Wilmer, Naiman, & Germine, 2012; Hartshorne & Germine, 2015). Patterns of performance across age replicate classic findings in lifespan

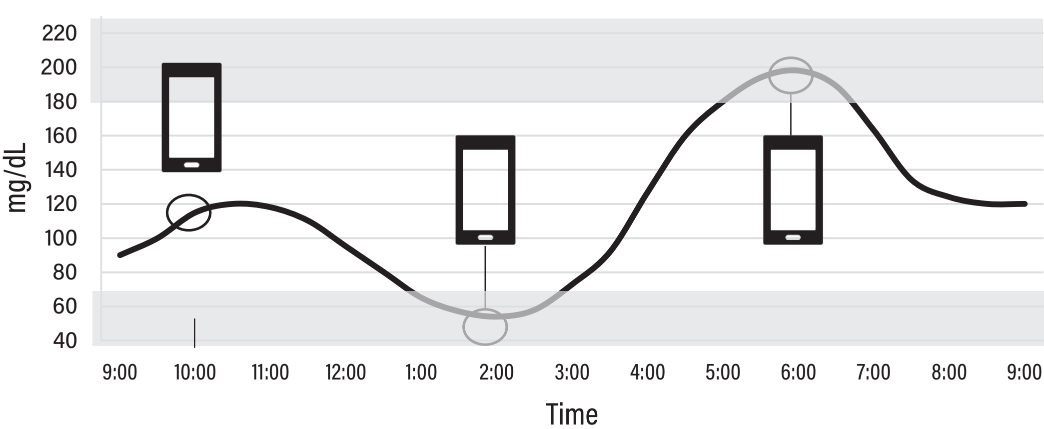

FIGURE 12.1. Cognitive EMA coupled with continuous glucose monitoring.

TABLE 12.2. EMA Cognitive Assessment

EMA cognitive assessments	Duration (seconds)	Description	Cognitive domain
Choice Reaction Time (Rutter, Vahia, Forester, Ressler, & Germine, 2020)	45	Two arrows in the same color, while a third arrow is in a different color, are presented. The participant must quickly select the direction in which the odd-colored arrow is pointing	Processing speed
Digit Symbol Matching (Hartshorne & Germine, 2015)	30	Participants quickly match a set of symbols to the numbers 1, 2, or 3, based on a key presented on screen	Processing speed
Visual Paced Serial Addition Test	60	Participants indicate whether last two numbers add up to more or less than 10	Cognitive control
Gradual Onset Continuous Performance Test (Fortenbaugh et al., 2015)	60	Participants tap the screen when they see a city scene and withhold a response when they see a mountain scene	Cognitive control
Flicker Change Detection (Wilmer et al., 2012)	60	Participants view an array of blue dots. Participants are asked to tap the dot that alternates from blue to yellow	Visual working memory
Multiple Object Tracking	60	Participants track dots as they move across the screen	Visual working memory

cognition using traditional neuropsychological assessments (Cattell, 1967; Hartshorne & Germine, 2015; Horn & Cattell, 1967), as well as age-related differences in cognition assessed in national samples (Hartshorne & Germine, 2015). These measures have been optimized for self-administration, broad accessibility, and participant engagement, using data from over 2 million participants from the testmybrain.org website. The EMA approach aligns well with the self-management expectations of living with T1D, which requires frequent, repeated interactions with technology throughout the day (e.g., checking blood glucose, counting carbohydrates before meals, administering insulin via insulin pump or injections).

Mobile Cognitive Assessment

Participants complete an initial self-administered cognitive battery (nonverbal reasoning, visual memory, decision making, word knowledge, and basic psychomotor speed) at home on a device of their choosing (computer or tablet is recommended) within 24 hours of the initial visit. After the baseline has been completed, the participant is prompted via the app to complete an initial "onboarding EMA" practice session. The onboarding EMA has more detailed task instructions and practice trials to ensure that all EMA tasks are understood before the EMA schedule begins. The following day, the EMA cognitive assessment schedule begins, delivered on a pseudorandom schedule for 20 days. Each EMA includes three discrete cognitive tests, one test from each cognitive domain, allowing us to investigate cognitive status varying over hours and days based on (1) a single common factor based on shared variance between the tests and (2) performance on each cognitive domain. All assessments are completed remotely through RedCap and a custom study page on TestMyBrain, a secure cognitive assessment platform. All cognitive assessments are implemented using a combination of JavaScript (including the TestMyBrain.js library) and HTML5 and are completed using the participant's smartphone. We chose these cognitive domains based on previous evidence of sensitivity to T1D-related cognitive impairment and insulin clamp studies; sensitivity to fluctuations in time-varying state factors such as fatigue, stress, and negative affect; and validation for brief, repeated administration using mobile devices, in naturalistic environments. For all tasks described above, 120 forms were generated based on validated algorithms to minimize practice effects. Cognitive test applications are linked with the EMA Application via established custom application program interface (API) integration with the TestMyBrain platform.

Contextual Factors

At the end of each EMA, participants report on their current location (work, home), social company (alone, with others), and whether anything distracted them during the cognitive tests (Sliwinski et al., 2018).

Passively Obtained Metadata

We use the EMA app to collect data pseudocontinuously and at the time of each EMA from sensors embedded in the participant's smartphone. These include information about ambient noise (dB) levels and GPS location, which will help us characterize and control for variability in testing conditions that may impact performance. Information about hardware, operating system, and the central processing unit (CPU) usage will also be captured to assist in interpreting cognitive data, as these device characteristics can confound smartphone-based cognitive assessment if not measured (Germine et al., 2019).

Device Audit

Throughout the study period, we are collecting continuous data on device characteristics (through TestMyBrain.org) in order to adjust for variations in technology across participants that could impact measurement properties of the tests. Device characteristics collected include device types, browsers, operating systems, and browser/OS updates that are released and enter the pool of potential devices. In addition, participants are asked to use the same device, software, and operating system for all within-person assessments when possible. We will exclude any devices that we find have a negative impact on the quality of our measurement (e.g., markedly poorer task scores when using a specific device based on online testmybrain.org data collection). For others, we will include device, operating system (OS), and browser as covariates in our statistical analyses.

Potential Pitfalls

All EMA research designs must strive to minimize participant attrition and missing data. In addition to financial incentives for completing individual study assessments, we provide participants with feedback on their baseline cognitive test performance after they return the CGM for download. This feedback will be in the form of an average age-adjusted percentile rank relative to TestMyBrain.org data, along with an explanation and contact information of a clinical neuropsychologist (Dr. Chaytor) if there are questions. We also return CGM data summary statistics to patients and their clinic providers. While EMA data collection in participants' real-world environment is integral to our research question, it also introduces less experimental control. We have taken steps to mitigate problems associated with reduced experimental control via certain aspects of our study design (e.g., exclusion of shift workers, no assessments in the early morning or late evening), as well as by collecting data on as many extraneous factors as possible (e.g., device type, sleep duration/quality, location, distraction, and noise data). In addition, there are important considerations when repeated discrete assessments (cognitive and psychological symptoms) are combined with passive continuous data collection (CGM). For example, the optimal CGM metrics/timeframes for impact on cognition are not known, so we have chosen to focus on the glucose window 60 minutes prior to each EMA. We will also explore other variables in exploratory analyses (e.g., nocturnal hypoglycemia/hyperglycemia prior to an entire assessment day).

A detailed understanding of the underlying factors that predict cognitive variability in adults with T1D is key to developing interventions that will make meaningful and lasting change in cognitive outcomes. Data generated via this project will be used to continue work focused on dissemination of a cognitive self-management tool based on the test battery used here. This will allow adults with T1D to self-monitor their cognitive performance over time and determine individual cognitive reactivity to glycemic fluctuations. This personalized data can be used by the patient and/or provider to improve short term individual functioning (e.g., academic and work performance). The remote assessment tools developed for this project will also be disseminated for research purposes to enable further investigations of cognition in T1D.

AA in Clinical Practice

AA/EMA has many possible clinical applications, including assisting with diagnostic evaluation and investigation, examining the mechanisms underlying symptoms, predicting symptom occurrence in the future, identifying symptom onset, monitoring treatment and efficacy, and using EMA to provide automated real-time interventions (Hoppmann & Riediger, 2009). Unfortunately, despite the potential clinical utility, its practical use in psychology and neuropsychology is still in its foundation (Ebner-Priemer & Trull, 2009). As a relatively new approach to assessment that departs from the basic foundations of clinic-based practice, widespread acceptance will likely be slow. This has been true of earlier technological advances (e.g., table-based test administration) that have subsequently been generally accepted by clinicians. While there will likely be clinical contexts in which this form of assessment will not be feasible or appropriate, we believe there is a role for AA within many clinical practices. In this section, we focus on the clinical application of AA in older adults for the detection of MCI and/or the progression of cognitive decline.

Clinical Applications in Aging and Mild Cognitive Impairment

While the older literature on AA in young children and older adults is relatively scarce (Hoppmann & Riediger, 2009), recent studies show that smartphone-based EMA in older adults is feasible (Brouillette et al., 2013; Munoz, Sliwinski, Scott, & Hofer, 2015; Schweitzer et al., 2017; Stawski, Mogle, & Sliwinski, 2011). By offering repeated assessment of cognitive functions over time, coupled with assessment of potentially reversible factors (e.g., perceived stress, sleep, negative affect), clinicians may be able to identify early evidence of cognitive change, as well as offer recommendations to maximize cognitive performance prior to, or after, traditional clinical services. EMA may provide a more sensitive identification of early cognitive and neuropsychiatric manifestations of neurodegenerative diseases, making it suited for monitoring the general aging population or those who may be at increased risk due to positive biomarker status or genetic risk. In fact, years prior to dementia diagnosis, patients already present subtle cognitive decline (Edmonds, Delano-Wood, Galasko, Salmon, & Bondi, 2015; Papp et al., 2020) and behavioral changes that can be more easily detected by repeated assessments (Anderson et al., 2016; Brouillette et al., 2013; Farias et al., 2009). In addition, intraindividual cognitive variability (within a test battery and over time) has been identified as an early marker of cognitive decline that is independent of absolute level of cognitive performance (Anderson et al., 2016; Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000; Murtha, Cismaru, Waechter, & Chertkow, 2002). As such, EMA may assist in making early clinical diagnosis before substantial cognitive and functional decline has occurred. Providing repeated and real-world assessments may reduce the margin of error normally associated with traditional neuropsychological testing and for this reason may better characterize cognitive decline (Schweitzer et al., 2017). Early diagnosis can lead to early intervention aimed at slowing decline, including cognitive rehabilitation, medication, and psychosocial interventions, as well as potentially preventing functional impacts of late diagnosis, determining needed services early, and supporting families in the care process. In an interesting study on ambulatory cognitive assessment and its correlation with neuroimaging findings, researchers found that, in contrast to the traditional neuropsychological tests used in the study, mobile assessment of semantic memory performance was significantly correlated with Alzheimer's disease neuroimaging markers, such as hippocampus volume, in older adults (Allard et al., 2014). Other validation work focused on smartphone-based EMA in clinical samples of older adults has also demonstrated promising initial results (Moore et al., 2017; Paolillo et al., 2018; Ramsey, Wetherell, Depp, Dixon, & Lenze, 2016).

In addition to aiding with early identification of cognitive decline in normal or at-risk aging populations, EMA could also be used to monitor cognitive change following an MCI diagnosis rather than relying on repeat neuropsychological evaluations in clinic. The problem of systematic missing data in longitudinal studies in older adults is well known, resulting in an underestimation of cognitive decline due to those with greater cognitive impairment being less likely to return for in-person follow-up assessments (Wang & Hall, 2010). Using auxiliary methods of detecting cognitive decline in those who do not return for follow-up assessment (e.g., phone assessments) can greatly improve detection of cognitive decline (Hall, Lipton, Katz, & Wang, 2015). Thus, the use of EMA cognitive assessments at regular follow-up intervals following an initial diagnosis of mild cognitive impairment (MCI) or mild dementia could help determine when additional in-person follow-up, and/or new treatment recommendations are warranted.

Since pharmacological and behavioral interventions are available to postpone the progression of Alzheimer's disease symptoms at the time of early diagnosis (Huang, Chao, & Hu, 2020; Jean, Bergeron, Thivierge, & Simard, 2010; Petersen et al., 2018), EMA may be used to monitor cognition and neuropsychiatric symptoms following interventions aimed at slowing decline. In addition, EMA can help identify patient preferences for treatments, particularly in the early stages of dementia (Saunders et al., 2018). The fact that AA provides data on cognitive performance under everyday conditions makes the results valuable for the patient's daily management. For example, in a study of elderly people in rural areas, researchers found that after engaging in specific intellectual activities, such as reading and completing crossword puzzles, the participants' semantic memory was better for the rest of the day (Allard et al., 2014). In practice, this observation could serve as an intervention strategy, such as recommending these types of activities at the beginning of the day. Diurnal variations in cognitive performance may also allow caregivers to plan activities to occur when patient cognitive functioning is less likely to be impaired. Also, EMA, particularly when coupled with GPS sensors, may be an important tool to monitor and create wander-management strategies in dementia (Vuong, Chan, & Lau, 2015). Indeed, managing changes in behavior and wandering is an important concern in the field of dementia, since both are associated with significant caregiver burden and negative health outcomes such as falls (Hashimoto et al., 2017; Neubauer, Azad-Khaneghah, Miguel-Cruz, & Liu, 2018). In addition to detecting problematic behavior, ecological momentary intervention could be used to prompt patients and/or caregivers (i.e., remind participant to take medication, alert caregiver that the patient has left his or her room).

One of the obstacles normally raised when it comes to applying AA to the elderly population is a possible concern that this population may have difficulty with computerized assessment. While this may be a challenge in some specific demographic groups, the majority of older adults in the United States have access to mobile devices and/or a tablet computer (Center, 2019). Further, the technology used can be adapted to specific populations (e.g., larger screen size, adapted sound volume). Newer touchscreen-based devices are very intuitive and user friendly, which may facilitate cognitive assessment in the face of some disabilities. Nevertheless, the clinical use of AA in more advanced cases of neurodegeneration is unclear and needs further study. AA has been validated with aging individuals without dementia (Moore et al., 2017; Paolillo et al., 2018; Parsey & Schmitter-Edgecombe, 2019; Ramsey et al., 2016) and for the detection of cognitive decline before dementia diagnosis (Schweitzer et al., 2017).

EMA can also be used to follow patients after receiving an MCI or dementia diagnosis via traditional clinical assessment. Researchers used EMA to capture health behaviors and mood following knowledge of beta-amyloid positive imaging results from patients with MCI, demonstrating that EMA can be a useful tool for monitoring adverse psychological events following disclosure of test results (Mattos et al., 2019).

Finally, to underline the promising importance of AA in clinical practice with older populations, the National Institutes of Health (NIH) through the National Institute on Aging (NIA) held a workshop on Applying Digital Technology for Early Diagnosis and Monitoring of Alzheimer's Disease and Related Dementias in 2019, with an accompanying notice of special interest with the goal of facilitating research on the use of "digital biomarkers," including both cognitive assessment and other digital data capture, that signal early changes associated with increased risk for dementia.

Further Resources Related to Clinical Use of AA in Other Populations

Examples of clinical application of AA in other clinical populations are listed below:

AA Including Cognitive Assessment

- AA used as a measure of *postconcussion symptoms* and recovery outcomes (Sufrinko et al., 2019)
- AA use in a brief intervention to reduce *cannabis use* (Prince, Collins, Wilson, & Vincent, 2019)
- AA as a measure of treatment effects in *obsessive–compulsive disorder* (Rupp et al., 2019)
- AA in monitoring and coaching in *chronic migraine* (Sorbi, Mak, Houtveen, Kleiboer, & van Doornen, 2007)

Behavioral Interventions Using AA

- AA addressing *alcohol* craving (Coates et al., 2017)
- Social support, self-management and *type 2 diabetes* management (Luscher et al., 2019; Pemu et al., 2019)
- Review of possible uses of continuous glucose monitoring (CGM) to enhance treatment and clinical decision making in patients with *type 1 and type 2 diabetes* (Brown, Basu, & Kovatchev, 2019)
- Review on the use of digital devices for *psychiatry and neuroscience* (Baker, Germine, Ressler, Rauch, & Carlezon, 2018)
- Use of biomedical sensors for *sports medicine* (Seshadri, Magliato, Voos, & Drummond, 2019)
- AA for improving *chronic pain* management (Jaén et al., 2019)
- Use of AA to avoid *suicide attempts* (Berrouiguet et al., 2019)
- AA as intervention for *major depressive disorder* (Colombo et al., 2019)

Future Directions

Ambulatory assessment is a promising tool for both research and clinical practice. Future research, clinical assessment, and intervention strategies are expected to emerge in the coming years as a result of advances in technology and broadened use in health settings. Among the most exciting aspects of AA and EMA study designs is the opportunity to more deeply explore biopsychosocial mechanisms that underlie human health and disease. Technological advances in physiological sensing capability, as well as machine learning techniques for prediction of cognitive change based on these data, are rapidly advancing. Our understanding of the real-world influences on cognitive performance will be increased exponentially by the ability to precisely measure these phenomena as they occur. Repeated measurement allows for identification of mediators and moderators of cognitive change over time. A key opportunity for future research is to identify the most optimal use of EMA in combination with traditional in-person clinical assessment. The combination of these methods may reduce some of the main obstacles encountered in the use of AA, such as the lack of qualitative data from trained observation and limited measurement of some cognitive constructs.

In addition, the combined use of EMA with brain morphology, functionality, and connectivity offers additional insights into neuropathological predictors of everyday cognition, thus enhancing the understanding of underlying brain mechanisms. In a study using electroencephalography measures, lower prefrontal cortex activity predicted depression symptoms measured by EMA (Putnam & McSweeney, 2008). In another study with structural and functional magnetic resonance imaging, reward-related brain function was correlated with natural positive affect measured through telephone-based EMA in adolescents with major depressive disorder (Forbes et al., 2009).

Conclusions

Recent advances in smartphone and other mobile technologies have resulted in new opportunities for ambulatory assessment of cognition in everyday environments. The use of ambulatory cognitive assessment, when applied in a careful and planned manner, can complement traditional neuropsychological assessment and provide an important tool for early diagnosis, monitoring, and intervention. This field holds immense promise for uncovering the everyday conditions, both internal and external, that influence cognitive performance in individuals over time. These insights can be harnessed to better understand the brain and behavior, and ultimately maximize functioning.

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CHAPTER 13

Virtual-Reality-Based Neuropsychological Assessments of Everyday Functioning

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Clinical neuropsychology is a question-driven service. Its value to patients, to referral sources, and to the health care system has required neuropsychologists to collect information from record review, interview, and formal assessment that addresses the clinical concerns of patients, their families, and referring providers. When neuropsychology emerged, brain visualizations were limited and behavioral manifestations of pathology-informed lesion localization (Lezak, 1983). While advances in neuroimaging have faded, the need for localization as a referral question for neuropsychologists (Bigler 2017; Dodrill, 1997) and other issues have emerged. Advances in technology have prompted a reexamination of how best to measure behavioral changes associated with neurological disease and injury (Bilder, 2011; Parsons, 2016). New questions for neuropsychologists fall into two major categories: (1) those with medical relevance; and (2) those with functional relevance. Medically relevant questions include assessing patients for evidence of cognitive changes potentially associated with disease or injury and using the pattern of deficits to help inform differential diagnosis, including assisting neurologists in differentiating between types of dementia. Neuropsychological test findings are also important in capturing the severity of cognitive deficits and contribute to disease staging.

Questions with functional relevance typically relate to capacities and the effects cognitive changes have on how a person performs important life tasks. These questions deal with a patient's ability to live independently and to make personal, financial, medical, and legal decisions. They also involve relating test data to the patient's capacity to perform tasks of everyday living (e.g., workplace; classroom; home; recreation; driving). To date, research has suggested a moderate relationship between traditional cognitive test performance and everyday functional capabilities (Chaytor & Schmitter-Edgecombe, 2003; Farias, Harrell, Neumann, & Houtz, 2003; Kibby, Schmitter-Edgecombe, & Long, 1998). While most neuropsychological evaluations do not address everyday activities per se, clinicians often have to address concerns about functional capacities (strengths and weaknesses) in their reports. In cases of well-preserved cognitive functioning or, conversely, for those with severe deficits, prediction can be straightforward. Nevertheless, life skills are complex and require not only intact basic skills but also the ability to integrate those skills in flexible and appropriate ways. Ecologically valid tests predict important aspects of real-life functioning.

Unfortunately, research to improve the predictive capabilities of the neuropsychological examination has lagged behind the importance of the question. Given the nature of the skills and behaviors involved in everyday tasks, we need assessments of everyday neuropsychological outcomes. Enhanced predictive ecological validity involves assessments of how patients successfully perform tasks and make correct judgments in real-life situations. Advances in technology and the ability to assess performance using virtual environments aid such efforts.

Functionally Relevant Neuropsychological Questions

Arguments about the balance between ecological validity in cognitive assessment (Neisser, 1982) and concerns about experimental control (Banaji & Crowder, 1989) can be traced back a few decades. Heaton and Pendleton (1981) discussed the need for research into the use of neuropsychological tests to predict everyday functioning. Literature reviews on ecological validity in neuropsychology found low-to-moderate correlations (0.2–0.5) in neuropsychological tests and everyday functioning (Burgess, Alderman, Evans, Emslie, & Wilson, 1998; Williams, 1996). The great variability among the skills needed for various daily activities resulted in concerns about the lack of similarity for an adequate study of these skills (Tupper & Cicerone, 1990, 1991). Williams (1988) suggested identification of skill clusters required for tasks relative to whether the skill is used in many tasks across environments (i.e., generic) or used in new tasks in a limited number of environments (i.e., specific).

Early formulations of ecological validity in neuropsychology emphasized the functional and predictive relation between a patient's performance on a set of neuropsychological tests and the patient's behavior in everyday life. Franzen and Wilhelm (1996) emphasized two requirements: (1) *verisimilitude*—the demands of a test and the testing conditions resemble demands in the everyday world of the patient; and (2) *veridicality*—the performance on a test predicts some aspect of the patient's functioning on a day-to-day basis (see Table 13.1).

An operational limitation of these definitions was that the technologies that were available when they were developed could not replicate the environment in which the behavior of interest would ultimately take place (Goldstein, 1996). While there have been a number of technological advances in past decades, most neuropsychological assessments today still have not been validated with respect to real-world functioning (Rabin, Burton, & Barr, 2007). Although there are a few exceptions (see Table 13.1), attempts at verisimilitude are at times limited by their focus on cognitive "constructs" (e.g., attention, executive function, memory) for identifying "functional" abilities (Chaytor & Schmitter-Edgecombe, 2003). A contemporaneous question for the verisimilitude approach is whether the assessment of functional capacity can offer the neuropsychologist

TABLE 13.1. Ecological Validity in Neuropsychology

Requirement	Define	Validity	Limitations	Current approaches
Verisimilitude	• Demands of a test and testing conditions must resemble demands in patient's everyday world • The "topographical similarity" (i.e., theoretical relation) between method by which data was collected and the skills required for successful praxes in the patient's natural environment	• Overlaps with face validity • Requires consideration of the testing environment and methods	• *Theoretical similarity*: Task demands on neuropsychological tests (e.g., list learning and recall) have a "theoretical" similarity to everyday tasks but may not reflect actual activities. • *Administrative controls*: Used to ensure reliability and internal validity in the laboratory (e.g., words presented at a controlled rate, the task is performed free from distractions, repeated opportunities to learn the list of words) and are different from everyday activities. • Tests may underestimate the implications of cognitive difficulties in everyday life. • Tests may overestimate functional difficulties (e.g., patient may use compensatory strategies in their everyday world).	• TEA • BADS • Rivermead • CAMPROMPT
Veridicality	• Performance on a test predicts some aspect of the patient's functioning on a day-to-day basis.	• Degree to which performance on a test predicts some aspect of the patient's everyday functioning	• Little is known about prediction of everyday behavior from neuropsychological tests. • Such an analysis is complicated by the difficulties inherent in capturing an individual's functioning in a reliable and valid numerical fashion. • Direct parallels between the demands found on traditional assessments and functional performance are often not evident (Makatura, Lam, Leahy, Castillo, & Kalpakjian, 1999; Wilson, 1993; Wilson, Cockburn, Baddeley, & Hiorns, 1989).	A number of studies have correlated neuropsychological test data with . . . • patient's vocational status (Bayless, Varney, & Roberts, 1989) • vocational functioning (Lysaker, Bell, & Beam-Goulet, 1995). • Rating scales designed to assess aspects of daily functioning (Dunn et al., 1990).

Note. TEA = Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996); BADS = Behavioral Assessment of the Dysexecutive Syndrome (Wilson, Alderman, Burgess, Emslie, & Evans, 1996); Rivermead = Rivermead Behavioral Memory Test (Wilson, Cockburn, & Baddeley, 1985); CAMPROMPT = Prospective Memory, Cambridge Test of Prospective Memory (Wilson et al., 2004).

data traditionally viewed as clinically relevant for understanding cognitive constructs disrupted relative to brain dysfunction. Conversely, will the verisimilitude approach provide an additional metric (e.g., lack of correspondence between cognitive construct models/taxonomies and functional imaging modalities; Price, 2018) that questions the applicability of conventional cognitive constructs as a framework for understanding brain-behavior relationships (e.g., Hommel et al., 2019; Jagaroo & Santangelo, 2017; Thomas, Ansari, & Knowland, 2019)? Likewise, while a number of studies have correlated neuropsychological test data with the patient's everyday activities, direct parallels between the demands found on traditional neuropsychological assessments and functional performance are often not evident (Makatura, Lam, Leahy, Castillo, & Kalpakjian, 1999; Olson, Jacobson, & Van Oot, 2013; Spooner & Pachana, 2006; Wilson, 1993; Wilson, Cockburn, Baddeley, & Hiorns, 1989).

Most neuropsychological tests in use today are construct-driven measures that fail to represent the actual functional capacities inherent in everyday cognitive tasks (Burgess et al., 2006). Tests like the Stroop, Wisconsin card Sorting Test, and Tower of London were not originally designed to be used as clinical measures. Instead, they were originally found to be useful tools for neuroscience studies in normal populations and then later were applied for clinical assessments of cognitive constructs. Burgess and colleagues (2006) make clear distinctions between the levels of explanation used in the cognitive neuroscience assessment of cognitive function (see Figure 13.1).

Burgess et al. (2006) begin with a distinction among the terms *construct, operations,* and *function* (see Figure 13.1). By "construct" they mean an abstract cognitive capacity that is inferred from research findings (e.g., correlational research). Operations

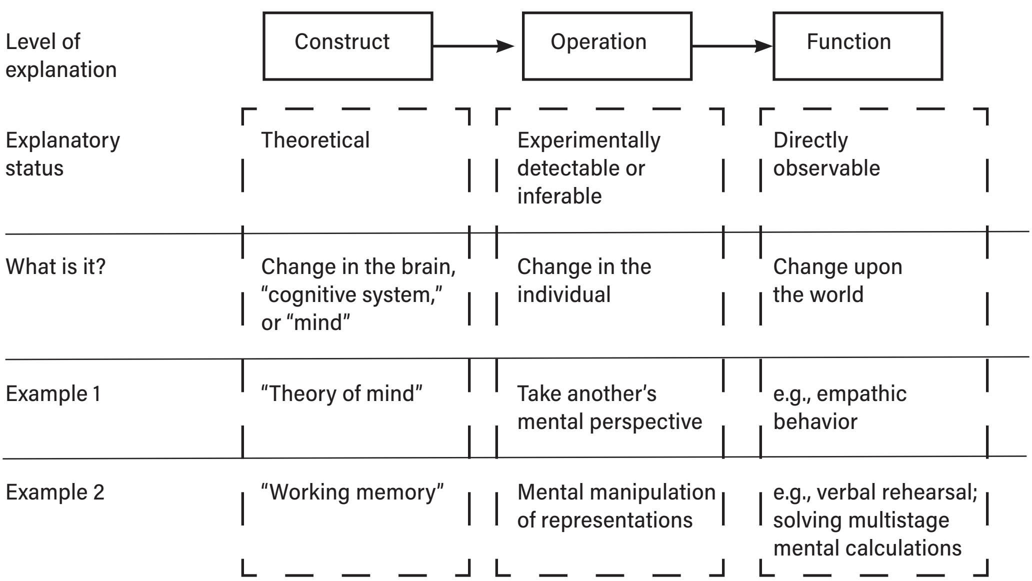

FIGURE 13.1. Levels of explanation for the neuropsychological domain of executive functioning Reproduced with permission from Burgess et al. (2006).

refer to the individual component steps of neurocognition that, while not directly observable, they can be inferred from an amalgamation of task analysis and change in a given dependent variable. Functions are understood to be directly observable behaviors that are the result of a series of operations. For Burgess and colleagues (2006), neuropsychologists need to develop more assessments that can further our understanding about how the brain enables persons to interact with their environment and organize everyday activities. Here they depart from the terms *verisimilitude* and *veridicality* when discussing "ecological validity." Instead, they emphasize the term *representativeness* to discuss the extent to which a neuropsychological assessment corresponds in form and context to a real-world (encountered outside the laboratory) situation. They use the term *generalizability* to discuss the degree to which poor performance on a neuropsychological assessment will be predictive of poor performance on tasks outside the laboratory.

According to Burgess and colleagues (2006), an apparent limitation in many neuropsychological assessments is that most are construct-driven tests that fail to represent the actual functional capacities inherent in everyday cognitive functions. Although these tests do appear to provide data regarding abstract cognitive constructs, functional information for predicting what situations in everyday life require these constructs is not readily apparent. This points to the need for tests that are both "representative" of real-world "functions" and that engender information that is "generalizable" for predicting functional performance across a range of situations. This "function-led" approach to creating neuropsychological assessments will include cognitive processing models that proceed from directly observable everyday behaviors backward to examine how a sequence of actions leads to particular behaviors (Burgess et al., 2006).

The Multiple Errands Test (MET) is a function-led assessment of everyday activities like planning, adapting, problem solving, and flexibility in real-life settings. Neuropsychologists use the MET to assess the patient's real-world cognitive functioning by requiring patients to encounter unpredictable conditions while planning and problem solving. Patients perform relatively simple but open-ended tasks (e.g., buying items, writing down information, traveling to a location) without breaking a series of arbitrary rules (Shallice & Burgess, 1991). The MET has been found it to be sensitive to failures in attentional focus and task implementation, as well as adequate for predicting behavioral difficulties in everyday life (Alderman, Burgess, Knight, & Henman, 2003). Despite some positive findings, the efficacy of using naturalistic tasks to evaluate the functional status of neurologic populations has yet to be definitively demonstrated (Robertson & Schmitter-Edgecombe, 2017). Practical limitations exist for many function-led and/or naturalistic task assessments conducted in real-life settings: time consuming, require transportation, involve consent from local businesses, costly, and are difficult to replicate or standardize across settings (Logie, Trawley, & Law, 2011; Rand, Rukan, Weiss, & Katz, 2009). Moreover, at times function-led assessments in real-world settings are not feasible for participants with significant behavioral, psychiatric, or mobility difficulties (Knight, Alderman, & Burgess, 2002).

Virtual-Reality-Based Neuropsychological Assessments

As noted previously, research to improve the predictive capabilities of the neuropsychological examination has lagged behind the importance of the question, and a paradigm change may be needed that employs the capabilities of modern technology to assess how patients perform and make judgments in order to be successful in real-life situations. The ability to capture behavior in relationship to life-like demands is now possible through use of virtual environments. (Campbell et al., 2009; Kane & Parsons, 2017, 2019; Parsons & Kane, 2019; Parsons, Carlew, Magtoto, & Stonecipher, 2017; Parsons & Duffield, 2019; Renison, Ponsford, Testa, Richardson, & Brownfield, 2012). This increased interest has been partially fueled by enhancements in three-dimensional rendering and increased system reliability. Today, virtual reality (VR) is experiencing a resurgence with the advent of more reliable hardware and software, cost-effective platforms, and enhanced usability in terms of size and appearance (Bohil, Alicea, & Biocca, 2011; Parsons, 2015).

The VR platforms available today offer advanced computer interfaces that allow clinicians to immerse their patients within computer-generated simulations of everyday activities. As a special case of computerized neuropsychological assessment devices (CNADs; Bauer et al., 2012), they provide enhanced computational capacities for administration, presentation of stimuli, response logging, and data analytic processing. Hence, they increase the ecological validity of neuropsychological assessments via the veridical control and rigor of laboratory measures and a verisimilitude that reflects real-life situations (Parsons, 2016). Many VR-based neuropsychological assessments have been modeled from, and validated with, traditional paper-and-pencil measures (see Table 13.2). The simulation technology found in state-of-the-art virtual environments appears to be well suited for the advancement of ecologically valid assessments in which three-dimensional objects are presented in a consistent and precise manner (Schultheis, Himelstein, & Rizzo, 2002). VR-based neuropsychological assessments can provide a balance between naturalistic observation and the need for exacting control over key variables (Campbell et al., 2009; Parsons, 2015; Matheis et al., 2007).

Virtual Environments Based on the Continuous Performance Task

A number of VR-based neuropsychological assessments have been developed that take cognitive construct-based stimuli from computer-automated neuropsychological assessments (e.g., continuous performance task; Stroop) and embed them into a VR simulation of a real-world setting. One example is the embedding of the Continuous Performance Task (CPT) into a virtual classroom. Parsons and colleagues performed an initial clinical validation of the Virtual Classroom CPT comparing children with attention-deficit/hyperactivity disorder (ADHD) to typically developing children. The Virtual Classroom CPT captured both attentional and behavioral abnormalities, including showing that children with ADHD (1) made more commission and omission errors; (2) exhibited more overall body movement; and (3) experienced greater levels of distraction. Measures in the Virtual Classroom CPT were significantly correlated with traditional measures and behavior checklists. Since the initial validation in 2007, a number of studies have replicated these results in children with ADHD (e.g., Adams, Finn, Moes, Flannery, & Rizzo, 2009; Bioulac et al., 2012; Diaz-Orueta et al., 2014; Pollak et al., 2009; Pollak, Shomaly, Weiss, Rizzo, & Gross-Tsur, 2010; see Table 13.2). Furthermore, the Virtual Classroom CPT has been validated in students with concussion (e.g., Nolin, Stipanicic, Henry, Joyal, & Allain, 2012) and neurofibromatosis type 1 (Gilboa et al., 2011). The Virtual Classroom CPT paradigm is perhaps the most widely validated of VR-based neuropsychological assessments to date. A recent normative study of AULA Nesplora's Virtual Classroom

TABLE 13.2. Examples of Construct-Driven VR-Based Neuropsychology Tests

Domain/task	Virtual environment	Population comparisons	Studies
WCST	Virtual Building	Multiple sclerosis	Pugnetti et al., 1995, 1998
	VRLFAM	mTBI	Elkind et al., 2001
CPT	Virtual Classroom	ADHD	Parsons, Duffield, & Asbee, 2019 (meta-analysis)
		NF1	Gilboa et al., 2011
		Concussion	Nolin et al., 2009, 2012; Gilboa et al., 2015)
		Spanish norms (*N* = 1,272)	Iriarte et al., 2016
Stroop	Virtual Classroom	Autism	Parsons & Carlew, 2016; see Duffield et al., 2018 for systematic review
		Validation with normal	Parsons & Carlew, 2016
		Validation with normal	Lalonde et al., 2013
	Virtual Apartment	Validation with normals	Henry. Joyal, & Nolin, 2012
		Aging	Parsons & Barnett, 2019
	Virtual HMMWV	Validation: Civilians Validation: Military	Parsons et al., 2011; Parsons, Courtney, Dawson, & Arizmendi, 2013; Parsons & Reinebold, 2012; Wu et al., 2010; Wu & Parsons, 2011a, 2011b; Wu & Parsons, 2012; Wu, Lance, & Parsons, 2013; Armstrong et al., 2013
PASAT	Virtual City	Validation: Civilians	Parsons et al., 2013; Parsons & Courtney, 2014
		Validation: Military	Armstrong et al., 2013; Parsons et al., 2012
List learning and memory	Virtual Office	mTBI	Matheis et al., 2007
	Virtual City	Validation with normals	Parsons & Rizzo, 2008
	Virtual City	Alzheimer's disease	Widmann, Beinhoff, & Riepe, 2012
	HOMES	Alzheimer's disease	Sauzéon et al., 2012
	VEGS	Aging and norms	Parsons & Barnett, 2017
		Validation with normals	Parsons & McMahan, 2017

Note. ADHD = attention-deficit/hyperactivity disorder; CPT = Continuous Performance Test; MCI = mild cognitive impairment; mTBI = mild traumatic brain injury; NF1 = neurofibromatosis type 1; VEGS = Virtual Environment Grocery Store.

CPT by Iriarte and colleagues (2016) had a normative sample composed of 1,272 participants (48.2% female; age range 6–16 years, M = 10.25, SD = 2.83). Normative findings revealed that the Virtual Classroom paradigm is significantly correlated with the traditional CPT. Furthermore, the Virtual Classroom CPT was found to be more sensitive to reaction time and rate of omission errors than the Test of Variables of Attention (TOVA); and was also rated as more enjoyable than the TOVA computerized battery.

A recent meta-analysis assessed both traditional two-dimensional (2D) CPTs and three-dimensional virtual classroom CPTs (Parsons, Duffield, & Asbee, 2019) for individuals with ADHD. Nineteen studies were identified as using the virtual classroom CPT that met selection criteria. Population differences were similar for the traditional CPT and virtual classroom CPT for the common metrics of omission errors (large effect), commission errors (large effect) and hit reaction times (small to trending toward medium at g = 0.45). Effect-size estimates were roughly equivalent with Huang-Pollock, Karahmas, Tam, and Moore's (2012) meta-analysis of 2D CPTs. However, group differences for omission errors and hit reaction times were augmented using the virtual classroom CPT compared to the traditional CPT (g = 1.18 vs. 0.81 and 0.45 vs. 0.14) but were reduced for commission errors (g = 0.70 vs. 0.81). In terms of ecologic validity, the current iteration of the VR classroom likely has some degree of verisimilitude (i.e., test or testing conditions must resemble demands found in the everyday world; Franzen & Wilhelm, 1996) but falls short of demonstrating veridicality. While some studies used head and body movements to assess hyperactivity, inattention, or susceptibility to distraction (Parsons, Bowerly, Buckwalter, & Rizzo, 2007), most failed to include such metrics. This is an important additional step toward a function-led assessment model that captures directly observable behaviors. Most of the reviewed VR classroom studies simply adapted a traditional test assessing dated theoretical cognitive constructs in a different environment, albeit a real-world one. This approach does not improve the ability of test performances to predict aspects of an individual's day-to-day functioning and adds little value over the traditional computerized 2D CPT.

Virtual Environments Based on the Stroop Test

A number of studies have looked at a VR-based Stroop task in which Stroop stimuli are embedded into various virtual environments. The first VR-based Stroop task was developed for assessing automatic and controlled processing of neurocognitive and affective stimuli. This Virtual Reality Stroop Task (VRST) places the participant in a simulated High Mobility Multipurpose Wheeled Vehicle (HMMWV) that passes through zones with alternating low threat (driving down a deserted desert road) and high threat (gunfire, explosions, and shouting among other stressors), while dual-task stimuli (e.g., Stroop stimuli) are presented on the windshield. Parsons and colleagues (2011) compared performance of the HMMWV VRST to traditional paper-and-pencil (Color Word Interference subtest from the Delis–Kaplan Executive Function System) and a 2D computer automated Stroop task (subtest from the Automated Neuropsychological Assessment Metrics).

The VRST presents each Stroop stimulus as a single item. In some situations, a single-item presentation is preferable to presentation in rows: (1) logging of reaction times for each stimulus to assess the impact of errors for individual stimuli; and (2) randomized counterbalancing of neutral, interference, cued, and facilitated trial types (Davidson, Zacks, & Williams, 2003). Moreover, the multi-item presentations found in paper-and-pencil versions of the Stroop may result in confounds from (or interactions with) visual distractor interference and may enhance the training/learning curve, resulting in greater practice effects (see Lemay, Bedard, Roulea, & Tremblay, 2004).

Results from an initial evaluation revealed that both the conventional and computerized Stroop produced more correct responses than the VRST. The Automated Neuropsychological Assessment Metrics (ANAM) and paper-and-pencil Stroop tests failed to create significant differences in performance between the Stroop conditions (Parsons et al., 2011). In a follow-up validation study, Parsons, Courtney, and Dawson (2013) replicated these findings. They also found that participants in the high-threat zones experienced a greater level of psychophysiological arousal. Analyses of the effect of threat level on the color–word and interference scores resulted in a main effect of threat level and condition. Findings from the virtual environment paradigm have supported the contention that stress and arousal associated with real-life performance demands may negatively affect cognitive processing in ways not assessed in traditional laboratory or clinical settings. In a replication study, Armstrong et al. (2013) established the preliminary convergent and discriminant validity of the VRST with an active-duty military sample.

The virtual Stroop paradigm has also been applied to a Virtual Classroom and a Virtual Apartment. In a psychometric evaluation of the Virtual Classroom Stroop, Parsons and Carlew (2016) conducted two validation studies aimed at investigating the effectiveness of a Virtual Classroom-based bimodal Stroop task for the assessment of motor and cognitive inhibitory control in both patients with autism and neurotypical participants. They were able to demonstrate impaired resistance to distractors in the VR version of the Stroop. This was not detected by conventional or computer versions of this test. Findings suggest that the Virtual Classroom Stroop may be successfully used in patients with autism for purposes of assessment.

The Virtual Apartment Stroop superimposes stimuli onto a large television set in a virtual living room. In a preliminary study, Henry, Joyal, and Nolin (2012) found that the Virtual Apartment Stroop is capable of eliciting the Stroop effect with bimodal stimuli. Initial validation data also suggested that measures of the VR Stroop significantly correlate with measures of the Elevator counting with distracters, the Continuous Performance Task (CPT-II), and the Stop-it task. Commission errors and variability of reaction times at the Virtual Apartment Stroop were significantly predicted by scores of the Elevator task and the CPT-II. Parsons and Barnett (2019) found that the classic "Stroop pattern" from traditional modalities (e.g., paper-and-pencil; computer-automated Stroop) was observed in the Virtual Apartment Stroop; participants performed less well when distractors were present. These results suggest the Virtual Apartment Stroop task has potential for distinguishing between inhibition of overlearned (prepotent) responses and resistance to distractors. This work was expanded to normative comparisons between younger and older adults with Parsons and Barnett (2019), demonstrating that participants in the older adult cohort performed significantly below participants in the young adult cohort.

Virtual Environments Based on the Paced Auditory Serial Addition Test

Numerous studies have demonstrated that the Paced Auditory Serial Addition Test (PASAT) is useful in detecting cognitive processing deficits. This test has demonstrated high levels of internal consistency and test–retest reliability, but it can create undue anxiety and frustration in participants, resulting in anxiety-related degradation of performance. Parsons and colleagues (2012, 2014) developed and validated a PASAT embedded in a VR environment. The Virtual Reality PASAT (VR-PASAT) was compared with the conventional auditory PASAT, as well as other standardized neuropsychological measures. Moderate relationships were found between VR-PASAT and other putative attentional processing measures. Results from active-duty military (Parsons, Courtney, Rizzo, Edwards, & Reger, 2012) and civilian (Parsons & Courtney, 2014) populations offer preliminary support for the construct validity of the VR-PASAT as a measure of attentional processing. Further, results suggest that the VR-PASAT may provide unique information related to salience processing not tapped by traditional attentional processing tasks. Furthermore, self-report of "likability" revealed a unanimous preference for the VR-based PASAT.

Virtual Environments Based on the Wisconsin Card Sorting Test

A number of early VR-based neuropsychological assessments (Delahaye et al., 2015; Elkind, Rubin, Rosenthal, Skoff, & Prather, 2001; Pugnetti et al., 1995, 1998) were developed to mimic the Wisconsin Card Sorting Test (WCST). One such measure required patients to reach the exit of a virtual building through the use of environmental cues (e.g., categories of shape, color, and number of portholes) that aided in the correct selection of doors leading from room to room (Delahaye et al., 2015; Pugnetti et al., 1995, 1998). Like the WCST, this measure employed a fixed number of trials and rule changes. Comparison of neurologically impaired patients and nonimpaired controls on both the VR task and the WCST revealed weak correlations between the two tasks, indicating that these measures were likely assessing different functional skills.

In a more recent virtual environment adaptation of the WCST paradigm, called the Virtual Reality Look for a Match Test (VRLFAM), Elkind and colleagues (2001) presented a beach scene in which participants were asked to deliver frisbees, sodas, popsicles, and beach balls to umbrellas. Each umbrella had one of the four objects on it (differing in type, color, and number). As the participant delivered the objects, he or she received verbal feedback. Similar to the WCST, the participant had 128 turns to twice match 10 times to color, object, and number. Comparison of healthy control performance on VRLFAM and the WCST indicated that all performance scales (with the exception of WCST perseverative errors) were directly related (Elkind, 2001).

While the virtual and paper versions of the WCST paradigm were found to be related, this may be problematic in that the original WCST has been found to have limited ability to differentiate between patients with frontal lobe pathology and control subjects (Stuss et al., 1983). In fact, the clinical use of the WCST has been a topic of discussion in that neuroimaging studies have revealed that the WCST does not discriminate between frontal and nonfrontal lesions (Nyhus & Barcelo, 2009; Stuss et al., 1983). Although the WCST and VRLFAM appear to provide data regarding "set shifting" and "working memory" constructs, functional information for predicting which situations in everyday life require these constructs is not readily apparent.

Some VR implementations offer little more than contextual environments modeled from traditional construct-driven assessments. This approach does not take full advantage of the capabilities of virtual environments that permit developing tests and scenarios that are more representative of real-world tasks, that evaluate the required cognitive skills to successfully perform these tasks, and that are "function-led."

Function-Led Virtual Environments

While results from virtual environments modeled from traditional paper-and-pencil paradigms can be helpful, there are times when neuropsychologists desire tests that are "representative" of real-world "functions" and to proffer results that are "generalizable" for predicting functional performance across a range of situations. A growing body of literature describes results from studies of virtual environments that proceed from directly observable everyday behaviors backward to examine the ways in which (1) a sequence of actions leads to a given behavior in normal functioning and (2) behavior might become disrupted (Parsons, 2016; Kane & Parsons, 2017). Table 13.3 provides a variety of examples of function-led domains (e.g., shopping, driving, office) and associated virtual environments (e.g., Virtual Supermarket). This table is not exhaustive, nor are domains/environments necessarily distinct, as various builds can include various settings, real-world activities, abilities assessed, and/or task demands. Function-led virtual environments are being designed and researched by other specialties such as occupational therapy and physical therapy. This may lead to different theoretical bases and outcome targets, and thus different psychometric properties compared to neuropsychological test development processes consistent with the Robertson and Schmitter-Edgecombe's (2017) review of performance-based naturalistic tasks.

Virtual Errands Test

One of the first of these function-led virtual environments can be found in the Virtual Errands Test (VET) that McGeorge and colleagues (2001) developed as a virtual analog to the original Multiple Errands Task. The VET tasks were designed to be vocationally oriented containing work-related errands. In a study involving five adult patients with brain injury and five unimpaired matched controls, participants completed both the real-life MET and the VET. Results revealed that performance was similar for real-world and VE tasks. In a larger study comparing 35 patients with prefrontal neurosurgical lesions to 35 controls matched for age and estimated IQ, the VE scenario was found to successfully differentiate between participants with brain injuries and controls.

Virtual Environment Grocery Store

Construct Validation in Healthy Participants

A Virtual Environment Grocery Store (VEGS) has been developed that uses a simulated shopping environment to assess the ways in which users complete a series of errands that require organization and planning while shopping (Parsons & McMahan, 2017; Parsons & Barnett, 2017). The VEGS allows the examiner to make systematic adjustments to an examinee's information load (which affects goal maintenance). It offers an advanced VR version of the Multiple Errands Task that includes assessment of learning, memory (including prospective memory), and executive functioning. The VEGS has a library of "multitask assignments" for empirical determination of an examinee's baseline performance, and then adds conditions in the environment that impact subsequent performance, including the ability to adjust the density of items on shelves, the similarity of packaging, and the intensity and types of realistic irrelevant distractions (e.g., loudness/

type of music in the background and loudspeaker announcements). In an initial validation of the VEGS, using a group of older (mean age = 75.21, *SD* = 8.31) and younger (mean age = 20.96, *SD* = 2.85) participants, VEGS correlated significantly with CVLT-II long delay free and cued recall (Parsons & Barnett, 2017). Younger adults did better on VEGS multitasking and prospective memory measures. As expected, using low-distraction conditions, Parsons and Barnett (2017) found no significant correlations between the VEGS measures and the traditional neuropsychology measures of executive functioning (Delis–Kaplan Executive Function System [DKEFS] Color–Word Interference Test). In other words, performance on the VEGS memory task was associated with traditional measures of memory, evidence of convergent validity, but not with traditional measures of executive function, evidence of divergent validity.

Impact of Distractors on Executive Control in Older Adults

In another series of studies (Parsons & McMahan, 2017), we aimed to assess everyday memory and performance under high- and low-distractor conditions in the VEGS. For the high-distractor condition, the VEGS was populated with human avatars who walked around the store or who spoke in groups of two or on phones. Distracting sounds were added that included laughter, coughing, dropped merchandise, and ring tones. Various announcements were given over the public address system. There was also a crying baby avatar. We expected that adding distractors into the VEGS would result in significant relationships between performance on the shopping tasks and traditional measures of response inhibition. Results using the low-distractor condition were similar to those reported in the study by Parsons and Barnett (2017). Significant correlations were observed between VEGS scores and CVLT-II delayed recall measures. In the high-distractor condition, correlations with CVLT-II delayed recall measures were again observed, as were correlations between VEGS and controlled processes—but not the automatic processes—of the DKEFS Color-Word Interference conditions. While congruent tasks like color naming and word reading were not related to VEGS shopping, incongruent (controlled processes) conditions of the DKEFS revealed significant correlations with distractor conditions of the VEGS. Specifically, the number of times that participants had to look at the map in the virtual environment was correlated with the percentage correct for both DKEFS Interference ($r = .26$, $p = .04$) and DKEFS Inhibition Switching ($r = .27$, $p = .03$). Furthermore, the time taken to complete DKEFS Inhibition Switching was correlated with prescription dropoff ($r = .50$, $p < .001$) and pickup times ($r = .50$, $p < .001$). This study provided preliminary validation of the VEGS's memory module with distractors. The additional distractors in the VEGS condition resulted in correlations between VEGS performance measures (e.g., number of instances participants had to look at the map for reminders; and amount of time to navigate to and from the pharmacist) and interference scores found on the DKEFS.

Multitasking in a Virtual City

A number of virtual environments with enhanced graphics (and usability) have been developed to model the function-led approach found in the MET. While some of these environments have focused on assessment of nonclinical populations (Logie et al., 2011), a number of virtual errand protocols have been developed to evaluate executive functions of clinical populations. The Multitasking in the City Test (MCT) is modeled after the MET and involves an errand-running task that takes place in a virtual city (Jovanovski, Zakzanis, Campbell, Erb, & Nussbaum, 2012a, 2012b). The MCT was designed intentionally to employ less explicit rule constraints, allowing researchers to investigate behaviors that are clearly not goal-directed. The MCT is made up of a virtual city that includes a post office, drug store, stationary store, coffee shop, grocery store, optometrist's office, doctor's office, restaurant/pub, bank, dry cleaners, pet store, and the participant's home. Although all buildings in the MCT virtual environment (VE) can be entered freely, interaction within them is possible only for those buildings that must be entered as part of the task requirements. Jovanovski et al. (2012b) found that although the patient sample (poststroke and brain-injured individuals) developed adequate plans for executing the tasks, their performance of the tasks revealed a greater number of errors. The MCT was significantly correlated with a rating scale completed by significant others.

Virtual Library

Virtual reality assessments modeled from of the MET to assess patients with neurological disorders are often placed in living or work settings (see Table 13.3). An example of a recently developed virtual environment for function-led assessment is the Virtual library task. Renison et al. (2012) were able to show that scores on the virtual library task and the real-world library task were highly positively correlated. This finding is important because the VR environment allows for automated logging of participant behaviors and has greater clinical utility than assessment in real-world settings. Comparisons of persons with TBI and normal controls supported the construct validity of the Virtual Library Task as a measure of executive functioning. The Virtual Library Task was found to be superior to traditional (e.g., WCST) tasks in differentiating between participants with TBI and healthy controls. The WCST failed to significantly differentiate between the two groups. This finding is consistent with studies that have reported no significant differences between control and brain-injured performances on the WCST (Alderman, Burgess, Knight, & Herman, 2003; Dawson et al., 2009; Ord, Greve, Bianchini, & Aguerrevere, 2009). The authors contend that the disparity between the demands of functional assessments and traditional testing environments most likely accounts for the differences (Manchester & Nicholas, 2004).

Virtual Environments Based on List Learning and Memory Paradigms

Virtual environments are also being used for assessment of memory in experimentally controlled simulations (Benoit et al., 2015; Mueller et al., 2012). For example, memory researchers have used virtual environments for neuropsychological assessment of object memory (Matheis et al., 2007; Parsons & Rizzo, 2008; Sauzéon et al., 2012; Widmann, Beinhoff, & Riepe, 2012). Matheis and colleagues (2007) utilized a Virtual Office to assess memory performance in both healthy controls and participants with traumatic brain injury. While immersed in the virtual office, participants performed a list-learning memory test that was followed by 30-minute and 24-hour recall and recognition trials. A significant relation was found between the Virtual Office and the California Verbal Learning Test. In a similar study, Parsons and Rizzo (2008) developed a virtual city task that reflected tasks found in the Hopkins Verbal Learning Test—Revised and the Brief

TABLE 13.3. Examples of Function-Led VR-Based Neuropsychology Tests

Domain/task	Virtual environment	Population comparisons	Studies
Multiple errands and multitasking	Virtual Shopping Tasks (e.g., VEGS)	OCD	Cipresso et al. (2013)
		Stroke	Josman et al. (2006, 2014)
		MCI	Werner et al. (2009)
		Validation with normals	Parsons & McMahan (2017)
		Aging cohorts	Parsons & Barnett, (2017)
		Validation with normals	Ouellet et al. (2018)
	Virtual Multiple Errands Task	Parkinson's disease	Pedroli et al., 2013; Cipresso et al., 2014
		Stroke	Rand et al., 2009; Raspelli et al., 2012
	Multitasking in the City Test	Stoke and TBI	Jovanovski et al., 2012a, 2012b
	Virtual Reality Activities of Daily Living	Normal vs MCI vs. mild AD	Tarnanas et al., 2013
	(2-module fire evacuation drill)		
	Edinburgh Virtual Errands Test	Validation with normals	Logie, Trawley, & Law, 2011
	Big-Store MET	Validation with normals	Antoniak et al., 2019
	MET-Home	Validation with stroke and matched normals	Burns et al., 2019
Street crossing	Virtual Reality Pedestrian Environment	EDS children	Davis et al., 2013
			Kim et al., 2010
	Road Crossing Virtual Apparatus	ADHD	
	Virtual Street Crossing Environment	Stroke/neglect	
Kitchen tasks	Virtual Kitchen	Brain injury	Cao, Douguet, Fuchs, & Klinger, 2010
	Nonimmersive Virtual Coffee Task (NI-VCT)	Validation with TBI and matched normals	Besnard et al., 2016

(*continued*)

TABLE 13.3. (*continued*)

Domain/task	Virtual environment	Population comparisons	Studies
Library	Virtual Library Task	TBI	Renison et al., 2012
Sorting furniture	Virtual Removals Task	Brain injury	Sweeney, Kersel, Morris, Manly, & Evans, 2010
Driving	Simulated Driving	Alcohol	Allen et al., 2009
	Virtual Town (based on the city of Paris)	TBI	Milleville-Pennel, Pothier, Hoc, & Mathe, 2010
		ABI	Schultheis, Rebimbas, Mourant, & Millis, 2007
		ADHD	Barkley, Anderson, & Kruesi, 2007; Barkley, Murphy, O'Connell, & Connor, 2005, 2007; Cox et al., 2008; Knouse, Bagwell, Barkley, & Murphy, 2005
		Validation with normals	Plancher, Barra, Orriols, & Piolino, 2012
		Normal, MCI, and AD	Plancher, Tirard, Gyselinck, Nicolas, & Piolino, 2012
		Children–young adult	Picard, Abram, Orriols, & Piolino, 2017
		Young vs. aging	Lecouvey et al., 2017
		Mild Alzheimer's	Lecouvey et al., 2019
Office (nonimmersive and MET based)	Jansari Assessment of Executive Functions (JEF)	Ecstasy/MDMA	Montgomery, Hatton, Fisk, Ogden, & Jansari, 2010
	JEF for Children (JEF-C)	Alcohol	Montgomery, Ashmore, & Jansari, 2011
		Cannabis	Montgomery, Seddon, Fisk, Murphy, & Jansari, 2012
		Nicotine	Jansari, Froggatt, Edginton, & Dawkins, 2013
		ABI	Jansari et al., 2014
		Caffeine & JEF vs. Stroop	Soar, Chapman, Lavan, Jansari, & Turner, 2016
		Frontal lobe lesions	Denmark et al., 2019
		ABI	Gilboa et al., 2019
Apartment	Virtual Multitasking Test (V-MT)	Aging	

Note. ABI = acquired brain injury; ADHD = attention-deficit/hyperactivity disorder; EDS = excessive daytime sleepiness; MCI = mild cognitive impairment; OCD = obsessive-compulsive disorder; TBI = traumatic brain injury; VEGS = Virtual Environment Grocery Store.

Visuospatial Memory Test—Revised. Prior to immersion in the virtual city, participants took part in a learning task in which they were exposed to language and graphic-based information without any context across three free learning trials. Following this, they were immersed in the virtual environment, wherein they followed a virtual human guide to five different zones of a virtual city. In each zone, participants searched the area for two target items (i.e., items from the learning phase). Next, participants performed short and long delay free and cued recall tasks. Comparison of results from the virtual city to traditional paper-and-pencil tasks revealed that the virtual city was significantly related to paper-and-pencil measures of both visually and auditorially mediated learning and memory.

Plancher, Nicolas, and Piolino (2008) used a virtual town environment to compare episodic memory of younger adults and older adults' performance on encoding (intentional vs. incidental) and exploration (active vs. passive). In the passive condition, participants were passengers in a virtual car. In the active condition, participant drove the virtual car. At the end of the simulation participants were asked to recall items and contextual information. Results revealed that older adults had diminished contextual memory but not factual memory. Moreover, intentional encoding was significantly different between aging cohorts. No effect for exploration type (active or passive) was observed. In a follow-up study (same VR town), Plancher, Gyselinck, Nicolas, and Piolino (2010) found that older aged participants were selectively impaired in their ability to associate several items of contextual information—specifically in spatiotemporal context recall. Further, comparison of traditional paper-and-pencil neuropsychological tests to VR-based neuropsychological assessments revealed that memory performances assessed using VR were more related to general cognitive functioning and subjective memory complaints. Plancher and colleagues (2012) also assessed healthy older adults, patients with aMCI, and patients with AD using a virtual environment. Results revealed that AD patients' performances were poorer than those of healthy individuals and patients with amnestic mild cognitive impairment (aMCI). Spatial allocentric memory was found to be useful for differentiating aMCI patients from healthy older adults.

Parsons and Barnett (2017) used the Virtual Environment Grocery Store (VEGS) to measure episodic memory in older adults. The VEGS memory scores showed construct validity in that they were significantly correlated with scores of standard neuropsychological tests of episodic verbal memory (convergent validity).

Another Virtual Shop requires participants to select a list of previously memorized items. Corriveau Lecavalier, Ouellet, Boller, and Belleville (2018) found that older participants performed less well than younger adults. Ouellet, Boller, Corriveau Lecacalier, Cloutier, and Belleville (2018) assessed older adults with subjective cognitive complaints on the same Virtual Shop task and on conventional paper-and-pencil measures of memory, executive functions, and a subjective measure of memory difficulties in daily life. Results revealed that performance in the Virtual Shop was correlated with conventional measures of memory.

VR, Teleneuropsychology, Biosensors, and Internet Navigation Skills

Virtual environments involve a highly integrative platform and has promise for technological integrations for neuropsychological assessment. For instance, virtual environments can include noninvasive imaging techniques (Makeig et al., 2009), as well as assessment and rehabilitation modalities (Bohil et al., 2011; Parsons, 2016). Virtual environments can be administered as immersive or nonimmersive (Rose et al., 1999). While immersive virtual environments (discussed later in the chapter) immerse the user into a 3D virtual environment where stimuli are presented via user-worn equipment (e.g., head mounted displays, haptic feedback), nonimmersive virtual environments present simulated environments and stimuli using a 2D presentation modality. These 2D presentations are amenable to remote assessment and have capabilities consistent with the growing needs for teleneuropsychology.

Teleneuropsychology, a specific implementation of telehealth, is a burgeoning tool for neuropsychologists and, because of recent virus pandemic needs, will likely become more pervasive in clinical practice (Hollander & Carr, 2020). Video-teleconference-based neuropsychological testing (i.e., teleneuropsychology) increasingly allows neuropsychologists to remotely administer neuropsychological tests (Cullum, Hynan, Grosch, Parikh, & Weiner, 2014). Although teleneuropsychology is in its relative infancy, practice recommendations (Grosch, Gottlieb, & Cullum, 2011) and reviews of the current evidence base are newly available and promising (Brearly et al., 2017), as many small studies have established the feasibility and reliability of video-teleconferencing based testing. Healthcare Information Portability and Privacy Act (HIPAA)-compliant virtual connections that allow for screen sharing will make possible the development of remote assessment capabilities using noninvasive VR measures.

Inclusion of biosensors with neuropsychological performance-based tests is also a growing research domain and offers compatibility with teleneuropsychology, computerized tests, and VR-based neuropsychological assessments (Parsons & Duffield, 2019). Investigators (e.g., Parsons, Duffield, & Asbee, 2019) postulate that expanding the behaviors that can be assessed and quantified during an evaluation can be vital for understanding brain–behavior relationships. The ability to generate multimodal data profiles (e.g., cognition + facial expressions + psychophysiology + eye-tracking) has the potential to vastly improve diagnostic accuracy, monitor condition and treatment progression (e.g., Bueno, Sato, & Hornberger, 2019), and truly capture the functional nature of human behavior. Biosensor integration may also be particularly suited to VR-based neuropsychological assessments (both immersive and nonimmersive) to capture physiological measures of attention and arousal as individuals navigate virtual challenges and tasks. Current clinical testing modalities are incapable of providing multimodal, multidimensional data relevant to task performance and to real-world functional outcomes (e.g., Guerra-Carrillo & Bunge, 2018).

Biosensor integration into neuropsychological assessment will also extend testing capabilities to those with physical disabilities where current assessment modalities are limited or completely precluded (e.g., Poletti et al., 2017). Technological advances generally, and biosensor integration in particular, may assist in disambiguating psychiatric and neurologic contributions to behavior change (e.g., Itti, 2015), improve the process approach (e.g., Au, Piers, & Devine, 2017), and revolutionize performance validity testing for moment-by-moment evaluation of effort, and somewhat relatedly enhance adaptive testing procedures (e.g., pupillometry metrics that infer cognitive load limits).

Virtual environments also provide function-led assessments of everyday activities in real-world settings (Logie et al., 2011; Kane & Parsons, 2017; Rand et al., 2009; Robertson & Schmitter-Edgecombe, 2017). Virtual environments (immersive or nonimmersive) simulating everyday technology use in the real world (e.g., online shopping) are also emerging. This is notable as individuals often complete daily household, social, and health-related activities online. A review of internet navigation skills (INS) included 17 studies examining INS in clinical populations. The INS domains included shopping, finances, health tasks, and general navigation. Results suggest that performance-based tests of INS discriminated between clinical and nonclinical groups (e.g., HIV, multiple sclerosis, traumatic brain injury). Performance-based tests of INS were associated with performance-based tests of everyday functioning capacity, domain-specific declines in manifest everyday functioning, and self-reported internet behavior, but not global manifest functional status (evidence of convergent ecological validity). These performance-based tests of INS were correlated with standard clinical neurocognitive tests, particularly executive functions and episodic memory. As this is an emerging literature base, it is predicated on small sample sizes, and many types of INS have not been examined in neuropsychological populations (e.g., health insurance navigation; Woods et al., 2019).

VR Technologies: Advantages and Areas Needing Development

Technological Advances and Affordability of New VR Platforms

Progress in the development and validation of VR-based neuropsychological assessments is increasing but faces professional barriers (see the following sections of this chapter). Predictive ecological validity may be substantially enhanced by assessing behavior in controlled life-like virtual environments that demand both the presence and integration of skills directly related to how patients perform and make judgments in order to be successful in real life situations. As mentioned earlier, recent (past 10–15 years) enhancements in three-dimensional rendering capabilities and shading have accelerated graphics considerably and allowed for greatly improved texture and shading in computer graphics. Moreover, today's VR platforms (hardware and software) have curtailed the limitations found in earlier platforms. Today's platforms are no longer large and unwieldy or difficult to operate. Likewise, today's VR platforms are much more affordable (see Table 13.4).

In addition to lowered cost and usability, the VR platforms available today have a number of other advantages (see Table 13.5). They offer advanced computer interfaces for immersing patients in computer-generated simulations of everyday activities. Given that today's VR-based assessments represent a special case of computerized neuropsychological assessment devices (Bauer et al., 2012), they have the advantage of enhanced computational capacities for administration efficiency, stimulus presentation, automated logging of responses, and data analytic processing (Parsons, 2016).

Need for Established Development, Administration, and Interpretation Guidelines

While VR-based psychological assessments have the potential to offer neuropsychologists ecologically valid assessments of day-to-day activities, a number of considerations go into the decision to add new technologies to one's battery of tests (Parsons, McMahan, & Kane, 2018). Multidimensional paradigm evaluation frameworks have been suggested for integrating the traditional psychometrics found in classical test theory with virtual environment platforms (Krohn et al., 2020; Parsons, 2011, 2016; Parsons, McMahan,

TABLE 13.4. Comparison of Today's Virtual Environment Platforms

System	Cost	Hardware	Resolution	Refresh rate	Field of view	Sensors/tracking	User interaction	SDK
Google Cardboard	$10-50	Depends on phone	Depends on phone	60 Hz	70 degrees	Head tracking (rotation):	Low level: gaze or button	Google VR SDK
Google Daydream	$70-150	High End Android Phone	Depends on phone	90 Hz	96 degrees	Head tracking (rotation)	Gamepad or joystick	Google VR SDK
HTC Vive *(now also available with eye-tracking)*	$800 *$1,600 with eye tracking)*	PC spec (minimum): NVIDIA GeForce GTX 970/AMD Radeon R9 290, Intel i5-4590/ AMD FX 8350, 4GB of RAM, HDMI 1.4 or DisplayPort 1.2, USB 2.0, Windows 7 SP1	2160 x 1200	90 Hz	110 degrees	Head tracking: Accelerometer, gyroscope, laser position sensor, front-facing camera (tracking in 15ft x15ft room size)	Controllers	HTC Vive SteamVR SDK
Oculus Rift	$400	PC spec (minimum): NVIDIA GTX 970/AMD R9 290, Intel i5-4590, 8GB RAM, Compatible HDMI 1.3 video output, 3 USB 3.0 ports and 1 USB 2.0 port, Windows 7 Sp1 64 bit	2560 x 1440 LCD	80 Hz	90 degrees	Oculus Insight 5 sensors	Updated Touch	Oculus SDK Suite
Oculus Quest	$400	No PC needed. HMD is powered by a self-contained Snapdragon 835 processor (CPU)	2880 x 1600 OLED	72 Hz	100 degrees (estimate)	Oculus Insight 4 sensors	Updated Touch	

(*continued*)

Varjo	$5,995	PC spec (minimum): NVIDIA GeForce GTX 1080/ AMD FX 9590, Intel Core i7-6700, 16GB RAM, 2 x DisplayPort 1.2 / 2 x mini DisplayPort 1.2	Combining two 1920 x 1080 low- persistence micro-OLEDs and two 1440 x 1600 low-persistence AMOLEDs	90 Hz	87 degrees	Head tracking; integrated 20/20 Eye Tracker	Integrated hand tracking by Ultraleap	Varjo Native SDK
Pico Neo VR	$450	PC spec (minimum): i5-4590/ GTX 970/4GB RAM	2560 x 1440	70 Hz	102 degrees	Head tracking (rotation) and positional tracking (forward/ backward)	Gamepad, joystick, of built in pad	Pico Mobile SDK
Playstation VR	$400	PS4 Gaming Console	1920 x 1080	120 Hz	100 degrees	Head tracking (rotation) and positional tracking (forward/ backward)	Gamepad, joystick or controllers	under development
Samsung Gear VR	$100	Compatible with following Samsung phones: Galaxy S7, S7 Edge, S6 Edge+, S6, Galaxy S6 Edge, Note 5, Note 7	2560 x 1440	60 Hz	101 degrees	Head tracking: Gyroscope, accelerometer, proximity sensor, touchpad	Gamepad, joystick, of built in pad for navigation	Oculus SDK Suite

Note. PC = personal computer; SDK = software development kit; Specs = specifications.

TABLE 13.5. Advantages and Disadvantages of VR When Compared to Traditional Paper-and-Pencil Tests

Advantages	Disadvantages
Administration	
• Virtual environments offer increased accuracy of timing presentation • Automatic randomization of stimuli • Adaptive testing protocols that offer alternate forms and reduced testing times • Monitor basal and ceiling levels to inform discontinuance of testing • Ease of adjusting language in which the test is administered • Administration of tests on portable devices (Samsung Gear VR)	• Problematic hardware and software interactions can result in test administration errors • Many virtual environments do not allow for "testing of limits" • Many virtual environments do not allow for flexibility in evaluations • Many virtual environments do not provide structured encouragement
Scoring	
• Virtual environments offer enhanced measurement accuracy—logging of response latency, strength, and variability • Integration of automate interpretive algorithms (e.g., decision rules) for determining impairment or statistical reliability • Performance measurement on time-sensitive tasks (e.g., reaction time)	• Virtual environments may mask deficits that would otherwise be apparent in some populations (e.g., persons with autism may perform better when faced with a computer)
Norms	
• Virtual environments offer enhanced logging for normative data collection and comparison • Ease of exporting responses for data analytic purposes • Automated data exporting for research purposes	• *Established guidelines* are lacking for the development, administration and interpretation of VR assessments • *Psychometric validation*: Need for validation (test–retest reliability; construct and criterion validity; sensitivity and specificity) of these VE-based assessments in large sample size studies. • *Manuals*: Virtual environments sometimes lack standardized instructions for administration and methods for scoring and interpreting test results. • *Equivalence*: VR tests may not be experientially or psychometrically equivalent to paper-and-pencil counterparts (validity)
Impact on participant	
• Virtual environments may increase openness and engagement of respondents • Decrease in examiner influence on responses • Portable VR devices (e.g., Samsung Gear VR) may increase accessibility and availability of neuropsychological services	• Anxiety and negative attitudes about computers (sometimes an issue for older adults or anyone with limited exposure to technology) may alter task performance

& Kane, 2018). At minimum, all VR-based psychological assessments need to have standardized instructions for administration and methods for scoring and interpreting test results provided in a test manual. Furthermore, systemized development standards should be created that would allow for a standard approach that ensures neuropsychologists that they have the basic information necessary to evaluate the quality of the VR-based neuropsychological assessment. The American Academy of Clinical Neuropsychology and the National Academy of Neuropsychology have established appropriate standards and conventions for computerized neuropsychological assessment devices. Likewise, VR-based neuropsychological assessments need to develop standards that address VR hardware/software platforms (e.g., Unreal; Unity; Virtual Battle Space; Cry development engines for building content), human factors (interface development that precludes the system becoming the task); data logging; and data security (see Kourtesis, Collina, Doumas, & MacPherson, 2019; Krohn et al., 2020; Parsons, McMahan, & Kane, 2018). Psychometric properties need to be established for both construct-driven and function-led virtual environments (Krohn et al., 2020; Parsons, 2011, 2016; Parsons et al., 2017; Parsons, McMahan, & Kane, 2018). Further issues regarding virtual environment-based tasks include establishing standardized guidelines for administration, interpretation, response validity (effort testing), reporting services, quality assurance standards, marketing and performance claims (made by developers of virtual environments), and patient-specific issues (sociocultural, experiential, and disability factors (Neguţ, Matu, Sava, & David, 2016a; Parsons, Barnett, & Melugin, 2015)

VR-Based Neuropsychological Assessments Must Be Sufficiently Standardized

The development of norms and interpretive approaches has the same importance in the production of VR-based measures as in the development of conventional and other computerized tests. In addition to assessing an individual's performance in relation to reference groups and estimates of that individual's estimated premorbid capabilities, VR tests may also be normed in relationship to day-to-day performance metrics. Different normative standards are necessary relative to the question to be addressed. Since a goal of scenario-based assessment is to provide data that has a stronger relationship to the demands of everyday life, then it will be important to develop norms and algorithms that relate virtual to real-world performance.

Although much work is needed in this area, VE-based assessment studies are increasingly establishing norms by demonstrating significant associations between virtual environments and conventional measures. As mentioned above, the Virtual Classroom represents a VR-based neuropsychological assessment that is approaching a normative standard. This is particularly true of Nesplora's Aula (virtual classroom). Iriarte and colleagues (2016) developed norms for the Nesplora Virtual Classroom from a sample composed of 1,272 participants (48.2% female; age range 6–16 years, $M = 10.25$, $SD = 2.83$). Normative findings related to omission errors, commission errors, and hit reaction time revealed that the Nesplora Virtual Classroom CPT paradigm is significantly correlated with the traditional CPT (omission errors; commission errors; hit reaction time) and was found to be more sensitive to reaction time and rate of omission errors than the TOVA. Findings from the normative study also revealed a general pattern of sex and age differences. Thomas Parsons and colleagues are conducting a multisite normative project for the VEGS at several institutions (including private practices): University of North

Texas, Oregon Health and Science University, Louisiana State University, Emory University, University of Texas, and the University College of Dublin. In the interim, meta-analyses have been published (and several more are underway) that compare traditional neuropsychological assessments and VR simulations (e.g., the virtual classroom; see the above discussion of Parsons, Duffield, & Asbee, 2019) to provide a preliminary source of normative data (e.g., Boccia, Nemmi, & Guariglia, 2014; Duffield, Parsons, Karam, Otero, & Hall, 2018; Kourtesis et al., 2019; Neguţ et al., 2016a, 2016b; Parsons, Duffield, & Asbee, 2019).

Outcome Measures for VR-Based Neuropsychological Assessments

An important emphasis in virtual environment research will be the standardization of measures used to assess outcomes. The selection of outcome measures for standardization needs to be relevant to the patient's treatment and health status, psychometrically sound, and related to pertinent functional and cognitive capabilities. Consistent with other Common Data Elements (CDE) Workgroups, a Neuropsychology and Technology Workgroup has been formed to establish core VR-based measures using previously validated paper-and-pencil (e.g., Wechsler Scales; CVLT, D-KEFS; WCST) and computer automated (e.g., ANAM; ImPACT; CANTAB) neuropsychological measures. Additional outcomes being considered are relations between virtual environment performance and academic performance, adaptive and daily living skills (including internet-related skills like online shopping), health-related quality of life, language and communication (including Boston Diagnostic Aphasia Examination), physical functioning, psychiatric functioning, social cognition (social role participation, social competence, and neurological symptoms.

In the area of function led assessment, multiple cognitive domains may be involved in the simulation of real-world tasks, and associations with traditional construct driven tests may be necessarily lower than is typically desired to establish construct validity. The degree to which a VE-based model using a function-led approach accurately predicts relevant real-world behavior may be more important than large-magnitude associations with traditional construct-driven paper-and-pencil tests (e.g., virtual shopping tasks; see also Renison et al., 2012). While conventional neuropsychological measures may help in assessing construct validity, more direct measures of real-life performance may be required to evaluate the unique contribution of function-led VR tests. These outcome measures may involve metrics to capture performance when individuals engage in actual daily living tasks and the creation of structured analog environments developed to produce quantitative and qualitative performance metrics. If neuropsychologists are to adopt VR-based assessments, these tests must demonstrate relevance beyond that which is available through simpler means of assessment (e.g., paper-and-pencil tests).

Issues for Use of Virtual Environments in Specific Patient Populations

In addition to psychometric issues, it is important that VR-based assessments be matched to the needs and capacities of the patient (Schultheis et al., 2002). VR-based assessments may be problematic for patients with autism spectrum disorder. The pronounced sensory issues commonly found in this population may be exacerbated by the use of dynamic stimulus presentations and stimulus intensity. While these are important concerns, there is no evidence of discomfort from two different studies with students diagnosed with autism using screen-based environments (Wallace et al., 2010; Parsons & Carlew, 2016). As we adopt newer and more immersive technologies, it is important to consider potential negative device effects and ensure that head-mounted displays provide an acceptable space for children. Some evidence suggests that children do not experience head-mounted displays any more negatively than screen-based media (Peli, 1998).

Neuropsychologists may have concerns that an older age patient will have more difficulty using this technology. While this is an important consideration, Dyck and Smither (1994) conducted a survey of adults over age 55 and found these older adults were less computer anxious and had more positive attitudes about computers than adults under 30. Older adults have been found to adopt novel technologies if those technologies appear to have value (e.g., for maintaining their quality of life; Heinz et al., 2013). Neuropsychologists may also be concerned that some older adults will have had frustrating experiences that lead to giving up on learning how to use new technologies. However, this effect should not be overgeneralized, as older adults are often interested in using newer technologies (Sayago, Sloan, & Blat, 2011). Independent of assessment modality, evaluation of memory performance in older adults may be confounded by stereotype threat. Chasteen, Bhattacharyya, Horhota, Tam, and Hasher (2005) found that invoking stereotype threat about memory abilities in older adults negatively impacts memory performance, especially when these adults are aware that their memory is being assessed. Subtle and unambiguous age-related stereotypes have also been found to influence older adults' performance on a number of cognitive tasks (see Lamont, Swift, & Abrams, 2015, for a meta-analysis), map learning (Meneghetti, Muffato, Suitner, De Beni, & Borella, 2015), driving a car (Lambert et al., 2016), and hand grip strength (Swift, Lamont, & Abrams, 2012). A potential benefit of a VR-based assessment is that these virtual environments could be designed to reduce stereotype threat by obscuring the true purpose of the task.

VR environments have been successfully applied to the study of age differences in spatial navigation among both healthy and demented aging. However, VR-based tasks may be complicated by visual, auditory, and motor impairment, or lack of familiarity with computers (Moffat, 2009). Moffat (2009) suggests adopting a number of helpful methodological practices in assessing older adults in research studies of navigation skills, such as (1) allowing aging patients to practice and ensure maximum familiarization with the computer platform, (2) including measures of computer experience, visual ability, and motor function, and (3) including assessments requiring the same sensorimotor capacities but not physical navigation.

Scenario Generators for Flexible Configuration and Administration

To be used in the context of neuropsychological evaluations, VR-based assessments must produce standardized norm-based metrics for interpretation. However, VR measures can also be developed to capture process data that assess strategies and approaches used by patients as they navigate tasks. Measuring process parameters will require that measures of these parameters be operationally defined. An optimal VR-based assessment system will require that the system be designed to permit the evaluator to adjust graphics, stimuli, other test parameters, and scenarios and to allow examiners to be flexible in how they incorporate VR measures into their assessment approaches. Greater flexibility can be achieved by developing VR-based neuropsychological assessments with scenario-generation systems that allow for modifications to the simulated real-world activities. VR measures should be developed so that they can be tailored to changes in technology and so that they can be adapted to different patient populations. Best practices for virtual environment platforms include comprehensive manuals, norms, ongoing improvements to operating systems, regular software updates, and hardware upgrades. These important considerations have been systematically addressed by Parsons, McMahan, and Kane (2018).

Summary and Conclusions

Progress in the predictive capabilities of traditional neuropsychological tests has lagged behind the technological advances that are so prevalent in society today. More recent developments in neuropsychological assessment have resulted in tests that lack conceptual or substantive advances over the older tests. Almost 25 years ago, Dodrill (1997) compared the progress in clinical neuropsychology to that of other neurosciences and found clinical neuropsychology to be lacking. By the 1990s, neuropsychologists were experiencing a shift in referrals from lesion localization to assessment of everyday functioning. With the advent and development of advanced technologies in the clinical neurosciences there was decreased need for neuropsychological assessments to localize lesions and an increased need for neuropsychologists to describe behavioral manifestations of neurologic disorders. Clinical neuropsychologists were increasingly being asked to make prescriptive statements about everyday functioning (Sbordone & Long, 1996). Given the nature of the skills and behaviors involved in everyday tasks, a paradigm change may be needed that shifts the assessment approach from task-based to scenario-based assessment. Enhancements to prediction and ecological validity may be found in approaches that assess behavior in controlled life-like virtual environments that measure both the presence and integration of skills directly related to how the patient would perform in a real-life situation. This chapter reviewed the potential for such approaches given technological advances and the ability to assess performance using virtual environments.

VR-based neuropsychological assessment allows neuropsychologists to expand methods for designing and implementing metrics capable of collecting information that provides an accurate picture of patient strengths and limitations. These VR-based neuropsychological assessments may improve the prescriptive statements neuropsychologists proffer by providing the neuropsychologists an opportunity to observe patient functioning in environments more closely mirroring the real world. Without VR this type of observation would be limited due to patient behavioral and physiological impairments as well as the practical limitations in attempting to assess behavior outside the laboratory or office environment. By adopting VR as a method for assessing patients, neuropsychologists increase the potentially positive impact of neuropsychological assessment for improving the daily functioning of patients through accurate understanding of neuropsychological deficits that enhance our ability to make relevant recommendations.

The challenge for neuropsychologists interested in developing VR-based assessment is designing tests that reflect everyday activities in a way that provides accurate information for making prescriptive statements to clients, parents, and teachers based on the best evidence available. As mentioned earlier, the practice of clinical neuropsychology is heavily rooted in psychometric assessment and the use of normative information. Adoption of VR-based neuropsychological assessments will require substantial research and development to establish acceptable psychometric properties and clinical utility. The implementation of VR assessment will likely require developing a library of VR scenarios that present pertinent life tasks and that capture critical aspects of performance. Norms from virtual environment studies are needed to describe the distribution of performances on a given VR-based test that can be considered the standard for the group concerned and that predict successful or unsuccessful real world performance. These norms will provide the context within which the performances of a patient external to the reference group can be interpreted. Although much work is needed in this area, VE-based assessment studies are increasingly interested in establishing norms by demonstrating significant associations between virtual environments and paper-and-pencil assessments.

Although a first step in validating new measures is to gauge the information captured against that provided by traditional test measures, the next step will be to evaluate the additional variance explained by implementing complex scenarios in addition to specific domain-based tasks. There is a need to develop a standardized library of tasks that present pertinent situations that make representative functional demands on the patient being assessed and that provide reliable outcome measures that account for the range and nature of responses available to patients within virtual environments.

While the needs for standardization are apparent, there is great potential for VR-based neuropsychological assessments to enhance our neuropsychological evaluations with ecologically valid assessment of patient functioning. Furthermore, the computerized nature of these tests allows for the accurate capture of neurocognitive data, as well as precise recording and scoring of neuropsychological test results. Several virtual environments have been developed for use in neuropsychological assessment. Although more validation studies need to be conducted with VR assessments, the benefits of using this technology for understanding daily functioning are well documented. In addition, smaller and more affordable equipment, as well as open-source VR software for psychological experiments (Neurovirtual 3D; Cipresso, Serino, & Riva, 2016), makes VR a viable option for use in psychological assessment.

Select limitations of new methods and technologies are often cited as cautions for adoption by (neuro)psychologists. No assessment tool or intervention technique is without limitations. Current practices in psychology (as noted throughout the cited literature) are ready for advancement and a potential paradigmatic shift. While not a sweeping criticism of current practices, we do want to underscore technologies that may enhance the state of our science.

As a field, we should embrace technological progress. We recently co-authored an article for *The Clinical Neuropsychologist* (TCN) for a special issue entitled “Are Modern Neuropsychological Assessment Methods Really ‘Modern’?” The introduction to this TCN special issue noted that neuropsychology is not alone in being slow to embrace technological advances for translational applications in clinical settings. Fair enough, but is that a justifiable reason to decide not to innovate (we refer readers to Figures 1 to 3 of Parsons & Duffield, 2019). Further, the TCN special issue introduction poses the following question (in relation to how our manuscript references neuropsychologists): “Are we lazy, uninformed, unimaginative or perhaps just under-resourced?” Our desire is not to denigrate our colleagues. We are not implying (here or in our peer-reviewed publications) that neuropsychologists are lazy—far from it. It is important to differentiate between “why” there has been slow technological adoption to “how” we can train future clinical neuropsychologists with the rapidly expanding reality of practicing neuropsychology in an increasingly digital era. We posit that the more our profession is involved in the development and validation of disruptive technologies for neuropsychology, the greater the probability we can learn from each other and advance together.

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PART II

EVERYDAY IMPACT OF NORMAL AGING AND NEUROPSYCHIATRIC DISORDERS

CHAPTER 14

Normal Aging and Everyday Functioning

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The intersection between what is considered "normal" aging and the early stages of disease can become difficult to disentangle as people grow older and the prevalence of cognitive decline and age-related pathologies increases. Normal age-related cognitive changes can range from very slight to a more pronounced impact on functional abilities, further blurring these boundaries. Some changes may be minor, such as having difficulty remembering where you put your keys, whereas others may have a greater impact on daily functioning and independence, such as repeatedly failing to take medications properly. This chapter focuses on what is typically considered normal age-related cognitive changes. Current research on structural changes found within the brain, cognitive changes and their impact on daily activities, and interventions to promote and maintain cognition and everyday function is also discussed. Finally, we address some current and future directions for research efforts in cognitive aging.

The Physiology of Aging

All a person's systems are ultimately affected by age. Although age-related changes in physical, sensory, and skeletal–motor systems may be more noticeable, with an obvious impact on daily functioning, changes within the brain also have an impact on cognition and daily functioning, though they may be more nuanced.

Although research in cognitive neuroscience has greatly advanced in recent years, there is still debate regarding the mechanisms, causes, and consequences of aging within the brain. However, normal age-related cognitive decline generally is less severe and happens without a pathological deterioration of the brain unlike what is seen in Alzheimer's disease (AD; Neuner, Wilmott, Burger, & Kaczorowski, 2017). Further muddying the waters is the fact that neural and cognitive research is often confounded by cohort effects, study design, repeated exposure of participants to many cognitive assessments in longitudinal studies, and participant attrition, resulting in the possibility of sample bias (Ahacic, Parker, & Thorslund, 2007; Boot, Simons, Stothart, & Stutts, 2013; Small, 2001). In addition to these general difficulties, there is a great amount of heterogeneity in the aging process, with both interindividual and intraindividual differences which can be somewhat explained by age-related phenotypes that predispose people to disease in their postreproductive life. The numerous interindividual differences found among older adults has cast some doubt on the generalization and inevitability of neurological declines, suggesting that some commonly held beliefs regarding age-related declines in cognitive abilities, such as memory loss as a result of nonpathological aging, may not be a part of normal aging (Small, 2001). Additionally, there is also great intraindividual variability in the aging process. This variability has been discussed in terms of cognitive plasticity (Nyberg, 2005) or the ability of the brain to change throughout the lifespan. Although it is generally accepted that neural plasticity is maintained throughout the lifespan, there is also some evidence of reduced plasticity in older adults, with losses in some domains and preservation in others (Goh & Park, 2009). Such reductions in plasticity may be due to both processing deficits (e.g., decreased cognitive speed), associated with frontal cortex changes, and production deficits (e.g., language, behavioral initiation), where neural correlates appear to be specific to the task at hand (Nyberg, 2005).

Until recently, it was widely believed that impairments found during the normal aging process were due to neuronal loss, usually found in the hippocampus and neocortical areas. However, recent development of stereological techniques and more accurate counting methods have revealed that there is no widespread neuronal loss throughout the brain (Goh & Park, 2009; Keller, 2006); rather, decreases in brain matter are more likely the result of reduced gray matter volume (Abe et al., 2008; Chung, Tymula, & Glimcher, 2017). In addition, research has also demonstrated that age-related reductions in gray matter are associated with decreased cognitive function, specifically in the domains of attention and executive function (Chung et al., 2017; Zimmerman et al., 2006).

The advancement of the cognitive reserve theory helps account for some of the heterogeneity related to normal cognitive aging (Anderson & Craik, 2017), as well as the differing presentations observed in persons with the same pathology (i.e., not every case of Alzheimer's disease is cognitively, behaviorally, or functionally the same; Satz, 1993; Stern, 2002; Whalley, Deary, Appleton, & Starr, 2004). This theory postulates that a greater number of novel environmental interactions (e.g., education, work, or leisure activities) results in greater neuronal development—including neurogenesis, migration, differentiation, arborization, synaptogenesis, synaptic sculpting, and myelination—throughout the lifespan (Evans et al., 2019; Perry, 2002). Early imaging research supports a neural basis for cognitive reserve (Clewett et al., 2016; Stern, 2003). As such, if pathology occurs that damages the neural structure within the brain, persons with a greater reserve may not demonstrate the same cognitive impact as others with the same pathology but less reserve, or observable deficits may not be manifest until a later time point when greater pathological damage has occurred.

A review of this theory demonstrates additional support for the protective nature of cognitive enrichment, through behavioral, nutritional, and pharmacological experiences, upon neural structures and functions (Milgram, Siwak-Tapp, Araujo, & Head, 2006). For example, Soldan et al. (2017) investigated the intersection of cognitive reserve and the risk for developing Alzheimer's disease. In this study, cognitive reserve was operationalized by a composite score based on three measures: (1) baseline reading level from the National Adult Reading Test (NART; Nelson, 1982), (2) baseline score on the vocabulary subtest of the WAIS-R (Wechsler, 1981), and (3) years of education. This study examined the long-term trajectories of 303 individuals who were cognitively normal at baseline and who were followed for 20 years. They found that persons who had higher levels of cognitive reserve at baseline had delays in the onset of symptoms of mild cognitive impairment. Once symptoms began, however, the rate of decline was faster for those with higher cognitive reserve. This finding suggests that cognitive reserve mediates declines by delaying disease onset rather than by slowing the process.

Typically, cognitive reserve is thought to encompass the impact of leisure activities, education, occupation, and mental activities pursued throughout the lifespan. Thus, there is not always consistency in how it is operationally defined across studies. There is some consensus, however, that more challenging measures with higher ceilings may provide better detection of changes for individuals who begin with high levels of cognitive functioning at the outset. It also may be important to include tests that are more pathologically oriented when examining specific conditions to increase sensitivity to change (Stern, 2012).

Upon evaluating some of the enrichment and intervention research, Salthouse (2006) also concluded that there is no solid evidence that cognitive stimulation actually slows the rate of cognitive decline. However, other researchers would argue that previous experiences and interventions do have an impact on the cognitive abilities of trained participants relative to control groups (Ball et al., 2002; Scarmeas & Stern, 2003; Willis et al., 2006; Rebok et al., 2014), in large part because boosting cognitive ability results in longitudinal declines originating from a higher level of cognitive function, and therefore not does not reach the threshold to impact functional abilities until later in life. This finding from the cognitive training research appears to be consistent with the benefit of cognitive reserve and would not have been observed within shorter follow-up studies. In the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) clinical trial, improvement on trained cognitive abilities observed at immediate posttest dissipated over time, unless boosted with additional training, but scores remained better than baseline cognitive scores for a significant portion of a 10-year follow-up. Also, importantly, greater cognitive decline in the control group did not occur until the fifth year of follow-up, allowing researchers to see significant protective effects of training on both cognitive and everyday functional abilities. However, even researchers who are not completely convinced by the evidence that increased cognitive activity slows cognitive decline have noted that adults should still be engaging in challenging cognitive activities, as they are not harmful and can be enjoyable (Salthouse, 2006), thereby resulting in a higher quality of life.

Another commonly espoused theory that complements the construct of cognitive reserve is the frontal lobe theory (Chung et al., 2017; Phillips & Sala, 1998; Zanto & Gazzaley, 2019). Although other areas of the brain may also exhibit deterioration, such as that found in the hippocampus, many researchers have targeted the frontal lobes as particularly relevant for cognitive function. That is, the frontal lobes appear to be particularly relevant for executive function (as described below), and age-related changes are typically more advanced in this area of the brain. Several researchers have further explored this theory and have begun to define the specific areas of the frontal lobes that are important to cognition. For example, the dorsolateral prefrontal cortex regions, involved in fluid intelligence tasks, appear to be a key contributor to age-related cognitive decline (Phillips & Sala, 1998), rather than some other areas falling under the "frontal lobes" umbrella, such as the ventromedial prefrontal area (MacPherson, Phillips, & Della Sala, 2002). Chung and colleagues (2017) found that a reduction of gray matter volume in the ventrolateral prefrontal cortex correlated with a loss of economic rationality and decision making, demonstrating an impact on executive function.

More recent research has focused on age-related phenotypes that may affect cognition. These phenotypes are observable characteristics of an individual that reflect the interaction of a person's genotype with their environment. For example, individuals with potential AD have been found to have very different clinical profiles when presenting for evaluation. They may present with mild (e.g., impairment in list learning) or much more severe memory loss (e.g., disorientation in time and place, poor recognition as well as recall). Additionally, they may or may not have difficulty with semantic memory, working memory, language, calculation, visual perception, spatial abilities, praxis (e.g., use of limbs), or frontal lobe function (e.g., lack of hygiene, social disinhibition). Snowden et al. (2007) reported that AD patients fell into three broad phenotypes or clusters: (1) those who had a young onset, a strong family history, characteristics of frontal lobe dysfunction (as well as likely posterior cortical deficits and autosomal dominant inheritance not associated with APOE ε4); (2) those with symptoms reflecting posterior hemisphere dysfunction, more likely female gender and middle age, and have a relatively low incidence of family history; and (3) those with symptoms of temporal (medial temporal and temporal neocortex) lobe dysfunction who show no gender bias, are older, have few neurological signs, and have a high incidence of family history of dementia and high APOE ε4 allele frequency. More recent studies have looked further into phenotypes and provide additional insight into genetic variations and mediation of cognitive decline (Brooks-Wilson, 2013; Chung et al., 2017; Vaiserman, Koliada, & Lushchak, 2018). Gene studies have found that variants at SPOE and FOXO3A are associated with longevity and may buffer the effects of aging and lead to a delay in health-related declines (Brooks-Wilson, 2013; Wang, Du, Li, & Qiu, 2019). For a review of this literature, see Wang and colleagues (2019).

Cognitive Changes

Cognitive abilities provide us with the flexibility to negotiate the world in which we live. Whether we are reading and following directions in order to cook a meal or program a DVR, preparing our tax returns, learning and remembering new information presented in a class, or driving a car, our cognitive skills allow us to engage in many unique and challenging situations. As a result, age-related decline in cognitive function can potentially impact the daily function of older adults.

Intelligence

In the absence of disease, such as dementia, age-related declines in intelligence tend to be minimal until the eighth decade of life (Park & Bischof, 2011; Schaie, 1996). Although the incidence of dementia increases with age, affecting between 5 and 10% of people over the age of 65, dementia is not an inevitable outcome of aging even into the tenth decade of life (Andersen-Ranberg, Vasegaard, & Jeune, 2001). Intellectual functioning has been categorized into two domains: crystallized and fluid abilities. Crystallized abilities, which include vocabulary, semantic knowledge, phonemic knowledge, and simple arithmetic, have been found to increase or remain stable into middle age, and any declines in these abilities tend to occur very late in life, if at all. The cumulative improvement of crystallized cognitive ability, which occurs throughout the lifespan primarily through education and enriching experiences, has been used as a definition of cognitive reserve. Fluid abilities, in contrast, which include memory, reasoning, speed of processing, and higher-order thought processes (Horn, 1982), may begin to decline in young adulthood, according to findings from the Seattle Longitudinal Study of Adult Intelligence (Schaie, 1994). However, age-related declines in fluid abilities are also not inevitable. Higher education and continued intellectual activity (increasing cognitive reserve), as well as expertise in a particular area, or improving basic fluid abilities through cognitive training, can enhance everyday functioning, which in turn can provide added years of independence and ultimately slow the progression to dementia (Cizginer et al., 2017; Compton, Bachman, & Logan, 1997; Edwards et al., 2017; Hall et al., 2009; Hoyer & Rybash, 1994; Wilson, Bienias, Berry-Kravis, Evans, & Bennett, 2002). Cognitive training has been shown to improve the trained basic cognitive abilities at the meta-analysis level (Karbach & Verhaeghen, 2014). The primary point of contention among scientists is whether or not such improvements transfer to untrained cognitive skills in older adults, and in particular everyday functioning (Simons et al., 2016). An attempt at consensus on best practices for methodological standards for behavioral interventions to improve cognitive function has recently been published (Green et al., 2019). Studies in this area will be discussed below in greater detail.

Memory

Memory loss is one of the most frequent cognitively related complaints of older adults. One reason for this frequency is that memory is fundamental to most everyday activities, and the inability to remember something can be embarrassing and quite obvious. Although some normal age-related memory decline occurs for many older adults, these changes typically do not have a significant impact on daily function. Intact memory functioning requires activation of both cortical and subcortical areas of the brain. When the hippocampus is damaged in Alzheimer's disease, profound memory loss occurs. Regardless of disease presence, research has linked memory decline to self-reported impairment in many instrumental activities of daily living (IADLs), including shopping, preparing meals, managing finances, and handling complex medication regimens (Arvanitakis, Shah, & Bennett, 2019; Sinclair, Morley, & Vellas, 2012).

Changes in the aging brain also occur in the temporal cortex, hippocampus, and limbic system, all of which are associated with memory (Eustache et al., 1995). Schofield et al. (1997) found that 31% of cognitively intact community-residing elders reported memory complaints. Given that there may be declines in metamemory as well (i.e., people forget that they forget), the prevalence of those with memory impairments may be even greater than reported. Similarly, Vogel (2008) found that while memory complaints in older adults were common, they were inconsistently associated with current cognitive impairment but predictive of future pathological changes.

It is believed that many age-related changes in memory are due to declines in short-term memory. The phrase "short-term memory" has been used to denote both the immediate recall of information as well as working memory. Working memory can be described as the ability to simultaneously store and manipulate information temporarily. Although the ability to immediately recall relatively simple information remains intact in normal aging, working memory is poorer, on the average, in older adults (Foos & Wright, 1992; Salthouse, 1992). For example, the ability to retain increasingly long strings of digits presented aurally, mentally manipulate those digits so that they are in reverse sequence, and recite them aloud is a classic working memory task, the performance of which declines with age. Although normal declines in working memory are expected with age, frank deficits in working memory may be suggestive of dementia and have been associated with early IADL impairments in Alzheimer's disease (Arvanitakis et al., 2019).

Prospective memory, or memory for future intentions, has also been studied with respect to aging. Successfully performing a prospective memory task requires remembering to do something, as well as remembering what to do. There is also a difference between remembering when to do something (time critical events), and simply remembering to do it. Cognitively normal older adults are particularly adept at carrying out time-dependent tasks in naturalistic settings (e.g., remembering to make a phone call at 2 p.m., or remembering to attend a scheduled appointment or take medications at certain times of the day). They are, however, motivated to do these types of tasks and can use cues or reminder systems as aids. Indeed, in a meta-analysis of prospective memory studies (Henry, MacLeod, Phillips, & Crawford, 2004), results showed that in laboratory studies of prospective memory older adults are at a disadvantage and perform more poorly than young adults. However, the opposite was true in naturalistic studies where older adults had the advantage. Once older adults start exhibiting deficits in these naturalistic prospective memory tasks, however, as with working memory, it may be an indication of cognitive decline.

Long-term memory consists of two broad classes of memory—declarative (episodic and semantic) and nondeclarative (procedural)—which are differentially affected by aging. The primary distinction between declarative and nondeclarative memory is that declarative (explicit) memory refers to conscious learning and nondeclarative (implicit) memory refers to unconscious learning. Nondeclarative memory can be described as unintentional, automatic, or without awareness, and it relies upon familiarity rather than deliberate study (Kausler, 1994; Smith, 1996). Use of nondeclarative memory occurs when one performs automatic skills such as flipping a light switch (Light & Albertson, 1989; Poon, 1985). Nondeclarative memory remains intact in normal aging as well as in the early stages of Alzheimer's disease (Kuzis et al., 1999). Older adults more often have difficulty with declarative memory as they age, and age-related impairments can be seen in both types of declarative memory: episodic and semantic. Episodic memory involves the recall of temporal (e.g., when) and spatial (e.g., where) information associated with past personal experiences/events. Semantic memory involves language and world knowledge, which are reinforced throughout the lifespan and thus are more resistant to age-related decline. Alternatively, episodic memory involves discrete occurrences and generally declines with age (Hooyman & Kiyak, 2005).

Executive Function

Executive function is one of the most complex cognitive functions and includes the ability to plan, sequence, organize, inhibit responses, think abstractly, monitor the self, and reallocate mental resources. As noted previously, these abilities are primarily associated with the frontal lobes of the brain, as demonstrated by the deficits in these skills observed in younger adults with acquired frontal lobe lesions. Some researchers have argued that the executive function impairments observed in normal aging are similar to those observed in younger individuals with frontal lobe lesions (Moscovitch & Wicour, 1992). Executive function is needed to complete tasks that require complex behavior or involve multiple steps. Many investigators have demonstrated age-related decline in prefrontal and frontal lobe function, associated with executive functioning (Glisky, Polster, & Routhieaux, 1995; Parkin & Java, 1999; Souchay, Isingrini, & Espagnet, 2000; West & Alain, 2000). Inhibition is one key aspect of executive function that declines with age. The ability to inhibit responses is as important as initiating them. Inhibition allows one to access, delete, or restrain cognitive behaviors (Hasher, Zacks, & Rahhal, 1999) and prevents "mental clutter," distraction, and interference, thereby facilitating the allocation of mental resources to the task at hand. Perhaps one of the most salient examples of successful inhibition is the ability to refrain from making hurtful or socially inappropriate comments. Research has indicated that some common genetic polymorphisms contribute to increased heterogeneity of executive function in older adults (Nagel et al., 2008). For example, McFall et al. (2014) performed a gene x environment study looking at executive function data from the Victoria Longitudinal Study concurrently and across 9 years. They were investigating the impact of an insulin degrading enzyme (IDE) genetic polymorphism and pulse pressure (an indicator of vascular health). Those older adults with the major IDE G allele (the insulin degrading enzyme) exhibited better executive function relative to those with the minor A allele. In addition, those with poorer (higher) pulse pressure performed more poorly on executive function tasks and had greater longitudinal decline. Interestingly, there was an interaction effect such that the effects of higher pulse pressure differed across the risk and protective allelic distribution of the IDE gene.

Reasoning

Reasoning is a cognitive ability that uses logic, knowledge, and principles to find solutions to a problem. It is a sophisticated problem-solving ability used in a variety of real-world tasks and requiring both memory and executive functioning. Age-related declines may become apparent when the task is unfamiliar or complex (Hayslip & Sterns, 1979). Not surprisingly, declines in reasoning can impair successful decision making in everyday situations such as financial investment or medical treatment. Laboratory tests of reasoning include measures such as Letter Series, Word Series, or Letter Sets. These types of measures present a series of letters, words, or numbers, followed by the question "What comes next in the sequence?" (A simple example might be 1 2 3 1 2 3 1 2 3.). While 1 is the correct answer, older adults with declining reasoning abilities may not be able to answer or may answer 4. Typically, a number of such series, with increasing difficulty, are presented, and the number correct within a prescribed timeframe is scored.

Attention

Attention encompasses a rather broad spectrum of abilities that range from automatic orientation toward a loud noise to remaining vigilant for long periods of time (i.e., sustained attention). Divided attention is quite commonly used in everyday contexts and occurs when people try to do two or more things at once ("multitasking"). This ability may or may not decline with age, depending on the individual, the difficulty of the tasks being performed, and, to some degree, the previous life experiences of the individual (Harada, Natelson Love, & Triebel, 2013). The use of a cell phone while driving is an example of a task requiring divided attention that can be difficult for all age groups. Selective attention is the ability to attend to relevant information while ignoring irrelevant information or distraction. This executive-function-based ability is another area in which age-related decline has been documented (Parasuraman & Greenwood, 1998).

Speed of Processing

Speed of processing refers to the rate at which information is perceived and processed. Facility in processing speed is one of the first cognitive abilities to decline with age (Schaie, 1994). Age-related decrements in speed of processing vary depending on task complexity (Allen, Wallace, & Weber, 1995; Bashore & Ridderinkhof, 2002; Bashore, Ridderinkhof, & van der Molen, 1997; Fisher, Fisk, & Duffy, 1995). Over the past decade, many studies have demonstrated relationships between cognitive processing speed and everyday function in older adults. Various indices of mobility have been linked to processing speed impairments in older adults, including number of falls (Vance et al., 2006), performance mobility via the Performance Oriented Mobility Assessment (Owsley & McGwin, 2004), life space (a measure of the extent of movement within an individual's environment; Stalvey, Owsley, Sloane, & Ball, 1999), and driving outcomes such as on-road driving performance, driving simulator performance, and crash risk (Clay et al., 2005). Slower processing speed is also related to slower performance of IADLs (Edwards et al., 2005). Processing speed is frequently a component of other cognitive abilities such as reasoning and executive function. For example, in the trail making test, individuals are presented with letters and numbers scattered over a sheet of paper and asked to "connect the dots," alternating between numbers and letters. This is a timed test, so those taking the test must start at 1 and draw a line from 1 to A to 2 to B to 3 to C, and so on. Those who can perform the task quickly and correctly would be representative of those with good executive function. Many measures of cognitive assessment include a time component, and those with poorer speed of processing would be penalized on those measures as well.

Daily Functioning and Aging

There is substantial evidence that cognitive abilities are important predictors of individual differences in the ability to function in everyday life; in this way, age-related cognitive decline can jeopardize independence. However, the ability to perform everyday activities relies on many functions (e.g., physical, sensory, and cognitive), and these functions are better predictors of real-world abilities than age per se. It is undoubtedly the case that a critical level of cognitive decline must occur before that decline begins to affect everyday abilities. It is not surprising that age-related cognitive declines are observable in a clinical or laboratory environment much earlier than are real-world functional declines. There is, for example, a considerable difference between someone's ability to perform an unfamiliar cognitive test in a laboratory and his or her ability to shop, balance a checkbook, drive a vehicle, or prepare a meal. It is perhaps because of the multiple determinants of everyday ability and the possibility of compensation in everyday life that decline in functional competence occurs at a later chronological age than decline in associated cognitive abilities (Allaire & Marsiske, 1999; Diehl, Willis, & Schaie, 1995). Furthermore, older adults who have had lifelong disadvantages (e.g., little education, low income) are at increased risk (Willis, 1996) for both cognitive and functional decline, and may exhibit decline at an earlier chronological age. These findings are consistent with the findings presented earlier relative to cognitive reserve.

Much recent research in the area of cognition and functional abilities has focused on the development of assessments that are predictive of difficulty in performing everyday activities, as well as the determination of those critical cut points in cognitive function that define impaired and nonimpaired function in everyday life. In the development of such measures, the emphasis has been to determine the bases of age-related functional problems (e.g., which cognitive abilities are relevant), as well as the development of interventions that would potentially maintain everyday function and independence. With an increasing number of older adults continuing to work and drive, the long-term goal is to identify how assessment can be improved to better address the difficulties older adults experience in performing everyday activities. Increasingly, rapid technological changes in vehicles, work environments, and communication are making it more and more difficult for older adults to remain current in these areas. Most noticeable in the current COVID pandemic, the use of online banking, zoom meetings, and online shopping and services have become more and more of a necessity. Keeping up with such changes may help older adults live independently, while falling behind may necessitate the need for assisted living or other living arrangements. We next summarize some examples of linking cognitive assessment to everyday ability in relation to aging, followed by a brief discussion of cognitive training and the role it may play in sustaining independence in older age.

Self-Reported ADL/IADL Function

Self-report is a common way of assessing everyday abilities among older adults. With age, older adults may begin to report increased difficulty, especially with the performance of daily activities that rely on cognitive function. Lawton and Brody (1969) defined specific categories of daily activities essential to maintaining an independent lifestyle. These include abilities such as financial management, medication management, ability to use the telephone, ability to prepare meals, and housekeeping (Fillenbaum, Heyman, Wilkinson, & Haynes, 1987). Because the performance of these *instrumental activities of daily living* (IADLs) is necessary to maintain one's household and therefore independence in the community, disability in IADLs typically precedes disability in the more basic *activities of daily living* (ADLs; self-care such as dressing, feeding oneself, and toileting). The U.S. National Health Survey of 2011 found that approximately 21% of older adults age 85 or older, 7% of those aged 75–84, and 3.4% of those 65–74 required assistance with at least some ADLs (Wolff, Feder, & Schulz, 2016; Adams, Kirzinger, & Martinez, 2012). With the dramatic change in demographics due to the aging baby boom generation, this represents a significant number of dependent older adults.

Performance-Based ADL/IADL Function

Research has shown that some older adults may not be able to validly evaluate their everyday abilities (Friedman et al., 1999; Rubenstein, Schairer, Wieland, & Kane, 1984).

For example, it has been reported that older adults with mild cognitive impairment, as well as healthy older adults, tend to overestimate their abilities (Rubenstein et al., 1984). In contrast, older adults suffering from depression tend to underestimate their abilities (Kiyak, Teri, & Borson, 1994). Because of these discrepancies, there has been an emphasis on developing performance-based measures of everyday abilities rather than relying solely on self-report of IADL ability (Diehl et al., 1995). Some of these measures—for example, those evaluated in the ACTIVE clinical trial; see section on training—include measures of everyday problem solving (Jobe et al., 2001; Schaie, 1996; Willis, Jay, Diehl, & Marsiske, 1992) and measures of everyday speed such as the timed IADL (TIADL). For example, the TIADL measure assesses IADL task completion accuracy and time for activities such as looking up a phone number, finding food items on a crowded shelf, making change, finding ingredient information on cans of food, and finding relevant information on medication bottles (Edwards et al., 2002; Owsley et al., 2001; Owsley, Sloane, McGwin, & Ball, 2002). While speed may not be a critical component in some IADLs (e.g., writing a check, managing one's medication schedule) it is becoming increasingly important with certain tasks such as obtaining prescriptions over the phone (frequently requiring entry of information over the telephone using an automated system), and other activities that will time out if not done quickly enough (e.g., online banking). Speed of processing is also a critical component of driving. Thus, both speed and accuracy are important in the development of performance-based assessments of current IADLs.

Mobility

One everyday ability that has been evaluated by self-report, performance measures, and multiple outcomes is mobility. Mobility is extremely important to older adults because it ensures access to social contacts and health care, and is critical for independence and a satisfying quality of life. Mobility, broadly defined as "a person's intentional movement throughout his or her environment" (Owsley & McGwin, 2004, p. 1901), can be assessed in a variety of ways. With increasing age, mobility limitations become more prevalent and are associated with impairments in sensory, cognitive, and/or physical functioning (Barberger-Gateau & Fabrigoule, 1997). Mobility limitations negatively impact quality of life by increasing the need for formal care and decreasing independence in nearly 20% of adults age 65 or older (Guralnik, Fried, & Salive, 1996). In addition, mobility limitations are associated with acute medical conditions (Branch & Meyers, 1987), depression (Seeman, 1996), and declining independence (Manton, 1988).

Some of the ways in which mobility is assessed as an IADL include a count of negative events (e.g., falls, vehicle crashes), actual performance (e.g., rapid-pace walk or driving performance), and self-report (e.g., regarding driving difficulty or driving habits). Frailty has been defined as a clinical phenotype that increases the risk of poor health outcomes (e.g., falls, disability, hospitalization, and mortality). Xue (2011) describes frailty as a well-defined syndrome with clinical manifestations including negative energy balance, sarcopenia, and diminishing strength and tolerance for exercise. Frailty has been operationally defined (Fried et al., 2001) as meeting at least three out of the five phenotypic criteria: poor grip strength, low energy, slow walking speed, low physical activity, and unintentional weight loss. Therefore, frailty has an obvious impact on mobility measures. A brief description of some of the research linking cognitive ability with mobility outcomes follows as an example of one area in which cognitive research is being translated into everyday applications.

Falls

Falls are one of the leading causes of injury among older adults and can be life-threatening. Nearly one-third of adults age 65 and older fall at least once each year (Bergland, Pettersen, & Laake, 2000; Stalenhoef, Diederiks, de Witte, Schiricke, & Crebolder, 1999). The result can be severe mobility restriction, as a result of a broken hip or even death (Cummings et al., 1995; Tinetti, Speechley, & Ginter, 1988). Falls relate to quality of life by limiting or eliminating one's ability to leave home for social events or, in more serious situations, even bathe and dress (Sicard-Rosenbaum, Light, & Behrman, 2002; Stalenhoef, Diederiks, de Witte, Schiricke, & Crebolder, 1999; Tinetti, Williams, & Gill, 2000).

Although some falls are caused by extrinsic agents (e.g., slippery floors), many can be linked to declining cognitive function (Fuller, 2000; Tinetti et al., 1988). Results from a large sample study found that impaired Useful Field of View (UFOV®) test performance (a measure of cognitive speed of processing) was associated with an increased risk of falls, suggesting that interventions to improve cognitive function may be helpful in reducing falls among older adults (Vance et al., 2006).

Driving

Driving is a vital means of maintaining mobility in many countries, and older adults in the United State report strong reliance on the personal vehicle for their transportation, and thus independence, needs (Jette & Branch, 1992). As individuals age, however, their driving skills may become compromised by declining visual and/or cognitive processing. Driving cessation poses a severe threat to mobility and can lead to decreased volunteerism, employment opportunities, social activities, and access to health care (Marottoli et al., 2000). Public concerns call for both effective evaluation of driving risk and proven rehabilitative programs, whenever available, for those at risk. There is a large literature relating visual and cognitive function to driving competence (Ball, Owsley, Sloane, Roenker, & Bruni, 1993). A meta-analysis evaluated the relationship between the UFOV® and objective measures of driving performance (Clay et al., 2005). Results showed converging evidence from multiple sites and investigators that the UFOV® test is strongly related to driving competence among older adults.

With respect to driving habits, many older adults begin to avoid specific driving situations, begin to limit their driving, or stop driving altogether in response to declining visual and cognitive abilities. Significant changes in all these driving habits are detected after age 75 (Ball & Owsley, 1991, 1993, 2000; Ball, Owsley, Sloane, Roenker, & Bruni, 1993; Ball & Owsley, 1998; Edwards, Ross, et al., 2008; Marottoli, Cooney, Wagner, Doucette, & Tinetti, 1994; Owsley, Ball, Sloane, Roenker, & Bruni, 1991; Owsley et al., 1998; Owsley, McGwin, Sloane, Stalvey, & Wells, 2001; Schaie, 1994; Sims, Owsley, Allman, Ball, & Smoot, 1998; Stalvey, Owsley, Sloane, & Ball, 1999). Cognitive losses have been associated with many of these outcomes. Specifically, deficiencies in executive function, mental status, speed of processing, and memory have been associated with decreased driving exposure, increased driving avoidance, increased self-reported driving difficulty, and driving cessation among older adults (Ball, Owsley, et al., 1998; Foley, Wallace, & Eberhard, 1995; Johansson et al., 1996; Stutts, 1998; Aust & Edwards, 2016; Ross et al., 2016).

Useful Field of View

One cognitive assessment that has been studied extensively with respect to its relationship to mobility outcomes is the UFOV® test. This test measures the speed with which an individual processes information of increasing complexity (Ball, Edwards, & Ross, 2007). Cutpoints predictive of everyday outcomes and norms for older populations are available (Ball, Wadley, Vance, & Edwards, 2007; Clay et al., 2005; Edwards et al., 2006). Research has also demonstrated that speed of processing training, which targets the speed with which complex visual information is processed, is one method by which the UFOV® can be enhanced (Ball & Birge, 2002; Willis, Tennstedt, et al., 2006).

In summary, it is important to note that the performance of "real-life" tasks relies on multiple complex cognitive abilities (Allaire & Marsiske, 1999; Willis, 1996) as well as on an individual's overall health, social skills, and social networks. Even so, the identification of specific cognitive skills that are related to specific functional declines has led to effective interventions.

Training

The concept of "brain training" or cognitive training has generated much interest in recent years, particularly due to the numerous commercial interests that now advertise the benefits of such training with the use of their products. Indeed, several of these entities have been fined for unsupported claims that they have made regarding specific products. There have also been controversy, concerns, and criticisms within the scientific community (Boot et al., 2013; Melby-Lervag & Hulme, 2013; Shipstead, Redick, & Engle, 2012; Simons et al., 2016), despite numerous published empirical studies demonstrating that certain core cognitive abilities can be improved through behavioral training (Au et al., 2015; Ball, Berch, et al., 2002; Bediou et al., 2018; Deveau, Jaeggi, Zordan, Phung, & Seitz, 2015; Karbach & Unger, 2014; Kramer, Larish, & Strayer, 1995; Schmiedek, Lövdén, & Lindenberger, 2010; Strobach & Karback, 2016; Valdés, Andel, Lister, Gamaldo, & Edwards, 2019). Green and colleagues (2019) summarized many of the issues that have been raised regarding cognitive training studies, based on a meeting that included scientists on both sides of the controversy to discuss potential methods for standardizing the design of such studies (including control group selection and assignment), selecting assessment and outcome measures, and blinding research participants as well as those assessing and/or training them; replication of results; and difficulties that arise in the absence of proper communication, dissemination, and publishing of results. These issues are not unique to cognitive training studies. In fact, they occur in drug trials and in many intervention studies dealing with improvement of performance or education.

With respect to improving or protecting the cognitive function of older adults, a variety of exercise, pharmacological, vitamin-based, and cognitive training programs have been developed, focusing on either particular fluid abilities or general strategies for daily living. For a recent review of cognitive training and a meta-analysis of interventions and their possible impact on cognitive aging in both healthy older adults and those experiencing mild cognitive impairment, see Basak, Qin, and O'Connell (2020). These authors analyzed 215 published studies and reported that cognitive training is effective in improving cognition in both healthy older adults, and in adults with MCI, even though not all 215 studies demonstrated positive effects. The results further suggested that cognitive plasticity is possible into late adulthood, even in those with early cognitive impairments (MCI).

One of the longest controlled studies evaluating cognitive training has been the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE clinical trial). This study is now in the 20-year follow-up phase. ACTIVE was a multisite, clinical, randomized, single-blind trial investigating the long-term effects of three cognitive training programs on cognitive measures, even though the primary and secondary outcomes focused on the improvement of everyday activities in older adults ($N = 2{,}802$; Jobe et al., 2001). Specifically, the effects of standardized memory, reasoning, and speed-of-processing interventions that initially required up to ten 60- to 75-minute training sessions, and booster training for half of the participants, were investigated in persons over a 10-year period, with 20-year follow-up of archival data on driving records, Medicare and Medicaid records, credit histories, and mortality records currently in progress. Memory and reasoning training involved teaching participants strategies such as mnemonic memory devices (Rasmusson, Rebok, Bylsma, & Brandt, 1999; Rebok & Balcerak, 1989) and finding patterns in series of words and letters that benefit reasoning abilities (Willis & Schaie, 1986). Training to improve processing speed used an individualized computerized practice involving more complex and challenging identification and localization of targets at increasingly faster paces (Ball, Wadley, Vance, & Edwards, 2007; Edwards, Wadley, et al., 2002). All three interventions were found to be effective at improving the targeted cognitive ability for up to 10 years, and all were found to improve self-reported IADLs (Rebok, Langbaum, et al., 2013). For those who received booster training, speed-of-processing training was found to transfer to everyday performance-based speed outcome measures at 5 years (Ball et al., 2002; Willis, Tennstedt, et al., 2006), as well as self-reported IADLs at 10 years (Rebok et al., 2013). Speed of processing training was also found to have long-term protective effects on a variety of mobility outcomes such as state-recorded crash risk (Ball, Edwards, Ross, & McGwin, 2010), driving cessation (Edwards, Ross, Ackerman, et al., 2008; Ross et al., 2016), and driving mobility (Edwards, Meyers, et al., 2009; Ross et al., 2016). Finally, Edwards et al. (2017) also reported a protective effect on dementia.

Speed-of-processing training has been more extensively evaluated relative to everyday outcomes, as well as in populations where more impairment was present at baseline. Older participants who have undergone such training have been found to have faster processing speed (i.e., cognitive laboratory tasks; Edwards, Vance, et al., 2005), faster everyday processing speed (i.e., everyday life tasks; Willis et al., 2006), better performance on TIADLs; (Edwards, Wadley, et al., 2002; Edwards, Vance, et al., 2005), faster complex reaction time (Roenker, Cissell, Ball, Wadley, & Edwards, 2003), and reductions in dangerous driving maneuvers (Roenker et al., 2003), and were less likely to experience extensive and clinically relevant declines in health-related quality of life (Wolinsky et al., 2006). For a detailed review of the training procedures and outcomes, see Ball, Wadley, et al. (2007).

As mentioned earlier, a recent comprehensive meta-analysis of 215 studies examining the differential effects of cognitive training in both healthy aging and MCI was done to compare the effects of different training modules (Basak et al., 2020). The authors reported that all training modules (both single-component and multicomponent) improved their targeted cognitive abilities with effect sizes between 0.19 and 0.46, and reported that training which targeted specific cognitive skills produced significant and moderate near transfer as well. The authors also reported that overall, executive functions training produced transfer to both trained and untrained cognitive skills. Furthermore, in assessing far transfer from different types of single-component training programs to everyday function, the authors reported that only processing speed training was significant.

The findings of Basak et al. (2020) are consistent with another systematic review and meta-analysis of the cognitive speed of processing training (Edwards Fausto, Tetlow, Corona, & Valdes, 2018), which evaluated 44 studies for this particular training from 17 randomized trials using the Institute of Medicine criteria. This analysis indicated that training enhanced neural outcomes, as well as the cognitive outcomes of speed of processing and attention. These training effects did not differ when compared to active or no contact control conditions. Training showed far transfer (i.e., saw an improvement in activities that is very different from what was actually trained) to everyday function and was enduring (in some cases across 10 years). Results were larger for adaptive training techniques (i.e., the training effects were more robust and had greater improvement on the outcome measures) as well as in community-based as compared to clinical samples. Training also positively enhanced health, well-being, and quality of life longitudinally. Although effects were somewhat smaller relative to healthy older adults, training was also found to be beneficial among individuals with diseases associated with cognitive decline (i.e., Parkinson's disease, stroke, HIV, and breast cancer).

As noted earlier, critics of cognitive training argue that empirical effects could be due to participants' expectations (Foroughi, Monfort, Paczynski, McKnight, & Greenwood, 2016; Simons et al., 2016) related to the expectancy value theory (Guo, Marsh, Parker, Morin, & Dicke, 2017). However, Kaur, Dodson, Steadman, and Vance (2014) reported that older adults who did not believe that speed of processing training would improve their cognitive abilities tended to benefit the most, and self-efficacy was not found to result in differing training effects (Sharpe, Holup, Hansen, & Edwards, 2014). Furthermore, results of two meta-analyses (Edwards et al., 2017; Hill et al., 2017) were not smaller (i.e., training effects, or effect sizes, were not smaller for the no contact control groups analyzed in the meta analyses relative to the active control groups) for active versus no contact controls. In addition, Edwards, Ruva, O'Brien, Haley, and Lister (2013) demonstrated that transfer of training gains to IADL performance was completely mediated by cognitive training gains, accounting for 87% of the variance.

Future Directions

With respect to normal aging, unquestionably, good cognitive function is of considerable importance for independent everyday function and quality of life. Cognitive reserve, developed throughout a lifetime of education, work, and leisure activities, has been shown to slow the impact of cognitive decline on everyday function and potentially delay loss of independence. Cognitive training also has the potential to improve cognition or protect against the impact of cognitive decline on these functions. In light of the recently published results and criticisms regarding cognitive training, a great deal of media attention has been focused on the findings that cognitive abilities can be improved or maintained in older age. This attention has resulted in insurance companies and other stake holders performing their own studies (American Automobile Association, 2016) to verify, for example, that cognitive training reduces driving claims, as well as crashes. As a result, cognitive training in older age has gained popularity and has been made more widely available through Medicare Advantage programs and insurance companies; even public libraries have made it available online during the COVID pandemic. Future directions in this area will involve additional field studies that evaluate the impact of assessment and training programs conducted in real-world settings (e.g., senior centers, medical offices) on both clinical and everyday outcomes. Given the preliminary evidence that cognitive training may slow progression to dementia, future work is needed to evaluate this outcome in trials focused on this outcome. Questions related to who is most likely to benefit from such programs, how much benefit can be expected, and for how long will need to be addressed in a systematic fashion (e.g., is it better to provide training before cognitive decline becomes evident, and would benefits persist longer with booster training administered each year in an ongoing basis?). An understanding of changes that occur in the brain as a result of training (based on early work in this area) will undoubtedly help to address some of these issues and solidify approaches to cognitive training in the future. Finally, as more and more studies are done on clinical populations, it will be important for scientists to work with physicians and other health professionals to educate and have them assess the everyday abilities of older adults (through performance-based tests as well as self-report and proxy report from family members), and to assist in clinical trials evaluating the impact of interventions on their patients' health and well-being.

Authors' Note

Karlene Ball owns stock in the Visual Awareness Research Group (formerly Visual Awareness, Inc.) and Posit Science, Inc., the companies that market the Useful Field of View Test and speed of processing training software. Posit Science acquired Visual Awareness, and Dr. Ball continues to collaborate on the design and testing of these assessment and training programs as a member of the Posit Science Scientific Advisory Board.

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CHAPTER 15

Everyday Functioning in Alzheimer's Disease and Mild Cognitive Impairment

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Alzheimer's disease (AD) is the leading cause of dementia, and dementia is one of the leading causes of impairment in everyday functions. The most recent estimates reported by the Alzheimer's Association indicate that 5.8 million Americans age 65 and older (about 10%) are living with AD (Alzheimer's disease facts and figures, 2020). Without significant breakthroughs in treatment and prevention, an estimated 13.8 million Americans age 65 or older will have AD by 2050 (Alzheimer's disease facts and figures, 2020). The most significant risk factor for AD is age. As a result of advances in other areas of medicine which have helped to extend life expectancy, the number of adults over the age of 80 is expected to approximately double between 2020 and 2050.

Over the past two decades, AD research and clinical management have undergone a paradigm shift to a focus on early detection and intervention, as well as a description of preclinical AD. This has placed an increased importance on the development of tools to assess the earliest changes in cognition that may herald later changes in everyday functions. Dementia due to AD has long been associated with changes in numerous functional areas, including driving, medication management, and other basic and instrumental activities of daily living. Even as the clinical focus shifts earlier in the disease continuum, identifying changes in the manner in which activities of daily living are managed will always be a crucial element of AD clinical assessment. Functional decline occurs with an insidious onset, threatens the safety of patients, and contributes substantially to the public health burden of the disease, given the duration of time individuals with AD spend in a state of dependence or disability.

AD as a Pathological and Clinical Entity

Formal diagnosis of AD has always relied on neuropathological examination. Alzheimer's neuropathological changes are lesions formed by amyloid plaques and tau neurofibrillary tangles (Hyman et al., 2012). These abnormal protein deposits tend to accumulate in a consistent pattern (Braak, Alafuzoff, Arzberger, Kretzschmar, & Del Tredici, 2006). Historically, these proteinopathies were only detected postmortem, but advancements in clinical research tools have brought living biomarker-based diagnosis to the forefront. Now, a biomarker-based definition of AD has become the leading, albeit controversial, model in research on the disease. Briefly, the National Institute on Aging-Alzheimer's Association (NIA-AA) research framework entails the following components (Jack et al., 2018). First, AD can be defined biologically without reference to a cognitive/ behavioral phenotype. Second, its core diagnostic features can be detected in living people. Third, its signature comprises the presence of aggregated beta amyloid (A), aggregated tau (T), and neurodegeneration (N); the first two are relatively specific to AD, and the third is nonspecific. Pathologic cutoffs for biomarkers continue to be optimized as measurement techniques improve (Bullich et al., 2017). The resultant binarized AT(N) framework provides for eight distinct biomarker profiles, some of which are considered Alzheimer's disease (e.g., A+T+N-) and others of which are considered non-Alzheimer's pathologic change (A-T+N+). The primary tools for measuring pathologic amyloid and tau are positron emission tomography (PET) imaging and cerebrospinal fluid analysis. Accumulation of amyloid plaques, not tau neurofibrillary tangles, occurs early in the course of AD (Tiraboschi, Hansen, Thal, & Corey-Bloom, 2004). Tau neurofibrillary tangles appear to be the major determinants of cognitive decline after the early stages of dementia (Tiraboschi et al., 2004).

One clear limitation of a biomarker-based definition of AD is that it omits clinical phenotypic information, including cognitive decline and functional decline. Individuals with positive biomarker profiles may or may not have cognitive decline and functional decline. As the principal theme of this volume is functional status, we emphasize that, within the NIA-AA 2018 research framework, a biomarker-based diagnosis of Alzheimer's disease does not provide information about a patient's functional status. Clinical assessment is therefore all the more critical.

There continues to be significant research into the causes of AD. The predominant theory in pharmaceutical research has been the amyloid cascade hypothesis, which suggests that there is an imbalance between the production and clearance of Aβ in the brain, which is the initiating event that leads to neuronal degeneration and dementia (Hardy & Selkoe, 2002). Additionally, given the relationship between cerebrovascular disease and AD, there has long been a suggestion that neurovascular dysfunction contributes to the decline in AD. The neurovascular hypothesis states that dysfunctional blood vessels may contribute to cognitive dysfunction by impairing delivery of nutrients to neurons and reducing Aβ clearance from the brain (Iadecola, 2004). More recent work has built upon this foundation to suggest that vascular disease, as indexed by chronic accumulation of small vessel ischemic changes, independently predicts diagnosis of AD (Brickman et al., 2012). Some research has suggested that, rather than tau and Aβ being precursors to neuronal degeneration and dementia in the brain, they are a by-product of an earlier pathological event. Oxidative stress causes the buildup of oxidative molecular damage and may contribute to AD (Tonnies & Trushina, 2017). Inflammation also may be a core mechanism of AD, wherein chronically activated microglia cause neuronal damage (Kinney et al., 2018).

The genetic underpinnings of the disease are multifactorial in most cases. The gene that appears to confer the greatest variance in risk for sporadic AD is *ApoE* (Sims, Hill, & Williams, 2020). Individuals with at least one ε4 allele of *ApoE* are at higher risk of developing AD than those with any combination of ε2 and ε3 alleles only (Liu, Liu, Kanekiyo, Xu, & Bu, 2013). Each copy of ε4 has been shown to lower the age of onset by almost 10 years (Corder et al., 1993). In rare cases, AD is inherited in an autosomal dominant pattern. The prevalence of dominantly inherited AD is below 0.1% (Harvey, Skelton-Robinson, & Rossor, 2003). This form of AD typically results in early onset with symptoms appearing as early as the third decade of life. It is caused by mutations in several genes linked to Aβ metabolism: *PSEN1, PSEN2,* and *APP.*

Diagnostic Criteria for Dementia and Major Neurocognitive Disorder Due to AD

The criteria for all-cause dementia are described in the 2011 revision of the NIA-AA diagnostic guidelines for AD (McKhann et al., 2011). Diagnosis of dementia, as described therein, entails the presence of cognitive or behavioral symptoms from two or more domains that represent a change from previous functioning, are not explained by delirium or a psychiatric disorder, and are documented through clinical interviewing and objective cognitive assessment. Critically, the changes must interfere with the ability to function in usual activities. With the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) came changes in the diagnostic frameworks of many disorders, including the neurocognitive disorders (American Psychiatric Association, 2013). Major neurocognitive disorder took the place of dementia as the term describing the presence of both cognitive decline and reduced independence in everyday activities. Despite the change in name, the criteria were essentially unchanged.

Once the NIA-AA 2011 clinical criteria for dementia are met, additional criteria are applied to determine whether the dementia is due to *probable* or *possible* AD. *Probable* AD entails insidious onset, progressive course, and exclusion of core features of other neurologic diseases. The amnestic presentation must have initial or most prominent cognitive deficits in learning and memory. The less common nonamnestic presentations must have initial or most prominent cognitive deficits in their respective domains (e.g., executive dysfunction in frontal predominant AD). An increased level of certainty for probable AD is applied to cases with a documented causative genetic mutation or a documented clinical decline over serial evaluations. The NIA-AA 2011 criteria offer two scenarios for a diagnosis of dementia due to *possible* AD. The first scenario is a clinical presentation with a course that is not clearly characterized by insidious onset and gradual progressive course. The second scenario is a clinical presentation with evidence of mixed etiology. The DSM-5 took a similar approach to the description of major neurocognitive disorder due to *probable* and *possible* Alzheimer's disease.

Diagnostic Criteria for MCI and Mild Neurocognitive Disorder Due to AD

Mild cognitive impairment (MCI) is a diagnostic entity that was formulated to capture cognitive impairments that are detectable on exam but have not yet prohibited independence in daily functioning. One clinical purpose of the specification of this category was to improve early detection of dementia (major neurocognitive disorder) due to Alzheimer's disease. A 2011 NIA-AA workgroup formalized the MCI diagnosis based on the prior decade of research on this topic (Albert et al., 2011). Diagnostic criteria include a concern regarding change in cognition (self-report, informant report, or clinician observation); evidence of performance below expectations in one or more cognitive domains; maintenance of independence in activities of daily living; and absence of dementia. Just as major neurocognitive disorder represents the DSM-5 formulation of dementia, mild neurocognitive disorder represents the DSM-5 formulation of MCI. Typically, when MCI or mild neurocognitive disorder is attributed to possible AD, the cognitive decline is observed in episodic memory (Albert et al., 2011).

Conversion from MCI to Dementia Due to AD

Researchers have become increasingly concerned about how to diagnose and treat AD early to prevent symptoms altogether, or at least delay or halt progression. Doing so would result in massive reductions in disability and health care costs. Studies have shown that individuals with MCI are at increased risk for development of dementia. Three-year conversion rates of elderly with MCI at baseline range from 27 to 46% (Ganguli, Dodge, Shen, & DeKosky, 2004; Tschanz et al., 2006), as compared to a rate of 3.3% of elderly without cognitive impairment converting in the same 3-year period (Tschanz et al., 2006). It is likely that patients with the amnestic subtype of MCI will progress to dementia due to AD, while those diagnosed with nonamnestic MCI more likely reflect other etiologies such as vascular dementia or "normal aging" (Levey, Lah, Goldstein, Steenland, & Bliwise, 2006; Portet et al., 2006). Greater than 50% of individuals with amnestic MCI have been shown to develop dementia within 3 years (Busse, Bischkopf, Riedel-Heller, & Angermeyer, 2003). Compared to a clinical diagnostic approach that makes minimal use of formal neuropsychological instruments, the use of actuarial neuropsychological criteria facilitates improved prediction of conversion to dementia over conventional MCI criteria (Bondi et al., 2014). Actuarial neuropsychological criteria also reduce the reversion from MCI diagnosis to normal cognition (i.e., false positives), a phenomenon more commonly observed in longitudinal studies that rely on impairment on a single memory test to define MCI (Bondi et al., 2014). The Jak/Bondi criteria for MCI (Jak et al., 2009) require that at least two scores within a cognitive domain fall at least one standard deviation below normative expectations. Improvement in prediction of future clinical status facilitates prediction of future functional status, as those with MCI are at risk for declining independence.

Clinical Assessment of AD

Memory clinics commonly employ a multidisciplinary approach to dementia diagnosis. A neurologist or other physician will collect a medical history and conduct physical and neurological examinations. The neurologic exam is often normal in the early stages of AD but is often abnormal in the early stages in other dementias, such as movement disorders (e.g., Parkinson's disease) and cerebrovascular disease. The physician will usually order laboratory tests such as B12, folate, RPR, liver function tests, and thyroid panels to identify treatable medical conditions that may be contributing to cognitive change. A computed tomography (CT) or magnetic resonance imaging (MRI) scan will usually be ordered to rule out a structural lesion (e.g. brain tumor, stroke) and to assess the localization and severity of cerebral atrophy. If the dementia is not too severe at presentation, a neuropsychologist will conduct an assessment. Neuropsychological assessment can be helpful in early detection of cognitive deficits, differential diagnosis, and tracking of changes over time in response to treatment or progression of disease. The neuropsychological battery should, at a minimum, assess episodic memory, orientation, naming, executive functions, and visuospatial functions to capture early cognitive changes, but other cognitive domains are measured as well. Ratings scales completed by collateral reporters measuring neuropsychiatric problems (Cummings et al., 1994; Grace & Malloy, 2001) and activities of daily living can also be useful diagnostic tools. Questionnaires of functional status in older adults include the Lawton-Brody Activities of Daily Living Scale (Lawton & Brody, 1969) and the Alzheimer's Disease Cooperative Study Activities of Daily Living Scale (Galasko et al., 1997). As will be discussed below, noncognitive problems are often important determinants of real-world functioning in people with dementia.

Neuropsychological Testing for AD

Individuals with AD generally show rapid forgetting on delayed memory tasks (Braaten, Parsons, McCue, Sellers, & Burns, 2006), resulting from decreased consolidation of both verbal and visual information (Kramer et al., 2003). The pattern of memory deficits can also differentiate AD from other dementias. Individuals with AD have more susceptibility to distractors in visual search tasks and experience more difficulty with dual-task performance (Baddeley, Baddeley, Bucks, & Wilcock, 2001). Deficits in semantic, or category, fluency tasks are evident early on in the disease process, especially when compared with performance on phonemic, or letter, fluency tasks (Greenaway et al., 2006; Murphy, Rich, & Troyer, 2006; Rascovsky, Salmon, Hansen, Thal, & Galasko, 2007). Again, this marked difference between semantic and phonemic fluency, with worse performance on semantic fluency tasks, can be used to differentiate AD from other dementias. In comparison, individuals with frontotemporal dementia (FTD) are more likely to demonstrate increased impairment on phonemic, as compared to semantic fluency, or similar impairment on both tasks (Rascovsky et al., 2007). Another prominent deficit in AD is in confrontation naming (Braaten et al., 2006; Greenaway et al., 2006), and individuals with AD may present early on with complaints of difficulties in word finding. However, individuals with semantic dementia may perform worse than individuals with AD on naming, and deficits on this task alone (as with any neuropsychological task) are not sufficient to diagnose a specific disease process (Kramer et al., 2003). Visuospatial problems are also common in AD. Deficits may be on construction tasks (Malloy, Belanger, Hall, Aloia, & Salloway, 2003), visual perception tasks (Ska, Poissant, & Joanette, 1990), or visual spatial organization (Greenaway et al., 2006). Deficits on tasks in this domain may contribute to difficulties in real-world functioning, such as driving (Uc, Rizzo, Anderson, Shi, & Dawson, 2005).

Neuroimaging in AD

Individuals with amnestic MCI display significant hippocampal atrophy on CT or MRI early in the disease process (Becker et al., 2006), but with less severity than that shown in later AD. Quantified structural neuroimaging has shown greater gray matter loss in converters to dementia relative to nonconverters in the hippocampal area, inferior and middle temporal gyrus, posterior cingulate, and precuneus (Chételat et al., 2005). Longitudinal studies of hippocampal volume show accelerated volume loss in this region in MCI individuals who convert to AD (Chincarini et al., 2016). Volume loss in the medial temporal lobe has been shown to be the most sensitive measure to identify AD (Zakzanis, Graham, & Campbell, 2003). Fluorodeoxyglucose (FDG) PET shows a typical pattern of bilateral hypometabolism in the parietotemporal, posterior cingulate, and hippocampal regions; in MCI, hypometabolism is observed primarily in the latter two regions (Mosconi et al., 2008). With the development of new radiotracers for AD biomarkers, amyloid PET and tau PET have been added to the diagnostic imaging toolkit, particularly for research applications. Amyloid PET imaging has about 90% sensitivity in differentiating AD from controls and about 84% specificity (Morris et al., 2016). Tau PET is a newer tool; the first FDA-approved radiotracer to detect tau was approved by the FDA in 2020, and there is evidence documenting good fidelity to neurodegenerative and clinical changes (Ossenkoppele et al., 2016).

Rating Scales

Most clinical trials for dementia have two primary outcome measures: an experienced clinician rating of functioning using a structured interview, and one or more neuropsychological tests. Some clinician ratings measure severity and others measure change. The scales that have been most commonly used include: the Clinical Dementia Rating (CDR) and the related CDR-sum of boxes (CDR-SB), the Global Deterioration Scale (GDS), the Functional Assessment Staging (FAST) procedure, Clinical Global Impressions of Change (CGIC) and Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-Plus; Reisberg, 2007).

The CDR, for example, is a structured interview that is rated on a five-point scale ranging from "no cognitive impairment" to "severe dementia" (Morris, 1993, 1997). The global score is derived from individual scores in six domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Information is collected from both a collateral source and the presenting patient, and level of ability is rated for each domain. Accurate ratings, particularly in the domains of community affairs, home and hobbies, and personal care, rely heavily on thorough assessment of change from previous level of everyday functioning. The clinical interviewer aims to identify both subtle and overt changes that may indicate a pattern of reduced independence due to cognitive decline. Individuals using the CDR should be trained according to a specific protocol, in order to increase reliability, but some subjectivity is unavoidable.

Activities of Daily Living

Basic activities of daily living (ADLs) include such self-care behaviors as grooming and bathing. Instrumental ADLs include more complex interactions with the environment such as cooking, bill paying, and medication management. These behaviors can be evaluated by direct observation or via informant ratings scales. It might be argued that observation in a standard environment is the superior method in that it is not subject to caregiver biases. However, the advantage of informant ratings is that they take into consideration performance over an extended period in the relatively unstructured home environment.

In the home, the patient often needs to initiate and organize an activity, unlike the case in the laboratory situation where the materials may be laid out and tasks prompted by the examiner. As will be discussed, deficits in executive functioning, including initiation, are what often cause ADL failures.

With regard to cognition, research has demonstrated that moderate dementia (a Mini Mental Status Examination [MMSE] score of 16 or below) seems to be a point at which most instrumental ADLs are lost, and many basic ADLs decline throughout the next year (Feldman, Van Baelen, Kavanagh, & Torfs, 2005). But it is common to observe some decline in instrumental ADLs in patients with milder cognitive impairment. It might be expected that memory dysfunction is the cause of failures in ADLs; indeed memory, and ADL deficits are related (Bombin et al., 2012; Farias et al., 2006). However, executive functioning has also been shown to be significantly related to performance on activities of daily living. Frontal lobe systems are disproportionately affected by aging, and this condition can result in deficits in planning, organization, self-control, and awareness of problems that affect the ability to care for one's self. In a study of community-dwelling individuals without dementia, executive function and depression severity accounted for a significant proportion of variance in instrumental ADLs, with executive function making the greatest contribution. Tests measuring other cognitive functions, such as memory, language, and spatial skills, did not contribute significantly to the prediction of functional status. Furthermore, executive measures accounted for more variance than other demographic characteristics such as general health status, age, and educational level (Cahn-Weiner, Boyle, & Malloy, 2002). In another study of patients with mild to moderate AD, frontal systems dysfunction accounted for 44% of the variance in instrumental ADLs and 28% of the variance in basic ADLs, independent of memory problems (Boyle et al., 2003). According to a meta-analysis of MCI studies, executive function measures explained the largest proportion of variance in functional status (McAlister, Schmitter-Edgecombe, & Lamb, 2016).

There is also a strong relationship between the presence of behavioral disturbance and poor performance of ADLs, especially instrumental ADLs, in dementia. Both MMSE scores and neuropsychiatric symptoms have been shown to be related to ADL performance (Tekin, Fairbanks, O'Connor, Rosenberg, & Cummings, 2001). Neuropsychiatric symptoms related to frontal lobe dysfunction (such as apathy and disinhibition) are particularly disruptive to ADLs. In fact, a stronger relationship has been found between ADL function and scores on the Frontal Systems Behavior Scale (FrSBe) than between ADLs and cognitive measures in dementia patients (Norton, Malloy, & Salloway, 2001). Behavioral disturbance also affects ADLs independent of cognitive deficits in AD (Boyle et al., 2003). In regard to the relationship between neuropathological changes and ADLs, a positive correlation exists between the total ADL scores and neuritic plaque and neurofibrillary tangle counts in AD patients (Sabbagh et al., 2010). ADLs do not correlate with age at death, age at symptom onset, dementia duration, gender, or education (Marshall, Fairbanks, Tekin, Vinters, & Cummings, 2006).

Instrumental ADLs

Driving

Changes in driving abilities reportedly begin early in MCI and worsen as illness severity increases (Davis & Ohman, 2017). Even in the preclinical phase of Alzheimer's disease, amyloid accumulation is related to self-reported driving errors (Ott et al., 2017). Review of research based on crash statistics, performance studies of drivers with AD, and testing of components of the driving test has shown mild driving impairment in individuals with probable AD (Clinical Dementia Rating = 0.5), similar to drivers aged 16–19 years, and those with blood alcohol concentration less than 0.08% (Dubinsky, Stein, & Lyons, 2000). As dementia severity increases (drivers with a Clinical Dementia Rating Scale equal to one [mild dementia]), a more significant problem arises with regard to crashes and driving performance measures (Dubinsky et al., 2000). Put another way, in the first year after diagnosis, individuals with AD have a similar rate of crashes as drivers of all ages, but higher than age-matched controls (Drachman & Swearer, 1993). But the risk of crashes increases dramatically in the next few years. If patients with dementia continue to drive for 5 years, 47% will be involved in accidents as compared to 10% of healthy controls (Friedland et al., 1988). Patients with preclinical AD (biomarker measurement) are also at higher risk for a failed road test (Babulal et al., 2018; Roe et al., 2017, 2018) and earlier time to driving cessation (Stout et al., 2018); naturalistically, patients with preclinical AD travel to fewer places, take fewer trips, and travel fewer days than those without preclinical AD (Roe et al., 2019).

In one on-road driving study, drivers with mild AD identified fewer landmarks and traffic signs, and made more at-fault safety errors (i.e., erratic steering, lane deviation, unsafe intersection behavior) as compared to controls. Roadside target identification was predicted by scores on tests of visual abilities and cognitive functioning (executive, memory and spatial tasks). Safety errors were predicted by performance on memory and visual perception tasks (Uc et al., 2005). Other studies have shown operational/tactical driving errors, such as hesitant driving, diminished awareness of traffic environment, problems with changing lanes smoothly/lane positioning, scanning behaviors, and judgment errors such as making a turn onto a one-way street (Fuermaier et al., 2019; Grace et al., 2005).

In individuals with mild AD, unsafe drivers (as determined through an on-road driving test) were impaired across all neuropsychological measures (Hopkins Verbal Learning Test [HVLT], Rey–Osterrieth Complex Figure [ROCF], Neuropsychological Assessment Battery [NAB] driving scenes, Trail Making Test [TMT], computerized mazes), except for finger tapping (Grace et al., 2005). Spatial (ROCF) and executive functioning tasks (TMT-B) distinguished safe from unsafe drivers (Grace et al., 2005). Other research studies have also shown that driving abilities are related to nonverbal executive functioning skills (Porteus mazes, computerized mazes, clock drawing; (Unsworth, Russell, Lovell, Woodward, & Browne, 2019), as well as visual attention skills (Whelihan, DiCarlo, & Paul, 2005).

Clinicians are only fair in predicting actual driving performance using standard road testing. In individuals with very mild to mild dementia, clinician accuracy ranged from 62–78%, with dementia specialists ranging from 72 to 78% and general practitioners from 62–64% (Ott et al., 2005). Research has indicated that, although MMSE scores may predict poor driving abilities at the lower end (< 19), one-third of those with AD who scored above 24 failed an on-road driving test as well, indicating a need for comprehensive assessment of abilities (Piersma et al., 2018). A review of the literature has indicated that support groups directed at assisting with transitioning away from driving may be helpful; interventions should also be directed toward helping patients remain safe while driving (Davis & Ohman, 2017).

Medication Adherence

Elderly with cognitive impairment are at higher risk for nonadherence to a medication regimen (Cooper et al., 2005). In a study of 1107 community-dwelling elders, Ganguli and colleagues (2006) found that inadvertent medication nonadherence increased with dementia severity. The levels of discrepancy between information patients provided to their physicians and the information they provided in response to detailed, standardized assessments also varied with dementia severity. Clinicians should therefore be alert to the possibility of receiving unreliable health information from even mildly demented patients, as it can have serious consequences. Underuse of prescribed medications can exacerbate an underlying medical condition (e.g., hypothyroidism) or further brain damage (e.g., stroke in an untreated hypertensive). Overuse can precipitate a toxic confusional state, a common reason for hospitalization in the demented elderly. As medication management difficulties can be quite subtle in MCI compared to AD dementia, the use of process-oriented assessment can be illuminating. For example, Wadley, Okonkwo, Crowe, and Ross-Meadows (2008) found that individuals with MCI were slower but not less accurate than older adults with normal cognition in performing a set of instrumental ADL tasks, including medication management.

In other chronic illnesses, adherence interventions have included home visits (Johnson, Taylor, Sackett, Dunnett, & Shimiz, 1978), simplifying medication regimens (Girvin, McDermott, & Johnston, 1999), special medication containers (Rehder, McCoy, Blackwell, Whitehead, & Robinson, 1980), electronic alarm reminders (Safren, Hendriksen, Desousa, Boswell, & Mayer, 2003), telephone reminders (Friedman et al., 1996), and psychoeducation (Bailey et al., 1990). Home visits for medication compliance are often impractical for real-world application in dementia clinics. While simplifying medication regime would benefit individuals with dementia, this is not always possible, as many such patients have multiple medical conditions requiring concurrent treatment. For individuals with dementia, several studies have advised customizing treatment to meet patients' needs and cognitive capabilities (e.g., Cohen-Mansfield, 2001; Gerdner, 2000). Thus, interventions to improve medication adherence in dementia patients are more likely to be successful if they focus on environmental modifications and mnemonic aids, rather than focusing on the patient's skills and knowledge. A multifaceted intervention utilizing an electronic reminder system, transdermal medication delivery, special medication containers, structuring of the home environment, and psychoeducation for caregivers is likely to be most helpful.

Financial Management

The unique risks of financial errors, particularly in late life, make the domain of financial management an area of grave concern across the AD spectrum. Performance-based measures of financial ability, including the Financial Capacity Instrument (FCI), are employed to assess this domain of everyday function. Marson et al.'s (2000) early work with the FCI showed that people with mild AD performed worse than cognitively intact older adults on more complex tasks (e.g., checkbook management) but performed normally on more basic tasks (e.g., counting currency). In comparison to demographically matched controls, individuals with AD who had mild to moderate levels of dementia performed worse in all areas of financial management on the FCI (Earnst et al., 2001). In individuals with AD in that study, basic monetary skills (naming and counting money), checkbook management, bank statement management, and bill payment were all correlated with working memory performance (Earnst et al., 2001). According to a 2017 meta-analysis, elder financial fraud affects at least 5% of cognitively intact, community-dwelling older adults annually (Burnes et al., 2017). Older adults with cognitive deficits may be at greater risk of financial exploitation. Indeed, in Earnst et al.'s (2001) study, financial judgment related to mail and telephone fraud was reduced in the AD group.

The financial management abilities of people on the AD spectrum without dementia are also of significant clinical interest. Research participants without a dementia diagnosis but with amnestic MCI possibly due to AD underperformed on aspects of financial abilities compared to unimpaired older adults; these deficits were observed in the areas of financial conceptual knowledge, bank statement management, and bill payment (Griffith et al., 2003). The magnitude of the overall deficit was equal to 1.7 standard deviation units. This suggests that financial abilities may degrade in a manner that evades detection, with a greater degree of performance change required before self-report or collateral-report of functional impairment emerges. Okonkwo, Wadley, Griffith, Ball, and Marson (2006) found that people with MCI were slower and more likely to commit errors on a multistep financial task. Despite the fact that most of their MCI sample had a diagnosis of amnestic MCI, their financial performances were correlated with attention and executive functions, rather than memory, echoing the aforementioned working memory correlation in AD by Earnst et al. (2001). Perhaps not surprisingly, there can be a substantial difference between subjective and objective indicators of performance on financial tasks. Individuals with MCI show reduced insight into their own financial abilities, as indexed by the split between subjective and objective indicators (Okonkwo et al., 2008).

Preliminary investigations of neuroanatomical correlates of financial capacity have uncovered relationships worthy of further investigation. In a small study of individuals with mild AD, medial frontal cortex volume accounted for about 34% of the variance in the FCI score (Stoeckel et al., 2013). Stoeckel and colleagues (2013) also showed that formal measures of attention partially mediated the relationship between medial frontal cortex volume and FCI score. Gerstenecker, Hoagey, Marson, and Kennedy (2017) studied anatomical changes in white matter tracts as they pertain to financial capacity in people with mild cognitive impairment and mild AD. Relative to healthy older adults, the MCI group showed a correlation between FCI score and fractional anisotropy, a measure of white matter integrity or coherence, in a number of tracts. The mild AD group showed an inverse relationship between FCI score and mean diffusivity along tracts predominantly in the anterior portion of the brain. These studies begin to elucidate the neurobiological mechanisms underlying reductions in financial capacity in AD.

Basic ADLs

Although subtle failures in instrumental ADLs are observed in individuals with MCI, failures in basic ADLs are much less common in MCI. As MCI progresses through mild dementia into the moderate dementia range, basic ADLs tend to decline. Many patients and families express curiosity about staging within the AD spectrum, and the progression of deterioration of ADLs can serve as a useful frame of reference in clinical feedback.

Falls

Researchers have predicted that three quarters of older people with cognitive impairment and dementia may fall each year (Shaw et al., 2003). Individuals with AD have a higher frequency of falls than other elderly persons (Morris, Rubin, Morris, & Mandel, 1987), and the number increases with dementia severity (Ganguli et al., 2006). About 60% of individuals with dementia fall per year (Tinetti & Williams, 1998), and falls have been found to occur in 7.4% of community residing patients with AD studied for a 2-week period (Bassiony et al., 2004). Individuals with mild to moderate AD also have a faster rate of decline in balance, fall risk, and mobility compared to age-matched healthy controls (Suttanon, Hill, Said, & Dodd, 2013). Noncognitive changes that increase the likelihood of falls in older adults may precede cognitive changes and be indicative of preclinical AD (Stark et al., 2013). Consequences of falls can be significant, including loss of independence, worsening of mobility, fractures, and even death (Wilson, Schneider, Beckett, Evans, & Bennett, 2002).

Difficulties getting up from a chair, previous falls, needing a helper when walking, and hyperactive symptoms are risk factors for falls (Kallin, Gustafson, Sandman, & Karlsson, 2005; Perttila et al., 2017). Sedative/opioid use, higher number of medications, drugs with anticholinergic properties, and some chronic medical conditions (e.g., osteoarthritis, diabetes) may be associated with a higher risk of falling (Perttila et al., 2017; Tinetti & Williams, 1998). Other risk factors have included male gender, stumbling/slipping, and gait and equilibrium disturbances, including vestibular deficits (Nakamagoe et al., 2015; Perttila et al., 2017; van Dijk, Meulenberg, van de Sande, & Habbema, 1993). A more recent study indicated that lower functional status, higher depressive symptom scores, and higher time on walk and dual task tests were associated with falls in MCI; in mild AD, lower time on a walk test and a turn to sit phase, and a higher visuospatial domain score were associated with falls (Ansai et al., 2019). Slow gait speed has also been shown to predict later falls in mild to moderate AD (Dyer, Lawlor, & Kennelly, 2020). In addition, caregiver burden may be related to incidence of falls (Maggio et al., 2010). Protective factors against falls have included good nutritional status and good physical functioning (Perttila et al., 2017). Those without falls often tend to be younger, with better cognitive functioning (Perttila et al., 2017).

Living Alone/Wandering

Individuals with cognitive impairment are at higher risk for harm due to wandering, which often occurs due to disorientation or confusion (Tierney et al., 2004). Critical wandering has been defined as anyone who wanders away from supervised care, lives in a controlled environment, or cannot be located (Butler & Barnett, 1991). The Alzheimer's Association estimates that 60% of people with AD will wander and become lost in the community at some point (Rowe, 2003; Rowe & Bennett, 2003). These incidents may result in injury or even death (hypothermia, drowning, dehydration; Byard & Langlois, 2019; Rowe & Bennett, 2003). In Virginia, for example, 16% of lost person cases reported to Search and Rescue (SAR) were individuals with AD, second in rate only to lost children. Extrapolating from previous research, authors estimated that over 125,000 critical wandering incidents occur every year in individuals with AD. To reduce wandering, recommendations have included that caregivers should use behavioral measures (recognition that changes in schedule or being left alone may trigger wandering), make environmental modifications (keep them oriented, design an interesting walking path), and control the exits (lock windows, gait stairs; "Alzheimer's Disease and Related Disorders SAR Research: Alzheimer's Overview," 2000–2007). More novel tracking devices have been developed, including wearable global positioning system (GPS) devices and temporary barcodes worn on the body. However, these devices raise the issue of the ethics of patient privacy, and patients should consent to their use (Landau & Werner, 2012; Mangini & Wick, 2017).

Caregiver Burden

As the severity of dementia progresses, caregivers of the individual with dementia must increase the amount of support for their loved one. Not unexpectedly, the demands placed on the caregiver may lead to an increase in emotional, physical, and financial stress. Up to 68% of caregivers have been shown to be highly burdened, with no difference between individuals with dementia who were institutionalized and those living in the community (Papastavrou, Kalokerinou, Papacostas, Tsangari, & Sourtzi, 2007). Studies have shown an increase in caregiver burden over time, with one study indicating that 47.4% of caregivers had significant burden at baseline, increasing to 56.8% at 3 years (Connors et al., 2020). However, this increase in burden was specific to those families without services. Caregivers show an increase in symptoms of depression (Manzini & do Vale, 2020; Papastavrou et al., 2007; Sink, Covinsky, Barnes, Newcomer, & Yaffe, 2006), and severe depression appears to get even worse as dementia progresses (Berger et al., 2005). The majority of dementia caregivers—an estimated almost three quarters of all caregivers—are women (Ory, Hoffman, Yee, Tennstedt, & Schulz, 1999). Women tend to show a higher level of burden, including higher levels of depression, as compared to men (Connors et al., 2020; Gallicchio, Siddiqi, Langenberg, & Baumgarten, 2002; Papastavrou et al., 2007; Thompson et al., 2004). Although there may be gender biases in reporting mental health symptoms (World Health Organization, 2002), as in other disorders, other factors may be influencing this increased burden for women as compared to men, such as the manner in which women and men cope with the increased stress (Thompson et al., 2004).

Sources of caregiver burden include (1) patient variables, such as severity and duration of the dementia, patient psychopathology, behavior problems, patient frailty, and ADL limitations; (2) caregiver variables, such as age and health of caregiver, level of education, gender, caregiver's time demands, religious beliefs, problem-solving skills, and perception of disease; and (3) environmental variables, such as financial resources, social support, and the quality of their prior relationship with the care recipient (Isik, Soysal, Solmi, & Veronese, 2019; Liao et al., 2020; Papastavrou et al., 2007; Rymer et al., 2002; Sugimoto et al., 2018).

With regard to cognitive deficits in the care recipient, only minimal research has thoroughly examined the relationship between patient cognitive deficit and caregiver burden. Many studies have not demonstrated that measures of general cognitive status alone predict burden (Coen, Swanwick, O'Boyle, & Coakley, 1997), although the severity of the dementia overall may show a relationship with caregiver burden (Donaldson, Tarrier, & Burns, 1998). Other research has indicated that the care recipient's perception of memory deficits is associated with level of caregiver burden (Rymer et al., 2002).

Over and above cognitive deficits, associated neuropsychiatric symptoms in the patient add significantly to caregiver burden (Connors et al., 2020; Isik et al., 2019; Liao et al., 2020; Mavounza, Ouellet, & Hudon, 2020; Reed et al., 2020). Disinhibition and apathy in the individual with dementia are particularly troublesome problems for caregivers (Boyle et al., 2003; Davis & Tremont, 2007; Rymer et al., 2002). Increased caregiver burden may also worsen the relationship between patient and caregiver, leading to further neuropsychiatric symptoms (Isik et al., 2019). With regard to institutionalization, caregivers with a high desire to institutionalize may have greater dementia knowledge, but also have higher burden, more family dysfunction, and decreased social support (Spitznagel, Tremont, Davis, & Foster, 2006). Less burdened relatives tend to use more problem-solving approaches to cope with the increased demands. Greater social supports and high premorbid relationship satisfaction with the care recipient have been shown to decrease level of burden, as well as reactivity to memory and behavior problems (Steadman, Tremont, & Davis, 2007; Yu, Wang, He, Liang, & Zhou, 2015). Psychoeducational support and/or comprehensive dementia care may be helpful in decreasing level of burden in caregivers (Reuben et al., 2019; Terracciano et al., 2020). Taking into account all of these factors is especially important in providing supports for these caregivers within the community.

Guidance for Clinicians

Deficits in everyday functions are direct consequences of cognitive decline in AD and its clinical precursor, MCI. Although disruption to functional status is, by definition, more subtle in MCI, accurate assessment of functional status is critical to the diagnosis of neurodegenerative conditions. The loss of episodic memory certainly confers risk for decline in activities of daily living, but it is important for clinicians to keep in mind that a strong relationship exists between performance on neuropsychological tests of executive functions and functional status as well. It is not uncommon to see patients whose memory impairment seems milder than expected given the degree of functional impairment, and this can sometimes be attributed to more severe executive dysfunction. Accurate diagnosis of MCI with the use of neuropsychological evaluation improves diagnostic stability and prediction of future progression. In the field of neurodegenerative disease, where treatments fall far short of desirable outcomes, one of the most powerful tools the clinician wields is facilitation of targeted future planning. With improved diagnostic accuracy, the clinician can discuss the prognosis of everyday functions and help patients and their support systems make arrangements to reduce the potential consequences of progressive decline. Problems in the areas of financial management, medication management, and driving are often encountered first. These require early attention, with gradually increased supervision that respects the needs for safety and autonomy. Later in the progression of AD, patients experience changes in more fundamental aspects of everyday functioning; falls and wandering, linked to reductions in balance and orientation, have received the most research attention. Environmental adaptations and technology can help improve safety in these areas. The challenge placed on caregivers constitutes a parallel public health crisis that deserves a high degree of clinician attention. Although many factors relate to caregiver burden, patient limitations in everyday functions constitute a primary contributor.

Summary

As the world population ages, AD is becoming an increasing public health crisis. AD is the most common cause of dementia, and although we have learned much about the risk factors and putative molecular mechanisms of the disease, to date no cure has been found. Patients with dementia (and even mild cognitive impairment) display progressive deficits in ADLs that are caused by both decline in cognition and increases in behavioral problems. Dementia is also associated with increased risk of falls, wandering and automobile accidents, and medication errors that may be fatal to the patient. Interventions focusing on modifying the environment, providing mnemonic aids, and assisting caregivers are likely to be most helpful in reducing real-world problems in patients with dementia.

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CHAPTER 16

Everyday Functioning in Vascular Cognitive Impairment

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The human brain is perfused by nearly 400 miles of blood vessels that stem from either the internal carotid artery (anterior circulation) or the vertebral artery (posterior circulation). Transient or permanent restriction of oxygen and metabolic exchange in a main source or distal branch of this system can produce a wide range of symptoms based on the affected cerebral circuitry. Theoretically, an individual with a small stroke (< 5 mm) in the association cortex would experience no discernible symptoms (historically referenced as "silent stroke"), whereas the same event in Broca's area, the hippocampus, or other critical neural hub would produce substantial impairment in cognitive function and ability to complete activities of daily living (ADLs).

Existing diagnostic criteria for vascular cognitive impairment (VCI), as well as all other acquired neurocognitive disorders, are based on the underlying premise that incident brain injury produces cognitive impairment, which in turn disrupts an individual's ability to perform basic and/or instrumental ADLs (American Psychiatric Association, 2013; Skrobot et al., 2018). In practice, establishing clear associations between neuroimaging, neurocognitive impairment, and ADL disruption is not straightforward. This is particularly true when considering the impact of vascular injury on ADL function. While there is consensus regarding best practices for neuroimaging and neurocognitive assessment of cerebrovascular injury, no agreement has been reached on best practices for ascertainment of ADL disruption (Fieo et al., 2018; Sikkes & Rotrou, 2014). This is quite remarkable given that ADL function differentiates Mild from Major VCI according to the updated diagnostic guidelines (Skrobot et al., 2018); this scheme also defines the critical difference between mild and major neurocognitive disorder defined by the fifth edition of the *Diagnostic and Statistical Manual of Manual Disorders* (DSM-5; American Psychiatric Association, 2013).

This chapter provides a critical review of the empirical literature related to ADL disruption in the context of VCI. We begin with a review of the revised diagnostic criteria for mild and major VCI, followed by a synopsis of the neurocognitive and neuroimaging signatures of ADL disruption. We then review methods of ADL assessment and discuss challenges with existing protocols related to sociocultural biases embedded in test content and norming procedures that inflate ADL impairment among ethnically diverse individuals. We conclude with opportunities for new research using data-driven models. Recommendations are discussed for catalyzing innovative research aimed at improving the identification, characterization, and prediction of ADL disruption associated with VCI.

Revised Diagnostic Criteria for VCI

In 2015, a multinational panel of clinical and research scientists was convened to update the nomenclature, diagnostic criteria, and assessment protocol for VCI. Referred to as the Vascular Impairment of Cognition Classification Consensus Study (VICCCS), the outcomes are documented in publications by Skrobot et al. (2018) and reviewed in detail by Iadecola et al. (2019) and Sachdev et al. (2019). The VICCCS guidelines replace older diagnostic schemes for VCI such as the State of California Alzheimer's Disease Diagnostic and Treatment Centers (Chui et al., 1992) and the National Institute of Neurological Disorders and Stroke—Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria (NINDS-AIREN; see Roman, 2005), both of which leaned too heavily on diagnostic symptoms of Alzheimer's disease (AD).

The revised guidelines for VCI were developed in parallel to the revision of the DSM-IV to the current DSM-5 (American Psychiatric Association, 2013). As noted above, the VICCCS and the DSM-5 criteria differentiate "Mild" from "Major" VCI according to the degree of ADL disruption (Table 16.1). Yet, somewhat inexplicably, neither provides guidelines for the assessment of ADLs. The two nosologies differ in two important ways. First, the DSM-5 criteria require evidence of attention or executive impairment when a temporal association between symptom onset and neuroimaging markers cannot be established (Table 16.2). Second, the VICCS criteria, but not the DSM-5, differentiate between subtypes of Major VCI.

TABLE 16.1. VICCCS Criteria for Mild and Major VCI

Mild VCI: Impairment in at least one cognitive domain and mild to no impairment in ADLs
Major VCI (VaD): Clinically significant deficits in at least one cognitive domain and severe disruption to activities of daily living.
A diagnosis of "possible" is required in the absence of MRI confirmation of cerebrovascular disease.
Does not meet criteria for drug/alcohol abuse/dependence within 3 months of diagnosis.
Does not meet criteria for delirium.

TABLE 16.2. Neuropsychological Battery Assessment Protocol

Animal naming
Controlled Oral Word Association (letter fluency)
WAIS-III Digit Symbol—Coding
Trail Making Test
Hopkins Verbal Learning Test—Revised
Rey–Osterrieth Complex Figure Copy
Boston Naming Test, 2nd Edition, Short Form
Simple and Choice Reaction Time
Neuropsychiatric Inventory, Questionnaire Version
Center for Epidemiological Studies-Depression Scale (CES-D), Short Form
Mini-Mental State Examination (MMSE)

Subtypes of VCI

The VICCCS guidelines describe four subtypes of major VCI. Three of the four subtypes differ according to the number and anatomical distribution of cerebrovascular events; the fourth (i.e., mixed dementia) reflects the presence of co-occurring neuropathology consistent with AD. At present, the empirical literature has not established distinct subtypes of mild VCI. Future studies employing advanced neuroimaging and analytic strategies sensitive to nonlinear patterns embedded in complex clinical data hold promise in this area. Later sections of this chapter offer a glimpse into a few attractive methods. Here, we provide a synopsis of the four subtypes of major VCI.

Subcortical Ischemic Vascular Dementia

Subcortical ischemic vascular dementia (SIVD) is the most common subtype of major VCI (Sachdev, Lipnicki, Crawford, & Brodaty, 2019). This subtype typically results from cardiac emboli that occlude deep penetrating lenticulostriate arteries from the middle cerebral artery (MCA) to perfuse white matter and subcortical gray matter nuclei (Paciaroni et al., 2012). Neuroimaging markers of SIVD are seen in nearly all community-dwelling adults age 80 and over (De Leeuw et al., 2001). As such, a simple binary classification of SIVD (present/not present) cannot distinguish normative (i.e., age-related) cognitive performance from Mild VCI. Furthermore, the onset of cognitive and ADL disruption related to SIVD occurs slowly and progressively, which differs markedly from the clinical presentation typical of large vessel strokes (Iadecola et al., 2019; Jellinger et al., 2013; Paul et al., 2000). The insidious onset of SIVD also carries a similar clinical profile as early-stage AD, both of which are frequently characterized by a gradual worsening of mental abilities in older adults.

Poststroke Dementia and Multi-Infarct Dementia

The second most common subtype of Major VCI results from stroke in one or more large cortical arteries. As noted above, large cortical infarcts produce a sudden onset of symptoms and one or more classic phenotypes such as aphasia, apraxia, and agnosia (Skrobot et al., 2018). Nearly 50% of individuals who experience a large cortical stroke will eventually meet criteria for Major VCI within 12 months of symptom onset (Tsai et al., 2019). This is not surprising given that about half (51%) of all cortical strokes involve the MCA, which covers a massive region of the lateral cortical surface as well as deep brain regions. The unique vulnerability of the MCA to embolic infarction is due to the tortuous anatomical path after the vessel emerges from the Sylvian fissure.

Mixed Dementia

Most individuals with cerebrovascular disease exhibit neuropathological features of AD or other age-related neurodegenerative disorders at autopsy (Lee et al., 2016; Soldan et al., 2020). The co-occurrence is not surprising given that advanced age is the primary risk factor for both conditions. This does not mean, however, that VCI exists only in the context of AD. Cerebrovascular disease is likely a sentinel event for amyloid deposition and development of phosphorylated tau characteristic of AD. This is supported by studies demonstrating increased risk for AD neuropathology among individuals with a wide variety of neurologic etiologies (e.g., traumatic brain injury, multiple sclerosis; see Hicks, James, Spitz, & Ponsford, 2019; LoBue et al., 2017; Louveau, Da Mesquita, & Kipnis, 2016; Sweeny et al., 2019), as well as by studies describing a correspondence between increased burden of white matter hyperintensities (WMH) in posterior brain regions and AD severity (Brickman et al., 2008, 2015; Lee et al., 2016). In terms of ADL impairment, individuals with mixed dementia are more likely to exhibit significant disruption in both basic (i.e., bathing, dressing, grooming) and instrumental (i.e., driving, financial management, medication adherence) ADLs compared to VCI alone. The broader disruption in ADLs is proportional to the increased involvement of both posterior and anterior brain regions by AD and vascular pathology among those with dual diagnoses (Cahn-Weiner et al., 2007).

Neurocognitive Phenotype of VCI

The neurocognitive phenotype of VCI involves a disproportionate degree of impairment on tests of working memory, executive function, psychomotor speed, and learning efficiency (for review, see Skrobot et al., 2018). By contrast, less severe abnormalities are seen on tests of core components of the language network (basic expression, comprehension, and repetition) and memory consolidation. This presentation is consistent with the neuropathological and neuroimaging features of SIVD that disrupt frontal-subcortical brain networks. In terms of ADL disruption, individuals with VCI exhibit more severe disruption on instrumental ADLs (IADLs) compared to basic ADLs (BADLs), a difference explained by the early and consistent involvement of executive brain regions in VCI.

Neuroimaging Signatures of VCI

Neuroimaging is required for the diagnosis of VCI (Skrobot et al., 2018; Paul & Salminen, 2019; Sachdev et al., 2019). The sensitivity of neuroimaging to detect cerebrovascular disease is dependent on the magnetic field strength of the scanner, with detection increasing at higher field strengths (Theysohn et al., 2011). In 2013, a standardized nomenclature for neuroimaging markers of cerebrovascular disease was established, referred to as the Standards for ReportIng Vascular Changes on nEuroimaging (STRIVE), was established (Wardlaw et al., 2013). The nomenclature defines the following imaging features: (1) recent small subcortical infarcts, (2) lacunes of presumed vascular origin (3) white matter hyperintensities, (4) perivascular spaces, and (5) cerebral microinfarcts.

Recent Small Subcortical Infarcts

Recent small subcortical infarcts (RSSIs) represent occlusions in perforating arterioles that perfuse the white matter, basal ganglia, thalamus, and/or pons. By definition, RSSIs are visible on neuroimaging within the first weeks of onset (Fisher, 2011). RSSIs account for ~25% of all ischemic infarcts (Sacco et al., 2006). Longitudinal studies show that 30–90% of RSSIs evolve into cavities referred to as lacunes. On neuroimaging sequences designed to highlight areas of increased signal from water (e.g., T2, fluid attenuated inversion recovery sequences; FLAIR; Wardlaw et al., 2013), RSSIs are visualized as small WMHs. Recent work suggests that RSSIs from the anterior circulation system are most prevalent among individuals with hypertension, whereas RSSIs from the posterior circulation are more frequently seen in individuals with diabetes (Eppinger et al., 2019). In a longitudinal study of 74 older adults with RSSIs, 61 participants (78%) showed evidence of cavitation, and all but a few cases showed WMHs on neuroimaging (Pinter et al., 2019).

Lacunes of Presumed Vascular Origin

Lacunes of presumed vascular origin are fluid-filled cavities in the brain that typically measure between 3–15 mm in diameter. Although previously thought to exclusively result from small subcortical lacunar infarcts, lacunes of presumed vascular origin may also result from small hemorrhages, microembolisms, and amyloid angiopathy (Wardlaw, Smith, & Dichgans, 2013). The location of the lesion is an important predictor of clinical symptomatology and an indicator of disease etiology. For example, lacunes that occur in deep white matter often do not render overt clinical symptoms and are believed to result from arteriosclerosis, endothelial dysfunction, and chronic ischemia (Wardlaw, Sandercock, & Dennis, 2003). Conversely, lacunes that occur in the basal ganglia often lead to pure motor or sensory stroke and are believed to result from thrombo-embolic occlusion of the perforating arteries (Wardlaw, Smith, & Dichgans, 2013). On MRI with fluid attenuated inversion recovery (FLAIR), lacunes of presumed vascular origin often appear as hypointense cavities with a hyperintense rim, but other variations of signal intensity have also been reported (Moreau, Patel, & Lauzon, 2012).

White Matter Hyperintensities

White matter hyperintensities (WMHs) are a hallmark neuroimaging signature of cerebrovascular disease (Paul & Salminen, 2019; Soderlund et al., 2003). Periventricular WMHs that are located confluent with the horns of the lateral ventricles appear as "caps" or "halos" of bright white signals and are believed to reflect "asymptomatic" aspects of normative aging (Murray et al., 2012). By contrast, WMHs that appear as isolated signals in deep white matter have a more sinister etiology and represent harbingers of future cerebrovascular events. Quantification of WMH burden in research is accomplished, most commonly, using automated or semiautomated computational algorithms. By contrast, visual rating scales are utilized in clinical practice. The VICCS guidelines recommend using the 4-point Age-Related White Matter Changes (ARWMC) scale (Wahlund et al., 2001) as the optimal and preferred method, with the Cardiovascular Health Study rating scale (Yue et al., 1997) serving as an acceptable alternative (Skrobot et al., 2018).

Recently, Jokinen et al. (2020) used a machine learning approach (i.e., a three-dimensional convolutional neural network [CNN]) to segment region-specific WMHs. The machine learning algorithm demonstrated better correspondence to cognitive performance (processing speed, executive function, and memory) than the rating scales. Our group reported similar results when comparing a semiautomated algorithm to visual rating scales (Garrett et al., 2004). Interestingly, results from the study by Jokinen et al. (2020) revealed that baseline WMH burden predicted the rate of cognitive and ADL decline in otherwise healthy older adults over a 3-year follow-up period. Additional explanatory gain regarding the functional consequence of WMHs can be obtained using diffusion tensor imaging (DTI). DTI measures the directional flow of water in brain tissue. More specifically, the technique quantifies the rate and directionality of hydrogen atoms coursing through brain tissue (Reginold et al., 2015; Seiler et al., 2018; Taylor et al., 2013). DTI is ideal for the assessment of white matter fasciculi because water preferentially flows along the length of these tracts due to the linear direction of the axons (and myelin).

In a study of 680 older adults (average age of 72), Seiler et al. (2018) described five white matter tracts that are uniquely vulnerable to WMHs. The tracts included the forceps major and minor, posterior thalamic radiation, inferior-fronto-occipital fasciculus, and the inferior longitudinal fasciculus. Across all tracts, lower fractional anisotropy (a ratio of directional vs. nondirectional water flow) was significantly associated with WMH volume. Numerous studies reveal inverse associations between cognitive performance and mean diffusivity in tracts affected by WMHs (Reginold et al., 2015), including regions of the tracts that are distal to the lesion. The observation of structural abnormalities in brain regions distant, but related to, focal injury has transformed conceptual models of brain function from a regional focus to a larger perspective of the brain as an interconnected network.

Perivascular Spaces

Perivascular spaces (PVS), referred to as Virchow-Robin spaces, are fluid-filled spaces that line the penetrating vessels of the brain. They are most commonly observed in the basal ganglia and centrum semiovale, and to a lesser extent, in the hippocampus (Francis, Ballerini, & Wardlaw, 2019). PVS appear as hyperintense signals on T2-weighted images, with signal intensities that are similar to cerebrospinal fluid (CSF). Most PVS do not exceed 3 mm in diameter and are often undetectable with low-resolution neuroimaging. However, enlarged PVS (10–20 mm) become increasingly detectable with older age (Groeschel, Chong, Surtees, & Hanefeld, 2006), particularly in the basal ganglia (Wardlaw et al., 2013). Indeed, a meta-analysis of 23 studies (N = 12,725) revealed the association of PVS in the basal ganglia with lacunes (OR = 3.56), microbleeds (OR = 2.26), hypertension (OR = 1.67), and older age (OR = 1.47) (Francis et al., 2019).

Manual annotation of PVS is time-intensive and susceptible to human error. For example, Dubost et al. (2019) reported enhanced detection and quantification of PVS in the basal ganglia, midbrain, centrum semiovale, and hippocampus using an automated program compared to visual rating scales. In a recent longitudinal study of older adults (N = 560, ages 65–84 years) with mild (44%), moderate (32%), and severe (23%) WMHs, baseline PVS volume was associated with decline in memory and processing speed (Jokinen et al., 2020). Future studies are needed that combine the strengths of high-resolution neuroimaging and automated detection algorithms to determine the explanatory relevance of PVS in conjunction with WMHs and DTI metrics of white matter microstructural integrity.

Cerebral Microinfarcts

Cerebral microinfarcts (CMIs) are microscopic ischemic lesions (100 μm–4 mm, mean diameter = 0.2–1 mm) that occur in 16–46% of older adults and over 60% of individuals with Major VCI (Brundel, de Bresser, van Dillen, Kappelle, & Biessels, 2012; Gurol, Biessels, & Polimeni, 2020). Prior studies using DWI reveal CMIs within 4 weeks of infarction (Ter Telgte et al., 2020; Li et al., 2013). After the DWI signal fades, chronic CMI burden can be estimated using mathematical algorithms that combine features from DWI, T1-, and T2-weighted scans (van Veluw et al., 2015a; van Veluw, Biessels, Luijten, & Zwanenburg, 2015b). However, results are heavily dependent on Tesla strength (van Veluw et al., 2016). A recent longitudinal study of community-dwelling older adults revealed multiple acute CMIs in about 15% of the sample, with chronic CMIs evident in nearly one-third (Ter Telgte et al., 2020). Baseline CMI burden corelated with cognitive performance.

Neuroimaging Correlates of ADLs in VCI

The LADIS (Leukoaraiosis and Disability Study) cohort ($N > 500$) reported that baseline WMH burden and total gray matter and hippocampal volume predicted cognitive impairment (i.e., processing speed, executive function, memory) and degree of ADL disruption. Volumes of lacunes, enlarged PVS, and cortical infarcts also contributed to prediction accuracy, but to a lesser extent. These results align with work completed by our group describing strong associations between subcortical WMH volume and IADL impairment among individuals with Major VCI (Boyle et al., 2003). Studies are needed that integrate multiple neuroimaging modalities (e.g., FLAIR and DTI) to leverage the unique dimensional strengths of each imaging approach.

Methods of ADL Assessment

While there is agreement on the use of specific neuroimaging and neuropsychological protocols to quantify brain injury, no consensus has been reached on best practices for the assessment of ADL impairment associated with the aforementioned injury. A common clinical strategy is to rely on the results of clinical neuropsychological testing.

However, neuropsychological performance and ADL function are nonorthogonal constructs that represent sequelae injury estimated from neuroimaging features. The lack of precision that is inherent to each approach may introduce error in the risk stratification of individual cases; this problem is magnified by the lack of integrated clinical expertise and siloed health care service. Existing methods to ascertain ADL status only worsen the clinical challenge.

Self-Report Assessment of ADL Status

Self-report questionnaires have been the mainstay of ADL assessment in research and clinical practice. Examples of self-report measures include the Lawton and Brody IADL Scale (Lawton & Brody, 1969) and the Patient's Own Assessment of Function Inventory (Chelune & Lehman, 1986). Self-report questionnaires such as the Lawton and Brody were introduced approximately 50 years ago and are quickly administered and scored, typically requiring less than 10 minutes. However, the validity of self-report scales is predicated on the false assumption that metacognitive skills are unaffected in the context of VCI, an argument that lacks face validity. Similar to other conditions that include cognitive impairments, individuals with Major VCI overestimate their ability to complete IADLs compared to ratings provided by their caregivers (Tezuka et al., 2013). The difference between self-report and collateral report is most extreme in cases with a right hemisphere infarct with consequent anosognosia (Vossel, Eschenbeck, & Fink, 2013). Collateral sources (e.g., spouses, significant others, adult children), on the other hand, tend to overstate ADL impairment. Collateral sources also differ markedly in the degree of first-hand knowledge of previous versus current ADL function of others.

Objective Assessment Using Task-Based Procedures

The challenges associated with self-report and subjective ratings of ADL function have prompted efforts to develop objective measures using task-based protocols. One example is the Naturalistic Action Test (NAT; Schwartz, Segal, Veramonti, Ferraro, & Buxbaum, 2002). The NAT requires individuals to perform real-life tasks that differ on the level of complexity (e.g., make toast, wrap a gift while avoiding distractions). The Neuropsychological Assessment Battery Daily Living Module (NAB-DLM; Stern & White, 2003) prioritizes language-based demands of everyday function. The NAB-DLM includes five subtests: (1) Daily Living Immediate and Delayed Memory; (2) Bill Payment; (3) Judgment; (4) Map Reading; and (5) Driving Scenes. The Daily Living Memory subtest requires individuals to learn and remember information related to medication instructions as well as a fictitious name, address, and phone number. Bill Payment requires individuals to demonstrate the steps involved in payment and recordkeeping of a fictitious utility bill. The Judgment subtest requires participants to answer questions pertaining to home safety, health, and medical issues. On Map Reading, participants are shown a fictitious map depicting highways, boulevards with street names, and directional markers, and then asked questions about the information (e.g., number of miles between points). On the Driving Scenes subtest, individuals are shown a line drawing depiction of a two-lane road viewed from the perspective of the driver. Subsequently, individuals are required to identify modifications that have been made to the scenes.

A problem with existing task-based protocols is that most were developed and normed for use in Caucasian populations. Closer examination of the item content on the NAB-DLM Bill Payment subtest, for example, assumes that individuals from diverse sociocultural backgrounds are equally familiar with the task demands. However, this is a false assumption. Ethnic minorities and individuals in the United States with limited financial resources are more likely to utilize alternative financial service providers (check cashing, money orders) than formal banking institutions and personal checking accounts (Cook, Kazantzis, Morris, Zahradka, & Firm, 2009; Goodstein & Rhine, 2017). Similarly, ethnic minorities use public transportation more frequently than white individuals (Cervero, 2007; Gautier & Zenou, 2010), yet the NAB-DLM Driving Scenes test depicts scenes from the perspective of the driver. Technical advances such as autopay bill payment and vehicles equipped with accident-mitigation devices will deepen the cultural divide due to the inequities that persist in access and utilization.

Another area in need of attention is the lack of ethnic diversity in normative data for existing task-based ADL measures. For example, the NAB-DLM norms include few black individuals over the age of 60 who have more than 12 years of education. Preliminary work completed by our group (Paul et al., 2021) reveals substantial differences in norm-adjusted scores on the NAB-DLM when comparing individuals by race. In a cohort of 79 older individuals with comorbid cerebrovascular disease and human immunodeficiency virus (HIV), subtle differences in raw scores (< 3 points per subtest) between black and white individuals translated into substantially different *T*-scores using the published norms (Stern & White, 2003). Average *T*-scores for black individuals were below the clinical threshold for impairment on the DLM Delayed Recall ($T = 36$) and Bill Payment ($T = 35$) subtests. Similarly, the average score on Bill Payment was below the threshold for impairment ($T = 34$) for ethnic minorities. By contrast, norm-adjusted NAB-DLM subtest scores were above the clinical threshold of impairment for white individuals. Further, correlations between NAB-DLM subtests and objective testing differed by race, reinforcing the challenge with using standard neuropsychological testing to predict ADL performance. These results are not unique to individuals with co-occurring cerebrovascular disease and HIV, but almost certainly apply to studies of ethnically diverse samples of VCI, probable AD, and other neurological conditions. Understanding the complex interplay between sociocultural factors, cultural relevance of test content, and normative expectations for ADL performance represents a major "blind spot" in the clinical care of individuals with acquired neurocognitive disorders from vascular mechanisms.

Misclassification of cognitive and ADL "impairment" is not a new problem. Palmer, Bäckman, Winblad, and Fratiglioni (2008) reported a type 1 error rate for cognitive impairment of 25% in a sample of mostly Caucasian healthy older adults age 50–79. Similarly, 20% of healthy adults with no history of neurological risk factors were misclassified as cognitively impaired when examined using just five memory tests, including the NAB Daily Living Memory subtests (Brooks, Iverson, & White, 2007). The risk of misclassification increases as a function of the number of tests administered (Binder, Iverson, & Brooks, 2009). Reliance on domains scores and more focal neuropsychological batteries reduce type 1 error, but increase type 2 errors. Addressing the inherent tension between these opposing factors requires alternative ways to conduct pattern analyses. Below we introduce analytic approaches that may help to identify classification algorithms that optimize sensitivity and specificity.

Recommendations for Future Research

Data-Driven Models to Advance the Conceptual Framework of ADL Decline in VCI

Common statistical models are inherently restricted by statistical assumptions (e.g., normality, linearity) and reliance on conservative significance thresholds to minimize chance findings. Additionally, traditional methods, such as logistic regression, require advanced selection of predictor variables before the relevance of the predictors is understood. As noted by Miller, Lubke, McArtor, and Bergeman (2016) and Miller, McArtor, and Lubke (2017), it is rarely possible to incorporate interactive and nonlinear effects into parametric models because the underlying data structure is unknown.

Data science and machine learning methods offer a complementary approach to offset the limitations of traditional statistics. Advances in data science are among the most exciting areas of clinical neuroscience. Methods that our group have deployed to identify novel cognitive phenotypes include hierarchical clustering and ensemble machine learning.

Hierarchical Clustering Algorithms

Models that manage multicollinearity among predictor variables (i.e., mutually shared information) by defining tunable parameters for each variable produce algorithms with high accuracy during model training, but limited generalizability. Inclusion of additional variables further reduces the reliability of the model due to overfitting. Traditional variable selection methods such as least absolute shrinkage and selection operator (LASSO) manage mutual information by reducing the size of certain predictor coefficients to "0," leaving only the most important predictors (Hastie, Tibshirani, & Wainwright, 2015). The result is a more parsimonious model that comes at the sacrifice of biological accuracy. Further, it is not possible to determine the relative ranking of variable "importance" without assuming normality and homoscedasticity of the data, neither of which is common in high-dimensional feature sets (Wilcox, 2018).

Methods that overcome these limitations include Hierarchical Density-Based Clustering (HDBScan; McInnes, Healy, & Astels, 2017), and Correlation Explanation (CorEx; Ver Steeg & Galstyan, 2014) (*http://github.com/gregversteeg*). These methods deemphasize the dependency of traditional strategies to employ categorical labels (e.g., major depressive disorder) and arbitrary cutoffs between "normal" and disease states (e.g., mild vs. major neurocognitive disorder). This approach aligns with the ongoing NIH Research Domain Criteria (RDoC) initiative that aims to cut across diagnostic categories by leveraging the richness of dimensional features (Cuthbert, 2014). Unpublished work from our group favors HDBScan for clustering of neurocognitive performance and ensemble machine learning for discovery of underlying features that explain complex clinical phenotypes using highly dimensional features (Paul et al., 2021).

Ensemble Machine Learning

A second method favored by our group is gradient-boosted multivariate regression (GBM), a form of ensemble machine learning that leverages the strength that comes from a "wisdom of crowds" approach (Miller et al., 2017). The boosting function combines multiple simple models into a composite that benefits from classification error and accuracy derived from individual models (termed "weak learners"). Prediction accuracy is enhanced by quantifying the difference between current approximation and the target vector (i.e., residual). The algorithm then trains weak learners that map feature vectors to the residual and combines the information on accuracy and error to derive an ensemble predictive classifier. GBM is reasonably robust to sample size variance, differences in base rates, and overfitting. We employed GBM to identify a combination of variables to predict cognitive decline on a screening measure administered to 121 community-dwelling older adults enrolled in a study focused on SIVD. Results from the GBM identified a combination of variables that distinguished cognitive subgroups using DTI in the corpus callosum, history of use of postmenopausal hormone replacement therapy, older age, and black race distinguished individual membership in each cognitive group.

GBM represents a pathway for developing and implementing clinical decision tools to identify individuals at risk for cognitive and ADL dysfunction. Additionally, GBM allows for true integration of multimodal neuroimaging outcomes (e.g., DTI, volumetrics). It is important to recognize that data science methods are vulnerable to overfitting and generation of algorithms that model noise and implicit biases that amplify, rather than mollify, sociocultural disparities. As such, the burgeoning enthusiasm for the application of data-driven methods to resolve vexing neurological conditions such as VCI must be tempered by responsible science using safeguards to prevent the introduction of algorithms into clinical practice that amplify and perpetuate sociocultural disparities associated with health inequities.

Summary

The clinical and research landscape of VCI has undergone a remarkable evolution in terminology, diagnostic criteria, and harmonization procedures. Nevertheless, critical knowledge gaps remain, particularly in terms of defining culturally appropriate methods for detection and monitoring of ADL status. Future studies that leverage advanced methods to examine interactions embedded in complex data are needed. Ideally, these tools will identify individuals at risk for ADL decline as well as delineate the combination of risk factors that serve as antecedents and therapeutic targets for intervention/prevention strategies designed to support functional independence among the global population of older adults at risk for VCI.

Clinical Recommendations

- Universal guidelines for the assessment of ADLs among individuals with VCI do not exist.
- Self-report measures of ADL status are prone to reporting bias, whereas task-based methods may artificially inflate the frequency of impairment among ethnically diverse samples.
- A multidimensional approach is needed to differentiate Mild from Major VCI.

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CHAPTER 17

Everyday Impact of Traumatic Brain Injury

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Traumatic brain injury (TBI) is not a misnomer, for the "traumatic" effects of such an injury can be long-lasting and profound. TBI most often results in diffuse injury to the brain, which can lead to a varied pattern of disruption in an individual's everyday life. Following a TBI, many individuals struggle with meeting the everyday demands of their household such as paying bills, caring for children, preparing meals, or attending appointments. Often, individuals with TBI struggle with returning to employment at the same level of performance as prior to the injury. Persistent cognitive difficulties together with emotional and behavioral difficulties and alterations in physical functioning, including pain and fatigue, can create lifelong challenges that impact daily living. This chapter begins with an introduction to brain injury and its resulting sequelae, followed by a discussion of the relationship between TBI and the performance of everyday activities, including instrumental activities of daily living (IADLs), financial management, driving performance, and vocational functioning, as well as practice guidelines for assessment and intervention.

Overview of TBI and Its Sequelae

Pathophysiology

Traumatic brain injury is broadly defined as an alternation in brain function caused by an external force that can occur in any number of ways including accidents in traffic, at home, at work, during sports activities, or on the battlefield. There are numerous potential sources of altered brain function in cases of TBI, and they typically occur in two stages. In the first stage, primary injuries are caused by mechanical forces. Linear acceleration–deceleration forces usually generate focal lesions when a moving skull is suddenly decelerated or when a stationary head is abruptly accelerated. As the brain continues its trajectory, damage incurred at its point of compression against the skull is called a "*coup* injury." A "*contre-coup* injury" refers to (hemorrhagic) contusions sustained to the opposite side of the brain when it rebounds. Orbitofrontal and anterior temporal regions are highly vulnerable because they are propelled over bony protrusions and cavities of the skull below. "Diffuse axonal injury" refers to microscopic damage caused by widespread stretching and shearing of axons deep in the brain. It occurs when a head movement is abruptly stopped and the brain continues to rotate within the skull (rotational forces).

Within 24 hours, a cascade of negative events can produce secondary injuries. Brain tissue may swell and become displaced, thereby causing further shearing and tearing of blood vessels. Consequently, blood clots may form either in the space surrounding the brain (e.g., extradural and subdural hematomas) or within the brain itself (intracerebral hematomas). Hematomas can force portions of brain tissue to shift into nearby spaces (herniation). Bleeding, edema, and development of hydrocephalus due to impaired circulation of cerebrospinal fluid may result in increased intracranial pressure. Limbic structures are particularly vulnerable to hypoxia and ischemia caused by metabolic and vascular disturbances, and by systemic complications that interfere with oxygen or blood supply to the brain (e.g., crushing and choking injuries, extensive blood loss). Tissue scarring can lead to delayed onset of seizures.

More recently, advances in neuroimaging have provided evidence that diffuse axonal injury after TBI has the effect of disconnecting or altering the functional brain networks. Sharp, Scott, and Leech (2014) mapped structural damage following TBI through the use of diffusion MRI and investigated the functional effects of the damage on large-scale intrinsic connectivity networks (ICNs). Two such ICNs, the salience network and the default mode network, are normally tightly coupled and are important in attentional control. The researchers demonstrated that damage to the structural connectivity of these networks produces predictable abnormalities of network function and cognitive control. Utilizing diffusion tensor tractography, Caeyenberghs et al. (2014) demonstrated that individuals with chronic TBI symptoms, in comparison to controls, demonstrated a weaker globally integrated structural network, resulting in a limited capacity to integrate information across brain regions. Even in subject groups characterized as having experienced a mild TBI and/or repetitive subconcussive injuries, researchers have used functional magnetic imaging to demonstrate alterations in the default mode network (Abbas et al., 2015) and decreased cross-frequency coupling in the resting state (Antonakakis et al., 2016).

Levels of Severity

The injured person's level of consciousness upon hospital admission, based on a standardized coma scale, and the duration of posttraumatic amnesia (PTA) are most commonly employed to classify the severity of TBI. PTA is defined as a period post-injury marked by confusion and inability to consistently and accurately recall ongoing events. Additional information regarding severity can be based on the presence or absence of abnormalities on structural brain imaging. A commonly used set of classification guidelines is provided in Table 17.1 (Brasure et al., 2012).

TABLE 17.1. Criteria Used to Classify TBI Severity

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	< minutes	30 minutes to 24 hours	> 24 hours
Alteration of consciousness/ mental state	A moment to 24 hours	> 24 hours	> 24 hours
Posttraumatic amnesia	0–1 day	> 1 and < 7 days	> 7 days
Glasgow Coma Scale (best available score in 24 hours)	13–15	9–12	3–8

Note. From Brasure et al. (2012).

Epidemiology

Traumatic brain injury is a leading cause of death and disability worldwide. The Centers for Disease Control and Prevention (CDC, 2019) reported that in 2014 about 2.7 million TBI-related emergency department visits, hospitalizations, and deaths occurred in the United States, with over 837,000 of these events among children. TBI contributed to the deaths of 56,800 people, including 2,529 children. TBI was diagnosed, alone or in combination with other injuries, in 288,000 hospitalizations. Between 2006 and 2014, age-adjusted rates of TBI-related emergency visits increased by 54%, hospitalization rates decreased by 8%, and death rates decreased by 6%. Moderate and severe TBI make up 20–30% of cases; the rest are mild. Men outnumber women by a 1.5 ratio, and incidence is highest for children and for people between the ages of 15 and 24 or over the age of 75. The leading cause of TBI is falls (48% of TBI-related injuries), which disproportionately affect children and older adults. Being "struck by/against" an object was the second leading cause of TBI-related emergency visits (17%). Falls and motor vehicle crashes were, respectively, the first and second leading causes of all TBI-related hospitalizations (52% and 20%, respectively). The CDC estimates that 2% of the U.S. population lives with disabilities directly attributable to TBI, with annual direct and indirect costs estimated at more than $76.5 billion.

Psychopathology

Psychopathology has been implicated both as a contributing factor to the risk for TBI and as a complicating factor in rehabilitation following injury. Substance misuse is a common problem, with data from various studies suggesting that between one-third and one-half of individuals affected by TBI have some history of alcohol abuse. In a 10-year review of the literature from 1994 to 2004, Parry-Jones, Vaughan, and Miles Cox (2006) found that the prevalence of alcohol intoxication at the time of injury ranged from 37–51%, mirroring the pre-TBI incidence of alcohol misuse, which was also 37–51%. Intoxication at the time of the injury can lead to more complications and longer acute hospital stays; and a history of alcohol abuse is strongly associated with increased morbidity and mortality. In general, alcohol misuse is associated with poorer outcomes, neurologically, medically, cognitively, and functionally (Parry-Jones et al., 2006).

The most commonly diagnosed mental health disorders following brain injury are depression and specific anxiety disorders, with a significant proportion of individuals having two or more diagnoses. Prevalence of depression following injury (Kreutzer, Seel, & Gourley, 2001) has been reported at nearly nine times the rate found in community samples, with a prevalence rate of 42% for major depressive disorder at 2½ years post-injury. Rates of suicide are also higher in this group, with suicide three to four times more likely compared to the general population (Teasdale & Engberg, 2001). A study of 76 individuals approximately 14 years following brain injury suggests that anxiety remains a significant problem for 44% of the group (Hoofien, Gilboa, Vakil, & Donovick, 2001). Even mild injuries can play a role in the emergence and expression of anxiety (Moore, Terryberry-Spohr, & Hope, 2006).

Cognitive Profiles Associated with TBI

Attention and Speed of Processing

Attention is particularly vulnerable to dysfunction following TBI. On objective testing, slowed speed of processing is almost universally reported, even 2–5 years after a severe injury (e.g., Perbal, Couillet, Azouvi, & Pouthas, 2003; Ríos, Periáñez, & Muñoz-Céspedes, 2004), and a meta-analytic study on mild TBI documented the largest effect size for speed-of-processing tests compared to other cognitive domains (Frencham, Fox, & Maybery, 2005). Difficulty dividing attention between stimuli and problems with working memory can occur regardless of injury severity and may persist for years (Serino et al., 2006; Vanderploeg, Curtiss, & Belanger, 2005). Disruptions of selective attention have been reported, as have difficulties with sustained attention.

Memory

Memory difficulties are among the most common difficulties experienced by TBI survivors (Shum, Harris, & O'Gorman, 2000; Zec et al., 2001). Free-recall tasks are typically more impaired than cued-recall or recognition (Nolin, 2006), and memory performance may be characterized by reduced semantic clustering during new learning and a high number of intrusions upon recall or recognition (Nolin, 2006; Zec et al., 2001). Prospective memory, or memory for actions to be performed in the future, can also be disrupted (Shum, Valentine, & Cutmore, 1999).

Executive Functioning

Executive functions are the higher-order cognitive skills necessary to successfully formulate and execute independent, goal-directed behaviors. Abstract reasoning and planning may be impaired, with difficulties more noticeable on relatively unstructured measures requiring self-generated strategies and organization than on structured tasks (Cockburn, 1995; Fork et al., 2005).

Draper and Ponsford (2008) investigated cognitive impairments 10 years following TBI in 60 participants and 43 controls. The TBI group demonstrated significant cognitive impairments on measures of processing speed, memory, and executive function, with the Symbol Digit Modalities Test, Rey Auditory Verbal Learning Test (AVLT), and Hayling C and Sustained Attention to Response Task (SART) errors most strongly differentiating the groups. Greater injury severity was significantly correlated with poorer test performances across all domains. This and many other studies have clearly demonstrated that cognitive impairments following TBI can persist for many years.

Additional Sequelae

Awareness

Self-awareness refers to the ability to recognize one's own cognitive and behavioral strengths and weaknesses and to appreciate how difficulties might impact aspects of everyday functioning. Comparison of self-ratings with those made by significant others indicates that persons with TBI may underestimate the extent or the impact of deficits pertaining to selective aspects of their overall functioning (Prigatano, 2005). Impaired self-awareness is associated with rehabilitation-related variables, including poorer compliance with participation (Lam, McMahon, Priddy, & Gehred-Schultz, 1998), increased length of rehabilitation stay (Malec, Buffington, Moessner, & Degiorgio, 2000), and reduced functional independence at discharge (Sherer, Hart, & Nick, 2003).

Sleep and Fatigue

Sleep disturbances and fatigue are both commonly reported following TBI and likely have a multifaceted and complex interaction with cognition, physical, and emotional functioning. They have been linked to anxiety, depression, pain, slowed information processing, and the need for increased effort in performing tasks (Ponsford et al., 2012; Duclos, Beauregard, Bottari, Oouellet, & Gosselin, 2015).

IADLs in TBI

The cognitive, physical, and emotional sequelae of TBI often impact the ability to engage in instrumental activities of daily living (IADLs; Pagulayan, Temkin, Machamer, & Dikmen, 2006). Difficulties in performing basic IADLs (e.g., dressing, bathing, grooming, eating) are common after severe injuries and are especially evident early in recovery secondary to both cognitive difficulties and physical sequelae such as weakness, incoordination, and balance problems. Such difficulties are commonly addressed by physical therapies (e.g., strengthening and normalizing muscle tone, improving balance and postural control, restituting gait patterns) and occupational therapies (e.g., compensatory training in using an unimpaired limb, assistive devices, cuing strategies). Over time, difficulties with basic self-care skills usually improve. In one study of nearly 1,800 individuals with TBI, only 3.2% of responders identified a persistent need for increasing independence in basic self-care skills at 1-year post-injury (Corrigan, Whiteneck, & Mellick, 2004).

In contrast, difficulties performing more complex IADLs such as shopping, cooking, housekeeping, and managing medication and finances have been shown to persist over time (Colantonio et al., 2004; Pagulayan et al., 2006). In one study of 210 individuals who had sustained moderate to severe brain injuries 3–5 years previously, only 30% reported difficulties completing personal care activities, while 60% reported that cognitive problems interfered with more complex daily activities (Dikmen, Machamer, Powell, & Temkin, 2003). In a study of long-term outcomes post-TBI that included participants up to 24 years post-injury, 88% of the 306 participants could bathe, dress, eat, transfer, use the toilet, and telephone independently (Colantonio et al., 2004), but even with assistance, 10% of the sample reported an inability to complete a variety of daily tasks such as shopping, meal preparation, housework, money management, and navigating in the community. A study of 141 adults with moderate to severe injuries at 10-years post-injury (Ponsford et al., 2014) indicated that while the majority of the sample felt independent in many personal activities, a significant minority required continued assistance with heavy domestic chores (30%) and shopping (20%). Corrigan et al. (2014) estimated that at 5 years post-injury, one-third of adults with moderate to severe injuries require supervision both overnight and in part of their waking hours. Although only about 10% of individuals with TBI require restricted living situations in the long term (Colantonio et al., 2004; Dikmen et al., 2003), difficulty with completing daily tasks increases risks for the individual and commonly causes an increased burden on family members and caregivers.

IADLs can be negatively impacted by a variety of brain injury sequelae. Preparing a meal, for example, requires the ability to plan and organize and to carry out a sequence of actions. It requires thinking ahead as well as focused attention and memory. Memory problems can also lead to safety concerns, such as leaving a pot on the stove. Add a distracting environment (e.g., background noise, children playing, or a telephone ringing) and the task can become nearly impossible for someone who experiences difficulties with divided attention or working memory. An added complication may be limitations in self-awareness that prevent the individual from recognizing the difficulties they are having and may interfere with their willingness to accept help with or use aids to complete everyday tasks. Concerns regarding their loved one's judgment and safety in the home and community have been shown to be a significant source of stress for caregivers (Kreutzer et al., 2009).

Assessment of IADLs

Assessment of IADLs is most often completed by an occupational therapist or a multidisciplinary team. Assessment tools include indirect measures such as questionnaires, rating scales, and interviews (both self-report and report by a significant other, caretaker, or therapist) as well as direct observation of activities performed in realistic environments (see Law, Baum, & Dunn, 2005). Some of the more commonly used rating scales and questionnaires for the assessment of IADLs are listed in Table 17.2. All of the measures listed are available for open access through the Center for Outcome Measurement in Brain Injury (COMBI). Decisions regarding specific instruments to be used should be guided by the assessment environment, the psychometric properties of the instrument, and the specific question being addressed. Input from the individual affected by TBI and a significant other or members of a treatment can jointly provide valuable insight into where problems arise on a daily basis.

Direct observation of IADL performance in a realistic environment is one of the best indicators of day-to-day functioning. Individuals can be rated on standard scales while completing IADLs, or they can be asked to complete a standardized measure of functioning such as the Multiple Errands Test (Dawson et al., 2009). Goverover and DeLuca (2015), as an example, assessed participants on their ability to use the internet to place an online order, as a means of capturing a realistic daily activity in a structured environment that can be replicated and standardized. The benefit of these types of assessment

TABLE 17.2. Measures of Functional Independence and Related Skills

Community Integration Questionnaire (CIQ)
Craig Handicap Assessment and Reporting Technique (CHART)
Disability Rating Scale (DRS)
Functional Independence Measure and Functional Assessment Measure (FIM & FAM)
Independent Living Scale (ILS)
Mayo Portland Adaptability Inventory (MAPI)
Neurobehavioral Functioning Inventory (NFI)
Participation Objective, Participation Subjective Questionnaire (POPS)
Patient Competency Rating Scale (PCRS)
Quality of Life after Brain Injury (QOL/BRI)
Sickness Impact Profile (SIP)
Supervision Rating Scale (SRS)

Note. Available online through the Centre for Outcome Measurement in Brain Injury (COMBI; *www.tbims.org/combi/list.html*).

measures is the ability to see in real time where in the process and ways in which behavior breaks down.

Advancements in technology have increasingly been adapted to assess functional behavior in a controlled and safe environment. Virtual reality applications are gaining recognition as useful tools for research, evaluation, and rehabilitation, allowing users to interact in a range of sensory-rich virtual environments and to obtain real-time feedback on their performance (Larson, Feigan, Gagliardo, & Dvorkin, 2014; Parsons, 2011; Zhang et al., 2003). Another application of technology has been the use of cameras and other remote sensing devices within the living environment to monitor behavior and the frequency and nature of difficulties experienced with independent living activities (Cook & Schmitter-Edgecombe, 2009).

Neuropsychological evaluation has also been used to predict performance of IADLs, with mixed results (Johnston, Shawaryn, Malec, Kreutzer, & Hammond, 2006). Although one review suggested that up to 85% of the variance in levels of functional abilities can be reflected in test scores (Acker, 1990), others have argued that the very nature of neuropsychological evaluation (e.g., testing in a quiet environment, provision of rules and structure, clear task demands, limited demands for multitasking) limits the applicability of neuropsychological test performance to predict performance in everyday environments, where individuals are faced with distractions, noise, and a need for self-direction and planning (Chaytor & Edgecombe, 2003; Manchester, Priestley, & Jackson, 2004). The neuropsychological evaluation can complement more real-world observations by providing hypotheses for *why* a breakdown in task completion is occurring (e.g., problems with attention, memory, and/or executive control), suggesting useful avenues for intervention.

Other factors that seriously impact completion of IADLs post-TBI are beyond the scope of the current discussion but require mention. Fatigue and sleep disturbance have been noted to negatively impact performance of daily activities (Ponsford et al., 2012; Duclos, Beauregard, Bottari, Ouellet, & Gosselin, 2015), as can chronic pain (Nicholson

& Martelli, 2004). Depression and anxiety can also negatively affect day-to-day functioning even many years post-injury.

It is worthwhile to consider the approach to disability taken by the International Classification of Functioning, Disability, and Health (ICF). The ICF focuses not just on individual abilities or limitations, but on the critical role played by environmental factors that can either support participation or restrict family and community involvement. Thus, one needs to consider access to financial and social resources, transportation, health, and community support. Laxe et al. (2012) discusses ways to link comprehensive TBI assessment with ICF nomenclature.

Summary

Not being able to live independently or to effectively complete day-to-day tasks can be devastating and severely limiting to a person's overall health, safety, finances, and satisfaction. Family members and caregivers are often faced with providing support for ADLs in already challenging situations, which can increase pressure within the household and on relationships. As the TBI population is a relatively young group, the cost of limitations in completing daily activities, both to the individuals involved and to society, is great. Assessment and rehabilitation of IADL performance in individuals with TBI are critical to improving long-term outcomes.

Money Management

Managing money and handling one's finances are an important aspect of everyday functioning and have been found to be related to success in the transition to independent living after TBI. Money management incorporates a broad range of tasks, from relatively simple ones, such as currency identification or calculating the correct change, to those tasks that are more complex such as interpreting bank statements, preparing budgets, completing tax returns, and negotiating bank loans. Effective money management requires planning and monitoring of financial actions in relation to personal resources and constraints.

Individuals with TBI may struggle with completing monetary transactions due to problems with attention (e.g., sustaining attention when calculating), comprehension (e.g., interpreting bills and statements), perception (e.g., visual recognition problems with currency), memory (e.g., paying bills on time), or executive functions (e.g., planning and monitoring expenses). Hoskin, Jackson, and Crowe (2005a) investigated the types of money management deficits seen in people with TBI and their relation to cognitive skills. They compared responses on a Money Management Survey (MMS) for a group of 35 people with acquired brain dysfunction (ABD) of heterogeneous etiologies to 15 control participants. Relative to controls, the TBI participants were reported to have more difficulty on a range of money management tasks, such as paying the rent or bills on time, spending all their money before the next pay day, needing to borrow money because they had run out, not checking their change, impulse buying, not leaving money for essentials, and experiencing difficulty using automatic teller machines.

Crowe, Mahony, O'Brien, and Jackson (2003) compared 90 people with ABD (30 mild, 30 moderate, and 30 severe) with 30 nonimpaired individuals of similar age, gender, and educational attainment on a questionnaire measure of ATM use. The ABD sample consistently confirmed that they had difficulty using automated transport ticketing machines, ATMs, and automatic telephone answering and responding devices. Understanding and remembering the instructions for these tasks appeared to be the major impediment to successful usage, and overall level of competence with automated machines was related to overall performance on a neuropsychological test battery. Hoskin and colleagues (2005a, 2005b) also examined the relationship between responses on the Money Management Scale and performance on a battery of neuropsychological tests. Measures of impulse control were significantly predictive of problematic impulse spending, and measures of memory were significantly predictive of late payment of bills or rent. They were able to discriminate between people with ABD who were independently managing their personal finances, with 83.7% accuracy from those who had been appointed an administrator to assist in financial management. Measures of attention/executive functions were most useful in predicting group membership. Bottari, Gosselin, Guillemette, Lamoureux, and Ptito (2011) examined the performance of 27 adults with moderate or severe TBI and 27 controls on a budgeting task. The adults with TBI experienced more difficulty with planning, carrying out the task, and verifying the attainment of the goal than controls, with planning (i.e., organizing and structuring the problem, staying focused on and remembering the goal) being particularly affected. Microanalysis of the performance of the adults with TBI suggested underlying deficits in executive functions (e.g., stopping in the middle of the task, insertion of irrelevant activities into the task, difficulty adapting to the novelty of the proposed scenario).

Other insights into money management skills after TBI come from a study of self-awareness where participants were asked to perform tasks, two of which were related to money management (i.e., simple math calculations used in daily activities and checkbook reconciliation) and to answer self-awareness questions related to the performance of these tasks (Abreu et al., 2001). The brain-injured patients rated their ability to complete the money management task more positively than their actual performance, and the largest indicator of impaired self-awareness (i.e., discrepancy between the brain-injured patients' self-rating and the rating of their clinicians) was consistently associated with impaired money management. A deficit in self-awareness within the money management domain leaves the person vulnerable to experiencing financial difficulties or financial abuse and failing to assist themselves by receiving financial assistance.

Research on money management in individuals with degenerative diseases has shed light on issues for consideration in individuals with TBI. The Measure of Awareness of Financial Skills (MAFS) was developed to both examine performance of money-related tasks and to evaluate discrepancies between self and other ratings of financial performance as an indicator of self-awareness (Cramer, Tuokko, Mateer, & Hultsch, 2004; Van Wielingen, Cramer, & Tuokko, 2004; Van Wielingen, Tuokko, Cramer, Mateer, & Hultsch, 2004). Individuals with mild dementia lacked awareness of difficulties performing complex tasks, whereas people with moderate/severe dementia lacked awareness concerning the difficulties they experienced across tasks, regardless of complexity. Individuals with dementia who experienced executive dysfunction were more likely than those without executive dysfunction to be unaware of impairment in performing simple as well as complex tasks. These findings echo the executive dysfunction observed by Hoskin and colleagues (2005b) in people with TBI who had been appointed an administrator to assist in financial management, suggesting that lack of awareness of impairments may have been central to their need for supervision.

Marson and colleagues (2000) developed the Financial Capacity Instrument (FCI) to assess domain-level financial activities and task-specific financial abilities in people with dementia. The FCI comprises 18 tasks (e.g., naming coins/currency, purchasing three grocery items, detecting mail fraud risk, prioritizing bills), nine domains (e.g., basic monetary skill, cash transaction, financial judgment, bill payment), and two global-level scores (with and without including investment decision making) and was found to reliably discriminate between healthy adults and people with moderate to severe TBI during hospitalization and after six months (Dreer, DeVito, Novack, & Marson, 2012). Initially, adults with TBI displayed significant impairment across most FCI domains. Six months later, improvement was seen for those with TBI on both simple and complex tasks, but they remained impaired relative to controls on many complex tasks (e.g., reading bank statements, paying bills, making investment decisions). Martin and colleagues (2012) extended this investigation to identify which cognitive domains were predictive of FCI performance. Working memory and executive functions were found to be associated with FCI performance (i.e., overall scores) at both initial hospitalization and six months post-injury.

This brief examination of money management in TBI indicates that many different types of cognitive deficits affect successful performance on money management tasks, but that deficits in self-awareness and/or other executive functions appear pivotal in terms of increased vulnerability. There is also evidence that specific types of cognitive deficits (e.g., memory, impulse control) relate to specific types of money management problems (e.g., remembering to pay bills, impulse spending).

Driving

Driving is a complex behavior that depends on effective and integrated functioning of a broad range of cognitive abilities in a rapidly changing and unpredictable environment. For many recovering from a TBI, the ability to drive is an indicator of regained independence and resumption of pre-injury lifestyle and is of significant concern for individuals, and their families (Rapport, Hanks, & Bryer, 2006; Liddle et al., 2011; Novack et al., 2010). Another chapter in this book (Chapter 9) deals comprehensively with driving, so comments here are restricted to studies related to individuals with brain injury. It has been shown in brain-injured populations that driving independence is associated with employment and job stability (Kreutzer et al., 2003), confidence, quality of life, resumption of previous activities, and social integration (Rapport et al., 2006). Moreover, it has been shown that *not driving* is particularly socially and functionally disabling (Rapport et al., 2006) in individuals recovering from TBI.

There is widespread agreement that individuals recovering from TBI experience residual cognitive impairments that may compromise their ability to drive safely (e.g., Rike, Johansen, Ulleberg, Lundquist, & Schanke, 2015; Hargrave, Nupp, & Erickson, 2012). Behavioral and/or emotional sequelae may also have an influence on driving performance, but in the interest of space, we will focus primarily on cognitive disturbances post-TBI that are especially relevant to successful driving performance (e.g., attention, information-processing speed, memory, planning, decision making, awareness) (Christie, Savill, Buttress, Newby, & Tyerman, 2001). Studies examining associations between specific aspects of cognitive functioning and driving performance have been inconsistent (e.g., Coleman et al., 2002; Ortoleva, Brugger, Van der Linden, & Walder, 2012).

Performance on the Useful Field of View (UFOV) test—a measure of speed of information processing, divided attention, and selective attention—has been associated with driving performance in TBI. Fisk, Novack, Mennemeier, and Roenker (2002) found that compared to young adult controls, individuals with TBI had slower visual processing, greater difficulty detecting stimuli throughout the peripheral field (e.g., at all eccentricities), and poorer selective and divided attention. In another study, Novack and colleagues (2006) found that younger age and poorer performance on the Trail Making Test Part B and UFOV subtests significantly predicted failure ratings on an on-road driving test in a moderate-to-severe TBI sample.

Many individuals with TBI exhibit operational deficits (e.g., difficulty performing secondary in-car tasks, steering, and speed control; Lew et al., 2005), but some individuals recovering from TBI have been found to drive safely by employing strategic and tactical skills (e.g., avoiding challenging situations, slowing down) to compensate for their operational deficits (Priddy, Johnson, & Lam, 1990). Since lack of awareness may result from TBI, assessment of self-knowledge of deficits and the awareness of the need to compensate for one's driving impairments is of utmost importance in predicting driving safety in TBI.

A large proportion of individuals suffering from TBI do return to driving, with percentages ranging across studies from approximately 32 to 80% (Lew et al., 2005; Schultheis, Matheis, Nead, & DeLuca, 2002), and many do so without assessment or advice from driving experts (Christie et al., 2001; Leon-Carrion, Dominguez-Morales, Barroso, & Martin, 2005). Leon-Carrion and colleagues (2005) note that individuals with TBI returned to driving if their physical functioning was greater than 80% as measured by a functional independence/functional assessment measure (FIM-FAM), regardless of their cognitive problems and often against doctor's advice.

The processes involved in returning to driving and driving cessation after TBI and how these evolve over time were examined by Novack and colleagues (2010) in a large, longitudinal examination of people with predominantly moderate-to-severe TBI. They reported that 42% reported driving within 1 year, and the proportion had increased to 53% by 5 years post-injury. Liddle and colleagues (2011) identified key transition points in relation to driving after brain injury: learning about and understanding the need for driving restriction; the "on-hold" period where future driving status is undetermined; and the process required for returning to driving. Frustration was expressed by all parties throughout the process, whether the ultimate outcome was return to driving or driving cessation; the need for information and practical support was identified as paramount.

Ponsford, Di Stefano, Charlton, and Spitz (2016) examined pre- and post-injury self-reported driver behavior and safety in 106 individuals with TBI who returned to driving after occupational therapy driver assessment and on-road rehabilitation. They found no significant difference between pre- and post-injury crash rates. Compared to pre-injury, 36.8% of drivers reported limiting driving time, 40.6% drove more slowly, 41.5% reported greater difficulty with navigating, and 20.0% reported more near-crashes. A subset of the sample (with greater injury severity) required driver rehabilitation. This group was significantly more likely to drive less frequently, drive shorter distances, and avoid driving with passengers, night and freeway driving, and busy traffic compared to the subset of the sample who passed their initial driver assessment and required no further intervention or rehabilitation.

Considerable controversy has arisen regarding the optimal method of determining fitness to drive by people with TBI (Baker, Unsworth, & Lannin, 2015). Studies have utilized diverse evaluation methods, including on-road or closed-circuit/off-road evaluations, driving simulations, neuropsychological assessment of driving-relevant abilities, and objective or subjective measurement of accident and violation rate. Several investigators have reviewed the strengths and weaknesses of these methods, and the cognitive, motor and sensory factors necessary for safe driving (Rizzo, McGehee, Dawson, & Anderson, 2001; Schulteis & Whipple, 2014). Even the most ecologically valid method, an on-road driving assessment, has several important weaknesses, such as increased safety risk for the driver, examiner, and other road users and the subjectivity of the driving evaluation (McKenna, Jefferies, Dobson, & Frude, 2004; Schultheis et al., 2002). The less demanding environmental conditions and decision-making processes found in on-road tests (e.g., predetermined routes, less busy times, instructions/cues provided by examiner) compared to the real world may also be limitations. Moreover, behavior during driving testing may not accurately represent an individual's behavior in everyday driving situations (e.g., more caution, motivation to drive safely) (Lane & Benoit, 2011).

Licensing authorities (e.g., Rapoport et al., 2015) use a variety of guidelines regarding driving with medical illnesses, including TBI and various models have been proposed for use in clinical practice (e.g., Classen et al., 2009; Lundquist, Alinder, Modig-Arding, & Samuelsson, 2011).

Ideally, an individually adapted combination of assessments is undertaken by a multidisciplinary team to evaluate the individual's capacities for driving, cognitively related skills, insight/awareness of any limitations to driving, and on-the-road skills.

Vocational Functioning

TBI can have a deleterious and long-lasting impact on vocational outcome. Efforts to accurately predict an individual's ability to return to competitive employment post-TBI are complicated by interactions from multiple factors, including premorbid individual characteristics, injury variables, post-injury sensory, physical and/or cognitive impairments, emotional and behavioral difficulties, and environmental factors (Shames, Treger, Ring, & Giaquinto, 2007). Chapter 7 in the present volume deals specifically and extensively with issues related to employment and heavily cites the research on return to work after acquired brain injury. As such, the discussion of these issues in this chapter is only cursory.

Return to work offers individuals a sense of value and purpose, opportunities for social engagement, and, of course, access to financial resources and health insurance. Although individual capacities and limitations play an important role in return to work, equally important are environmental factors related to the degree to which the work can be adapted or the person is otherwise supported in the workplace. Vocational rehabilitation services, including vocational assessment, job coaches, and supported employment options, have been found to be a cost-effective way to help brain-injured workers return to and maintain their employment (Wehman, Gentry, West, & Arango-Lasprilla, 2005; Kendall, Muenchberger, & Gee, 2006). Other environmental factors such as reliable housing, access to transportation, flexibility in work schedules, and general labor market conditions can also have an impact on successful return to work. Walker, Marwitz, Kreutzer, Hart, and Novack (2006) found that those employed in manual labor jobs at the time of injury demonstrated the lowest level of return to work at 1 year post-injury compared to those who were employed in professional/managerial jobs.

As might be expected, a lack of awareness of one's strengths and weaknesses is a negative predictor of return to work (Shames et al., 2007). Post-acute emotional adjustment, including the incidence and severity of depression and anxiety following TBI, also impacts the likelihood of returning to work, and clients who show less effective coping and higher levels of hopelessness are less likely to be employed. A history of past or current substance abuse also leads to less successful vocational outcomes (MacMillon, Hart, Martelli, & Zasler, 2002).

Wehman et al. (2009), however, reminds the clinician that a key ingredient to promoting successful vocational reentry is not a client-based variable, but a service provider's belief that every person, regardless of disability, is employable when provided with the right type, level, and intensity of support, and when efforts are made to establish appropriate employment placements/positions that are able to accommodate limitations, while also valuing a client's unique skill set and presence.

Summary and Conclusions

TBI involves diffuse insult to the brain and a variety of long-lasting consequences that may negatively impact daily living. Individuals with moderate-to-severe injuries, approximately 20–30% of the TBI population (Langlois, Rutland-Brown, & Wald, 2006), tend to experience the most impact on daily functioning, though even individuals with mild injuries also can be affected. Although the exact pattern of impairment will vary from individual to individual, most often some aspects of daily living are affected following injury, with more substantial difficulties experienced in the early stages of recovery. TBI leads to permanent and pervasive impairments in daily living in a small proportion of cases, with approximately 10% of affected individuals requiring long-term assisted care environments (Colantonio et al., 2004; Dikmen et al., 2003).

The cognitive sequelae of TBI often affect the skills necessary for completing everyday tasks, including IADLs, financial management, and driving, as well as the ability to return to work. Measures of executive functions often serve as the best neuropsychological predictors of everyday abilities across domains of function because they tap the underlying skills (e.g., planning, sequencing, and organization) vital to completing daily tasks. Measures of executive functioning and verbal memory have been linked to functional outcome over and above other neuropsychological indices (Hanks, Rapport, Millis, & Deshpande, 1999). Speed in processing information and complex attentional skills are crucial for driving and rapid decision making across tasks and are often negatively impacted by TBI. Memory impairments can limit one's ability to learn new skills (e.g., vocational training), keep in mind appointments, or remember errands that need to be completed. For a subset of individuals with TBI, disturbances in self-awareness can negatively impact rehabilitation outcome.

Neuropsychological evaluation provides only an indirect link to everyday functioning. For intervention purposes, it is vital to obtain additional information on behaviors as they occur in more naturalistic environments. An interview with the affected individual and a significant other can identify the types of situations in which difficulties are likely to arise and can provide direct targets for intervention. Functional assessment, involving the direct observation of the client in different situations or completing everyday tasks, can also be a useful tool. Neuropsychological test performance and behavioral data provide complementary information and lead to a more clearly defined view of a person's abilities and disabilities. Identifying when a breakdown in functioning occurs (behavioral data) and for what reason (neuropsychological data) can help tailor a more individualized rehabilitation regimen that is most likely to benefit the client.

Practice Guidelines

General Guidelines

- Due to the multifaceted/multifactorial impact of TBI, a thorough review of cognitive, emotional, and physical factors is warranted in any neuropsychological evaluation.
- Clinicians should consider premorbid and postmorbid emotional functioning and its transactional impact on current symptomatology and cognitive functioning.

Assessment of IADLs

- In situations where a more direct assessment of everyday functioning is desirable, several psychometrically sound instruments are available to the clinician to provide a snapshot of daily living, some at little to no cost. Use of informant ratings or team observations is recommended, especially in settings where self-report may be less accurate (e.g., impaired self-awareness).

Financial Management

- Clinicians should remain vigilant of the risk for financial difficulties or abuse in this population. Limited self-awareness, along with general executive dysfunction, in particular, can lead to increased vulnerability to negative financial consequences.

Driving

- Speed of processing deficits, executive dysfunction, and lack of awareness of deficits have all been identified as limiting factors in return to driving post-TBI. When dysfunction in these areas is noted, the clinician is advised to consider their impact on return to driving.
- Most of the research on return to driving suggests that a comprehensive assessment involving multiple types of driving assessment is warranted. Clinicians are advised to familiarize themselves with return-to-driving procedures in their local community.

Vocational Functioning

- Addressing underlying factors (e.g., emotional distress, substance abuse, etc.) that may interfere with a client's ability to fully engage in the vocational re-entry process is recommended early and on an ongoing basis in the rehabilitation and recovery process.
- Implementation of a neuropsychological evaluation early in the course of recovery is recommended to inform treatment planning and identify necessary support services.

- Emphasizing client-focused interventions that demonstrate a high degree of ecological validity (i.e., relevant to client's interests/expected work duties) can aid in engagement and success.
- Educating oneself on public funding sources can be important in aiding clients in the return-to-work process. Many can benefit from accommodations or more formal vocational rehabilitative assistance.

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CHAPTER 18

Cognitive Functioning and Everyday Tasks in Multiple Sclerosis

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Ecological validity is a central issue for the field of clinical neuropsychology. Neuropsychologists routinely extrapolate the neuropsychological test results of their patients to real-world activities. Yet, in many cases the actual empirical data supporting such an extrapolation is limited or nonexistent. If patients are impaired on tasks such as the Wisconsin Card Sorting Test (WCST) or the California Verbal Learning Test–3 (CVLT-3), will they have difficulty with real-world tasks that purportedly require the cognitive functions measured by these tasks? As a more specific example, if patients perform poorly on tasks measuring information-processing speed and attention, such as the Symbol Digit Modalities Test (SDMT) or the Paced Auditory Serial Addition Test (PASAT), will their driving skill or their ability to carry out daily household tasks such as cooking be impaired? The goal of the present Chapter is to provide a review of some of the existing data relating to the ecological validity of neuropsychological tests in people with multiple sclerosis (PwMS). Cognitive problems are very common in multiple sclerosis (MS), and there is a growing body of literature suggesting that such cognitive difficulties have consequences for important real-world tasks. Before reviewing this literature, we summarize what is known about some of the basic characteristics of MS, including pathophysiology, symptom profile and diagnostic issues, epidemiology and disease characteristics, and cognitive functioning and depression.

General Characteristics of MS

Pathophysiology

MS was originally thought to be an organ-specific T-cell mediated autoimmune disease that results in demyelination in the central nervous system. However, subsequent successful trials of therapies targeting B-cells have brought this initial conceptualization into question (Dobson & Giovannoni, 2019). A slow-acting virus or a delayed reaction to a common virus has also been considered as a possible cause of this demyelination (Arnett, 2003; Compston et al., 2005; Paty & Ebers, 1998; Tröster & Arnett, 2006). Multiple discrete plaques are formed, in part, by proliferating astrocytes that result in demyelination. Myelin sheaths within plaques are either destroyed or swollen and fragmented. This process disrupts neural transmission. MS plaques appear as ill-defined, pale, pink-yellow lesions in the untreated brain. Axons and cell bodies of neurons often remain intact, though some cell death is thought to occur with progression of the disease (Brass, Benedict, Weinstock-Guttman, Munschauer, & Bakshi, 2006). MS plaques can occur in the brain and/or spinal cord, and their location is highly variable among patients. Within the brain, plaques near the lateral and third ventricles are most common. The frontal lobes are the next most commonly affected, even when the size of the frontal lobes, relative to the rest of the brain, is taken into account. Plaques are also frequently observed in other major lobes of the brain, the optic nerves, optic chiasm, or optic tracts, as well as the corpus callosum, the brainstem, and the cerebellum. Plaques are also found in white matter regions of the thalamus, hypothalamus, and basal ganglia. The majority of plaques (about 75%) are observed in the white matter, but some occur in the gray matter and in the juncture between the gray and white matter (Pittock & Lucchinetti, 2007). (For a more comprehensive review of the pathophysiology of MS, see Dobson & Giovannoni, 2019.)

Symptom Profile and Diagnosis

Symptoms from demyelination in MS most often reflect functions associated with the affected areas. The most common symptoms at MS onset are muscle weakness, paresthesias (usually numbness and tingling in the limbs, trunk, or face), gait/balance problems, and visual disturbances. Urinary disturbance, fatigue, and problems with balance are also common (Arnett, 2003; Paty & Ebers, 1998). Significant cognitive difficulties and problems with depression are very common symptoms as well, as discussed in detail below. Symptom onset is typically acute or subacute, with many MS symptoms being transient and unpredictable. For example, visual disturbances and paresthesias may last for seconds or hours. Because of the short-lived and sometimes unusual nature of symptoms, it is not uncommon for patients in the early stages, prior to formal diagnosis, to be labeled with somatoform disorders.

Currently, the diagnosis of MS is based on guidelines from the 2010 McDonald criteria (Polman et al., 2011), and most recently refined by Thompson and colleagues (Thompson et al., 2018). Under these new criteria, lesions should be separated in both time and space. McDonald and colleagues (and, subsequently, Thompson et al., 2018) also lay out specific criteria for defining lesions detected on MRI as abnormal and characteristic of MS. With this new diagnostic system, MRI data are considered preferable to other paraclinical tests; however, additional tests are considered useful when clear-cut MRI findings are not evident or in the case of atypical clinical presentations. In particular, the presence of oligoclonal IgG bands in the cerebrospinal fluid (CSF) different from those in the serum, or elevated IgG, can be used. Furthermore, visual evoked potentials (VEPs) can be used to supplement the clinical examination to reveal evidence of additional lesions.

New attacks, relapses, or exacerbations commonly occur in MS and imply new disease activity. The latest classification of course types for MS has been provided by Lublin (2014). The most common course type is *relapsing–remitting.* Approximately 85% of patients have this type at initial diagnosis. It is characterized by clearly defined disease relapses. Recovery is highly variable, ranging from complete recovery back to prerelapse baseline to sequelae and residual deficit. A central feature of this course type is the absence of disease progression between relapses. *Secondary progressive* is the next most common type of MS. It begins as a relapsing–remitting course, but progression of the disease is evident even between relapses. It is important to note, however, that relapses and remissions may or may not occur once patients enter a secondary progressive course, but disease progression occurs. Individuals with relapsing–remitting MS typically develop the secondary progressive type within 10–15 years, but these numbers may change with the continued development of better disease-modifying medications that, thus far, have mostly targeted relapsing-remitting type. The *primary progressive type* affects approximately 5–15% of patients and involves an unremitting disease progression for most patients. That said, occasional stabilization and even improvement in functioning can occur, but there are no clear relapses. A fourth category is *clinically isolated syndrome (CIS).* This is characterized by a single clinical episode that reflects a focal or multifocal inflammatory demyelinating event in the CNS. The duration of the attack must be at least 24 hours but in someone not known to have MS. A diagnosis of MS would not be made in the case of CIS, unless the patient has future attacks that fulfill the dissemination in space and time criteria, whereby the CIS attack would be considered their first attack. Of note, the term *chronic progressive* formerly encompassed all progressive types (Arnett & Strober, 2014).

Complete remission is common following the initial episode of symptoms for relapsing–remitting MS. Subsequent episodes are unpredictable, occurring weeks to years later, and symptoms associated with them remit less completely or not at all. Relapses are highly variable, lasting days to weeks, and more rarely, hours or months (Compston et al., 2005; Paty & Ebers, 1998).

Epidemiology/Disease Characteristics

MS is about three times as likely to affect women compared to men (Dobson & Giovannoni, 2019), and symptom onset occurs in most (about two-thirds of) patients between the ages of 20 and 40. Onset before age 15 in MS is rare; late onset after age 40 is also relatively uncommon and is typically characterized by a quicker progression and greater morbidity. Following disease onset, the average life expectancy of patients is estimated to be greater than 30 years, but as with many aspects of this disease, variability is great (Arnett & Strober, 2014).

The incidence and prevalence of MS are quite variable geographically. Relatively few cases occur near the equator, with the greatest number of cases found in the northern and southern latitudes (from about 60 to 300 per 100,000). Initial prevalence estimates indicated that MS affects about 400,000 individuals in the United States and more than two million people worldwide (Reich, Lucchinetti, & Calabresi, 2018); however, recent data indicates these numbers could be much higher, with almost one million people in the United States now thought to have MS (National Multiple Sclerosis Society, 2017). Individuals who live north of 40 degrees latitude are approximately three times more likely to have MS compared with residents living in southern regions. Such a discrepant geographic pattern implicates an environmental contribution to the disease. Relatedly, vitamin D appears to play a role. As Correale and Gaitan (2015) note, MS is associated with vitamin D deficiency, and a reduced risk of MS associated with sunlight exposure and vitamin D supplements suggests that it may play some protective role. Furthermore, higher levels of circulating vitamin D are associated with lower MS risk. Other well-studied environmental factors include Epstein–Barr virus (EVB) and smoking. Individuals who have had symptomatic EBV (mononucleosis) are twice as likely to get MS as those who are EBV negative (Handel et al., 2010). Smoking has been shown to increase the risk of MS by 50% (Palacios, Bronnum-Hansen, & Ascherio, 2011). These environmental risks are significant, but genetic factors also appear to play a role in MS, though findings are variable. In the United Kingdom and Canada, concordance for female monozygotic twins is about 30%; however, rates are under 9% in southern Europe. About one in eight PwMS have a family history of MS (Dobson & Giovannoni, 2019).

While it has long been believed that MS disproportionately affects white people of northern European descent, more recent population-based studies suggest that African Americans may in fact experience the highest rates in the United States (Langer-Gould, Brara, Beaber, & Zhang, 2013; Wallin et al., 2012) with more rapidly accumulating disability (Kister et al., 2010). In contrast, though Hispanics have been found to demonstrate a younger age of disease onset, they also more frequently manifest the relapsing-remitting form of the disease (Amezcua, Lund, Weiner, & Islam, 2011). The risk of MS appears to be lowest for Asian Americans (Langer-Gould et al., 2013).

Cognitive Sequelae/Profiles

Since Rao and colleagues' (Rao, Leo, Bernardin, & Unverzagt, 1991) seminal study on the prevalence of cognitive deficits in MS, other investigators have supported their finding of close to a 45% prevalence in community-based samples (Amato, Zipoli, & Portaccio, 2006; Jonsson et al., 2006; McIntosh-Michaelis et al., 1991). Over half of patients in clinically based samples (about 55–65%) have typically been shown to have significant cognitive problems (Amato et al., 2006; Bertrando, Maffei, & Ghezzi, 1983; Feinstein, 2004). In their study, Rao and colleagues (1991) compared 100 community-based patients with MS with 100 matched healthy controls on an extensive neuropsychological battery. They found that memory and complex attention/speeded information processing were the cognitive domains most affected in MS; this finding has been supported by subsequent work. Other domains commonly affected include verbal fluency, working memory, and executive functions involving problem solving and abstract reasoning (Amato et al., 2006; Arnett & Strober, 2014; Benedict et al., 2002; Bobholz & Rao, 2003; Feinstein, 2004; Rao et al., 1991; Wishart et al., 2004).

As Rao and others have noted, however, about 80% of patients with cognitive deficits are relatively mildly affected. Only approximately 5% of patients experience global cognitive deficits that would be consistent with dementia. Even mild cognitive problems, however, have been shown to be associated with difficulty in everyday activities in MS (e.g., work, homemaking, personal care activities, social activities) (Higginson, Arnett, & Voss, 2000). Thus, even mild cognitive difficulties in MS are a concern in a context of ecological validity.

Nature of Neuropsychological Deficits

In the following sections, the percentage of patients with deficits in a particular domain is noted. This determination is based on the percentage of patients who fell below the fifth percentile of controls in Rao, Leo, Bernardin, and Unverzagt's (1991) seminal study. We chose this study because it includes a representative community sample of patients with MS and provides one of the best samples of control participants in the literature.

Memory

Difficulties encoding and/or retrieving both verbal and visual information are the most common type of memory deficit in MS. On neuropsychological testing, these problems are typically manifested as immediate and delayed recall memory deficits. About 30% of patients have substantial problems, another 30% have moderate problems, and the remaining 40% have mild or no problems with this type of memory (Brassington & Marsh, 1998). Delayed recall deficits are usually a function of deficient immediate recall, not forgetting. The learning curve across repeated trials is similar in slope in MS compared with controls but is lower in magnitude. Percent retention, recognition, and incidental memory following a delay, and remote memory are usually intact in MS (Arnett & Strober, 2014).

Working Memory/Attention/Information-Processing Speed

Working memory deficits and problems with speeded information processing are nearly as common in MS as long-term memory problems. Working memory, defined as the ability to maintain and manipulate information "online," is commonly impaired in MS (D'Esposito et al., 1996; Foong et al., 1999; Grigsby, Ayarbe, Kravcisin, & Busenbark, 1994; Grigsby, Busenbark, Kravcisin, Ayarbe, & Kennedy, 1999; Hancock, Bruce, Bruce, & Lynch, 2015) in patients with relapsing–remitting (Grigsby et al., 1999) as well as progressive (Grigsby et al., 1994) subtypes. It can be difficult to separate speeded information processing from working memory/attention because attention is typically necessary for performing any speeded cognitive task. Of note is that DeLuca and colleagues (DeLuca, Chelune, Tulsky, Lengenfelder, & Chiaravalotti, 2004) have reported that processing speed deficits, as measured by the Processing Speed index from the Wechsler Adult Intelligence Scale–III (WAIS-III), are common to both relapsing-remitting and secondary progressive MS subtypes. In contrast, working memory deficits, as measured by the Working Memory index from the WAIS-III, only emerge in patients with a secondary progressive course. One limitation of their study is that the Processing Speed index requires fine motor speed, something that is commonly impaired in patients with MS. The authors did attempt to control for this potential confound by covarying out Finger Tapping test speed, but motor writing impairments may still have exacerbated differences with controls. Using the Sternberg task, an experimental measure that controls for perceptual and motor difficulties, Archibald and Fisk (2000) showed that both relapsing–remitting and secondary progressive MS course types demonstrated significantly slower processing speed compared with controls as the working memory demands of the task increased. Generally, patients with MS show significant difficulty on tasks requiring rapid and complex information processing, like those requiring swift application of working memory operations, attentional switching, or rapid visual scanning. About 20–25% of patients with MS have impairments in this cognitive domain (Rao, Leo, Bernardin, & Unverzagt, 1991). Simple attention span is usually intact, but mild impairments are sometimes found.

Executive Functioning

The next most common cognitive domain typically affected in MS is executive functioning, with approximately 15–20% of individuals with MS showing impairments here (Rao, Leo, Bernardin, & Unverzagt, 1991). Deficits in cognitive flexibility, concept formation, verbal abstraction, problem solving, and planning are commonly found (Amato et al., 2006; Arnett & Strober, 2014; Benedict et al., 2002; Bobholz & Rao, 2003; Feinstein, 2004).

Verbal/Linguistic Function

Aphasias are unusual in MS (Arnett, Hussain, Rao, Swanson, & Hammeke, 1996), but mild confrontation naming difficulties are sometimes seen. Similarly, alexia, agraphia, and apraxia are very rare (Mahler, 1992). With that said, speech abnormalities such as dysarthria and hypophonia are common in MS (Hartelius, Runmarker, & Andersen, 2000; Hartelius, Runmarker, Andersen, & Nord, 2000), as are deficits in verbal fluency. A recent meta-analysis suggested that letter–word and semantic fluency tasks are equally sensitive to verbal fluency problems in MS (Henry & Beatty, 2006). Data from our lab indicate that the later parts of verbal fluency tasks may be most sensitive to cognitive problems in MS. In particular, we found that patients with MS did not differ significantly from controls in the first 15-second interval of the task, but robust differences were found for the overall task (Smith & Arnett, 2007). We speculated that the initial, more automatic part of the tasks, wherein examinees often produce a large proportion of their words, is not sensitive to fluency deficits in MS, but the more effortful later parts of the task requiring more controlled cognitive processing are sensitive. Overall, 20–25% of patients typically show deficits on verbal fluency tasks (Rao, Leo, Bernardin, & Unverzagt, 1991).

Visuospatial Function

Visuospatial deficits occur with reasonable frequency in MS, with 10–20% of patients showing substantial difficulty with higher-order visuospatial skills involving angle matching or face recognition (Rao, Leo, Bernardin, & Unverzagt, 1991).

Intellectual Function

Although verbal intellectual functioning is impaired in about 20% of patients with MS (Rao, Leo, Bernardin, & Unverzagt, 1991), most patients score within the broad normal range on general measures of intelligence.

Possible Causes of Cognitive Deficits

Cognitive deficits are primarily a direct consequence of the location and extent of brain damage. Because most research in cognition in MS is conducted on participants who are not experiencing acute attacks, there are limited data on cognition during a clinical exacerbation. However, Foong and colleagues (1998) examined memory and attentional performance in a small sample of patients with MS tested during and after an acute exacerbation. They reported that, in a subgroup of patients in whom gadolinium-enhanced lesion load decreased following remission, attentional performance improved during recovery, whereas memory performance remained consistently impaired. These findings suggest that some limited aspects of cognitive dysfunction observed during acute exacerbation may be reversible. However, there is clear evidence that overall cognitive impairment is associated with total white matter lesion burden in MS, as measured by T1 magnetic resonance imaging (MRI) lesion volume (Brass et al., 2006; Rao, Leo, Haughton, St. Aubin-Faubert, & Bernardin, 1989). There is also evidence that subcortical gray matter deterioration is associated with overall neuropsychological functioning in MS (Brass et al., 2006; Minagar et al., 2013), in some cases more highly than lesion volume (Sanfilipo, Benedict, Weinstock-Guttman, & Bakshi, 2006). Some work has shown that this relationship holds even in CIS patients (Štecková et al., 2014). Thus, cognitive problems caused by primary influences are generally not reversible. Additionally, there is some evidence that frontal lobe lesions are associated with deficits on executive tasks such as the Wisconsin Card Sorting Test (WCST; Arnett et al., 1994); however, the association between lesions in other brain areas and specific cognitive deficits is less clear (Brassington & Marsh, 1998).

There is also evidence that cognitive problems can appear very early on in the disease course. Jonsson and colleagues (2006) found that 44–48% of patients with MS displayed cognitive impairments within the first year of their diagnosis. Feuillet and colleagues (2007) even found significant evidence of cognitive impairment in over 50% of patients with CIS suggestive of MS, though Reuter et al. (2011) found somewhat lower prevalence. It has also been demonstrated that once cognitive problems are present, they are likely to progress. Two longitudinal studies have now shown that patients who initially display cognitive problems are most likely to show progression of such difficulties. Kujala, Portin, and Ruutiainen (1997) demonstrated this outcome in a 3-year longitudinal study, and Bergendal, Fredrikson, and Almkvist (2007) showed evidence for such progression over an 8-year follow-up period.

Secondary causes of cognitive impairment arise from factors/conditions associated with the disease, such as depression, anxiety, or fatigue. Cognitive problems caused by a secondary influence are potentially reversible if the secondary influence is successfully treated. Although many early studies often reported null findings in this realm (Good, Clark, Oger, Paty, & Klonoff, 1992; Schiffer & Caine, 1991), more studies conducted since then have often shown that depression is associated with impairments in speeded attentional functioning, working memory, and executive functions (Arnett, Higginson, Voss, Bender, et al., 1999; Arnett, Higginson, Voss, Wright, et al., 1999; Denney, Lynch, Parmenter, & Horne, 2004; Gottberg, Einarsson, Fredrikson, von Koch, & Holmqvist, 2007; Sundgren, Maurex, Wahlin, Piehl, & Brismar, 2013).

The presence of unmeasured moderators might explain some of the discrepancies in the literature on cognitive problems and depression in MS. In a theoretical review paper (Arnett, Barwick, & Beeney, 2008), we articulated a comprehensive model that explains how the relationship between cognitive dysfunction and depression may be moderated by factors such as stress, social support, cognitive schema, and coping. In one empirical study we found that coping strategies significantly moderated the relationship between cognitive dysfunction and depression (as measured by the combined Mood and Evaluative scales from the Chicago Multiscale Depression Inventory (CMDI; Nyenhuis et al., 1995). Specifically, patients with MS and cognitive difficulties were at risk for depression only if they used high levels of avoidance coping or low levels of active coping (Arnett, Higginson, Voss, & Randolph, 2002; Rabinowitz & Arnett, 2009). The influence of moderators such as coping style might explain some of the discrepancies in the literature outlined above. Longitudinally, we have found that negative evaluative depression symptoms are more consistently associated with cognitive dysfunction than mood symptoms (Arnett, 2005).

A number of studies have now shown that cognitive reserve moderates the relationship between measures of MS severity (e.g., MRI indicators; Expanded Disability Status Scale [EDSS] scores) and cognitive outcomes. The typical finding is that PwMS who have higher levels of cognitive reserve are less likely to show cognitive impairments, even when they have levels of disease severity comparable to those with lower levels of cognitive reserve (Amato et al., 2013; Sumowski et al., 2013).

Besides depression impacting cognitive functioning or cognitive functioning resulting in depression, it is also possible that both common problems in MS could result from some third variable, for example, a common neurobiological factor such as inflammation in the basal ganglia and white matter. We have also previously proposed (Arnett, Higginson, & Randolph, 2001) that, given that left frontal hypoactivation is common in depression in general (e.g., Davidson, 1992; Niemiec & Lithgow, 2005) and that the left frontal brain region appears to be important in performance on executive and working memory/speeded processing tasks associated with depression in MS, differential white matter lesion damage and/or hypoactivation in this region could result in both depression and cognitive problems.

Primary problems with visual acuity as well as problems with output modalities (e.g., fine motor skills, oral–motor speed) can also compromise performance on higher-level cognitive tasks requiring these outputs and thereby confound interpretation of test results. It is unclear whether higher-order visual deficits are a function of primary visual disturbances involving blurred vision and diplopia (Rao, Leo, Bernardin, & Unverzagt, 1991), though a study from our lab suggests that such factors may play an important role (Bruce, Bruce, & Arnett, 2007). Research from our lab also suggests that rudimentary problems with oral–motor speed differentially contribute to performance on commonly used cognitive tasks in evaluating MS, such as the oral version of the SDMT (Arnett, Smith, Barwick, Benedict, & Ahlstrom, 2008; Smith & Arnett, 2007). Such problems in oral–motor speed appear to magnify the relatively poorer performance of patients with MS on such tasks.

Depression

The prevalence of depression is high in patients with MS (Arnett, 2003; Fischer et al., 1994; Goldman Consensus Group, 2005; Minden & Schiffer, 1990). The lifetime risk for depression has been estimated at around 50% (Patten & Metz, 1997), compared with a lifetime risk in the general population of around 10–15% (American Psychiatric Association, 1994). Point prevalence rates are also high, with the most rigorous community-based study showing 26%, with a confidence interval ranging from about 19% to 33% (Viner et al., 2014). The latter range is very similar to that suggested by a recent study using a variety of self-report depression measures (Strober & Arnett, 2015). Because of its high prevalence, importance to quality of life and patients' well-being (Kenealy, Beaumont, Lintern, & Murrell, 2000), and possible influence on the disease course itself (Ackerman et al., 2000; Mohr et al., 2000), depression has been intensively studied in MS. The significance of depression in MS is also underscored by the fact that depression scores are highly predictive of suicidal intent in patients with MS (Feinstein, O'Conner, & Feinstein, 2002).

Depression in MS has been shown to be treatable through brief and even telephone-based cognitive-behavioral therapy (CBT; Mohr et al., 2000, 2005) as well as group therapy. In addition, cognitive-behavioral stress management training has been shown to reduce emotional distress in patients with MS (Fischer et al., 1994), and psychopharmacological treatments have been shown to be effective in treating depression in these patients (Mohr & Goodkin, 1999). Nonetheless, depression has been historically undertreated in MS, despite the fact that successful treatment of depression is associated with greater adherence to immunotherapy (Mohr, Likosky, et al., 1999).

A number of factors have been found to have a strong association with depression, including reduced social support (McCabe, McKern, & McDonald, 2004; Bambara, Turner, Williams, & Haselkorn, 2011), dysfunctional attitudes and negative cognitive schema (Bruce & Arnett, 2005), perfectionism and physical disability (Smith & Arnett, 2013), stress and maladaptive coping (Pakenham, 1999; Tan-Kristanto & Kiropoulos, 2015), and the extent of lesion damage in the brain (Bakshi et al., 2000; Feinstein et al., 2004; Gold et al., 2014). Recent research has also shown that reduced functional connectivity at rest in hippocampal structures is associated with depression in MS (Rocca et al., 2015). Not surprisingly, depression has also been shown to be related to sexual dysfunction in MS (Demirkiran, Sarica, Uguz, Yerdelen, & Aslan, 2006; Zivadinov et al., 2003). Additionally, research has consistently demonstrated that depression is highly negatively correlated with quality of life in MS (D'Alisa et al., 2006; Janardhan & Bakshi, 2002; Patti et al., 2003; Fernández-Jiménez & Arnett, 2014) and that effective treatment of depression may alleviate this effect (Hart, Fonareva, Merluzzi, & Mohr, 2005). Effective treatment of depression in patients with MS has also been found to improve adherence to disease-modifying treatment (Mohr, Goodkin, Gatto, & Van Der Wende, 1997; Bruce, Hancock, Arnett, & Lynch, 2010).

There is no consensus regarding the nature of depression in the MS literature. Some investigators have presented evidence that neurovegetative symptoms of depression are not valid indicators because of their overlap with MS symptoms (e.g., sleep disturbance, fatigue, sexual dysfunction; Beeney & Arnett, 2008; Mohr, Goodkin, Likosky, Beutler, et al., 1997; Rabinowitz, Fisher, & Arnett, 2011; Randolph, Arnett, Higginson, & Voss, 2000), whereas others have provided evidence to the contrary (Aikens et al., 1999; Moran & Mohr, 2005). This debate suggests that caution is warranted in interpreting neurovegetative symptoms of depression as such in any individual patient with MS (for a more extensive treatment of this issue, see Strober & Arnett, 2015).

Although cognitive reserve has mostly been examined in the context of cognitive outcomes, recent work has explored its applicability to depression. Cadden, Guty, and Arnett (2018) found that cognitive reserve moderated the relationship between MS disability and depression. Specifically, the measure of MS disability, EDSS, only predicted depression in those PwMS with low-cognitive reserve but not high-cognitive reserve.

Ecological Validity of Cognitive Tests in MS

Perhaps the seminal study examining the ecological validity of cognitive tests in MS was Rao, Leo, Ellington, and colleagues' (1991) comprehensive examination of the impact of cognitive dysfunction on employment and social functioning. These investigators divided their sample of 100 patients with MS into groups of 52 "cognitively intact" and 48 "cognitively impaired" patients. To demarcate their groups, they first determined the mean number of "failed" tests from a comprehensive neuropsychological battery of 31 test indices that a matched control group of 100 participants had taken. These investigators determined that less than 5% of controls failed (i.e., they scored below the fifth percentile) four or more tests in the battery. Thus, failing four or more tests was operationalized as failing the entire battery. Participants were then administered a number of measures pertaining to real-world skills, including the EDSS (Kurtzke, 1983), the Incapacity Status Scale (ISS; Kurtzke, 1981), and the Environmental Status Scale (ESS; Mellerup, Fog, & Raun, 1981). The EDSS is a standard measure of physical/neurological disability in MS that focuses primarily on ambulation; the ISS measures basic activities of daily living (ADLs) such as stair climbing, dressing, and bed and chair transfers; and the ESS assesses degree of social handicap from illness in seven domains, including employment, social activities, personal assistance required, community assistance required, financial status, need for transportation, and modifications to personal residence. An occupational therapist also conducted a 2-hour evaluation in patients' homes. Patients were rated on the Barthel Index (BI; Mahoney & Barthel, 1965), the Klein–Bell ADL (Activities of Daily Living) Scale (Klein & Bell, 1982), and a homemaking evaluation. In the last-named assessment patients performed three tasks: cooking a simple dessert, demonstrating the operation of household appliances, and making a bed. The Klein–Bell Scale includes ratings in six ADL domains (dressing, elimination, mobility, bathing/hygiene, eating, and communication). Finally, the BI provides an overall summary score reflecting level of dependence on others for ADLs. Patients and significant others also completed various self-report measures pertaining to emotional functioning, as well as a measure of sickness-related disability. Because of its relevance to the topic at hand, the results of Rao and colleagues' seminal study are variously described in the relevant sections that follow.

Independent Activities of Daily Living

ADLs involve a variety of basic functions such as dressing oneself, bathing and hygiene, eating, and communicating, among others. Impairments in ADLs are extremely common in MS. In one of the most representative samples of patients with MS reported in the literature to date, Sarah Minden and her colleagues (2006) noted that almost two-thirds of over 2,000 patients with MS in the Sonya Slifka Longitudinal MS Study needed help from another person to perform routine or instrumental activities of daily living. Several studies have now examined the relationship between cognitive dysfunction and ADLs in MS. In a study examining 31 cognitively and functionally impaired patients with MS, Higginson and colleagues (2000) used standard clinical neuropsychological tests of memory and attention, in addition to two batteries of memory and attentional tests designed to be more ecologically valid, to predict ADLs in MS. The standard clinical tests included the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987), 7/24 Spatial Recall Test (Rao, Leo, Bernardin, & Unverzagt, 1991), PASAT, and oral SDMT

(Smith, 1982). The ecologically valid batteries were the Rivermead Behavioural Memory Test (RBMT; Wilson, Cockburn, & Baddeley, 1985) and the Test of Everyday Attention (TEA; Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). The ESS (described earlier) was used to measure ADLs. The standard neuropsychological tests were quantified into one index based on the number of scores below the 16th percentile of the MS sample; a comparable strategy was conducted using the subtests from the ecologically valid batteries. These investigators found that both summary indices were significantly (r = .40) correlated with the ESS. More specifically, the following standard subtests were significantly ($p < .05$) correlated with the ESS: CVLT Long-Delay Free Recall, PASAT, and Symbol Digit; on the RBMT, the Name, Belonging, and Story-Delayed subtests; and on the TEA, the Elevator Counting with Distraction, Elevator Counting with Reversal, and Time per Switch from the Visual Elevator task. In a stepwise regression analysis including the two summary indices, only the ecologically valid cognitive index significantly predicted ESS score after level of physical disability (EDSS score) was controlled for.

Grasso, Troisi, Morelli, and Paolucci (2005) examined the relationship between two measures of ADLs (the BI and the Rivermead Mobility Index [RMI]) and cognitive functioning in a group of 230 patients with primary and secondary progressive MS who had undergone a 3-day-a-week, 8-week rehabilitation treatment program. Cognitive functioning was categorized in EDSS format for functional systems (none, minimal, moderate, and severe impairment) by using the results of a neuropsychological evaluation. These investigators found that worse overall scores on the BI were significantly associated with worse cognitive performance. They also found that patients who were not severely impaired cognitively had a probability of improvement on the RMI that was almost twice as high as that of the severely impaired group. These authors speculated that cognitively impaired patients with MS may not be able to benefit from rehabilitation treatment because they may be unable to collaborate with the rehabilitative team in an effective way. One limitation of this study is that, given the broad-based nature of a measure such as the BI, it is unclear which aspects of ADLs were associated with cognitive impairments. Also, the authors did not describe the neuropsychological battery used, nor did they attempt to examine the association between ADLs and specific types of cognitive difficulties.

In a study with implications for rehabilitation, Basso and colleagues (Basso, Lowery, Ghormley, Combs, & Johnson, 2006) examined whether self-generated encoding improved memory for names, appointments, and object locations in a sample of patients with MS and moderate-to-severe memory problems. They found that, compared with a didactic procedure for encoding information, even patients with moderate–severe memory problems had better recall in ADLs when the information was self-generated. As these authors speculate, it may be that memory-impaired patients with MS would be able to improve their ability to remember names, appointments, and object locations—basic ADLs—if they developed strategies to encode this information themselves.

One limitation of the studies that have been conducted on cognitive dysfunction and ADLs in patients with MS is that most have used subjective reports of ADLs (but cf. Rao, Leo, Ellington, et al., 1991). As Goverover and her colleagues (2005) have noted, subjective reports may be limited in their accuracy in that the relationship between subjective and objective indicators of ADLs is often weak. In response to this gap in the literature, Goverover et al. conducted a study that examined instrumental ADLs using both subjective (Functional Assessment of Multiple Sclerosis [FAMS] and Functional

Behavior Profile questionnaire completed by both patients and significant others) and objective measures (Executive Function Performance Test [EFPT]). In the EFPT, patients carry out six ADLs, including hand washing, simple cooking, telephone use, medication management, and bill paying (a more complex cooking task was also included). These investigators found that self-reported measures of ADLs were not significantly correlated with EFPT scores. These results suggest caution in interpreting self-reported ADLs in MS, because they may not accurately reflect patients' ability to actually perform various ADLs. However, it is also notable that the authors failed to find significant correlations between self-reported ADLs and EFPT scores in the healthy controls, suggesting that self-report measures and the EFPT measures may be tapping into different aspects of ADL functioning. It may also be the case that the novelty of the environment in which the EFPT tasks were completed provided an additional executive challenge that the participants do not experience in their home environments (e.g., using an unfamiliar stove and utensils to prepare a casserole vs. preparing a familiar recipe at home with frequently used appliances and utensils). This additional executive demand may result in poorer performance and a discrepancy between participants' self-ratings and their performance on the objective measure.

Overall, the existing data on the association between cognitive dysfunction and performance of ADLs in patients with MS indicate that there is a consistent relationship regardless of whether ADLs are measured via actual performance or self-report, despite the fact that there may be little association between objective and subjective measures of these ADLs. The data also suggest intriguing clues regarding what might be helpful to patients in rehabilitation. Patients with mild–moderate (but not severe) cognitive impairments appear to show some benefit from rehabilitation programs, even if the outcome measure for the rehabilitation is not cognitive (i.e., mobility). That said, even patients with more severe memory impairments appear to be able to improve their memory of important everyday activities if they self-generate the information that needs to be remembered. Caution is warranted with such an extrapolation, however, because in each of these latter cases, only one study reported the finding.

Driving Ability

Several studies on the relationship between cognitive functioning and driving in MS have been published. Schultheis, Garay, and DeLuca (2001) appear to have published the first empirical study examining this issue. These investigators compared 13 patients with MS and cognitive impairments with 15 cognitively normal patients with MS and 17 healthy controls on two computerized measures of driving ability. Most of the patients with MS had a relapsing–remitting course type, though a definitive course type could not be ascertained for almost 30% of the sample. The computerized driving tasks included the Neurocognitive Driving Test (NDT) and the Useful Field of View (UFOV) test. The UFOV quantifies the visual field area in which drivers rapidly process visual information; it consists of three subtests involving visual information processing, divided attention, and selective attention. The UFOV generates an overall score and also categorizes participants according to risk level (low, moderate, high). The NDT is also computerized and assesses driving-related skills in an ecologically valid format. The NDT has two composite scores, one involving response latency and the other involving errors. Schultheis and colleagues found that cognitively impaired patients with MS performed significantly more slowly than both cognitively intact patients with MS and healthy controls on the response latency score from the NDT. The groups did not differ on errors on the NDT. On the UFOV test, significantly more cognitively impaired patients with MS (29%) were classified in the high-risk group for probability of driving difficulties compared with both the cognitively intact participants with MS and the healthy controls (0% for both). The cognitively impaired group with MS also performed significantly worse than the other two groups on the central vision and processing section of the UFOV. Additionally, cognitively impaired patients with MS performed significantly worse than healthy controls on the selective attention subtest of the UFOV. Thus, these investigators reported the first clear evidence that cognitive impairment in MS was associated with driving difficulties on a simulated test, especially on driving-related activities involving rapid information processing. These findings dovetail nicely with the numerous studies that have demonstrated that deficits in information-processing speed are one of the most commonly observed cognitive problems in patients with MS.

Kotterba, Orth, Eren, Fangerau, and Sindern (2003) extended Schultheis and colleagues' (2001) work by comparing the performances of 31 patients with relapsing–remitting MS in a driving simulator with those of 10 healthy matched controls. The driving simulation, conducted using the computer-aided risk (CAR) simulator, involved participants driving for 60 minutes on a "highway." Various obstacles were presented to the drivers, as well as a variety of driving conditions. Concentration errors were identified, including errors of omission—disregarding the speed limit, traffic lights, or the right of way—as well as of commission—turning too far to the right or left or touching curbstones or the opposite lane. Finally, accidents were tallied. Participants were also administered the MS Functional Composite (MSFC) and the EDSS. Kotterba and colleagues found that the accident rate and the number of concentration faults were significantly higher in patients with MS compared with controls. Interestingly, neither the EDSS nor the two physical components of the MSFC were correlated with either of these difficulties; however, the cognitive index from the MSFC was significantly correlated with concentration errors on the CAR.

One limitation of Kotterba and colleagues' (2003) study is that differential levels of fatigue may have played a role in the poorer performance of patients with MS; however, the authors did not report on fatigue levels of the sample. Another limitation of this study is that the authors used only one test to measure cognitive dysfunction, the PASAT, which is the only measure used to assess cognition on the MSFC.

Shawaryn, Schultheis, Garay, and DeLuca (2002) conducted a study similar to Kotterba's (2003) investigation in that they examined the relationship between MSFC scores and driving indices in 29 mostly relapsing–remitting patients with MS. In addition to using the NDT and UFOV measures described above, these investigators included number of self-reported motor vehicle collisions (MVCs), as well as number of violations and crashes formally reported to the Department of Motor Vehicles (DMV) from the states in which participants lived. These investigators found that the cognition index from the MSFC (the PASAT) was significantly inversely correlated with all three UFOV indices, in addition to the response latency index from the NDT. The hand and leg/ambulation components of the MSFC were significantly correlated with the measure of selective attention from the UFOV, and the MSFC hand index was also significantly associated with response latency on the NDT. These authors also found that the overall MSFC (but none of the subcomponents) was inversely correlated with number of reported

DMV crashes. One limitation of this study is the finding that education was significantly correlated with overall UFOV score. It was unclear from the follow-up analyses whether this overall UFOV score would still have been significantly predicted by the cognitive component of the MSFC if education had been covaried out of the equation. Other limitations (acknowledged by the authors) included relatively small sample size, in addition to a limited range of physical disability in the sample.

Schultheis, Garay, Millis, and DeLuca (2002) compared 13 cognitively impaired and 14 cognitively intact, mostly relapsing-remitting patients with MS with 17 healthy controls on the numbers of formal MVCs and motor vehicle violations (MVVs) during the previous 5-year period. The cognitively impaired group with MS showed a significantly greater incidence of one or more MVCs compared with both of the other groups; the groups did not differ on the number of MVVs. The authors' findings on MVCs were especially striking in that the cognitively impaired group with MS also reported driving fewer days per week than the other groups.

Studies conducted since the first edition of this book have generally supported the initial findings on the ecological validity of neuropsychological tests in predicting driving performance either on the road tests (e.g., Devos et al., 2017) or in off-road simulators (Akinwuntana et al., 2018). A recent comprehensive review conducted by Krasniuk and colleagues (2019) concluded that the Stroke Driver Screening Assessment and UFOV test were best in predicting fitness to drive in adults with MS (level B). However, they further noted that much more research needed to be conducted in this area, especially involving Class I studies.

These recent studies examining the ecological validity of neuropsychological tests in the context of driving are provocative. One limitation of existing studies that we identified in the first edition of this book is that the possible mediating role of depression was not examined. Since then, at least two studies have included depression measures. One of these studies found that depression was not correlated with driving variables (Devos et al., 2017), and the other simply included depression as a descriptive variable but did not examine it in relation to driving variables (Akinwuntana et al., 2018). Given that depression appears to be associated with cognitive dysfunction in some MS samples (e.g., Arnett, 2005; Denney et al., 2004; Sundgren, Maurex, Wahlin, Piehl, & Brismar, 2013), more work in this area is necessary.

Medication Management/Adherence

Individuals with MS often have complicated medication regimens, including disease-modifying therapies (DMTs) as well as symptomatic treatments, such as those for bladder dysfunction or spasticity. In recent years, treatment options have greatly expanded with more than 15 DMTs currently approved by the FDA. Options for route of delivery now include IV infusion, subcutaneous injection, intramuscular injection, and oral methods. Dosing varies from twice daily to once a year. Adherence is known to be variable in MS. In a meta-analysis completed by Menzin et al. (2013), treatment adherence rates to DMTs ranged from 41 to 88% across 24 studies. Maintaining adherence to variable medication schedules over what is typically many years of use places demands on executive, attentional, memory, and, to some degree, motor skills. While factors beyond cognition such as tolerability, expense, and communication between patient and care providers influence adherence rates, in a report completed by the Global Adherence Project, "forgetting" was the most frequent patient-reported reason for treatment nonadherence (Devonshire, 2011). Further, adherent patients indicated significantly lower levels of cognitive impairment on a self-report measure. Given that the efficacy of DMTs in reducing the frequency of exacerbations and disability progression has been well established (Burks, 2005; Coppola et al., 2006; Sandberg-Wollheim, 2005), as has the long-term nature of damage done by increasing lesion loads, it is critical to examine any factors that negatively impact treatment adherence. This issue is particularly important when one considers that adherence to DMTs is not only associated with decreased frequency of relapse and slowed disease progression (Steinberg, 2010; Tan, Cai, Agarwal, Stephenson, & Kamat, 2011), but may actually improve cognitive functioning in patients with relapsing-remitting MS (e.g., Barak & Achiron, 2002; Fischer et al., 2000; Kappos, 2009; Mattioli, 2011; Pliskin et al., 1996; see Patti, 2009, for a review). While several investigators have examined the relationship between medication adherence and patient perception of cognitive functioning, few have examined the relationship between objective cognitive functioning and medication adherence in MS. Bruce and colleagues (2010) reported on a sample of 55 patients with relapsing-remitting MS being treated with an injectable DMT (glatiramer acetate, interferon beta-1b, or interferon beta-1a), who participated in an 8-week observation period in which their adherence to their DMT was measured using self-report, a medication diary, and needle disposal bottles fitted with electronic monitoring caps that recorded time and date for each needle disposal. Poorer adherence was significantly associated with poorer performance on measures of prospective memory, list learning, and list recall. Findings also suggested a strong relationship between co-occurring mood and anxiety symptoms and poor adherence. In another investigation, Settle et al. (2016) found that participants with MS who performed more poorly on the SDMT triggered more alerts on an electronic medication adherence monitoring system than those who performed in the unimpaired range.

Several questions remain regarding the relationship between cognition and DMT adherence in MS. Given the importance of adherence to DMTs in preventing progression and relapse, future research should address possible methods of remediation of deficits associated with nonadherence. Further, given possible differential challenges in adhering to injectable versus oral medications, neuropsychological research into the role of cognition in medication adherence may be critical in order to enable neurologists to make informed treatment recommendations. While adherence research in MS has tended to focus on adherence to DMTs, another potential area of exploration includes how cognitive changes might affect adherence to other medical treatments, such as clean intermittent self-catheterization, as examined by Vahter et al. (2009). The authors found that the number of lessons required to learn the procedure was negatively correlated with visuospatial memory, though, overall, the ability to learn the procedure was not dependent on cognitive performance. Though based on a small sample, when the researchers followed up with the study group after 3 months, six participants had stopped using the procedure, four of whom demonstrated "significant impairment in executive functions." The authors interpreted this finding as suggesting that patients with significant executive dysfunction may require more assistance in adhering to interventions. In a broader sense, neuropsychological evaluation could serve a useful role in identifying patients who may require case management or increased nursing intervention in order to adhere to specific physical therapy recommendations and complex DMT treatment schedules, or simply to maintain routine neurology follow-up.

Vocational Status

Unemployment rates in MS populations have been reported to be as high as 80% (Scheinberg et al., 1980), with some research showing that 70–80% of patients with MS are unemployed within 5 years following diagnosis (Kornblith, LaRocca, & Baum, 1986). A Norwegian study conducted by Glad and colleagues (Glad, Nyland, Aarseth, Riise, & Myhr, 2011) suggests a reason for the variability in reporting, noting very different rates of unemployment in their “benign” (35.0%) versus “non-benign” (82.8%) MS groups. However, as Glad et al. observe, it is important to be aware that research on vocational functioning in MS may not generalize across nations due to differences in social welfare networks, health care coverage, and legal protections for workers with disabilities that may serve to influence whether someone with MS remains employed. With this caveat in mind, in a longitudinal study spanning 7 years, Ruet et al. (2013) reported that in their sample of 65 “newly diagnosed” patients with MS in France, 81.5% ($n = 65$) worked at baseline whereas only 54.1% ($n = 48$) of the participants who continued in the study were working at follow-up. Because MS affects many individuals in the early stages of their careers, work disability due to MS may affect attainment of life goals, worsen financial difficulties, and exacerbate caregiver stress. In addition to its obvious financial importance, employment has also been found to be related to quality-of-life ratings in MS (Koch, Rumrill, Roessler, & Fitzgerald, 2001). Considering the immense importance of mitigating disability due to MS, clinicians should be aware of factors that reliably predict change in employment status in order to assist patients with treatment planning and better focus rehabilitation efforts.

Several studies have examined factors associated with work status change in MS. Greater physical disability (Edgley, Sullivan, & Dehoux, 1991; Kornblith et al., 1986; Krause, Kern, Horntrich, & Ziemssen, 2013; Smith & Arnett, 2005), increased age (Beatty, Goodkin, Monson, Beatty, & Hertsgaard, 1995; Edgley et al., 1991; Glad et al., 2011; Krause et al., 2013; Kornblith et al., 1986), longer diagnosis duration (Krause et al., 2013; Strober & Arnett, 2016), and less education (Edgley et al., 1991; Glad et al., 2011; Krause et al., 2013; Kornblith et al., 1986) have been found to be related consistently to unemployment in MS. Factors that have less consistent support include gender (males are more likely to be employed) and depression (Glad et al., 2011; Krause et al., 2013).

The majority of published empirical studies examining neuropsychological test data and their relationship to unemployment in MS have found that individuals with MS who are unemployed perform more poorly on cognitive measures (see Clemens & Langdon, 2018, for a review). Regarding specific measures, the SDMT (Benedict et al., 2005; Buhse, Banker, & Clement, 2014; Krause et al., 2013; Morrow et al., 2010; Strober & Arnett, 2016; Strober, Chiaravalloti, Moore, & DeLuca, 2014) and the PASAT (Covey et al., 2012; Krause et al., 2013; Ruet et al., 2013) appear to have the most robust support as measures that distinguish people with MS who maintain employment versus those who stop working.

While cross-sectional differences in cognitive performance between individuals with MS who are employed and those who are not have been reported frequently, studies addressing this question from a longitudinal perspective are less common. Morrow et al. (2010) sought to provide neuropsychological markers of “clinically meaningful” cognitive decline in a 3-year longitudinal study, and they reported that a decline of 2 raw score points on the CVLT-II total learning or 4 raw score points on the SDMT produced odds ratios of work status deterioration of 3.7 and 4.2, respectively. A well-designed study conducted by van Gorp and colleagues (2019) in the Netherlands followed 124 employed participants with relapsing-remitting MS and 60 healthy controls over the course of 2 years. After 2 years, the participants with MS were divided into sustained employment or decreased employment (left employment or reduced work hours by at least 20%) groups. At baseline, these groups did not differ on demographic variables such as age, gender, or education level and were similarly equivalent on disease variables such as anxiety, disease duration, and use of immunomodulatory treatment. However, at baseline the participants who would go on to have decreased employment at 2 years demonstrated worse physical disability (as measured by the EDSS), poorer performance on measures of complex attention and executive functioning, worse self-reported cognitive functioning, and more depression and fatigue versus the group that maintained employment. In a regression analysis, only physical disability and executive functioning (as measured by PASAT, Trail Making Test, Delis-Kaplan Executive Functioning System Color-Word Interference Test and Design Fluency Test) emerged as significant predictors of group status at 2 years, with a moderate effect.

In a study utilizing a sample of 52 employed participants with MS, Benedict and colleagues (2014), found poorer performance on the PASAT predicted negative work events (e.g., verbal reprimands), requiring accommodations at work (e.g., rest breaks) and reduced hours at work. In the longitudinal study described previously, Ruet et al. (2013) classified participants as cognitively impaired if they performed at or below 1.5 standard deviations below the control group mean on at least two tests in the cognitive battery. Using this standard, they found that 52.3% of their sample was classified as cognitively impaired at baseline. This status was a significant predictor of employment status at 7-year follow-up in a logistic regression analysis. When performance on specific tests was considered, a composite score made up of performance on the SDMT and the PASAT at baseline (defined as a measure of information processing speed) was also a significant predictor of vocational status at follow-up, though memory and verbal fluency performance at baseline were not. Similarly, Corey, Shucard, Shucard, Stegen, and Benedict (2013) reported that in a sample of 47 participants with MS and 47 participants with systemic lupus erythematosus, a composite score made up of the PASAT, SDMT, and Delis–Kaplan Executive Function System was a significant predictor of vocational status in a cross-sectional analysis, with no differential effect based on disease status. No such relationship was found for the "nonexecutive" measures including Judgment of Line Orientation (JLO), Controlled Oral Word Association Test (COWAT), CVLT-II, and Brief Visuospatial Memory Test-Revised (BVMT-R).

We reported findings that were inconsistent with these results (Smith & Arnett, 2005). In a community-based sample of 50 individuals with MS, we controlled for the effect of participants' education levels, depression levels, medication effects, and age on their test performance. After doing this in a multivariate analysis, we found that participants who cut back on their hours due to MS, who left their jobs due to MS, and who remained employed full time were not significantly different on a variety of cognitive measures commonly found to detect impairment in MS (the PASAT, the oral SDMT, the Selective Reminding Test, the Tower of Hanoi, the COWAT, and the 7/24 Spatial Recall Task). Additionally, when asked what MS symptoms precipitated their employment status change, only a relatively small percentage of participants (10% of the group that cut back on hours and 29% of the group that left jobs) reported that cognitive symptoms were responsible. This finding is consistent with the results of Edgley and colleagues (1991), who found that only 12% of their unemployed sample reported cognitive symptoms (when asked in an open-ended format) as a primary reason for having discontinued employment and Glad et al. (2011), who found no association between cognition and unemployment in a "benign" MS group. It may be that, although cognitive impairment is common in patients with MS who have had to stop working, it is not the deciding factor for patients who are considering leaving their jobs. This hypothesis is supported by the finding that the majority (86%) of the unemployed patients with MS in our sample (Smith & Arnett, 2005) reported that they left their jobs due to physical or neurological symptoms. It may be that, although patients with MS experience difficulties at work due to their cognitive symptoms, physical symptoms pose the greatest challenge and result in the most disability.

Many areas for future research remain to be explored. The extent of the impact of cognitive impairment on employment in MS is still unclear, though most studies support a relationship. Changes to the health insurance system in the United States through the Affordable Care Act may influence this area of inquiry in that individuals may feel less pressure to remain employed in order to maintain insurance coverage and not be disqualified due to a preexisting condition. Further investigations into these questions will improve our understanding of the impact of cognitive symptoms in MS and may help cognitively impaired individuals with MS decide between struggling to maintain employment or facing early retirement on disability.

Social Functioning and Quality of Life

Quality of life (QOL) includes a person's life satisfaction, happiness, and standard of living, and within the health sciences, health-related quality of life (HRQOL) is frequently the focus of investigation. The concept of HRQOL specifically refers to the amount a person or group is affected by physical or mental health problems. HRQOL is distinct from QOL, which is decidedly "more difficult to conceptualize and operationalize because it is affected by economic, political, cultural, and spiritual factors that are not the primary focus for health-care providers" (Shawaryn, Schiaffino, LaRocca, & Johnston, 2002, p. 310). "Social functioning" represents another difficult-to-define concept, closely related to QOL. In the current review, we explore the literature regarding the relationship between cognitive dysfunction, social functioning, and HRQOL in MS.

Investigations of different aspects of social functioning and their relationship to cognitive functioning in MS have yielded mixed findings, particularly in relation to whether social functioning is correlated with cognition or mood measures. In an exploration of the relationship between cognitive functioning, fatigue, depression, and dyadic adjustment in MS, King and Arnett (2005) found that neither patient nor significant-other ratings of dyadic adjustment were significantly correlated with performance on measures of speeded attention/working memory or long-term memory. However, they reported that executive dysfunction was a significant predictor of significant-other-rated dyadic adjustment; this indicates that the significant others of patients experiencing greater executive dysfunction rated the quality of their relationships more negatively. Importantly, in this investigation, cognitive dysfunction was found to be a weaker predictor of poor dyadic adjustment than fatigue or depression.

Phillips et al. (2014) found that depression scores mediated participant report of emotion regulation difficulties in MS, while there was no significant relationship with cognitive measures (a go-no-go task and the COWAT). The same lead investigator also reported that participants with MS performed more poorly than controls on an emotion perception task, performance on which was related to QOL measures (Phillips et al., 2011). Examining another aspect of social functioning in a German sample, Pöttgen, Dziobek, Reh, Heesen, and Gold (2013) reported that participants with MS demonstrated poorer performance on a test of theory of mind compared to age- and education-matched controls. While performance on the theory of mind task correlated with performance on tests of verbal learning and memory, executive functioning, and the SDMT, there was no such relationship with depression (as measured by the Hospital Anxiety and Depression Scale). In another German sample, Kraemer et al. (2013) reported that 25 participants with "early-stage" relapsing-remitting MS performed more poorly than 25 healthy controls on an emotional prosody task, but this performance was not correlated with performance on executive functioning measures (a letter–number sequencing task, Trail Making Test, and a Stroop task).

In a longitudinal investigation in individuals with MS enrolled in a subcutaneous interferon β-1a drug trial, Patti et al. (2012) reported no significant differences between cognitively impaired (defined by scoring at least one standard deviation below the mean on at least three cognitive measures on Rao's Brief Repeatable Battery) and cognitively intact participants with MS on the Environmental Status Scale, a measure of social functioning. Furthermore, social functioning did not significantly decline over the 3 years of observation.

Overall, individuals with MS experience poorer QOL when compared with neurologically healthy individuals (Benedict et al., 2005; Shawaryn, Schiaffino, et al., 2002) and individuals with other chronic illnesses (Rudick, Miller, Clough, Gragg, & Farmer, 1992). With the increased emphasis on patient-reported outcome research, accelerated by the establishment of the Patient-Centered Outcomes Research Institute in 2010, measurement of HRQOL has become increasingly sophisticated and central to outcome research. As such, investigators have examined the relationship between cognitive dysfunction and HRQOL. However, as Baumstarck-Barrau et al. (2011) noted, research in this area has revealed inconsistent findings regarding the impact of cognitive change on QOL in individuals with MS (we discuss these inconsistencies below).

Several early investigations failed to account for the role of depression in the relationship between cognition and QOL (e.g., Barker-Collo, 2006; Cutajar et al., 2000; Shawaryn et al., 2002). As noted in our earlier review on this topic, many studies have now demonstrated that depression is significantly associated with worse performance on cognitive measures, particularly those measuring complex information processing, such as the PASAT. If the patients who are experiencing more depression are also experiencing more information-processing dysfunction, then depression may be a mediator in this relationship, as, not surprisingly, depression has been found to be significantly negatively correlated with HRQOL (Amato et al., 2001; Spain, Turbridy, Kilpatrick, Adams, & Holmes, 2007).

Investigators who have controlled for depression in their analyses of this question have often reported that there is a small to no relationship between cognitive functioning and QOL in MS. Benedict and colleagues (2005) found that performance on the BVMT-R Recognition index was a significant predictor of QOL as measured by the

MSQOL-54P, an expansion of the Short Form Health Survey 36 (SF-36) questionnaire, though performance on a variety of other measures sensitive to deficits typically seen in MS (COWAT, JLO, CVLT-II, SDMT, PASAT, and WCST) was not significant. Additionally, the BVMT-R Recognition index was no longer a significant predictor when noncognitive variables were entered into the regression model. In a study using the SF-36, Spain and colleagues (2007) found that performance on the SDMT did not predict overall physical and mental health subscale scores in a regression model when other disease variables (e.g., EDSS, depression, fatigue, pain) were entered. Similarly, in a French study, Baumstarck-Barrau et al. (2011) reported that in a sample of 124 participants with MS, no significant relationship was found between ratings on the Multiple Sclerosis Quality of Life Inventory and performance on the cognitive measures that compose the Rao Brief Repeatable Battery, though marital status, physical disability, and depression were significant predictors. Baruch et al. (2015) reported no significant differences between adults with pediatric-onset MS and adults with adult-onset MS on measures of HRQOL, fatigue, social support, and depression, though the participants with pediatric-onset MS scored more poorly on the SDMT. Grech et al. (2015) examined the relationship between performance on an extensive battery of executive functioning measures (Iowa Gambling Test, several measures from the Behavioural Assessment of the Dysexecutive Syndrome, verbal fluency, a reading span task, measures from the TEA, the Hayling Sentence Completion Test, Trail Making Test, and SDMT) and QOL in a highly educated (> 50% of the sample reported a college or postgraduate degree), minimally physically disabled (mean EDSS = 2.90) sample of 107 individuals with MS. Despite the lengthy battery, none of the measures analyzed were found to be significant predictors of overall QOL. While the authors report that the error score on Trails B was found to be a significant predictor of physical health QOL, when overall physical disability was controlled for in the analyses (with poorer performance predicting poorer physical QOL), the restricted range of this predictor suggests that this finding may be unreliable. Adding further evidence, Giovannetti and colleagues (2016) also reported that once anxiety and depression were entered into a hierarchical regression, processing speed (as measured by the SDMT) was no longer a significant predictor of HRQOL in 181 participants with MS. Similar results were found in a smaller sample ($n = 55$) but one using a more extensive cognitive battery by Yalachkov et al. (2019).

However, when Ryan and colleagues (2007) examined predictors of psychological distress, global life satisfaction, and HRQOL in a sample of 74 individuals with MS, they found that cognitive functioning (as measured by a composite score based on performance on the SDMT, the Brief Test of Attention, JLO-Short Form, WAIS-III Letter–Number Sequencing, a Stroop test, COWAT, CVLT-II, and WCST) was a significant predictor of life satisfaction and HRQOL (i.e., more cognitive impairment was related to poorer life satisfaction and HRQOL), though the effect size was small. The authors reported that psychological distress and cognition were not significantly related in their sample and noted that this was in contrast to previous findings suggesting that patients with MS with higher levels of depression tend to perform more poorly on neuropsychological measures. However, rather than using a measure assessing depression symptoms such as the BDI, they examined the relationship between cognition and psychological distress in general, which may explain the discrepancy.

In a large sample of MS patients, Benito-Leon, Morales, and Rivera-Navarro (2002) examined the relationship between cognitive dysfunction and HRQOL using the FAMS

QOL questionnaire. This 52-item measure has six subscales that measure mobility, symptoms, emotional well-being, general contentment, thinking/fatigue, and family/social well-being. Cognition was measured by the Mini-Mental State Examination (MMSE) and the clock-drawing test. The researchers reported that both cognitive tests were significantly negatively correlated with all six subtests of the FAMS, indicating that low HRQOL was associated with higher levels of cognitive impairment. The authors also found that physical disability, as measured by the EDSS, and depression and anxiety, as measured by the Hamilton Depression Rating Scale and the Hamilton Anxiety Rating Scale, were significantly correlated to the FAMS, with increased physical disability, depression, and anxiety associated with decreased HRQOL. A positive aspect of this study is that performance on the clock-drawing test is typically not affected by an individual's level of depression (Herrmann, Kidron, & Shulman, 1998; Wolf-Klein, Silverstone, & Levy, 1989). It may therefore be concluded that the association between performance on this test and HRQOL was not likely due to depression.

Hoogs, Kaur, Smerbeck, Weinstock-Guttman, and Benedict (2011) examined performance on the neuropsychological measures making up the Minimal Assessment of Cognitive Function in MS (MACFIMS) and the ability to predict a dichotomous rating (poor vs. good) of QOL, while controlling for demographic variables, fatigue, and depression. The investigators reported that in their sample of 132 patients with MS, both physical disability and performance on the SDMT were significant predictors of physical HRQOL (as measured by the Sickness Impact Profile). Performance on the SDMT was also a significant predictor of poor versus good overall HRQOL and psychosocial QOL.

Other investigators have sought to increase the specificity of their findings by selecting more homogeneous groups of participants. Glanz and colleagues (2010) reported that in their investigation of the relationship between QOL and cognitive functioning in a sample of patients with "limited cognitive impairment and minimal physical disability," performance on the PASAT was correlated with aspects of the SF-36, while performance on the SDMT was correlated with a measure of social support (poorer performance linked to worse social support). These relationships held even after depression (measured by the Center for Epidemiologic Studies Depression Scale [CES-D]) was controlled for in the analyses. In a sample of 30 extremely impaired patients with MS, Kenealy and colleagues (2000) found that patients with intact autobiographical memory, as measured by the Autobiographical Memory Interview, reported the highest levels of depression, as measured by the Hospital Anxiety and Depression Scale, and the lowest levels of HRQOL, as measured by the SF-36. Surprisingly, the patients with impaired autobiographical memory (60% of the sample) reported higher levels of HRQOL than their intact counterparts. The authors interpreted these findings to suggest that severe cognitive impairment may affect the ability to accurately judge one's own HRQOL. This study suggests that cognitive impairment may not only negatively affect QOL, but also, in cases of severe impairment, might affect the ability of patients with MS to make accurate self-ratings.

The results of the research summarized above are difficult to interpret, given the variability in the level of cognitive impairment in the participants included, generally small sample sizes, and variations in the cognitive batteries used. Additionally, a number of researchers did not control for the possibly confounding effects of comorbid depression on the relationship between cognitive dysfunction and HRQOL. However, it appears that cognitive dysfunction may have some negative impact on HRQOL, though the magnitude of this relationship appears small and the role of depression and the specific cognitive domains involved remain unclear.

Sexual Functioning

Sexuality is influenced by a complex interplay of psychological and physiological factors. In general, people with MS experience lower levels of sexual activity, sexual relationship satisfaction, and sexual satisfaction (McCabe, McKern, McDonald, & Vowels, 2003). Disruption of sexual functioning in MS may be influenced by a variety of symptoms, such as impaired mobility, depression, spasticity, impaired sensation, and bowel and bladder functioning (see Kessler, Fowler, & Panicker, 2009, for a review and recommendations for intervention), in addition to any possible contributions from cognitive dysfunction. Because sexuality is often considered a sensitive topic, it has been historically underresearched. This problem is compounded by the fact that the sexuality of women (who are disproportionately affected by MS) and people with disabilities has typically been neglected (Bronner, Elran, Golomb, & Korczyn, 2010; Dupont, 1995; Schmidt, Hofmann, Niederwieser, Hapfhammer, & Bonelli, 2005). Despite Rao, Leo, Ellington, and colleagues' (1991) finding that cognitively impaired patients with MS reported more sexual dysfunction relative to healthy controls, to our knowledge, few empirical studies have been done on the relationship between objective cognitive measures and sexual dysfunction in MS and there has been little research in this area in neurological populations in general. As noted in the first edition of this work, many questions remain as to the relationship between cognitive dysfunction in MS and sexual dysfunction. Unfortunately, in the intervening time since the first edition of this work, it appears that no new empirical research has been published examining the relationship between sexual functioning and cognition in MS. Although an investigation of this relationship would certainly be complicated by the myriad psychosocial and physiological factors that also contribute to sexual functioning, literature in other populations (e.g., brain injury) suggests that this may be a fruitful avenue of exploration.

Everyday Functioning Assessment Recommendations for Clinical Practice

Although, as noted earlier, much more research needs to be done to assess the ecological validity of neuropsychological tests in MS, much has been learned that could be applied clinically. One general recommendation that can be derived from the existing literature is that clinicians should routinely screen the everyday functioning of MS patients in the domains of routine activities of daily living, driving, medication adherence, vocational performance, sexual functioning, social functioning, and general quality of life. In each of these domains of functioning, MS patients with more cognitive impairments tend to have more difficulty. As such, clinicians should be especially attuned to the possibility of everyday functioning problems in patients who have cognitive difficulties. At this stage of our knowledge, it is difficult to make translational suggestions from the research literature about specific cognitive functions that predict deficits in particular domains of everyday functioning. There is a lack of specificity and consistency of findings in this regard. Still, when MS patients seen for neuropsychological testing show cognitive deficits, clinicians should be especially attuned to the possibility that aspects of everyday functioning may be affected.

The central purpose of clinical neuropsychological evaluations is to characterize the nature of patients' neurocognitive strengths and weaknesses. However, clinicians hope to be able to extrapolate from such evaluations to how patients are functioning in their daily lives. The present review shows that such extrapolations in MS are reasonable. Although, again, specificity is lacking in terms of particular cognitive deficits predicting impairments in specific everyday functioning domains, cognitive deficits generally are associated with more problems in everyday functioning.

Summary and Conclusions

Research over the past 20–25 years has produced evidence to support the ecological validity of neuropsychological measures commonly employed to measure cognitive dysfunction in individuals with MS. These measures have been shown to predict driving difficulties, impairments in ADLs, reduced HRQOL, work/vocational difficulties, and (though limited) medication adherence. The literature on sexual dysfunction is sparse and inconclusive at this point. Overall, the weight of existing research suggests that the tests most often used in assessing cognitive status in patients with MS are predictive of important real-world behaviors. As research moves toward greater understanding of the pattern and prevalence of cognitive impairments seen in MS, it is important to understand how these impairments affect patients in their daily lives. Future work is needed to replicate some findings, fill in some of the gaps outlined in this Chapter, and define more precisely the kinds of dysfunctional cognitive operations that are problematic for specific daily tasks and activities. Such work should aid rehabilitation efforts that could be oriented toward circumventing the specific impaired cognitive functions necessary to perform everyday tasks and toward developing alternative strategies that allow patients with MS to function more effectively as they attempt to cope with what can be a devastating disease. Additionally, more work examining the possible role that treatable factors such as depression may play in the relationship between cognitive dysfunction and everyday activities is likely to be fruitful.

Authors' Note

This chapter represents an equal contribution by both authors.

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CHAPTER 19

Everyday Impact of HIV-Associated Neurocognitive Disorders

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Human immunodeficiency virus (HIV) is a retrovirus that causes acquired immune deficiency syndrome (AIDS), a disease in which the immune system begins to fail, leading to the emergence of life-threatening opportunistic infections. It is estimated that 37.9 million people worldwide are living with HIV, and in 2018, approximately 1.7 million people became newly infected with HIV, a number that has gradually declined from a peak of 2.9 million new infections in 1997 (UNAIDS, 2019). Similarly, an estimated 690,000 people died of AIDS-related illnesses in 2019, down from a peak of 1.7 million in 2004 (UNAIDS, 2019). Many of these gains have been driven by declines in transmissions and AIDS-related mortality in eastern and southern Africa. Although HIV is more commonly thought of as an illness attacking the immune system, approximately 30–50% of people with HIV (PWH) have been shown to experience some form of cognitive impairment (Heaton et al., 1995, 2011) due to the effects of the virus in the central nervous system (CNS).

Combination antiretroviral therapy became the standard of care for HIV in 1996 because of its ability to dramatically reduce the amount of virus in the body. Since then, there have been many advances in antiretroviral treatment (hereafter referred to more generally as ART). As a result, the estimated survival time after HIV infection, and the time between HIV infection and AIDS diagnosis, has increased substantially, transforming HIV from an almost uniformly fatal illness into a chronic but relatively stable condition for individuals with access to ART (Rodger et al., 2013). However, modern ART has not eliminated HIV-related neurocognitive disorders, and these impairments remain a significant clinical concern (Heaton et al., 2010, 2011; Sacktor et al., 2002; Schouten, Cinque, Gisslen, Reiss, & Portegies, 2011). For example, cross-sectional data from a multisite study of 1,555 HIV-infected individuals (the CNS HIV Antiretroviral Therapy

Effects Research [CHARTER] project) suggests that approximately 50% of HIV-positive individuals still have some form of neurocognitive impairment (Heaton et al., 2010). A review of other studies reached a similar conclusion (Schouten et al., 2011).

Increasingly, attention has focused on the everyday, "real-world" effects of HIV-associated neurocognitive disorders (HAND; see below), given that individuals are living longer than ever with HIV, and many individuals are experiencing a "second life" with the advent of ART therapy (Rabkin & Ferrando, 1997). These everyday outcomes are the focus of this Chapter, but in order to provide context for these effects, we first provide background information on the neurological and systemic impact of HIV infection.

Structural and Neurobiological Aspects of HIV

Life Cycle of the Virus

HIV infection exerts pathogenic effects on both the immune system and the nervous system. HIV belongs to the family of retroviruses, which means that its replication cycle includes a step of reverse transcriptase-mediated conversion of the viral ribonucleic acid (RNA) genome into a deoxyribonucleic acid (DNA) copy. Because HIV is a retrovirus, any drug used to combat HIV infection is referred to as an "antiretroviral." Currently, seven major classes of antiretrovirals are in general use: nucleoside analog reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transfer inhibitors (INSTIs), fusion inhibitors, postattachment inhibitors, and CCR5 antagonists. These current HIV therapies inhibit the viral replication process at various stages (described below): the binding and entry stage (fusion inhibitors, CCR5 antagonists, postattachment inhibitors), the reverse transcription stage (NRTIs and NNRTIs), or the protein cleavage stage (PIs). Newer classes of antiretrovirals that focus on inhibiting the virus at other stages are integrase inhibitors, which aim to block the insertion of the viral DNA into the host cell's DNA.

HIV infection of a host cell occurs when an HIV particle encounters a target cell with a cluster of differentiation 4 (CD4) surface molecules. T4-lymphocyte cells (also known as "T-helper" cells, or T-cells) are generally thought to be the main target receptor for HIV due to their abundance of CD4 receptors. HIV also binds to specific chemokine receptors (i.e., CCR5 or C-X-C motif chemokine receptor 4 [CXCR4], among others) on the surface of the host cell, which pull the virus and host cell membranes together, allowing fusion to occur. The HIV RNA, proteins, and enzymes then enter into the cytoplasm of the target cell, and viral RNA is converted to DNA by a viral enzyme called *reverse transcriptase*. This DNA then enters the cell nucleus, where the viral DNA is inserted into the host chromosomal DNA via another viral enzyme called *integrase*. The resulting integrated DNA virus (called a *provirus*) may remain latent for hours to years before becoming active through transcription, in which the cell creates new HIV via copying of DNA into RNA. Each RNA strand is processed, and a corresponding string of proteins is transformed or "translated" into various new viral proteins that are needed to make new virus. In the final step, the new virus is assembled in a complex process involving the cleaving of proteins into smaller proteins by a viral enzyme called *protease*, followed by the budding of the new viral particles off the host cell, creating a new virus. Once this virus is assembled and matures, it can then infect new cells and create new virus (for more thorough reviews, see Stevenson, 2003; Trkola, 2004). Thus, the clinical course of HIV infection is associated with a progressive decline in CD4 T-cell levels and an increase in the amount of the virus in the body (i.e., viral load). When the CD4 cell count drops below a critical level, T-cell mediated immunity begins to fail, and opportunistic infections are common. A diagnosis of AIDS is therefore determined by either a CD4 cell count dropping below 200/mm^3 or the presence of an AIDS-defining medical condition such as an opportunistic infection.

HIV and the Central Nervous System

HIV enters the brain early after infection (Sonnerborg et al., 1988), and although it is generally not thought to productively infect neurons (Wiley, Schrier, Nelson, Lampert, & Oldstone, 1986), it promotes an inflammatory response in the CNS that is characterized by chronic activation in perivascular macrophages and microglia and related accumulation of neurotoxic cellular byproducts. As a result, widespread neuronal and glial pathology occurs, particularly in the basal ganglia and the frontal–striatal–thalamocortical circuits (Brew & Barnes, 2019; Morgello, 2018). Nonetheless, the neuropathological damage due to HIV infection is evident in both subcortical (e.g., Kure et al., 1991) and neocortical (e.g., Everall, Luthert, & Lantos, 1991; Masliah et al., 1992) structures. Age-related pathological changes can also occur, including cerebral [β]-amyloidosis, Tau pathology, and arteriolosclerosis (Soontornniyomkij, 2017). In addition, HIV encephalitis (HIVE), a pathology-based diagnosis characterized by high brain viral burden, neuroinflammation (Achim & Wiley, 1996), and the presence of multinucleated giant cells and microglial nodules, commonly occurs with severe cognitive impairment, that is, dementia (Wiley & Achim, 1994). Neuropsychological (NP) assessment appears to be more sensitive to abundant HIV presence in the brain, although the association of virological markers with antemortem NP data have not been consistent in milder forms of HAND (Brew & Barnes, 2019). Synaptodendritic changes, or the pathological processes of pruning and loss of dendritic complexity that affect synaptic functioning, are also evident and may be more accurate markers of HIV-associated neural damage, as these changes correlate closely with the presence and severity of cognitive impairment (Avdoshina et al., 2020; Everall et al., 1999; Masliah et al., 1997).

The neurodegenerative changes associated with HIV are also reflected in neuroimaging findings. Computed tomography (CT) and magnetic resonance imaging (MRI) investigations have found that PWH show increased ventricular and sulcal spaces, reduced gray and white matter volumes, and white matter signal abnormalities, with findings generally more prominent in the basal ganglia and white matter (e.g., Jernigan et al., 1993; Post, Berger, & Qeuncer, 1991). White matter hyperintensities seen on MRI have been related to dendritic loss in the frontal cortex (Archibald, 1998), as well as HIV encephalitis (Miller et al., 1997). These alterations in brain volume and white matter can appear within a few months of HIV infection (Kelly et al., 2014; Ragin et al., 2012, 2015). Increased alterations in cortical thickness, brain volumes, and white matter are seen across more advanced disease stages (Alakkas et al., 2019; Stout et al., 1998) and with greater comorbidities (Archibald et al., 2014; Saloner et al., 2019), which may become even more relevant in the future with the aging of PWH. However, these brain alterations may also depend on viral load or CD4 cell count (Fennema-Notestine et al., 2013; Jernigan et al., 2011), with greater alterations in PWH without virologic suppression or with residual immunosuppression.

Magnetic resonance spectroscopy (MRS), a neuroimaging methodology that measures concentrations of metabolites in the brain, may prove to be a useful biomarker of HAND. Studies have found increases in concentrations of myoinositol and choline in the white matter of individuals in the early stages of HIV infection, ostensibly reflecting glial activation and an inflammatory process that could lead to HIV-associated neurotoxic effects. Decreases in *N*-acetyl aspartate (a neuronal marker) and additional increases in myoinositol and choline occur in symptomatic HAND, suggesting increased glial activation and further neuronal damage with HIV progression (see Ances & Hammoud, 2014, for a review). Additional studies using MRS have shown that levels of *N*-acetyl aspartate and glutamate are associated with neurocognitive functioning in PWH (Ernst, Jiang, Nakama, Buchthal, & Chang, 2010; Mohamed, Barker, Skolasky, & Sacktor, 2018), and changes in glutamate/glutamine and *N*-acetyl aspartate in basal ganglia are associated with neurocognitive decline (Gongvatana et al., 2013).

Neurocognitive Impairment

Diagnostic Criteria

Neurocognitive disorders associated with HIV range from subtle deficits to a severe and incapacitating dementia. The diagnostic terms in common use are based on (1) the presence of neuropsychological impairment, and (2) whether these impairments impact everyday activities. Historically, most studies used the diagnostic criteria proposed by either the American Academy of Neurology (AAN) AIDS Task Force (1991) or Grant and Atkinson (1995). However, with the evolution of HAND during the ART era, the National Institute of Mental Health and National Institute of Neurological Diseases and Stroke tasked a workgroup to revisit the AAN criteria (Antinori et al., 2007). This group established a revised nosology consistent with the Grant and Atkinson (1995) approach. The new criteria emphasized the *neurocognitive* complications of these conditions, excluding the motor, social/personality, and emotional abnormalities that were part of the AAN criteria. The revised nosology includes the mildest (“asymptomatic”) form of impairment, in which individuals evidence objective cognitive impairment, but the impairment does not significantly affect everyday functioning (Grant & Atkinson, 1995). It is important to include this classification because such impairments still predict symptomatic decline (Grant et al., 2014) and mortality (Ellis et al., 1997); thus, individuals with asymptomatic impairments may warrant close monitoring for potential worsening, perhaps requiring a change in treatment approaches.

The revised criteria for HAND were also more specific than previous criteria in terms of defining cognitive impairment. For each diagnosis, the cognitive impairment cannot be explained by other comorbidities, nor can it be the result of a delirium:

- *Asymptomatic neurocognitive impairment (ANI).* Performance needs to be at least one standard deviation (*SD*) below the mean of demographically adjusted normative scores in at least two cognitive domains (attention/information processing,

language, abstraction/executive, complex perceptuomotor skills, memory [including learning and recall], simple motor skills, or sensory perceptual abilities). At least five cognitive domains need to be assessed.
- *Minor neurocognitive disorder (MND).* MND meets the ANI criteria above. In addition, the neurocognitive abnormality must result in at least mildly impaired everyday functioning and cannot meet criteria for dementia.
- *HIV-associated dementia (HAD).* HAD requires (1) acquired moderate to severe cognitive impairment (at least two *SD* below demographically corrected normative means in at least two different cognitive areas [see above]), and (2) marked difficulty in everyday functioning due to the cognitive impairment.

The workgroup also added the qualifier of *in remission* for all three diagnoses, since there is evidence that the neurocognitive impairment may fluctuate in some individuals (Heaton et al., 2015). The impact of the cognitive impairments is a critical feature of the diagnoses and reinforces the need for robust and standardized methods of assessing real-world functioning.

NP Functioning and Treatment

In the era preceding ART, neurobehavioral complications were found in approximately 30–50% of PWH, with greater proportions of cognitive impairments emerging in late-disease stages (Heaton et al., 1995; McArthur & Grant, 1998; White, Heaton, & Monsch, 1995). ART provided substantial improvements in the systemic health of PWH since its advent in 1996, and there has been a dramatic increase in the time from infection to a diagnosis of AIDS, as well as survival time (Detels et al., 1998; Porter et al., 2003). PWH on ART have lower rates of HAND than those who are treatment naïve (Becker et al., 2015; Sacktor et al., 2002, 2006), and ANI appears to represent the majority of cases in the era of potent ART (Heaton et al., 2010). However, the treatment benefit of ARTs for neurocognitive functioning may not equal that seen for other symptoms. While there has been a decrease in impairment severity, the prevalence of impairment has not dramatically declined. In addition, although there was preliminary evidence that early initiation of ART would improve neurocognitive performance (e.g., Ferrando et al., 1998; Letendre et al., 2004; Parsons, Braaten, Hall, & Robertson, 2006), recent evidence from large-scale trials do not appear to support this hypothesis (Wright et al., 2015).

Consistent with its frontostriatal neuropathogenesis, NP deficits in HIV infection are seen in domains that are highly dependent on these circuits, such as attention/working memory, learning, motor skills, speed of information processing, and executive functioning (Becker et al., 1995; Heaton et al., 1995, 2011; Hinkin, Hardy, et al., 2002; Reger, Welsh, Razani, Martin, & Boone, 2002). Even the mildest forms of HAND can have substantial effects on the everyday life of affected individuals. Given the continued prevalence of neurocognitive disorders, there is reason to suspect that individuals may be living longer with HIV-related cognitive impairments, highlighting the importance of research into the ramifications of these impairments on daily functioning. Although the literature still leaves much to be explored, a significant amount of evidence suggests that HIV-related neurocognitive dysfunction significantly affects both laboratory and real-world measures of everyday functioning, as well as survival time, in a subset of individuals.

Everyday Impact of HIV Infection

Research to date indicates that HIV-associated functional impairments have significant implications for HIV-infected individuals, caregivers, and society as a whole, including reducing the available workforce, amplifying the economic burden of government-supported health care coverage, and increasing the prevalence of drug-resistant viral strains via inadequate medication adherence (Marcotte & Scott, 2008; van Gorp, Baerwald, Ferrando, McElhiney, & Rabkins, 1999). In order to more thoroughly investigate these functional impairments, researchers developed methods specifically tailored for individuals with HIV infection that more directly assess real-world functioning (e.g., Albert et al., 1999; Heaton et al., 2004; Marcotte et al., 2004; Scott et al., 2011; Woods et al., 2017), as traditional NP tests have limitations as measures of daily functioning (Heaton et al., 2004), and performance-based measures may have stronger relationships to objective functional markers than self-report of functioning (Blackstone et al., 2012).

Instrumental Activities of Daily Living

Although a subset of individuals experience declines in everyday abilities due to the CNS effects of HIV infection, these declines are not universal and are generally only evident in more complex everyday tasks, known as instrumental activities of daily living (IADLs). These include skills such as money management, meal preparation, medication management, and job-related skills. Declines in basic activities of daily living (BADLs), such as bathing, grooming, and dressing, are typically the result of advanced physical symptoms, and a cognitive etiology is only evident in severe HAD. Given that the neurocognitive deficits associated with HIV are more likely to be subtle, assessing complex IADL functioning is important.

In an attempt to objectively investigate the effects of HIV on IADL functioning, Heaton and colleagues (2004) examined 267 HIV-infected individuals on a comprehensive functional battery, including standardized instruments assessing grocery shopping, cooking, financial management, medication management, and vocational functioning. On these assessments, participants performed the required tasks with mock scenarios and items just as if they were carrying out the tasks in everyday life. For example, the cooking task required individuals to follow recipes and coordinate the timing of a meal, using mock food items and a microwave and hot plate.

Cognitively impaired HIV-positive participants performed significantly worse on all functional measures compared to HIV-positive participants without cognitive impairment; this difference was particularly evident on a global measure composed of test results from the entire functional battery (i.e., Functional Deficit Score [FDS]). The largest group differences were reported in vocational skills, followed by finances and medication management. Impairments in executive functioning, learning, verbal abilities, and attention/working memory were most predictive of performance on the functional measures. Importantly, both the NP and functional battery performances were independent predictors of real-world functional status, based on complaints of cognitive difficulties, level of dependence/independence in IADLs, and employment status. Thus, although the NP impairment was generally in the mild or mild-to-moderate range in the cognitively impaired group, the impairment resulted in a substantially increased risk for IADL dependence. These results also suggest, however, that even though neuropsychological assessments provide valuable information regarding functioning outside of the laboratory, they may not capture all of the components that are involved in successful execution of these tasks in real life. Therefore, functional tests may complement traditional cognitive testing in accurately determining everyday outcomes.

This study also highlighted the potential importance of considering affective status in assessing everyday functioning capacity, in that depressed mood was an independent, significant predictor of both objective (i.e., functional battery) and subjective (i.e., cognitive complaints and IADL dependence) everyday functioning. This suggests that some individuals may have had the ability to function at higher levels, but they failed to do so because of their affective symptoms. This finding has also been observed in a sample of older adults with HIV. In a cross-sectional study, Morgan and colleagues (2012) administered several measures of everyday functioning (e.g., IADL and BADL, self-report indices of quality of life, and objective measures of functioning, including employment and Karnofsky Performance Scale [KPS] ratings) to individuals who were either ≤ 40 years or ≥ 50 years, including 103 HIV-positive and 87 HIV-negative. They found that the older HIV-positive group had significantly greater declines in both IADL and BADL, higher rates of unemployment, and lower KPS ratings compared to all other groups. In addition, there were synergistic effects of HIV infection and aging on IADL/BADL decline severity, Karnofsky score, and employment status, suggesting that older age may exacerbate the adverse effects of HIV on daily functioning. Current major depressive disorder (MDD) was also a significant predictor of functional outcomes in the older HIV-positive group. Thus, similar to results from Heaton et al. (2004), both depressed mood and neurocognitive impairment were significant predictors of poorer functioning.

Quality of Life

Advanced HIV disease stage and disease-related medical symptoms, such as opportunistic infections and constitutional symptoms, have been consistently shown to be predictive of worse quality of life (QOL), especially in the pre-ART era (e.g., Revicki, Wu, & Murray, 1995). Comorbid substance abuse and psychiatric disorders, including depression, have also been associated with significantly worse QOL outcomes in HIV-infected individuals (e.g., Liu et al., 2006; Sherbourne et al., 2000). In addition, HIV-associated cognitive impairment significantly impacts QOL, even after controlling for relevant medical factors (Kaplan et al., 1995; Parsons et al., 2006; Revicki et al., 1995; Tozzi et al., 2004; Trepanier et al., 2005). The effects of ART use on QOL, however, have been surprisingly inconsistent. With successful long-term ART treatment, improvement may be seen in QOL (e.g., Carrieri et al., 2003; Jaquet et al., 2013; Parsons et al., 2006), although the effect may be greater for mental health QOL than for physical health QOL (Liu et al., 2006). On the other hand, a number of studies have shown that ART regimens, especially regimens from earlier years, can also have detrimental effects on QOL due to adverse side effects and toxicity associated with the drugs (Liu et al., 2006; Rabkin, Ferrando, Lin, & McElhiney, 2000). With the continued increase in life expectancy for individuals with

HIV, greater attention will likely be focused on maximizing QOL by developing more efficient and less toxic medication regimens (e.g., Maiese, Johnson, Bancroft, Hunter, & Wu, 2016).

Survival

In the pre-ART era, opportunistic infections (e.g., cryptococcus, cytomegalovirus) and cancers (e.g., Kaposi's sarcoma) commonly occurred because of the gradual decline of the body's immune system due to AIDS. These conditions often led to functional decline and ultimately death because of the body's loss of immune competence. However, HIV-associated neurocognitive impairments were also associated with an increased risk for death, independent of other disease or medical factors. Before effective ART therapy, HIV-infected individuals who were diagnosed with dementia had an average survival time of 6 months after diagnosis (McArthur et al., 1993), although a subset of patients exhibited a survival period of a year or longer in one study (Bouwman et al., 1998). After controlling for relevant biological variables, even milder neurocognitive impairments increased an individual's risk for death (Mayeux et al., 1993; Wilkie et al., 1998). For example, Ellis and colleagues (1997) found elevated mortality risk for individuals with minor cognitive/motor disorder (MCMD) and asymptomatic NP impairment when compared to NP normal participants, even after adjusting for other significant predictors of mortality. Psychomotor performance in particular was predictive of mortality in one early study (Sacktor et al., 1996).

Since the introduction of combination ART in 1996, estimated survival time with HIV has significantly increased, and the presence of risk factors for mortality (e.g., elevated viral loads) has concurrently decreased. At the same time, a dramatic increase occurred in survival time following a diagnosis of dementia (Dore, McDonald, Li, Kaldor, & Brew, 2003; Sacktor, 2018). It was suggested that the relationship between NP impairment and survival may depend on level of virological response to ART, as Tozzi and colleagues (2005) found a significant association between neurocognitive impairment and risk of death in participants with inadequate viral suppression, but no such relationship in those with adequate viral suppression due to successful ART treatment. A recent study by Banerjee, McIntosh, and Ironson (2019) examined whether HIV-associated neurocognitive impairment (NCI) predicted mortality in a sample of 209 HIV-positive adults who were followed over a 13-year period. The HIV-Dementia Scale (HDS), a brief cognitive screening tool, was administered along with the Beck Depression Inventory-II; mortality data were collected through publicly available death records. Thirty-one (14.8%) subjects scored in the NCI range. By the end of the follow-up period, 58 (27.8%) subjects in the sample had died. Baseline NCI predicted earlier mortality, with a two-fold increased risk of death. Other factors, including older age, African American race, lower education, and CD4 cell counts below 200 cells/mm, were significantly associated with mortality as well.

The cause of decreased survival in cognitively impaired individuals is still unclear. One potential mechanism may be a more virulent strain of the disease in impaired individuals, although this virulence is not being captured by standard disease markers, which are normally controlled for in analyses. Alternatively, particular host biological features may make some individuals more susceptible to the virus. Cognitive deficits might also affect patients' abilities to manage their disease (e.g., resulting in less effective medication adherence) or effectively use their available resources and support, as HIV treatment and maintenance are complex processes.

Medication Management

It is critical that HIV-infected individuals effectively manage their antiretroviral medications. Deviations from the prescribed dosing and dietary instructions decrease the drug concentrations, lower the likelihood of viral suppression, and increase the infectiousness of HIV and risk for progression to AIDS (Bangsberg et al., 2001; Kalichman et al., 2010; Viswanathan et al., 2015). Moreover, suboptimal adherence may lead to development of a drug-resistant strain of the virus; in fact, there is evidence of increasing rates of drug resistance among newly diagnosed patients (Beyrer & Pozniak, 2017). Adherence rate thresholds have varied slightly in recent years, with some studies showing viral suppression achieved among PWH who had 75–79% adherence, suggesting adherence of 80–90% may still be efficacious (Viswanathan et al., 2015). Unfortunately, other recent reviews still show poor adherence in some PWH, both intentional and unintentional, with multiple factors such as denial of diagnosis, fear of stigma, forgetting doses, cognitive limitations, and changes in daily routines contributing to suboptimal adherence (Iacob, Jacob, & Jugulete, 2017). Thus, adherence still remains a significant clinical concern, despite reductions in the complexity of antiretroviral dosing.

Approaches to adherence assessment include self-report questionnaires, performance tests of medication management, and electronic pill bottle caps that record when participants open the bottle to take their medications (i.e., Medication Event Monitoring System [MEMS] caps). Relatively consistent predictors of nonadherence have emerged, including adverse side effects of drugs due to toxicity (Carr, 2003), negative health beliefs regarding treatment (e.g., Horne et al., 2004), comorbid psychiatric disorders (Moore et al., 2012; Starace et al., 2002), comorbid substance abuse (e.g., Hinkin et al., 2007), and younger age (e.g., Hinkin et al., 2004). In addition, neurocognitive impairments appear to be a risk factor for medication nonadherence. Overall, studies have suggested that HIV-infected individuals with impairments in episodic memory (e.g., Obermeit et al., 2015), prospective memory (e.g., Woods et al., 2009), and executive functioning (e.g., Hinkin, Castellon, et al., 2002) may demonstrate significant difficulties with medication management.

In a series of early studies, Albert and colleagues (1999, 2003) examined how much of the nonadherence seen in PWH reflects the *inability* to adhere, and the extent to which individuals with cognitive impairment may adjust the way in which they manage their medications. The authors used a standardized, performance-based test of medication management skill, the Medication Management Test (MMT), which assessed the ability of participants to interpret prescription label information and dispense medications from prespecified prescription medication bottles. They found that individuals with impairments in memory, psychomotor speed, and executive functions displayed performance decrements on this test, as evidenced by difficulties following label information and correctly pouring different medications. Interestingly, they also found that cognitively impaired individuals reported more "fixed" medication regimens (i.e., taking their medications on the same schedule for 3 days), suggesting that these impaired individuals had compensated, to some degree, for their cognitive deficits. Heaton and colleagues (2004) also reported significant differences on a modified version of the MMT between

HIV-positive individuals with and without NP impairment, finding that impairments in learning and abstraction/executive functioning were the strongest predictors of failing the task. However, a later study of 448 PWH reported that performance on the MMT was related to self-reported adherence only in those who were immunosuppressed (i.e., with a CD4 count < 200; Patton et al., 2012). Moreover, the authors found that performance on the MMT was associated with premorbid factors such as word reading and education, as well as performance in attention/working memory and learning. Taken together, these findings suggest potential caution in interpreting the MMT as a measure of medication management ability without appropriate consideration of collateral information.

In another series of studies, Hinkin and colleagues (Hinkin, Castellon, et al., 2002; Hinkin et al., 2004, 2007; Levine et al., 2006) studied adherence as measured by bottle cap openings (MEMS caps), potentially providing a more objective estimate of adherence in everyday life. They found that HIV-positive individuals with impairments in attention, memory, executive functioning, and psychomotor speed were more likely to have lower adherence rates across all age groups. Importantly, the impact of cognitive impairment was most significant in those individuals with complex medication regimens (three or more doses per day). Furthermore, HIV-positive individuals under 50 years of age and those with substance use disorders were less likely to be adherent, regardless of cognitive status.

Recent studies have also attempted to understand the cognitive mechanisms of medication adherence in order to identify remediation targets. For example, Thaler et al. (2015) reported that longitudinal increases in intraindividual variability in cognitive performance, which may serve as an indicator of declining executive control, were associated with reductions in medication adherence. In this study, 150 HIV-positive individuals completed baseline neuropsychological testing and returned monthly over the course of six months, with medication adherence rates recorded for each preceding month. Participants with increasing intraindividual variability in cognitive performance became poorer adherers at approximately twice the rate of those with stable or decreasing intraindividual variability.

In addition, several studies have examined the potential of prospective memory, which describes the ability to execute a future intention (i.e., “remembering to remember”) in the absence of explicit cues, as a predictor of medication management. Examples of prospective memory in daily life include remembering to take a medication after a meal or remembering to send an email to a colleague later in the day. In fact, the most commonly reported reason that HIV-positive persons give for missing medication doses is “forgetting” (Chesney et al., 2000). Initial studies indicated that HIV infection is associated with a breakdown in the strategic (i.e., executive) encoding and retrieval aspects of prospective memory (Carey et al., 2006). Importantly, evidence also points to the ecological relevance of prospective memory in HIV infection. Studies have shown prospective memory impairment to be a significant, independent predictor of both subjective medication adherence (Woods et al., 2008) and objective medication adherence as measured by MEMS (Doyle et al., 2015; Woods et al., 2009) in PWH, especially with longer delay periods. These effects appear to be robust as well. In Woods et al. (2009), 79 HIV-infected individuals were classified as either Adherent ($n = 48$) or Nonadherent ($n = 31$) based on the outcome of a 4-week continuous observation period of adherence measured by MEMS caps. Nonadherence was defined as $< 90\%$ adherence to the target ARV. All participants completed assessments of prospective memory, neuropsychological functioning, and psychiatric status prior to starting the MEMS observation period. Nonadherent participants performed significantly worse than the Adherent participants on the prospective memory assessment, with HIV-associated prospective memory impairment at baseline associated with an almost six times greater likelihood of being classified as "nonadherent" (based on pill-bottle cap opening data) at 5-week follow-up.

There have been limited studies aimed at improving adherence to ART. A study using the Disease Management Assistance System (Andrade et al., 2005) suggested an early potential path for remediation of medication management deficits. This study was a randomized trial in which the treatment group received simple auditory reminding devices that notified individuals of the timing and dosing of their medications. Adherence rates did not significantly differ between the treatment group (80%) and the control group (65%), although an analysis of a subgroup of individuals with memory impairment revealed significantly greater adherence in the treatment group (77%) when compared to the control subjects (57%). Further studies have shown some evidence for improvement in antiretroviral adherence with use of text messaging or other mobile phone reminders, especially those that incorporate additional behavior change techniques (Rooks-Peck et al., 2019; Shah, Watson, & Free, 2019). In their review, Shah and colleagues identified 19 trials of mobile phone interventions for improving adherence. The trials had varying intervention styles, including via text message, mobile phone call, delivery of personalized health-related mobile imagery (e.g., a picture to serve as a reminder to take their medication), and mixed interventions. Objective measures included MEMS, pill counts, and biological outcomes (CD4 count and viral load). Secondary outcomes included subjective measures of self-reported adherence. The authors of the review concluded that specific interventions, with proven effectiveness, should be the focus of implementation strategies, rather than simply using mobile phone-based methods themselves as the intervention, and that interventions targeting a wider range of adherence barriers may be most effective. Few studies have examined potential differences in outcomes in individuals with neuropsychological impairment.

Vocational Functioning

Unlike most dementing disorders, the incidence of HIV infection tends to be highest in younger individuals who, prior to their illness, had many years of possible work life ahead of them. In the mid-1990s, many HIV-infected individuals experienced a "second life" as a result of available ART treatments, including a dramatic change in their health and functional outlook (Rabkin & Ferrando, 1997). It was proposed that this change created new opportunities for individuals to return to work, even for those who were unemployed or on disability for years (Martin, Arms, Batterham, Afifi, & Steckart, 2006). However, the complex symptom constellation associated with HIV infection, including opportunistic infections, physical limitations, fatigue, or cognitive impairment, provides a multitude of reasons for work-related disability, and it is still unclear whether this change in outlook has resulted in a shift in functional outcomes, including employment. Given that early studies estimated the productivity loss due to HIV infection may be in the tens of thousands of dollars per year (Liu, Guo, & Smith, 2004) and that employment has been consistently associated with both physical and mental-health related quality of life in PWH (Rueda et al., 2015), it is particularly important to examine the factors that contribute to vocational decline as well as the successful return to work.

Early investigations examined trends in PWH and group differences in employment status and job performance between HIV-positive and HIV-negative groups. In the early 1990s, 52% of HIV-infected individuals were unemployed and had quit the labor force entirely, with only 29% employed full-time (Sebesta & LaPlante, 1996). Employed individuals with AIDS also worked fewer hours than both HIV-infected individuals without AIDS and HIV-negative individuals (Leigh, Lubeck, Farnham, & Fries, 1995). More recently, Annequin, Lert, Spire, Dray-Spira, and the ANRS-Vespa2 Study Group (2016) found that unemployment rates among PWH living in France were twice as high as those seen in the general population. In a similar study in Sweden, from 1996 to 2016, PWH were consistently less likely to be employed compared to HIV-negative individuals, although significant increases in employment rates were also seen over that time span (Carlander, Wagner, Yilmaz, Sparén, & Svedhem, 2021). In all studies, those with symptomatic HIV were more likely to be unemployed than asymptomatic individuals.

Neurocognitive status also appears to be important in prediction of disability status in PWH. In early work, Albert and colleagues (1995) reported a relative risk ratio for work disability of 2.76 for initially asymptomatic PWH when compared to HIV seronegative participants during 4.5 years of follow-up. This increased risk was largely the result of a higher risk for a subset of participants who developed severe NP impairment, as PWH who did not evidence NP impairment at follow-up did not have an elevated risk of disability. Heaton and colleagues (1994) found unemployment to be almost three times higher in HIV-positive, neurocognitively impaired individuals than in HIV-positive, neurocognitively normal individuals (26.9 vs. 9.7%, respectively), even in those with only mild impairment. After removing participants with potentially disabling medical conditions, this relationship still held (17.5 vs. 7.9%, respectively). In employed participants, those with NP impairment evidenced a higher rate of difficulty performing their jobs. Similarly, in a study of advanced HIV disease, unemployed participants were twice as likely to be NP impaired as employed participants (22 vs. 11%), with physical limitations and performance on the Trailmaking Test Part B significantly predicting employment status (van Gorp et al., 1999).

In the current ART era, studies also indicate that prospective memory impairment may be a relevant predictor of unemployment in PWH, even when considered alongside functioning in other neurocognitive domains. Woods and colleagues (2011) recruited 59 unemployed and 49 employed PWH to undergo comprehensive neuropsychological and medical evaluations, including measures of prospective memory. The unemployed participants performed significantly worse on time-and-event based prospective memory, and individuals with the lowest prospective memory scores were approximately eight to nine times more likely to be unemployed compared to those with the best prospective memory performance. Significant group differences were seen in executive functions and verbal fluency, and unemployed participants also reported higher levels of affective distress. In a multivariable regression, though, prospective memory was the only remaining predictor for unemployment.

It is possible that HIV-positive individuals may stop working due to physical decline or because they are eligible for disability based on an AIDS diagnosis (i.e., developing an AIDS-defining medical condition or a CD4 cell count below 200/mm^3). Objective measures of vocational functioning may assist in disentangling these possibilities. Heaton and colleagues (1996) utilized a standardized battery of vocational-related tasks (Valpar International Corporation, 1986, 1992) that provided estimates of 13 job abilities as identified by the U.S. Department of Labor (1991). Participants completed both manual (e.g., placing wires through loops) and computerized (e.g., size discrimination, tracking) tasks, including work samples. This battery enables a comparison of current performance (on the work-sample battery) with previous ability, as specified by jobs that individuals have held throughout their work history.

In this unique study, the HIV-positive, NP normal; HIV-positive, NP impaired; and HIV-negative, cognitively normal groups were matched on prior work history, indicating likely equivalent premorbid vocational functioning. However, the HIV-positive, NP impaired group performed significantly worse on the work sample than the HIV-positive, NP normal and HIV-negative groups. Furthermore, although the latter two groups demonstrated higher current functioning than expected, given their work history (a person's work often does not require his or her highest ability levels), the HIV-positive, NP impaired group had reduced abilities compared to their prior work history, suggesting a decline from previous functioning. A similar pattern of results was found in a larger cohort from the ART era, with the discrepancy between prior work ability and current vocational functioning being almost three times greater in the NP impaired group (Heaton et al., 2004). The presence of an AIDS diagnosis, high levels of depression, and deficits in executive functions, verbal functioning, and attention/working memory were the strongest predictors of work-sample performance.

Studies have also examined predictors of returning to work, since successful ART treatment may give HIV-infected individuals the potential to be productively employed, even after years of being out of the labor force. Although ART increases the probability that HIV-positive individuals will remain employed (Goldman & Bao, 2004), some previous longitudinal studies in Western countries following individuals on ART suggest that only a small proportion of individuals who were unemployed at baseline were employed at follow-up (e.g., Lem et al., 2005; Martin et al., 2006; Rabkin, McElhiney, Ferrando, Van Gorp, & Liu, 2004). The strongest predictor of employment and number of hours worked in these studies was the receipt of disability payments (those receiving payments were less likely to return to work), with past or current diagnosis of depressive disorder, physical limitations, and worse performance on NP measures also significantly predicting change in employment and number of hours worked. The link between disability benefits and unemployment is consistent, with surveys finding that the most significant barriers to returning to work for PWH was the potential loss of disability benefits and publicly funded health insurance (Brooks, Martin, Ortiz, & Veniegas, 2004). This reluctance to endanger benefits, though controversial, likely reflects fear that benefits may not be reinstated once taken away, even with worsening health (Razzano, Hamilton, & Perloff, 2006), Moreover, treatment of HIV/AIDS is expensive, and health insurance agencies may be reluctant to pay for the high costs of medical care. HIV-positive individuals may enter the workforce after many years of being unemployed, whereupon they are more likely to land low-wage or part-time positions that are more likely to provide inadequate or minimal health insurance (Lem et al., 2005). In a recent comprehensive review, PWH continued to experience many barriers to employment, including interfering physical symptoms of the disease, side effects of HIV medications, burdens from rigorous medication regimens, and the need for frequent medical visits. Additionally, PWH reported fewer employment options due to outdated job skills, long absences, and fear of discrimination in the workplace (Maulsby, Ratnayake, Hesson, Mugavero, & Latkin, 2020).

In contrast to previous reports, a large study of employment status among PWH in rural South Africa showed that employment levels among PWH had recovered to approximately 90% of baseline levels 4 years after initiating antiretroviral therapy (Bor, Tanser, Newell, & Barnighausen, 2012), suggesting potential differences based on setting. Other studies in non-Western settings also show large effects of HIV treatment on employment (Larson et al., 2009; Thirumurthy, Zivin, & Goldstein, 2008; Thirumurthy et al., 2011). In addition, an earlier study examining a number of predictors for returning to work found that 52% of individuals from a sample in the United States who were unemployed at baseline found some sort of employment during 2 years of follow-up (van Gorp et al., 2007). Only performance on a measure of learning (California Verbal Learning Test [CVLT]) predicted finding employment; older age, presence of an AIDS diagnosis, and length of unemployment comprised barriers to finding work. Similar to this study, a study of 174 PWH participating in a workforce reentry program in the United States reported that 42% had found either part-time or full-time employment after 24 months; however, neurocognitive functioning did not significantly predict employment outcomes (Chernoff, Martin, Schrock, & Huy, 2010).

Although programs aimed at helping HIV-infected individuals return to work have been described (e.g., Kohlenberg & Watts, 2003), few studies have examined the effectiveness of an occupational rehabilitation program with HIV-infected individuals. Kielhofner and colleagues (2004) employed a program that combined psychoeducation with occupational therapy services, addressing a range of physical, psychosocial, and environmental issues. The authors reported that of 90 participants who completed the return-to-work program, 60 (66.7%) returned to work. Conyers and Boomer (2014) explored the role of vocational rehabilitation services by examining factors such as health risk behavior, access to medical/mental health care, supplemental employment services, job confidence, reduced stigma, and health perception. They found that the use of vocational rehabilitation services had a significant direct effect on supplemental employment services, health risk behaviors, and access to care.

Despite some promising initial results, more prospective studies are needed to thoroughly examine the predictors of successful reentry into the workforce for HIV individuals, especially as increasing numbers of individuals may participate in vocational rehabilitation or assistance programs (Conyers, Richardson, Datti, Koch, & Misrok, 2017; McGinn, Gahagan, & Gibson, 2005).

Automobile Driving

Similar to employment, driving an automobile is a task that younger PWH would be expected to undertake. Driving is a complex activity, requiring intact attention, perception, tracking, choice reactions, sequential movements, judgment, and planning. Assessment of driving abilities is challenging, as there is currently no clear standard for the concept of "impaired driving skills" (Marcotte & Scott, 2004). However, there is evidence, via a number of methodologies for assessing driving abilities, that a subset of HIV-infected individuals with cognitive impairment experience an overall reduction in driving abilities.

Investigations of driving ability in cognitively impaired HIV-positive individuals using objective laboratory tests have yielded a detailed picture of the deficits associated with a subset of participants. Marcotte et al. (1999) utilized an interactive, computer-based driving simulator to study 68 HIV-infected individuals at varying disease stages, assessing lane tracking, divided attention, driving in traffic, and crash avoidance. Cognitively impaired individuals had an increased propensity to "swerve" in their lane, resulting in a five times higher likelihood of failing the lane-tracking task. In addition, participants with cognitive impairment displayed a significantly higher number of simulator crashes on a city driving simulation compared to cognitively intact individuals, with those diagnosed with MND having the highest number of crashes. Impairments in the domains of abstraction/executive functioning and attention/speed of information processing were most often associated with poor performance on the simulations.

These findings were later extended by using a multimodal assessment that included a 35-minute on-road driving evaluation, computer-based simulations that emulated city driving and assessed navigation skills, and NP testing (Marcotte et al., 2004). The on-road evaluation was designed to be lengthy enough to obtain an adequate sampling of behaviors (e.g., both residential and highway driving) without being overly taxing to participants. The simulations were designed to capture abilities that are not normally assessed in driving evaluations, such as quick decision making (i.e., in emergency or novel situations) and the ability to effectively navigate using a map.

Forty HIV-positive and 20 HIV-negative control participants were tested with these assessments. The HIV-positive, NP impaired participants, in contrast to the HIV-negative and HIV-positive, NP normal groups, were classified as unsafe in the on-road evaluation at a higher rate (36 vs. 6%), had more crashes on simulated routine and emergency driving tasks, and made almost three times the number of navigational errors as the other groups. In contrast, the HIV-negative and HIV-positive, NP normal participants performed similarly on all evaluations, indicating that HIV seropositivity alone does not increase the risk for driving impairment. Performance on the neuropsychological tests, number of crashes on city driving, and route efficiency on the navigation task were all independent predictors of on-road performance, suggesting that direct assessment of driving skills (e.g., via simulator) yields data relevant to real-world performance above and beyond NP data alone. In this study, impairment in executive functioning was the strongest predictor of failing the on-road evaluation. Notably, some of the individuals who failed the on-road driving test lacked awareness of their performance (these individuals had impairments that were generally greater than mild, particularly in executive functioning and learning), indicating that clinicians should be cautious in relying on a patient's self-report of driving ability.

These authors also investigated whether the inclusion of visual attentional processing data could assist in identifying HIV-positive individuals who are at risk for poor driving performance (Marcotte et al., 2006). The Useful Field of View (UFOV; Visual Resources, 1998) test has shown particular success in identifying older at-risk drivers (e.g., Ball, Owsley, Sloane, Roenker, & Bruni, 1993; Myers, Ball, Kalina, Roth, & Goode, 2000; Owsley et al., 1998). The UFOV is a computerized measure that assesses the amount of time it takes an individual to accurately acquire both central and peripheral visual information without head or eye movements. This study found that HIV-positive participants performed significantly worse on the UFOV compared to HIV-negative participants, with the greatest differences seen on a divided attention subtest. These declines in visual attention were not solely the result of advancing disease or high levels of general cognitive impairment, as individuals impaired on the UFOV covered the spectrum of disease stages and severity of cognitive impairment, suggesting a process occurring at least partially independent of disease progression, as well as a cognitive deficit not entirely captured by conventional NP tests. Importantly, the UFOV "high-risk" group had a significantly greater number of on-road crashes in the previous year compared to those who were not at high risk. Furthermore, a classification of "NP impaired" *and* "high risk" on the UFOV yielded a positive predictive value of 75% and a negative predictive value of 95% for crashes in the past year. This finding suggests that UFOV impairment may be riskiest in the presence of other cognitive impairments, as individuals may not be able to compensate for the UFOV deficit with other cognitive skills, such as deciding on an appropriate driving action (i.e., executive skills) or executing an appropriate motor response (i.e., motor skills).

Later studies expanded this work to driving simulator performance in middle-aged and older adults with HIV. Foley et al. (2013) examined the performance of older adults living with HIV on a route-planning virtual city driving simulator task. They reported that older adults were both less efficient and slower on the task than younger adults living with HIV, especially those individuals with cognitive impairment. Cognitive functioning accounted for over 50% of the variance in driving simulator performance. Furthermore, measures of attention/working memory and visuospatial functioning showed the highest associations with both efficiency and speed on the simulator.

As part of a cross-sectional pilot study, Vance and colleagues (2014) recruited 26 middle-aged PWH (40+ years) to examine the potential combined impact of HIV-associated cognitive deficits and age on functional outcomes, including driving. Older age and poorer UFOV performance were both found to be related to slower reaction times in the driving simulator. Better performance in speed of processing, executive functioning, memory, and better everyday functioning were associated with better driving simulator performance outcomes. These findings suggest that increased age and HIV-associated cognitive deficits can independently influence everyday functioning outcomes, including driving behavior, and the combination of both may have an even stronger effect on functioning and performance.

Most studies have examined performance in community, nonprofessional drivers. However, a recent study by Gouse and colleagues (2020) examined driving abilities in professional truck drivers. Forty drivers (20 HIV-positive and 20 HIV-negative) completed a standard neuropsychological battery, two driving simulator tasks, and a driving history questionnaire. PWH performed significantly worse and demonstrated impaired overall cognitive performance on the neuropsychological battery compared to their HIV-negative counterparts. Moreover, drivers with neurocognitive impairment were more likely to crash on the simulation compared to drivers without neurocognitive impairment.

Risky Behaviors

Investigations have also focused on areas of functioning that are relevant not only to the everyday abilities of HIV-infected patients, but also to the management and prevention of the disease. Decision making and risky behaviors have been emergent areas of research, given that high-risk sexual behavior can both increase the spread of HIV and endanger already infected individuals by potentially exposing them to drug-resistant strains of the virus. In addition, risky decision making can lead to an increase in (1) drug abuse; (2) poorer everyday outcomes; and (3) likelihood of transmitting the disease through injection drug use, which accounts for a substantial proportion of new HIV cases in the United States.

Infection with HIV has long been associated with high-risk behaviors, such as unprotected sex and intravenous drug use (e.g., Wolitski, Valdiserri, Denning, & Levine, 2001). Several factors have been associated with increased risk behaviors in HIV-infected samples, including demographic factors such as age (e.g., Mansergh & Marks, 1998), drug abuse (e.g., Rhodes et al., 1999), beliefs about HIV and its treatment (e.g., Dilley, Woods, & McFarland, 1997), and mental health status (e.g., Otto-Salaj & Stevenson, 2001). However, studies have also investigated the cognitive and personality factors that may be associated with risky behavior in relation to HIV and drug use. Martin and colleagues (2004) used the Iowa Gambling Task (IGT) to investigate whether HIV-infected individuals with substance dependence would display poorer decision-making abilities than substance-dependent individuals without HIV infection. The IGT, created by Bechara, Damasio, Tranel, and Damasio (1997) to assess various cognitive components of decision making, involves selecting cards from four decks that have different contingencies for monetary rewards and losses, with the overall goal of making as much money as possible. Over time, prudent decision makers realize that two decks offer large payoffs but also increased losses (resulting in a net loss by the end of the task), whereas the other two decks offer smaller gains but fewer losses (resulting in a net gain by the end of the task). Martin and colleagues (2004) found that the HIV-positive individuals with substance dependence made significantly more disadvantageous choices on the IGT and did not learn to avoid the disadvantageous decks over time, indicating that HIV infection may be associated with an increased level of cognitive impulsivity.

The IGT was also employed by Hardy, Hinkin, Levine, Castellon, and Lam (2006), who similarly found that HIV-positive individuals evidenced worse performance on the IGT compared to HIV-negative individuals. Notably, they also found that HIV-positive participants had an increased likelihood of selecting cards from a deck that resulted in infrequent, large penalties (as opposed to frequent, small penalties). In addition, selection of cards from this deck was associated with measures of inhibitory processing and delayed recall in exploratory analyses. This finding suggested that individuals who frequently chose from these decks might have difficulty inhibiting their selections and remembering the previous losses due to their infrequency.

Subsequent studies also indicated that personality traits may be worth considering in predicting engagement in risky behaviors; that is, long-standing traits, which may predate active substance use or HIV disease may influence an individual's decision making. A number of studies reported that the dispositional trait of sensation seeking, defined as the need to maintain a high level of arousal accompanied by a willingness to take risks to reach that arousal state (Zuckerman, Bone, Neary, Mangelsdorff, & Brustman, 1972), is associated with risky sexual practices among individuals with HIV (e.g., Crawford et al., 2003; Kalichman, Heckman, & Kelly, 1996). Gonzalez and colleagues (2005) investigated the contributions of executive functions, HIV serostatus, and the trait of sensation seeking on risky sexual practices in polysubstance abusers. Sensation seeking, but not executive functions, was associated with risky sexual practices in the past 6 months in both HIV-infected and HIV-seronegative groups, but this relationship was primarily driven by the association between the two within the HIV-infected group. Based on the results of these and similar studies (e.g., Moore et al., 2005), both decision making and temperamental characteristics are important to consider in assessing risk-behavior patterns in HIV-infected individuals, especially when taking into account the actions that an individual might undertake in the real world, such as driving.

Multitasking

While the performance-based functional tests mentioned earlier in this Chapter (i.e., medication management test) are reasonably sensitive to HIV-associated declines in IADL, questions remain regarding the extent to which the highly structured nature of these tests fully captures the various cognitive abilities involved in successful everyday functioning, including the complexities and environmental demands of daily life. Most individuals do not carry out activities of daily living by following specific instructions in a tightly controlled environment, but instead operate in open-ended situations with multiple competing demands (Burgess et al., 2006). Thus, measuring an individual's ability to multitask, or prioritize, organize, and structure a course of action in the face of competing alternatives, may be of particular importance in assessing IADL functioning. However, this skill is not readily measured by standard neurocognitive or functional tests.

A small body of literature has investigated the potential relevance of multitasking in PWH and its relationship to IADL functioning. Scott and colleagues (2011) developed a standardized measure of multitasking, the Everyday Multitasking Test (EMT), that involved balancing the demands of four interconnected performance-based functional tasks (financial management, cooking, medication management, and telephone communication). The multitasking assessment required participants to complete as much of four separate tasks as possible within a 12-minute time limit. PWH demonstrated significantly worse overall performance, an elevated number of errors, and fewer attempts at performing tasks simultaneously on the multitasking test as compared to an HIV-seronegative group. More importantly, multitasking deficits were uniquely predictive of IADL dependence in PWH beyond the effects of depression and global neurocognitive impairment. In a follow-up study in older adults living with HIV, Fazeli and colleagues (2017) similarly showed that neurocognitive abilities were moderately associated with multitasking performance on the EMT, but they also found that metacognition, or awareness of one's cognitive abilities, partially mediated the relationship between neurocognitive functioning and multitasking performance. More accurate global metacognition, and better global and domain performances, except delayed recall and verbal fluency, were also significantly associated with a greater total number of tasks attempted. Better metacognition accuracy was also correlated with more simultaneous task attempts, fewer omission errors, and fewer total errors, whereas traditional neurocognitive measures were not. These findings suggest that the ability to maintain and monitor multiple tasks may be specifically supported by metacognitive processes that are important for successful everyday task completion. Focusing on treatment of functional difficulties, Casaletto et al. (2016) showed that goal management training could improve EMT performance in PWH with comorbid substance use disorders, suggesting a potential novel remediation for such difficulties.

Online Tasks

Because of shifts in how individuals approach financial management, shopping, and information navigation, emerging research has focused on developing online tasks that more closely mirror internet navigation for everyday tasks, such as online shopping, banking scenarios (e.g., transferring funds between accounts), pharmacy requests, and health records review. In a small sample of PWH, Woods and colleagues (2016) examined performance on two novel, web-based tests, one of online pharmacy skills (e.g., online refill of a medication) and one of health records navigation (e.g., checking test results and requesting a follow-up appointment) on a website designed to simulate an electronic health care management interface. PWH with HAND performed significantly worse than HIV seronegative and PWH without HAND on accuracy for both tasks. Interestingly, worse accuracy on these tasks was associated with lower health literacy and poorer performance on the MMT. Similarly, Woods et al. (2017) showed that PWH with HAND were significantly more likely to fail an online shopping task modeled after major shopping websites (e.g., Amazon.com) than neurocognitively normal PWH and HIV- participants. Those with HAND also showed lower rates of accuracy on an online banking task in which they were asked to perform typical transactions (e.g., paying household bills) compared to neurocognitively normal PWH. HAND was also associated with poorer overall performance compared to HIV-positive normal on the online banking task. Internet-based task scores correlated with episodic memory, executive functions, motor skills, and numeracy in the HAND group. Notably, all of these results reflected difficulty in accuracy, with minimal differences between groups in completion time of the tasks. Woods and colleagues' findings suggest that the development and validation of effective Internet training and compensatory strategies may help improve the household management of individuals with HAND.

Interventions

Although historically few studies investigated the degree to which cognitive impairments associated with HIV are remediable, and whether such treatments might result in improved everyday functioning, the pace of this work has been increasing over the past decade. One popular approach has been the utilization of computerized cognitive training. In a review of 13 training studies in PWH, Vance and colleagues (2019) concluded that cognitive training may improve functioning in targeted cognitive domains, such as memory (e.g., declarative, verbal, procedural), speed of processing, executive functioning, reasoning training, and psychomotor functioning. However, the authors also concluded that studies to date also have significant limitations. For example, they are frequently pilot studies, with small sample sizes, inadequate control groups, and lacking in information regarding what training doses (e.g., how hours of training over what time period?) might be most effective for various subgroups. Most studies also had limited follow-up (only assessing individuals immediately at the conclusion of training) and did not assess the degree to which cognitive improvement translates into improved everyday functioning.

Other intervention studies have focused on specific constructs believed to be important in the successful completion of everyday tasks. Prospective memory has been one particular area of interest (Avci et al., 2018). For example, using strategic supports in encoding, monitoring, and cue detection, Woods et al. (2021) were able to improve naturalistic, time-based prospective memory. Lastly, there are also noncognitive, behavioral interventions that may result in improved cognition, and perhaps downstream improved everyday functioning. Such approaches include increased physical activity, dietary modifications, improved sleep hygiene, efforts to improve antiretroviral adherence, and mindfulness-based stress reduction. See Montoya, Henry, and Moore (2019) for a review of such approaches.

Given that HIV is now a stable disease for many individuals, the impact of cognitive rehabilitation on functional status remains a fertile theme for future research.

Clinical Recommendations

- Although cognitive deficits are typically less severe now than in previous eras, they remain prevalent, and clinicians should be mindful that patients, even those with well-controlled disease, may experience difficulties with everyday functioning associated with such deficits.
- Such difficulties may be exacerbated by aging, the presence of mood disorders, and other co-occurring conditions.
- Although self-reports remain prone to bias, they are still the most easily accessible and practicable method for first ascertaining possible everyday problems.
- While objective, performance-based measures of everyday functioning hold promise, the availability of such measures is limited; however, methods development continues, and clinicians should stay current with the literature as new approaches emerge that increasingly reflect modern tasks (e.g., internet shopping and banking).
- Ideally, clinicians should incorporate a multimodal approach to the assessment of everyday functioning (self-report, informant report, performance-based measures) whenever possible.
- Most interventions reported to date have taken place within small pilot studies and are not readily translatable for implementation in clinical settings. However, work continues in this area, and more widespread applications may become available.

Summary

Extensive research has suggested that HIV-associated cognitive impairments significantly influence one's ability to carry out common activities required for independent, productive daily living. These activities include such behaviors as managing and adhering to medications, driving an automobile, maintaining premorbid levels of employment and vocational skills, and avoiding risky behaviors. Although these deficits are more likely to be seen in individuals with more severe HAND (e.g., MND or HAD), even the milder impairments that are most often associated with HIV infection can influence daily functioning (e.g., Albert et al., 1995; Heaton et al., 2004) and even survival (Grant et al., 2014; Sacktor, 2018). Although these impairments occur only in a subset of HIV-infected individuals, they still impart large societal costs, including increased costs of care, reducing the available workforce, and potentially spreading drug-resistant strains of the virus with inadequate antiretroviral adherence. Because of these costs, interventions to improve various aspects of everyday functioning continue to emerge, although none have become common practice.

The process of identifying functional deficits is challenging, and multimodal approaches to measure everyday functioning that integrate self-report, informant-report, performance-based tasks, or other objective indicators are likely to be more sensitive in detecting difficulties compared to any singular approach (Blackstone et al., 2013; Doyle et al., 2013). Moreover, isolating HIV-associated functional deficits has proven complex (e.g., Obermeit et al., 2017), as a number of factors could contribute to deficits in daily functioning, including comorbid medical or psychiatric conditions or substance use disorders. As the study by Heaton and colleagues (2004) illustrates, psychiatric factors (e.g., depression) need to be carefully considered as potential sources of functional impairment, as they may predict functioning independent of cognitive and/or functional performance. Often, studies do not thoroughly assess for psychiatric cofactors that may be contributing to functional difficulty, despite the high rates of disorders such as depression in HIV-infected populations. If these factors do not directly affect an individual's capacity to perform an activity, they certainly affect whether he or she *actually performs* the activity, as well as the accuracy of self-report measures that assess functional impairment. Indeed, the identification and remediation of psychiatric symptoms may prove important in preventing disability and negative functional outcomes as individuals continue to live longer with HIV infection (Benson et al., 2018; Grelotti et al., 2017).

Future Directions

As discussed in the first edition, cultural considerations remain a critical issue in the assessment of everyday functioning. HIV significantly impacts the ability to carry out common activities required for independent living. However, most research has been, and continues to be, conducted predominantly in Western countries with mostly English-speaking populations. With the highest rates of transmission in non-Western countries and in ethnic minority populations within Western countries, it is important to better characterize the complex relationships between HIV, neurocognitive impairment, affective symptoms, and everyday functioning among varied groups. Although one might expect a disease to have similar effects across cultures, the potentially differing everyday demands, the diverse nature of affective and psychiatric illness across cultures, and the general complexity of these relationships suggest that more focused and comprehensive study is needed to better answer such questions.

Further research is also needed to better characterize HIV-associated functional deficits in aging populations. As HIV has been transformed from an almost uniformly fatal illness into a more chronic condition through more effective drug regimens, more individuals are living longer with HIV, raising important questions about the additive or interactive effect of aging and HIV-related decline. Initial studies show the impacts of both neurocognitive and medical risk factors on employment status (Kordovski, Woods, Verduzco, & Beltran, 2017), medication management (Thames et al., 2011), and driving (Thames, Arentoft, Rivera-Mindt, & Hinkin, 2013) in older adults living with HIV.

In addition, as antiretroviral treatments continue to improve and reduce viral burden, including the development of long-acting treatments, it will be important to further our understanding of the mechanisms by which cognitive and everyday functioning impairments remain prevalent. This can be accomplished by better characterizing different neurobehavioral phenotypes seen in PWH, as well as better understanding the underlying biological mechanisms resulting in brain alterations (e.g., inflammation, gut dysbiosis, metabolic syndrome).

Lastly, over the past few decades there has been a growing appreciation of the importance of quality of life and functional outcomes in pharmaceutical and other interventions for neurologic conditions. Further development of new functional measures that could be completed within the constraints of a clinical trial would significantly advance our knowledge regarding the impacts of such treatments on real-world performance.

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CHAPTER 20

The Influence of Depression on Cognition and Daily Functioning

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In this Chapter we discuss how depression may negatively influence both cognitive and everyday functioning abilities. We review the prevalence of depression and some common treatment options, followed by a discussion of underlying neurobiological and genetic correlates. A large body of research has focused on depression and depressive symptomatology, but the exact relationships among depression, cognition, and everyday functioning remain unclear, although some studies have found cognitive impairment to mediate the relationship between depression and everyday functioning (McIntyre et al., 2013). A subset of depressed individuals shows mild to moderate neuropsychological (NP) impairment, and there is evidence of mood-dependent NP impairment as well as difficulties that persist in some patients after acute mood symptoms clear. Thus, a large portion of the Chapter focuses on how depression affects cognition and how this effect may translate into difficulties in everyday life. We recognize that environmental factors can influence depression development, and so we have included these in our comprehensive model (Figure 20.1); however, we do not discuss environmental factors in detail.

On the following pages, we use "depression" as a general term that refers to level of depressive symptoms as determined by self-report (e.g., Beck Depression Inventory–II) or clinician rating (e.g., Hamilton Depression Rating Scale). Studies of "depression" do not necessarily encompass the multifaceted clinical syndrome of major depressive disorder (MDD). MDD or a single major depressive episode (MDE), as specifically defined in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), can include difficulties with not only mood, but changes in sleep, interests, energy, psychomotor performance, and cognition (American Psychiatric Association, 2013). When studies describe research participants who have met criteria for MDD or MDE, we clearly

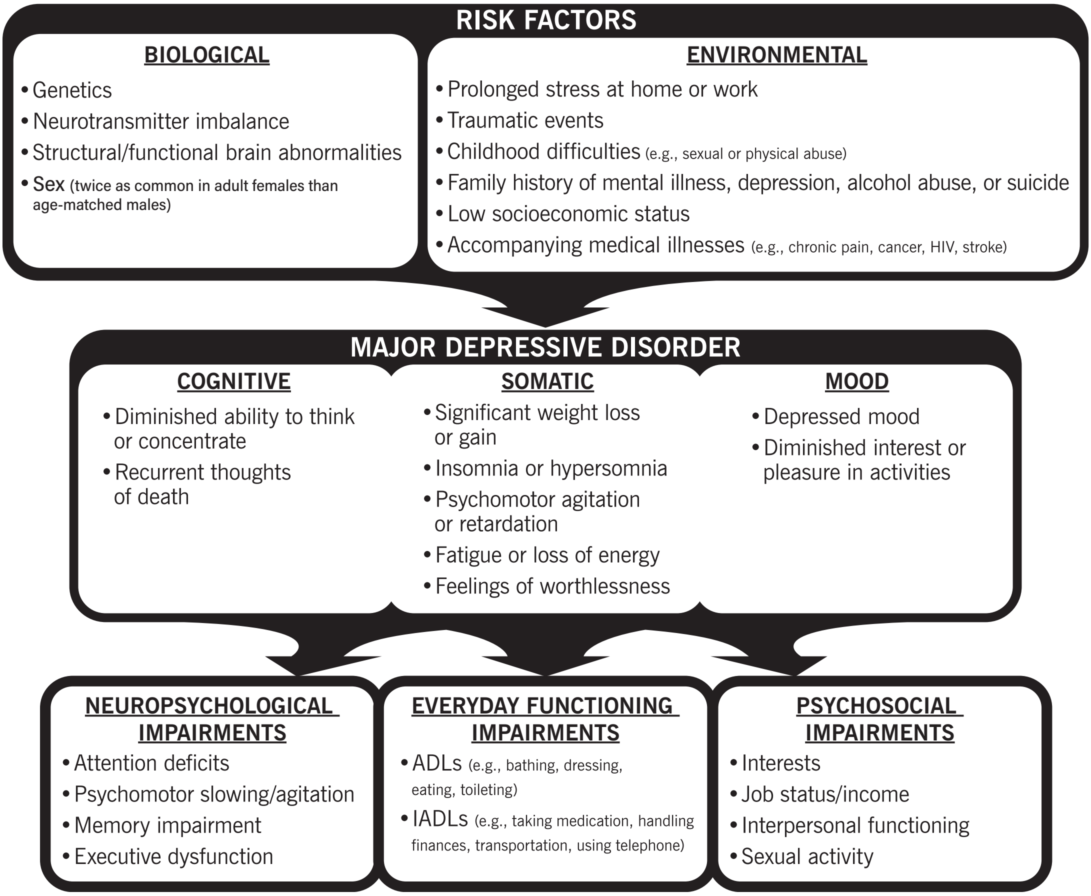

FIGURE 20.1. Biological and environmental contributions to the multifaceted diagnosis of major depressive disorder, both of which can also lead to neuropsychological, everyday, and psychosocial impairments.

indicate this. Otherwise, the reader can assume that the studies we discuss refer to participants with significant depressive symptoms who may or may not meet the criteria for MDD or MDE.

It is also notable that we have not included a detailed discussion of bipolar disorder in this Chapter, but rather an abbreviated overview of the most current literature in the subsection *Depression in the Context of Other Neurological/Psychiatric Conditions*. There is strong evidence that individuals with bipolar disorder have significant cognitive impairments and that the level of impairment may be more severe than in persons with MDD (Porter, Robinson, Malhi, & Gallagher, 2015). Furthermore, these NP impairments in persons with bipolar disorder may relate to difficulties in everyday functioning (Depp et al., 2012). Indeed, the evidence is strong that neurocognitive deficits in persons with bipolar disorder are present outside of affective episodes, whereas the evidence for such deficits among persons with MDD is less clear.

Prevalence of Depression

Depression is extremely common; the National Epidemiological Survey on Alcohol and Related Conditions (NESARC-III) estimates that 20.6% of American adults will have at least one depressive episode in their lifetime (Hasin et al., 2018). Although MDD is more common among women than among men, the disorder affects all genders, ages, and races (Kornstein et al., 2000). Research suggests a general underdiagnosis of MDD, especially for patients who have comorbid physical illnesses such as asthma or diabetes, probably because both patients and physicians attribute depressive symptoms to medical causes (Moussavi et al., 2007). Moreover, there are racial and ethnic disparities in screening, diagnosis, and treatment of depression due to differences in access to affordable, culturally appropriate, and linguistically appropriate care, as well as differences in the clinical presentation of depression (Shao, Richie, & Bailey, 2016). A recent analysis of data from 2005 and 2010 indicated an incremental economic burden of MDD at $210.5 billion, a 5-year increase (2005 to 2010) of 21.5% (Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015). Physical and psychiatric comorbidities were found to account for the largest proportion of this dramatic economic burden increase. Furthermore, depression was the second leading source of the global burden of disease among all diseases and disorders, as measured by disability adjusted life years (DALYs) and years living with disability (YLDs) in the year 2010 (Ferrari et al., 2013). Prevalence rates of depression among adults 65 years old and older are estimated to be 15–20% (Geriatric Mental Health Foundation, 2008), although this is likely an underestimation as geriatric depression often goes undetected and untreated (Center for Disease Control and Prevention, 2009). Older adults with co-occurring depression and chronic illnesses have a significantly higher disease burden than those who only have a chronic illness (Unützer et al., 2009).

The course of depressive illness can be variable. Some individuals have severe depression that is treatment resistant, whereas others respond well to treatment. Even at subsyndromal levels (i.e., instances where full criteria for MDD are not met), depression seems to have a significant effect on daily functioning and may cause particular difficulties with psychosocial functioning (Judd, Schettler, & Akiskal, 2002).

Individuals with depression can experience mental, role-emotional, and social dysfunction that is at least as debilitating as serious medical conditions. To highlight the fact that disability is not just the result of a medical or biological dysfunction, the World Health Organization revised its International Classification of Functioning, Disability, and Health (ICF) in 2001 to strengthen the notion that MDD should be placed on an equal footing with all health conditions (resolution World Health Assembly 54.21). Because the lifetime risk of depression is 5–10 times greater than that of many medical conditions and may occur at a time when severe medical illness is unlikely, depression may be more debilitating on a long-term and population basis. This seriousness of disability is compounded by underdiagnosis of depression, consequent lack of treatment for MDD, and the fact that those in the young-to-middle age range are particularly vulnerable to this disorder. A study of 240,000 people in 60 countries showed that depression alone is more debilitating than chronic physical diseases, including asthma, angina, arthritis, and diabetes. Moreover, patients with the burden of such physical diseases have an increased risk of depression, and, not surprisingly, those with both MDD and a physical disease have lower health scores than those with physical health problems alone (Moussavi et al., 2007).

Despite the prevalence of depression, there has been a relative dearth of research focused on its cognitive and everyday consequences. The lack of focus on daily functioning is likely a result of several factors: (1) There are numerous efficacious treatments for depressive symptoms, and it is often assumed that cognitive and daily functioning problems will improve simultaneously with treatment of the underlying mood disturbance; (2) the severity of depressive symptomatology and functional disability can vary greatly; (3) everyday functioning is difficult to measure; and (4) a consensus definition of impairment in daily functioning has not been formulated.

Treatment of Depression

Although many efficacious treatments for MDD exist, many individuals go undiagnosed and untreated (Gelenberg & Hopkins, 2007). Even with optimal pharmacological treatment, a significant proportion (20%) of individuals are "treatment-resistant" and fail to achieve symptomatic remission, defined as > 80% reduction in symptom severity on standardized rating scales (Keitner, Ryan, & Solomon, 2006; Culpepper, Muskin, & Stahl, 2015). This is important because people who achieve remission are more likely to return to normal psychosocial functioning than those who experience residual symptoms (Culpepper et al., 2015). Of these residual symptoms, sad mood and concentration problems have the strongest associations with impairment in everyday functioning (Culpepper et al., 2015).There are likely different cognitive and functional outcomes for those individuals who are treated, those who are not, and those who fail treatment. Likewise, the treatment outcome for patients with comorbid medical issues and depression requires that both mental and physical health issues be addressed. In patients with co-occurring mental and physical illnesses, treatment is often focused on more obvious physical diseases while depression is left unaddressed (Andrews & Titov, 2007). Below we briefly examine psychopharmacological, specialty procedures and psychosocial treatments for depression.

Psychopharmacological Treatments for Depression

Psychopharmacological treatments for depression are widely used. In fact, a recent report by the Centers for Disease Control and Prevention showed that approximately one in eight Americans over the age of 12 reported antidepressant use in the past month (Pratt, Brody, & Gu, 2017). Most "first-line" antidepressant agents are norepinephrine, serotonin, or dopamine reuptake inhibitors (e.g., selective serotonin reuptake inhibitors [SSRIs]) and target one or more of these systems. Recent meta-analyses support the efficacy and acceptability of 21 different antidepressant agents currently licensed in the United States and the European Union (Cipriani et al., 2018). Although some head-to-head trials support the superiority of some agents over others (Cipriani et al., 2018), in general all antidepressants are similarly effective: about one-third of all patients "get better" with several weeks of one of these first-treatments (Culpepper et al., 2015). Early detection is important since duration of depressive episode > 2 years is associated with worse outcome (i.e., not achieving remission in the first 6 months of treatment), as are comorbid chronic pain, medical and psychiatric disorders (e.g., substance use), and post-traumatic stress disorder (Kraus, Kadriu, Lanzenberger, Zarate, & Kasper, 2019).

Modern definitions of “getting better” with treatment focus on attaining *remission* of symptoms (e.g., > 80% reduction of symptom severity on standard rating scales) rather than simply treatment *response* (i.e., 50% reduction in symptom severity) because patients with residual symptoms have poorer life quality and everyday functioning. Those with residual symptoms are also three times as likely to relapse into another depressive episode over a 12-month follow-up compared to those without residual symptoms (i.e., 75% vs 25%). Of residual symptoms, sadness and concentration problems have the greatest impact on work, home management, close relationships, and social activities (Culpepper et al., 2015).

Treatment of the person who does not respond to initial trials of antidepressants is a complex topic and so is only briefly covered here. Assessment of initial misdiagnosis may be in order, as is consideration of “missed diagnosis” (e.g., alcohol use disorder), which may hinder response to treatment of depression. If adherence, dose, and duration of therapy have been adequate, the next steps may include switching to another antidepressant. For the person who has failed two initial trials of first-line agents, the next step may be combination therapy with two or more agents targeting different systems (Culpepper et al., 2015). Augmentation with lithium or non-antidepressants (e.g., atypical antipsychotics, thyroid hormone) and many other avenues may be considered.

One of these avenues is to consider novel agents. In 2019, the U.S. Food and Drug Administration approved esketamine (i.e., the *S*-enantiomer of ketamine) nasal spray for treatment-resistant depression. Double-blind studies have shown that esketamine is well tolerated and effective in rapidly reducing depression symptoms, including suicidality in patients with treatment-resistant depression (Papakostas et al., 2020).

Finally, long-term maintenance treatment (i.e., at least 6–12 months) with antidepressant medication seems important as it has been shown to provide better outcomes for individuals with depression than brief, short-term psychopharmacological intervention (Chisholm, Saxena, & van Ommeren, 2006). This regimen is particularly recommended for individuals with three or more lifetime major depressive episodes, particularly if two of these episodes are “severe” (Culpepper et al., 2015).

The effect of pharmacological treatment on cognitive functioning has not been well established because of the difficulties involved in disentangling the contribution of the depressive symptoms and medications. Some research suggests that SSRIs may negatively influence general memory abilities, resulting in forgetting (Wadsworth, Moss, Simpson, & Smith, 2005). The design of many observational studies does not allow for the disorder and treatment to be teased apart. In recent reviews of placebo-controlled clinical trials, antidepressants appear to have some benefit on immediate and delayed memory and psychomotor speed (Papakostas, 2015; Rosenblat, Kakar, & McIntyre, 2016). Yet, further trials with cognition as a primary outcome are needed. Although the long-term effect of esketamine on cognition has not yet been well studied; one study did find that participants did worse on cognitive tests at 40 minutes postdose but returned to their baseline performance by 2 hours post-dose (Morrison et al., 2018).

Procedural Treatments for Depression and Treatment-Resistant Depression

Some patients do not respond despite optimal treatment with standard antidepressants trials and proper augmentation strategies. For those with severe treatment-resistant depressions, often associated with suicidality, the gold standard therapy is still electroconvulsive treatment (ECT), which produces remission in 80% of patients. Stigma associated with this treatment, the usual need for hospitalization to administer a course of therapy, and patient concerns about adverse effects on memory (even though these effects resolve over time) have all contributed to a decline is its use (Kraus et al., 2019).

A new domain in nonpharmacological approaches to depression is "neuromodulation," indicating that entire brain networks rather than molecular-transmitter systems are targeted, though in more subtle fashion than traditional electroconvulsive therapy (ECT). One representative of this class is repetitive transcranial magnetic stimulation (rTMS) of the nondominant prefrontal cortex. This treatment is effective for major depressive disorder, can be used in an outpatient setting, has few adverse effects (e.g., mild headache, skin irritation), and is safe. A variation of this technique, theta-burst stimulation (TBS), has comparable response rates to rTMS; one advantage is that a treatment session takes < 4 minutes (versus > 40 minutes for TMS). Magnetic seizure therapy (MST) uses high doses of TMS to induce a seizure; an advantage over standard ECT is that stimulation is more superficial and therefore appears to result in few adverse cognitive effects (Kraus et al., 2019). Description of other rarely used procedural techniques (e.g., vagus nerve stimulation, deep brain stimulation) can be found elsewhere (e.g., Kraus et al., 2019).

Psychosocial Treatments for Depression

Several structured evidence-based psychotherapeutic interventions have been shown to produce substantial improvements in both mood and quality of life. For example, cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT) have been shown to be effective in the treatment of depression. CBT is a short, structured therapy that focuses on the here and now and seeks to change maladaptive thoughts that may negatively affect behavior and/or change behaviors to improve mood (e.g., behavioral activation). IPT also focuses on current difficulties but in relation to interpersonal relationships, rather than maladaptive thoughts, under the premise that depressive symptoms will decrease with the resolution of interpersonal problems. The cost efficacy of psychotherapy is comparable to generic antidepressants treatment, but it is less available (Chisholm et al., 2006), but medical models integrating primary care and mental health care are on the rise. Meta-analytic review of psychotherapeutic interventions for MDD generally show that reduction in depressive symptoms from psychological forms of intervention is equally as effective as pharmacological treatment with medium-to-large effect sizes, and that combined pharmacotherapy and psychotherapy is more effective in symptom reduction than pharmacotherapy alone (Karyotaki et al., 2016).

Both pharmacotherapy and psychotherapy approaches to the treatment of depression appear to improve overall quality of life and functioning, and combined pharmacotherapy and psychotherapy is better than either treatment alone; however, the effect sizes are in the small-to-medium range (Kamenov, Twomey, Cabello, Prina, & Ayuso-Mateos, 2017). Initial treatment with antidepressant medications and/or an indicated psychosocial intervention can lead to significant gains in terms of more years of healthy life; long-term maintenance treatment leads to even higher gains (Chisholm et al., 2006). Furthermore, maintenance treatment with an antidepressant medication and evidence-based psychotherapy (e.g., CBT) has been shown to decrease risk for relapse compared to medication alone (Karyotaki et al., 2016).

Neurobiology/Neuroanatomy of Depression

Catecholamine Hypothesis

Conventional hypotheses regarding the neurobiological underpinnings of depression suggest that abnormal levels of monoamine neurotransmitters are associated with the illness. The so-called catecholamine hypothesis suggests that individuals with depression have depleted levels of several neurotransmitters, particularly serotonin and norepinephrine (Ferrari & Villa, 2017). As a result, many antidepressant medications seek to boost the availability of these neurotransmitters by facilitating their release into the synaptic cleft or by blocking their reuptake. Although the monoamines clearly have a large role in the development, and consequently the treatment, of depression, more recent hypotheses show that there are likely numerous other factors related to depression and that the underlying biology of this disorder is complex. For example, more recent research has examined other possible neurobiological contributions to depression, including: changes in neuroplasticity and neurotrophins (e.g., Brain-Derived Neurotrophic Factor [BDNF]) in brain regions associated with depression (see the next section), mitochondrial dysfunction, and involvement of neuroinflammatory processes (Dean & Keshavan, 2017; Ferrari & Villa, 2017). Some hypothesize that different neurobiological contributions may account, in part, for the heterogeneous symptom presentation. For example, there is growing evidence that neuroinflammation may be more associated with the atypical depression subtype (Woelfer, Kasties, Kahlfuss, & Walter, 2019). While more work is needed, a better understanding of the neurobiological underpinnings of depression may lead to other pharmacological and nonpharmacological treatment options and more personalized treatments.

A description of the underlying neurobiology of depression would be incomplete without mentioning the hypothalamic–pituitary–adrenal (HPA) axis, which plays a role in emotional behavior and is responsible for regulating stress. The HPA has been found to be dysregulated in persons with mood disorders and may serve to identify persons who may be at risk for development of serious depressive symptoms, as well as those who will have higher chronicity of depressive symptoms and greater recurrence of symptoms over time (Murri et al., 2014; Stetler & Miller, 2011).

Neuroimaging Evidence of Brain Systems Involved in Depression

Neuroimaging studies have provided rich evidence of structural, functional, and connectivity abnormalities in the limbic-cortical and cortico-striatal regions and networks of persons with depressed mood (Graham et al., 2013). Structural neuroimaging of persons with depression reveals increased white matter abnormalities and decreased size of the medial systems of the prefrontal cortex (i.e., orbitofrontal cortex, ventromedial prefrontal cortex, and anterior cingulate cortex), lateral prefrontal systems (i.e., ventrolateral prefrontal cortex and dorsolateral prefrontal cortex), and subcortical systems, including the striatum and hippocampus (Wise, Cleare, Herane, Young, & Arnone, 2014). Of all these regions, reduction and altered shape of the hippocampus in MDD has been replicated most frequently across studies (Liu et al., 2017). Functional neuroimaging using tasks involving emotion processing of people with depression shows increased activation of the medial prefrontal cortex, amygdala, and hippocampus and reduced activation of the lateral prefrontal cortex and striatum (Wise et al., 2014). This pattern of response is consistent with the dysfunctional emotion processing theory of depression, in which individuals have an exaggerated emotional response to negative stimuli and reduced response to positive stimuli and reward processing. Similarly, Chamberlain and Sahakian (2006), in a review of the NP of mood disorders, have suggested that the orbital frontal and anterior cingulate regions of the frontal lobe in connection with subcortical structures may underlie the "affective" symptoms observed among individuals with depression. Positron emission tomography (PET) studies have also shown increased metabolism in the medial prefrontal cortex (Wise et al., 2014). Furthermore, a meta-analysis of 10 PET studies aimed to understand the neurochemical changes in MDD have shown reductions in serotonin 1 (5-HT1A) receptor binding in the mesiotemporal cortex and some surrounding structures (Wang et al., 2016). However, at this time, the usefulness of 5-HT1A receptor binding in diagnosing and treating MDD is not established.

Genetics of Depression

Genetic studies of depression often focus on genes that may impact monoamine neurotransmitters. Polymorphisms in the serotonin transporter promoter region (5-HTTLPR) have received a great deal of scrutiny and have been linked to bipolar disorder, depressive traits, and suicidal behavior, but they have yet to reveal a direct association with MDD (Kiyohara & Yoshimasu, 2010). More recent studies have also used polygenic risk scores to examine the genetics of depression. These studies suggest that the genetic associations are complex and currently only explain a small percentage of variance (~2%) in depression phenotype (Mistry, Harrison, Smith, Escott-Price, & Zammit, 2018).

Cognitive Impairment in Depression

Mounting research suggests that depression is a disorder of impaired NP networks (Rayner, Jackson, & Wilson, 2016). Cognitive impairment appears to be more prevalent among depressed individuals who are older, have a poorer response to antidepressant medications, suffer recurrent episodes, and have a younger age of onset (Jaeger, Berns, Uzelac, & Davis-Conway, 2006).

The diagnosis of "major depressive disorder," as presented in the DSM-5, is based on a list of heterogeneous symptoms (American Psychiatric Association, 2013), and some of these symptoms are cognitive in nature. Specifically, one of the criteria, "reduced ability to think or concentrate," may be related to attentional deficits. Decreased attention and concentration can include indecisiveness, negative automatic thoughts, and negative thought rumination, which have been shown to impact social problem solving (Donaldson & Lam, 2004). Another criterion, "psychomotor agitation or retardation," is often manifested as slowness or reduction in speech, facial expression, and fine and gross motor movements. In NP terms these deficits may be manifested through decreased psychomotor speed and speed of information processing (Bennabi, Vandel, Papaxanthis, Pozzo, & Haffen, 2013).

In the past, the term *pseudodementia* was used to describe primarily older patients with NP difficulties caused by a psychiatric illness rather than by a neurodegenerative disease (Kiloh, 1961). It is important to distinguish between the manifestations of cognitive difficulties in patients with these very different diagnoses. Mood-induced cognitive difficulties typically develop over a fairly short period of time and distress the patient, unlike similar changes due to a neurodegenerative disease (Kang et al., 2014). Patients with dementia rarely show improvements in cognitive tests of memory, whereas many patients with depression improve over time (Connors, Quinto, & Brodaty, 2019). Underlying global abilities that may be lost in dementia, such as language and learning skills, are still intact in depressed individuals (Arnold, 2005). In more recent years, use of the term *pseudodementia* has declined as the term is confusing and inaccurately describes the syndrome, may downplay the substantive cognitive problems experienced by individuals with depression, and does not account for the complex relationship between depression and neurocognitive decline due to underlying brain changes (e.g., vascular depression, prodromal dementia; Brodaty & Connors, 2020).

In terms of the severity of cognitive impairment, it has been repeatedly demonstrated that individuals with schizophrenia have moderate-to-severe cognitive impairment and people with nonpsychotic depression have mild-to-moderate cognitive impairment compared to healthy comparison participants (Harvey, 2011). A study comparing NP impairment in individuals with schizophrenia, nonpsychotic depression, and healthy controls showed that individuals with schizophrenia have the most significant cognitive impairment; however, individuals with nonpsychotic depression showed NP impairment in two of seven cognitive domains, as compared to zero domains among healthy comparison participants (Rund et al., 2006). Although severity of depressive symptoms did not directly correlate with NP performance, 24% of the patients with recurrent MDD had moderate cognitive impairment, and 4% of patients had severe impairment (impairments were most common in working memory and reaction time).

The Impact of Severity, Clinical State, and Remission of Depression on Cognition

The evidence is somewhat mixed as to whether the overall extent of depressive symptoms relates to cognitive ability. The study described above reported no correlation between severity of depressive symptoms and NP performance. However, a meta-analysis found significant associations between severity of depressive symptoms and cognitive performance in the domains of episodic memory, executive function, and processing speed; however, depression severity only accounted for a small percentage of variability in cognition (McDermott & Ebmeier, 2009). While severity of depressive symptoms likely contributes to severity of cognitive impairment, the severity of symptoms does not fully account for cognitive impairment (Rock, Roiser, Riedel, & Blackwell, 2014).

The evidence is stronger that some persons with depression who have cognitive impairments will continue to have such problems after they have returned to a euthymic state or their symptoms have remitted, with different patterns of impairment between late-onset and early-onset MDD (Bora, Harrison, Yucel, & Pantelis, 2013; Roca et al., 2015). Remitted MDD individuals in euthymic states still show significant attention and executive functioning impairments as compared to healthy controls, with impairments in inhibitory control the most consistent finding across studies (Bora et al., 2013; Rock et al., 2014). Such persistence of cognitive difficulties may suggest an underlying neural dysregulation that influences the presentation of cognitive symptoms associated with MDD (Bora et al., 2013). The cause of NP impairment in depressed individuals does not appear to be simply a result of low mood; instead impairment may be a manifestation of many neurobiological traits.

Another important issue to clarify is whether or not subjective cognitive complaints (i.e., self-reported forgetfulness) correlate with objective findings from NP testing. Skeptics suggest that cognitive deficits in individuals with depression are a result of loss of motivation or attention, not a reproducible neural dysfunction. Some studies do find an association between subjective and objective cognitive functioning even when accounting for affective symptoms. However, many studies do not find a significant association between subjective and objective function, but do find an association between subjective cognitive complaints and depressive symptoms (Burmester, Leathem, & Merrick, 2016). A large cross-sectional study of 1,000 community-dwelling adults aged 51–99 years old found that subjective cognitive complaints were unrelated to objective cognitive impairment but were significantly associated with depressive symptoms (Zlatar, Moore, Palmer, Thompson, & Jeste, 2014). The validity of self-ratings must be taken into consideration when exploring NP deficits. Additionally, although self-ratings may not be related to objective NP ability, they may be reflective of genuine psychological distress and should not be clinically disregarded.

The Effect of Treatment on Cognition

What remains particularly unclear is whether pharmacological treatments for depression contribute to the cognitive deficits in this disorder; however, it would be a misconception to think that cognitive problems among individuals with depression are an epiphenomenon caused by the treatment of the disorder. A review showed that, at least in specific executive functioning domains (e.g., set shifting), cognitive deficits do not necessarily improve with resolution of clinical symptoms. Deficits on executive functioning tasks are consistent with damage to dorsal and ventral portions of the prefrontal cortex (Austin, Mitchell, & Goodwin, 2001). These persisting cognitive deficits may have considerable implications for everyday functioning and quality of life in persons treated for depression.

Cognitive Domains Commonly Impaired in Individuals with Depression

Although individuals with depression may show cognitive impairments in a range of domains, we have chosen to focus on impairments in the areas of executive functioning, learning and memory, attention, motor skills, and psychomotor speed because they appear to be the most common (Tavares, Drevets, & Sahakian, 2003). The majority of NP deficits observed in those with depression are consistent with the frontosubcortical pathology described in the previous neurobiology/neuroanatomy section. Other cognitive abilities impaired in individuals with depression, such as an abnormal response to negative feedback and an affective processing bias, are reviewed elsewhere (Chamberlain & Sahakian, 2006; Tavares et al., 2003).

Executive functioning deficits are found in 20–30% of patients with MDD and are some of the most frequently identified and debilitating impairments of the disease (McIntyre et al., 2013). Some evidence suggests that attention and executive functioning deficits in depression may be trait-based and not a direct result of the depressive symptoms. This finding is supported by the earlier cited fact that remitted MDD individuals in euthymic states still show significant attention and executive functioning impairments, as compared to healthy controls without evidence of lifetime MDD (Bora et al., 2013; Roca et al., 2015). This does not mean that impairments in these domains are not related to clinical state. For example, in a cohort of individuals with mild to moderate levels of depression, executive functioning was the only impaired domain, and certain executive functioning deficits were related to severity of depressive symptoms (Grant, Thase, & Sweeney, 2001). Executive functioning impairments are more visible when the severity of the depression increases (Snyder, 2013). Impairments in executive functioning may be particularly relevant to everyday functioning. Preliminary evidence of the effect of executive dysfunction has been shown in areas of daily functioning, such as difficulties with planning and executing goal-directed activities. For instance, depression can lead to impairments in vocational and social abilities. Additional details regarding the effect of depression on executive functioning ability are reviewed elsewhere (Snyder, 2013).

Learning and memory problems in individuals with depression have been clearly identified and can be found on both verbal and visual learning and memory tasks (Austin et al., 2001). One interesting study showed that individuals with depression (in either a current episode or with evidence of a past episode) had difficulties with delayed recall but did not have any problem with habit-learning tasks, suggesting dysfunction of medial temporal systems rather than striatal systems (MacQueen, Galway, Hay, Young, & Joffe, 2002). Deficits were shown to be related to number of previous episodes, but independent of current mood state. Research suggests that verbal memory is worse in participants with remitted depression compared to healthy controls; however, this finding is primarily observed in older adults with much smaller effect sizes in younger adults (Bora et al., 2013). In summary, the evidence is somewhat mixed with regard to the root cause of learning and memory difficulties in persons with depression. The variability in findings may be due to methodological problems and the heterogeneity of MDD.

Attentional impairments and psychomotor slowing are other common impairment in persons with depression (Lee, Hermens, Porter, & Redoblado-Hodge, 2012; McIntyre et al., 2013), and, again, these symptoms can aid in the diagnosis of a major depressive episode. Psychomotor slowing can negatively influence performance on NP tests that are sensitive to generalized slowing (Bennabi et al., 2013).

Cognitive Problems in Older Individuals with Depression

Some of the most consistent evidence linking depression to NP dysfunction comes from studies of older people. Given that depression and cognitive problems are independently prevalent among older adults, the combination of the two is a particularly important concern (Steffens et al., 2006). Late-life depression has been particularly associated with deficits in executive functioning and speed of information processing, but associations with episodic memory and visuospatial skills are also reported (Wang & Blazer, 2015). However, studying the relationship between cognition and depression in older adults is complicated, as late-life depression is a risk factor for age-associated dementia (e.g., Alzheimer's disease) and is associated with early symptoms of dementia (Bennett & Thomas, 2014). Nevertheless, given that difficulties with daily functioning are common among older adults, the presence of depression may exacerbate these difficulties, whether objective cognitive impairment is present or not. Therefore, it is recommended that cognitive functioning in older adults with depression be closely monitored (Bennett

& Thomas, 2014). The particular impairments in daily functioning are further discussed in the depression and everyday functioning section, “Depression and Everyday Functioning” later in the Chapter.

Cognitive Impairment in Psychotic versus Nonpsychotic Depression

Data indicate that cognitive impairment tends to be worse in those with psychotic as compared to nonpsychotic depression (Sheffield, Karcher, & Barch, 2018). Individuals with psychotic depression have been found to have more diffuse cognitive impairment as compared to those with nonpsychotic depression, with deficits in executive function, processing speed, and learning being the most consistently reported (Sheffield et al., 2018; Zaninotto et al., 2015). The implications of psychotic versus nonpsychotic depression for daily functioning have not been well explored, but one can hypothesize that the additional cognitive impairment in persons with psychotic depression may translate into additional functional difficulties.

Mood-Congruent Cognitive Processing

Interestingly, persons with depression tend to show preferential processing for emotional stimuli with a negative tone (Ellis & Moore, 2001). For example, depressed patients are able to more easily recall a story with negative emotional content, and they show an above-average ability to recall negative emotional events from the past (Gaddy & Ingram, 2014).

Depression and Everyday Functioning

Depression and Performance of Activities of Daily Living and Instrumental Activities of Daily Living

Lack of energy, loss of interest, apathy, and insomnia can make it difficult for individuals suffering with depression to independently carry out basic self-care such as personal hygiene (activities of daily living [ADLs]) and to complete more complex tasks such as making and keeping appointments (instrumental activities of daily living [IADLs]). The presence of depressive symptoms is associated with a decline in performance of ADLs, particularly among older individuals. For example, following hospitalization due to medical conditions, 30–60% of older adults experience a decline in their ability to perform ADLs, and depression is associated with greater risk for decline in ADLs following hospitalization (Hoogerduijn, Schuurmans, Duijnstee, de Rooij, & Grypdonck, 2007). Other studies have confirmed that depressive symptoms are strongly associated with poor functional performance, and depression scores for older individuals were significantly higher for those who reported experiencing ADL decline (Iosifescu, 2012; Schillerstrom, Royall, & Palmer, 2008). Among community-based samples of older adults, NP impairment and depression appear to be two of the strongest predictors of daily functioning problems even when controlling for baseline cognitive function, alcohol consumption, and chronic health conditions (Stuck et al., 1999).

Among persons with a primary major depressive episode and severe depressive symptoms (e.g., Beck Depression Inventory *M* = 34.3; *SD* = 11.0), in one study cognitive impairment was strongly associated with impairment in IADLs, such as medication taking and finance handling, whereas level of depressive symptomatology and age were more strongly associated with impairments in basic ADLs (McCall & Dunn, 2003). Severity of depression and age were also associated with patients' satisfaction in role functioning and relationships.

Depression and Psychosocial Functioning

Like cognitive problems, psychosocial dysfunction is both part of the MDD diagnostic criteria as well as a consequence of the disorder. Specifically, depression is associated with declines in job status, income, and sexual activities; difficulties with marriage; and problems in familial relationships and friendships. Patients with more severe depressive symptomology exhibit higher levels of psychosocial dysfunction (Lam, Kennedy, McIntyre, & Khullar, 2014). Additionally, in persons with depression, there is a relationship between cognitive dysfunction and psychosocial dysfunction, particularly in older adults and in those with more severe depression (Cambridge, Knight, Mills, & Baune, 2018). Residual and pervasive depressive symptoms following treatment may lead to continued psychosocial dysfunction, suggesting that functional recovery lags considerably behind clinical recovery (Kennedy, Foy, Sherazi, McDonough, & McKeon, 2007). Additionally, problems in planning, working memory, and attention may be linked to permanent changes in the brain function of individuals with depression. These deficits in cognitive functioning may directly affect social functioning (Kennedy et al., 2007). Others may argue that low mood has less of a direct effect on neurocognitive integrity and a more consequential effect on psychosocial functioning, as difficulties in this domain may be more visibly troublesome.

Depression and Medication Adherence/Management

Although antidepressant medications are effective in reducing symptoms in many individuals with depression, this efficacy does not in itself ensure adherence to prescribed medications. In fact, randomized controlled trials of treatments for depression show that 20–40% of patients stop their treatments prior to completing a 6-month trial (Frank & Judge, 2001). Moreover, a large study examining antidepressant adherence using insurance claims found that adherence to antidepressants decreased from 41% at 3 months to 21% at 12 months (Keyloun et al., 2017). A recent systematic review identified a strong relationship between nonadherence to antidepressant medications and worsening of clinical outcomes (i.e., increased severity of depressive symptoms; increased relapse; increased emergency department visits), which directly relate to increased economic burden (Ho, Chong, Chaiyakunapruk, Tangiisuran, & Jacob, 2016). Reasons for nonadherence to medications include negative attitudes toward medication, depression, fear of medication dependence, side effects, and illness denial, although it has been suggested that beliefs about the efficacy of antidepressant medications may outweigh side effect problems (Byrne, Regan, & Livingston, 2006; Hansen & Kessing, 2007). Cognitive impairment may be another predictor of nonadherence (e.g., if people have difficulty remembering to take their medication, they are less likely to be adherent). This is especially true of elderly patients with memory problems (Ayalon, Arean, & Alvidrez, 2005).

Several psychosocial treatments have been designed to help individuals improve their adherence abilities. Briefly, collaborative interventions that involve the patient, significant others, as well as the physician, have proven to be the most helpful for improving adherence in this group (Vergouwen, Bakker, Katon, Verheij, & Koerselman, 2003). Even relatively simple adherence interventions, such as use of external reminders or construction of a positive attitude toward medication, appear to improve medication adherence (Patel & David, 2005). Cultural considerations must be taken into account when addressing adherence, as some ethnic/racial groups may have different depression treatment preferences. For example, Hispanic individuals may have a preference for psychotherapy or combination therapy as opposed to pharmacotherapy alone (Lewis-Fernandez, Das, Alfonso, Weissman, & Olfson, 2005).

Depression and Vocational Functioning

In addition to having a direct impact on simple daily functions, depression can negatively affect the ability to seek out and maintain employment. One study estimated the cost of time lost at work due to depression in 2010 to be $78.1 billion (Greenberg et al., 2015). Although depression may impact the likelihood of garnering employment, many individuals with depression are employed. Within the working population, depression prevalence rates have been estimated at approximately 6–7% (Birnbaum et al., 2010; Kessler et al., 2006). This likely underestimates the actual prevalence, given that individuals with depression often report physical problems (e.g., back pain) instead of emotional or psychological problems. Failure to report depression in the workplace may be driven by associated stigma as well as compensation policies (i.e., employees may be paid when on leave for physical problems but not emotional problems).

The World Health Organization reports that depression is the leading cause of disability worldwide (World Health Organization, 2017). Several studies show the widespread impact of depression on days of work lost due to short-term disability. In a 12-year study of employees (two-thirds of whom were women) at a major national bank, depression accounted for 65% of total short-term disability days, with an average of 44 days of work lost. For comparison purposes, employees tended to take an average of 42 days for heart disease and 39 days for lower back pain (Rytsala et al., 2005). In another large study of U.S. workers, MDD was associated with an average of 27.2 work days lost (Kessler et al., 2006). Greater duration away from work related to depression has been shown to strongly be associated with longer duration of depression and moderately associated with severity of depression, comorbid mental or physical disorders, history of previous sick leave, and older age (Lagerveld et al., 2010). A recent meta-analysis found that a number of empirically-based workplace interventions reduce depression symptoms among employees, with some evidence that these workplace interventions may improve occupational outcomes (e.g., absenteeism; Joyce et al., 2016).

Depression and Driving

As shown in other functional domains, it is difficult to disentangle the impact of depressive symptoms and treatment for depressive symptoms on driving ability. Older epidemiological studies suggest that individuals who are taking sedating antidepressant medications may be at greater risk for traffic accidents (Ray, Fought, & Decker, 1992). However, more recent reviews examining the relationship between antidepressants in cohort studies, as well as experimental studies (e.g., on the road tests, driving simulators), have highlighted the mixed findings in the literature. Several reviews conclude that there is currently not enough evidence to generate inferences regarding the relationship between SSRI/SNRI use and traffic safety, but that risk of accidents may depend on a number of factors such as dosage, acute effects when starting the medication, and the presence of sedating side effects (Hetland & Carr, 2014; Ravera, Ramaekers, de Jong-van den Berg, & de Gier, 2012). A study of healthy controls in comparison to participants with treated and untreated depression found that participants with treated and untreated depression performed worse than healthy control participants; however, participants on antidepressants (SSRI or SNRI) performed better on a driving test than those with untreated depression (van der Sluiszen et al., 2017). Finally, an experimental study that examined driving ability before and after starting antidepressants found that psychomotor skills and driving ability significantly improved after 4 weeks on antidepressants (Brunnauer et al., 2015).

Depression and Quality of Life

Undoubtedly, depression can negatively impact a person's quality of life (IsHak et al., 2011). The difficulty with studies of depression and quality of life is that some investigators feel that poor quality of life is simply part of the depressive illness and is not distinct from depressive symptomatology. Multiple studies have shown, however, that greater levels of depression are related to poorer quality of life (IsHak et al., 2011). Given the strong correlation between depressive symptoms and quality of life, one review called for the treatment of depressive symptoms in improving overall quality of life (Hansson, 2006). Moreover, a recent meta-analysis found evidence for the positive impact of psychotherapy and pharmacotherapy on quality of life in depression (Hofmann, Curtiss, Carpenter, & Kind, 2017).

Depression in the Context of Other Medical/Psychiatric Conditions

Thus far, we have discussed the impact of depression on cognition and everyday functioning in isolation, but it is well known that depression and/or depressive symptoms are a common consequence of many medical, neurological, and psychiatric conditions. Covering all aspects of the effects of depression on daily functioning in the context of all other medical conditions is not feasible in this Chapter; however, it is worth providing a couple of examples of how depressive symptoms can influence everyday functioning in the presence of comorbid syndromes.

Clinically significant depressive symptoms are common among individuals with HIV infection (Ciesla & Roberts, 2001). A large study of the everyday functioning abilities of individuals living with HIV infection found that depressive symptoms, as measured by the Beck Depression Inventory, were a significant predictor of employment status (Heaton et al., 2004). Levels of depressive symptoms and levels of functional impairment, as measured by laboratory-based IADL tests, were also correlated with patients' complaints of cognitive difficulties. Depressive symptoms uniquely contributed to participants' subjective complaints, as the symptoms did not strongly relate to levels of functional impairment. Finally, higher levels of NP impairment, functional impairment, and depressive symptoms contributed to greater dependence in the performance of daily activities (e.g., cooking, shopping, laundry). A recent study found that high cumulative depressive burden over time was associated with worsening neuropsychological functioning among those with HIV (Paolillo et al., 2020).

Depressive symptoms can also play a role in severe mental illness and are associated with greater cognitive, social, and everyday functioning impairments in patients with schizophrenia and bipolar disorder. The mechanism, however, of the depressive symptoms of cognitive impairment and real-world disability in schizophrenia and bipolar disorder may be different (Harvey, 2011). Among individuals living with schizophrenia, episodic major depression and more chronic, mild depression are highly prevalent and occur during all phases of the illness. A modest (and often uncorrelated) association between severity of depressive symptoms and cognitive functioning has been observed in those with schizophrenia (Bowie et al., 2008, 2010). Depressive symptoms do appear to be predictive of real-world, objective outcomes involving interpersonal skills and work skills independent of NP problems or other psychiatric symptoms among individuals living with schizophrenia (Bowie et al., 2008; Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006). Moreover, persons with schizophrenia who did not report depressive symptoms overestimated their cognitive and everyday functioning, whereas those with self-reported depression had cognitive and functional ratings that were both more negative/impaired and more accurate (Durand et al., 2015). In other words, depression in schizophrenia is associated with insight and awareness into objective levels of cognitive and functional impairments. These findings have important clinical implications, as the accurate self-assessment of cognitive and everyday functioning may reduce failure experiences and improve motivation to exert effort to set and achieve realistic functional goals.

In contrast, current depressive symptoms are more strongly related to cognitive impairment in persons with bipolar disorder than in individuals with schizophrenia (Harvey, 2011), and cognitive impairment still persists in periods of euthymia. Bowie and colleagues (2010) found that the ability to perform critical functional skills (interpersonal skills and work skills) were directly predicted by depressive symptoms in bipolar disorder, and this relationship was significantly mediated by performance-based measures of social skills. As with individuals with schizophrenia, this relationship was independent of NP problems or other psychiatric symptoms. Depression also appears to impact self-assessment of cognition and functioning differently among individuals with bipolar disorder. In a recent preliminary study, patients with bipolar depression significantly underestimated their everyday activities and cognitive functioning compared to ratings provided by high-contact clinicians (Harvey, Paschall, & Depp, 2015). Additionally, patients' self-reported ratings of functioning were unrelated to objective measures of cognition or everyday functioning but were related to greater self-reported depressive symptoms. According to the investigators, these findings suggest that patients with bipolar disorder may either have limited awareness of objective deficits (or lack thereof) or they are using their mood state to index their functioning. In conclusion, depressive symptoms are an important factor for understanding everyday functioning regardless of the clinical population.

Validity Testing

Depression has been shown to interfere with effortful processing on cognitively demanding tasks, thereby emphasizing the importance of including validated symptom and/or performance validity tests in neuropsychological evaluations of patients with depression. Suboptimal performance on symptom or performance validity tests could indicate intentionally poor performance, pursuit of secondary gain (e.g., compensation, attention), or disengagement from the task (e.g., preoccupation with suicidal thoughts, fatigue). If a pattern of NP results indicates inconsistent effort was applied to the testing situation, performance on the evaluation is likely an underestimate of the patients' cognitive abilities. In this situation, results of the evaluation will lack some validity and should be interpreted with caution. Research has shown that valid performance on symptom validity tests (e.g., validity scales on personality measures such as the Minnesota Multiphasic Personality Inventory) appears to mitigate the effects of overreporting/exaggeration of depressive symptoms (Rohling, Green, Allen, & Iverson, 2002). Additionally, several well-validated embedded (e.g., CVLT-II Forced Choice) and standalone (e.g., Test of Memory Malingering) performance validity tests are available, which, when paired with behavioral observation and clinical judgment, can help gauge the validity of neurocognitive testing. The current recommendation is to incorporate validated standalone and embedded validity measures throughout testing, as effort and validity can fluctuate (see the American Academy of Clinical Neuropsychology Consensus Conference Statement for a more in-depth discussion on this topic; Heilbronner et al., 2009).

Clinical Recommendations

The critical impact of depression and cognitive impairment on the inability to function in daily life situations highlights the need for clinicians to regularly screen and assess these multiple domains. For a number of reasons, patients may not realize or acknowledge they are depressed. For example, some patients may have more limited insight, may not know that factors like appetite, sleep disturbance, and concentration difficulties are non-affective components of depression, have less access to health care, or may not endorse depression symptoms due to stigma. Therefore, some patients may have less awareness of the consequences of depression; this is more so the case for older adults (Centers for Disease Control and Prevention, 2009). Including depression screening instruments in clinical visits can be an essential step in identifying those in need of further services and treatment. The Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) for younger and middle-aged adults and the Geriatric Depression Scale (GDS; Montorio & Izal, 1996) for older adults are brief, reliable, and well-validated self-assessments of depressive symptoms. Additionally, given the impact of both mood symptoms and cognitive deficits on everyday functioning, it is recommended that clinicians assess cognitive symptoms in their depressed patients. Unfortunately, there is not yet a consensus-based NP battery for assessing cognitive function in MDD as there is for other psychiatric illnesses (e.g., MATRICS for schizophrenia; McIntyre et al., 2013). Clinicians can administer several reliable and valid cognitive screening instruments such as the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), and make recommendations for follow-up assessment based on established cutoff scores. Given the significant, and somewhat independent, impact of depressive symptoms and cognitive deficits on everyday functioning, it is recommended that clinicians do not limit their assessment of depressive symptoms and cognitive functioning to the initial screening visit, but continue to monitor changes in these factors over the course of depression treatment as well as after remission (Iosifescu, 2012).

It is common to receive referral questions such as "Does the patient have the capacity to live independently, manage his/her own disability payments, and function in the community?" Direct assessment of everyday functioning can add significant information to help answer these types of referral questions, above and beyond information gleaned from the assessment of mood symptoms and cognitive ability. The "gold standard" for assessing everyday functioning is direct observation. Unfortunately, however, direct observation is rarely feasible. Alternative methods of assessing everyday functioning include ratings by high-contact clinicians, patient self-report instruments (e.g., Lawton and Brody Activities of Daily Living Scale; Lawton & Brody, 1969), proxy reports from confidants or caregivers (e.g., Specific Levels of Functioning [SLOF] scale; Schneider & Struening, 1983), or performance-based measures of functional capacity (e.g., UCSD Performance-based Skills Assessment-Brief [UPSA-B]; Mausbach, Harvey, Goldman, Jeste, & Patterson, 2007). It is critical that appropriate training be obtained for both administration and interpretation of cognitive screening batteries and performance-based measures of functional capacity in order to obtain valid patient data. Finally, we want to acknowledge the additional clinician and patient burden associated with recommending assessments of depressive symptoms, cognitive ability, and everyday functioning. Given the global economic burden of MDD, largely attributable to annual loss of workdays and other functional impairments, coupled with the general inability of conventional pharmacotherapy in mitigating cognitive deficits (McIntyre et al., 2013), the benefits of assessment and a more rapid treatment development plan appear to greatly outweigh the added time burden.

Summary

Future Directions for Research

There continues to be a growing body of research focusing on the impact of depression on multiple aspects of everyday functioning and cognition; however, significant work remains. There is a push in the mental health field for more personalized medicine; therefore, further research into the interplay among depressive symptoms, cognitive abilities, biological underpinnings, psychosocial factors, and real-world functional outcomes is needed to expand our understanding of depression and personalized treatment. Along these same lines, the relationship between depression and everyday functioning in the context of other medical and psychiatric conditions needs to be assessed. It is important to note that much of depression research has been conducted in North America in primarily non-Hispanic white populations; more research into psychosocial and sociocultural factors are needed in order to inform how to best assess for and treat depression among all persons. Finally, as discussed in this Chapter, everyday functioning is difficult to measure objectively; in the coming years, technological advances may also further improve our understanding of the relationship between depression and everyday functioning and could also be helpful in improving or sustaining independent functioning. Research using technology to both assess and intervene upon everyday functioning is growing; however, commonplace use of technology in a clinical setting for understanding everyday functioning is still lacking.

Conclusions

The multifaceted syndrome of depression is a common problem among individuals worldwide. The effects of this syndrome extend beyond its clinical symptoms (e.g., low mood, loss of interest in previously pleasurable activities) to problems with cognition and everyday functioning (see Figure 20.1). Cognitive problems are most prominent in the areas of executive functions, attention, learning and memory, and psychomotor slowing. One of the major implications for everyday functioning in individuals with depression is decreased ability to function in an employment setting, and depression has been shown to be a major contributor to short-term disability claims among those who are employed. Efficacious treatments for depression are available (both pharmacological and psychosocial) and may help to resolve clinical symptoms, cognitive problems, and difficulties in everyday functioning, although it remains difficult to tease apart the various contributors to cognitive impairment and everyday functioning. In summary, given the damaging effect that depression can have on daily functioning, all clinicians would benefit from being particularly sensitive to the high base rates of depression (regardless of clinical population), and there is a strong recommendation for routine depression screening.

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CHAPTER 21

Cognition and Daily Functioning in Schizophrenia

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Features of Schizophrenia

Schizophrenia is known for its dramatic clinical features, including psychotic symptoms (e.g., hallucinations and delusions), negative symptoms (e.g., flattened affect, reduced motivation, reduced speech), and disorganized symptoms (e.g., vague or tangential speech, odd behaviors; American Psychiatric Association, 2013). Less obvious to many people is that schizophrenia is also characterized by prominent cognitive impairments. Although schizophrenia has long been seen as a disorder of the brain and as a condition characterized by perceptual aberrations, it has only recently been viewed as a neurocognitive disorder. In this regard, it is different from many of the other neurological conditions covered in this volume. The cognitive impairments in schizophrenia now are a recognized core part of the illness (Green, Horan, & Lee, 2019). The cognitive deficits associated with schizophrenia are fairly broad and encompass a wide range of domains, including aspects of cognition that are social in nature (e.g., understanding the emotional and mental states of others, detecting and processing social cues) and nonsocial cognition (e.g., speed of information processing, attention, memory, reasoning). This broad pattern of impairment, along with the fact that some patients perform in the normal range on certain tests, are among the reasons that it has been difficult to identify particular neural circuits specific to schizophrenia.

Among the many cognitive domains affected in schizophrenia, some have been selected as particularly important for clinical trials. Based on a careful literature review and consensus meetings sponsored by the National Institute of Mental Health (NIMH), the following separable cognitive domains were selected as important to assess in treatment studies of cognition in schizophrenia: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition (Nuechterlein et al., 2004). This seven-domain conceptualization of cognition in schizophrenia has been supported with confirmatory factor analysis (McCleery et al., 2015).

Interest in nonsocial cognition, sometimes referred to as "neurocognition," in schizophrenia began with Eugen Bleuler (1857–1939) and Emil Kraepelin's (1856–1926) early observations of aberrant attentional processing in the illness. Research in this area took off with the advent of experimental psychology and clinical neuropsychology post-World War II and subsequently flourished with the emergence of cognitive neuroscience in the late 20th century (Green & Harvey, 2014). In contrast, social cognition is a relatively new area of investigation in this population. Research in this domain emerged in the 1990's and has grown exponentially since then (Green et al., 2019).

Studies of social cognition in schizophrenia have examined constructs such as social perception, theory of mind, emotion processing, social knowledge, and attributional bias (Green, Olivier, Crawley, Penn, & Silverstein, 2005; Pinkham et al., 2014). *Emotional processing* refers broadly to aspects of perceiving and using emotion. For example, an influential model of emotional processing includes four components: identifying emotions, facilitating emotions, understanding emotions, and managing emotions (Mayer, Salovey, Caruso, & Sitarenios, 2003). *Theory of mind*, also called mentalizing, typically refers to the ability to infer the intentions and beliefs of others. *Social perception* refers to the ability to judge social roles (e.g., intimacy and status) and social context; the term can also refer to one's perception of relationships between people, in addition to perception of cues that are generated by a single person. *Social knowledge* (also called social schema) refers to the awareness of the rules and goals that characterize social situations and guide social interactions. *Attributional bias* refers to how one explains the causes for positive and negative outcomes and how the meaning of events is based on this attribution of their cause.

Cognitive impairments (social and nonsocial) are relatively common in schizophrenia. It has been estimated that 90% of persons with schizophrenia have clinically meaningful deficits in at least one cognitive domain and that 75% have deficits in at least two (Palmer et al., 1997). Others have suggested that even these relatively high rates of impairment may be underestimates and that almost all individuals with schizophrenia may perform at a level below what would be expected in the absence of illness (Keefe, Eesley, & Poe, 2005; Wilk et al., 2005). Such estimates are based on the cognitive performance of patients compared to their unaffected monozygotic twins (Goldberg et al., 1990) or to estimates of expected levels based on premorbid functioning (Kremen, Seidman, Faraone, Toomey, & Tsuang, 2000). Additional evidence for the association between schizophrenia and cognitive impairment is provided by patients with superior intellectual ability. These individuals tend to exhibit performance on neuropsychological tests that, despite being within normal limits, falls far below expectations based on their intellectual ability (Vaskinn et al., 2014).

Cognitive impairments in schizophrenia have been noted and clearly described for well over a century and so cannot be considered a new discovery (Bleuler, 1950; Kraeplin, 1971). Because the impairments were appreciated so long ago, the recent surge in interest is more of a rediscovery than a discovery. At any rate, much more is known now about the nature of the deficits. The impairments are now clearly viewed as "core" features of the illness and not as secondary to it. The term *core* means that the impairments do not result merely from the presence of psychotic symptoms (e.g., distractibility due to hallucinations) or from the psychopharmacological treatments (e.g., sedation due to antipsychotic medications). Evidence for the central nature of these deficits in schizophrenia comes from several lines of research, as discussed briefly here.

1. Many patients demonstrate cognitive or intellectual impairments before the onset of psychotic symptoms and other clinical features of the disorder (Bora et al., 2014; Fusar-Poli et al., 2012); hence the cognitive impairments predate and show a different time course than clinical features of illness.

2. Cognitive impairment (at attenuated levels) can be detected in first-degree relatives of patients with schizophrenia who are not psychiatrically ill (Bora et al., 2014; Sitskoorn, Aleman, Ebisch, Appels, & Kahn, 2004; Snitz, MacDonald, & Carter, 2006). The presence of deficits in unaffected relatives suggests that some of the impairments reflect predisposition to schizophrenia, as opposed to the presence of the illness. For this reason, cognitive impairment is being used as an endophenotype in genetic studies of schizophrenia.

3. The magnitude of the cognitive impairment is relatively stable across the clinical state, with the level of impairment on some cognitive measures being quite similar when patients are either in or out of a psychotic episode (Heaton et al., 2001; Szöke et al., 2008). Hence, the impairments can occur in the absence of clinical symptoms of schizophrenia.

4. Cross-sectional correlations between cognitive performance and ratings of psychotic symptom severity are typically very small (Ventura, Thames, Wood, Guzik, & Hellemann, 2010). The low correlations are especially true for psychotic symptoms. Correlations with negative and disorganized symptoms are sometimes larger, but still relatively modest (O'Leary et al., 2000; Ventura et al., 2010).

5. The effects of antipsychotic medications are much larger on psychotic symptoms of schizophrenia than they are on cognition (Keefe et al., 2007). There may be greater cognitive benefits for second-generation antipsychotic medications compared to first-generation medications, but even so, this discrepancy of cognitive and clinical effects is true for both types of drugs. This suggests that the antipsychotic medications act on different neural systems from those that underlie the cognitive impairments (Coyle, 2006; Moghaddam & Javitt, 2012; Stone, Morrison, & Pilowsky, 2007).

Based on these converging lines of evidence, it can be concluded that cognitive impairment is a central feature of schizophrenia and that this feature is very prevalent. Although this conclusion seems obvious now, it reflects a recent shift in focus: away from the typical psychotic and negative symptoms that are part of the diagnostic criteria to the less dramatic, but more enduring, cognitive deficits.

Disability in Schizophrenia

Schizophrenia is a highly disabling illness that impacts essentially every aspect of daily functioning, including social networks, closeness to family members, school and vocational success, performance of activities of daily living (ADLs), and degree of independent living. When we consider all causes of disability, schizophrenia ranks among the top causes of disability worldwide (WHO, 2018). This high ranking is true for both men and women, even though schizophrenia tends to have earlier onset and be somewhat more severe for men.

Functional outcome in schizophrenia is typically assessed through semistructured interviews or surveys in which the participant describes his or her participation in various daily activities. Self-report ratings of functioning can be supplemented with ratings from caregivers, but typically they are not. It is rare for outcome studies in schizophrenia to use observations of behaviors in the community, so questions are sometimes raised about the validity of self-report measures (Bellack et al., 2007). Nonetheless, self-report ratings are generally considered to be acceptable measures of functioning for patients who are clinically stable (Birchwood, Smith, Cochrane, Wetton, & Copestake, 1990).

The relatively poor functional outcome in schizophrenia has changed little over the last century, even with the introduction of efficacious antipsychotic medications in the 1950s (Jääskeläinen et al., 2013). This reality creates a confusing situation in which antipsychotic medications (both first- and second-generation medications) are highly effective in reducing psychotic symptoms, but patient outcomes have not improved. It is hard to understand why, if our drug treatments are so good, the outcomes are so bad. One way to resolve the situation is to differentiate the types of outcome in schizophrenia. There are at least three distinctly different types of outcome in schizophrenia: clinical, subjective, and functional (Brekke, Levin, Wolkon, Sobel, & Slade, 1993; Brekke & Long, 2000). The clinical outcome includes levels of persisting psychotic and negative symptoms; subjective outcome refers to how good the patients feel about themselves and how satisfied they are with their lives. Neither of these types of outcome has a strong relationship to functional outcome, which includes social functioning, vocational success, and degree of independent living.

Making the distinction among different types of outcomes helps clarify the picture. Antipsychotic drugs are clearly effective in reducing symptoms in the majority of patients, and this effect is related to clinical outcome. However, antipsychotic medications have modest effects on other features of illness, such as cognitive impairments (Sinkeviciute et al., 2018; Woodward, Purdon, Meltzer, & Zald, 2005). As we will see in the next section, level of cognitive functioning is related to degree of daily functioning in schizophrenia. Hence, the features of illness that are related to functional outcome (e.g., cognitive impairments) are minimally impacted by drugs; instead the drugs improve aspects of illness such as psychotic symptoms that have comparatively less impact on daily functioning. The result of this mismatch is a major public health concern: Most patients with schizophrenia do not successfully reenter the community (defined by social or work achievements) after onset of illness (Hegarty, Baldessarini, Tohen, Waternaux, & Oepen, 1994; Helgason, 1990; Jääskeläinen et al., 2013; Wiersma et al., 2000). The treatment of schizophrenia can be viewed in terms of short-term and long-term phases. When someone experiences a psychotic episode, the first challenge is to reduce symptoms and to clinically stabilize the individual. The second phase occurs after the individual is stable and he or she is seeking a return to work, school, or family. The first phase tends to be managed successfully with medications and treatment teams; the second phase tends to end in disappointment.

Cognitive Impairment and Disability in Schizophrenia

There is a rather large literature on the relation between nonsocial cognitive impairment and functional outcome in schizophrenia; a PubMed query using the search terms "schizophrenia," "cognition," and "functioning" yields over 100 published articles on this topic each year since 2010. Many of the earlier published studies have been included in three literature reviews from our group (Green, 1996; Green, Kern, Braff, & Mintz, 2000; Green, Kern, & Heaton, 2004) and in a meta-analysis by Fett and colleagues (Fett et al., 2011). These reviews concluded that cognitive deficits show reliable relationships to functional outcomes in schizophrenia. Many of the studies also included patients with schizoaffective disorder. Among the studies, functional outcomes have included types of community functioning (social outcome, vocational success, and independent living), as well as the degree of success in acquiring skills in psychosocial rehabilitation programs. Participation in psychosocial rehabilitation groups can be considered a daily activity for many people with schizophrenia, so it is reasonable to consider success in these programs as a form of functional outcome. Across studies, the consistency of relationships is striking, and this overall conclusion is no longer a subject of debate. The strengths of the associations are typically in the medium range (e.g., $r = .3$) when separate cognitive domains are considered. The relationships can be much stronger ($r = .5$ or greater) when multiple cognitive domains are combined into composite scores (Green et al., 2000). At this point, the simple conclusion that cognitive performance is related to daily functioning in schizophrenia is clear and warranted. However, several follow-up questions have received careful attention.

Do the Relationships Hold for Prospective, as Well as Cross-Sectional, Associations?

One of the reviews was devoted to prospective studies in which baseline nonsocial cognition was correlated with community functioning (defined in terms of work status, social functioning, or degree of independent living) at a minimum 6-month follow-up (Green, Kern, et al., 2004). This review included 18 longitudinal studies, all of which appeared subsequent to the earlier review published in 2000. Based on the survey of these studies, it appears that cognitive impairment at baseline is a reasonable predictor of later community functioning. In fact, several of the studies found good associations with outcome 2–4 years after baseline assessment (Dickerson, Boronow, Ringel, & Parente, 1999; Friedman et al., 2002; Gold, Goldberg, McNary, Dixon, & Lehman, 2002; Robinson, Woerner, McMeniman, Mendelowitz, & Bilder, 2004; Stirling et al., 2003).

Several studies in the review examined baseline prediction of *changes* in functional outcome, instead of only functional status at follow-up (Friedman et al., 2002; Smith, Hull, Huppert, & Silverstein, 2002; Woonings, Appelo, Kluiter, Slooff, & van den Bosch, 2003). Such findings of baseline nonsocial cognition predicting change in functional outcome indicate that cognitive status has value for predicting how well people will benefit from interventions that are designed to improve community functioning (e.g., skills training programs). It is also possible to examine change in cognition over time, as opposed to change in functioning, and two of the studies found correlations between cognitive change and functioning (Friedman et al., 2002; Stirling et al., 2003). It should be noted that these studies examined cognitive decline, not improvement. In the absence of a potent cognitive enhancer, it has been hard to study correlates of cognitive improvement.

Are Some Cognitive Domains More Strongly Related to Outcome Than Others?

The findings in this regard have been mixed, with some studies suggesting that verbal learning (Fett et al., 2011; Green et al., 2000) or speed of processing (Fett et al., 2011; Gold et al., 2002) may be particularly important for functional outcome. However, looking across studies at this time, it is not obvious that one domain is particularly important to outcome compared to others. Instead, most or all of the cognitive domains appear to be related to functioning, at least when findings are averaged across subjects (Evans et al., 2003; Green et al., 2000; Velligan, Bow-Thomas, Mahurin, Miller, & Halgunseth, 2000).

More recently, researchers turned their attention to the role of social cognition in outcomes. Medium to large associations between social cognitive domains and community functioning have been reported, with theory of mind showing the strongest relationship ($\hat{\mu}_{\rho}$= 0.48) (Fett et al., 2011). The meta-analysis reports that social cognition explains an estimated 16% of the variance in community functioning, while neurocognition accounts for approximately 6% (Fett et al., 2011). The association between social cognition and functioning appears to hold over time; work from our lab has found significant associations between baseline social cognition and community functioning up to 5 years later (Horan et al., 2012; McCleery et al., 2016). Taken together, these findings suggest that interventions targeting social cognitive deficits have the potential to impact outcomes for people with schizophrenia.

Are Specific Cognitive Domains Related to Specific Aspects of Functioning?

At this point, it is difficult to draw connections between specific cognitive domains and particular aspects of outcome (e.g., work vs. social outcome, skill acquisition vs. independent living). Some support for specific differential relationships between cognitive constructs and different aspects of functional outcome has emerged from individual studies. However, meta-analytic results indicate that the effect sizes and associated confidence intervals largely overlap for most associations between individual cognitive domains and aspects of functioning (Fett et al., 2011). Thus, the magnitude of some associations between specific cognitive domains and aspects of functioning may not meaningfully differ from each other.

Nonetheless, it may be useful to consider predictors and correlates of work performance, especially because work outcome (whether someone has a job, how many hours a week, how long he or she has maintained the job) is a rather concrete, objective, and verifiable outcome. As expected, both the likelihood of having a job and the length of job tenure are consistently related to cognitive abilities (Bell & Bryson, 2001; Bryson & Bell, 2003; Gold et al., 2002; Kaneda, Jayathilak, & Meltzer, 2009; Reddy & Kern, 2014; Rosenheck et al., 2006).

One type of outcome that might be expected to be related to cognitive functioning, namely, medication adherence, is not consistently related. For example, a large-scale multisite 2-year follow-up study of patients with first-episode schizophrenia did not find level of cognitive functioning to be a predictor of medication adherence (Perkins et al., 2006). Instead, beliefs about the need for medication and the efficacy of the medications predicted adherence. Similarly, a review of the literature concluded that there is little support for cognitive status as a predictor of medication adherence (Lacro, Dunn, Dolder,

& Jeste, 2002). One might expect lack of medication adherence to be related to memory failure, and, in fact, studies have found associations between prospective memory (i.e., remembering to perform a previously planned task) and medication adherence (Lam, Lui, Wang, Chan, & Cheung, 2013; Raskin et al., 2014). However, in schizophrenia it appears that factors related to insight, as well as belief in the need and value of treatment, may be more important than level of cognitive functioning (Brain et al., 2013).

Even when specific relationships to a type of outcome are uncovered, they may change over time. For example, one study reported that vigilance is more important than verbal memory in explaining work performance during a structured 26-week vocational program (12 vs. 4% variance explained)—but only for the first half of the program (Bryson & Bell, 2003). The pattern was reversed for the second half of the program, in which verbal memory was a stronger predictor than vigilance (11 vs. 6%). In this case, familiarity with the tasks appeared to change the type of cognitive demands. Given this level of complexity, it is safe to say that it will take more time and more studies with differentiated assessments to form conclusions about highly specific relationships to outcome.

Are the Relationships Present for Other Major Psychiatric Disorders?

Patterns of relationships are not diagnostically specific to schizophrenia, but they also apply to other psychiatric disorders. Chapter 20 in this volume examines cognition and functioning in depression, so here we briefly consider the data for bipolar disorder. Compared to the large number of studies on this topic in schizophrenia, the literature on bipolar disorder is modest. However, systematic reviews of the findings to date suggest that similar relationships between cognition and functioning are present for bipolar disorder and that the strengths of these associations are comparable to those seen in schizophrenia (Baune, Li, & Beblo, 2013; Bowie et al., 2010; Depp et al., 2012). Bipolar disorder is associated with cognitive impairment even when patients are in a euthymic state (Baune et al., 2013; Depp et al., 2012), so many of the same concerns that apply to schizophrenia, about achieving adequate community functioning after acute treatment, also apply to bipolar disorder.

Mechanisms through Which Cognition Influences Outcome in Schizophrenia

Although the connections between cognitive status and daily functioning are clearly documented at this stage, we know relatively little about the mechanisms through which the linkages exist. The identification of mechanisms is important for several reasons. One reason is that it enables investigators to test statistically the adequacy of models of outcome in schizophrenia using techniques such as path analysis and structural equation modeling (Bellack et al., 2007). Given the highly complex nature of community functioning in schizophrenia and its reliance on a host of clinical, personal, and social factors, it is safe to assume that many of the observed effects between cognition and community activities involve mediators that act between cognitive processes and functional outcomes.

A second reason to identify mechanisms is that identification of key mediators can also suggest specific therapeutic targets. For example, a mediator of functional outcome would be a likely target for intervention in itself, especially if the mediator was thought to be more proximal to the outcome of interest. This situation could exist if a mediator, based on a well-grounded theoretical model, was thought to be closer to community outcome or vocational success than the basic cognitive process. An important goal in this area is to map out the key connections to outcome to help interpret treatment effects and to suggest new interventions.

Researchers have started to propose and test promising mediators between cognitive processes and outcome. One proposed mediator between nonsocial cognition and functional outcome is social cognition. Numerous reports have linked measures of social cognition to nonsocial cognition, on the one hand, and functional outcome, on the other (Kee, Green, Mintz, & Brekke, 2003; Kee, Kern, & Green, 1998; Mueser et al., 1996; Penn, Spaulding, Reed, & Sullivan, 1996). More recently, studies have combined all three types of measures into single analyses and have evaluated directly whether aspects of social cognition (e.g., emotion perception and social perception) act as mediators between nonsocial cognitive processes and functional daily outcomes (Addington, Saeedi, & Addington, 2006; Brekke, Kay, Lee, & Green, 2005; Couture, Granholm, & Fish, 2011; Green, Hellemann, Horan, Lee, & Wynn, 2012; Schmidt, Mueller, & Roder, 2011; Sergi, Rassovsky, Nuechterlein, & Green, 2006; Vauth, Rüsch, Wirtz, & Corrigan, 2004). Many early studies tested for mediation using multiple regression models and Sobel's test. More recently, researchers have applied sophisticated statistical procedures, such as bootstrapping and structural equation modeling or path analysis, to test for mediation/indirect effects and provide an estimate of the proportion of variance in functional outcome explained by the mediation model. The results are consistent: Social cognition appears to be a mediator for functional outcome (Brekke et al., 2005; Schmidt et al., 2011; Sergi et al., 2006), with approximately 25% of the variance in functional outcome being explained by such mediation models (Schmidt et al., 2011). While simple, single mediator models can point to important variables, multistep pathways with intervening variables can be informative about the pathway(s) to functional outcome in schizophrenia. However, these models are difficult to test because they usually require a large number of variables and a large sample size. Beyond social cognition, additional mediators for the pathway between cognition and functional outcome have been proposed, including beliefs and motivational factors (Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006; Green et al., 2012; Harvey, Koren, Reichenberg, & Bowie, 2006; Lin et al., 2013; Quinlan, Roesch, & Granholm, 2014; Ventura, Hellemann, Thames, Koellner, & Nuechterlein, 2009). Defeatist beliefs are a type of dysfunctional attitude in which an individual holds generalized negative beliefs about their ability to successfully perform tasks (Couture et al., 2011; Grant & Beck, 2009). A model proposed by Beck and colleagues (Beck & Rector, 2005; Rector, Beck, & Stolar, 2005) posits that for individuals with schizophrenia, impaired ability to successfully engage in activities (e.g., due to cognitive impairments) leads to discouraging life experiences, which in turn lead to development of negative and dysfunctional attitudes and beliefs. As dysfunctional attitudes and beliefs become entrenched, they are hypothesized to contribute to reduced motivation and drive to engage in activities, which are reflected in motivational negative symptoms (i.e., anhedonia and avolition).

Indeed, a study from our group using structural equation modeling found support for a single pathway from cognition to functional outcome via social cognition, defeatist beliefs, and motivational negative symptoms (Figure 21.1) (Green et al., 2012). A large Italian multisite study found evidence for multiple indirect pathways between cognition and functioning that included internalized stigma, resilience, and engagement with services in addition to social cognition, negative symptoms, and functional capacity (Galderisi et al., 2014). Further research is needed to settle the question of whether single versus multiple pathways (e.g., one through cognitive abilities, another through motivation) are most informative for understanding the key steps to functional outcome in schizophrenia.

Interventions for Impaired Cognition and Social Cognition in Schizophrenia

Because of the findings that cognition is related to community functioning in schizophrenia, as well as the evidence that cognition is a core feature of schizophrenia, cognition has become a treatment target. Cognition lies at the root of the fact that patients with schizophrenia experience high levels of disability and have difficulty entering the community. A common opinion is that the antipsychotic medications may have reached the limits of their treatment potential. For these reasons, the development of new drugs to enhance cognitive functioning in schizophrenia has become both a scientific focus and a public health priority.

Until recently, however, a number of obstacles prevented any drug from receiving Food and Drug Administration (FDA) approval for this purpose (Marder & Fenton, 2004). First, there was no consensus on how to measure cognitive performance as an end point in clinical trials. It was essential to find an end point for clinical trials that was based on a broad, interdisciplinary consensus process. Other significant barriers to drug development for cognitive enhancement in schizophrenia included the lack of a

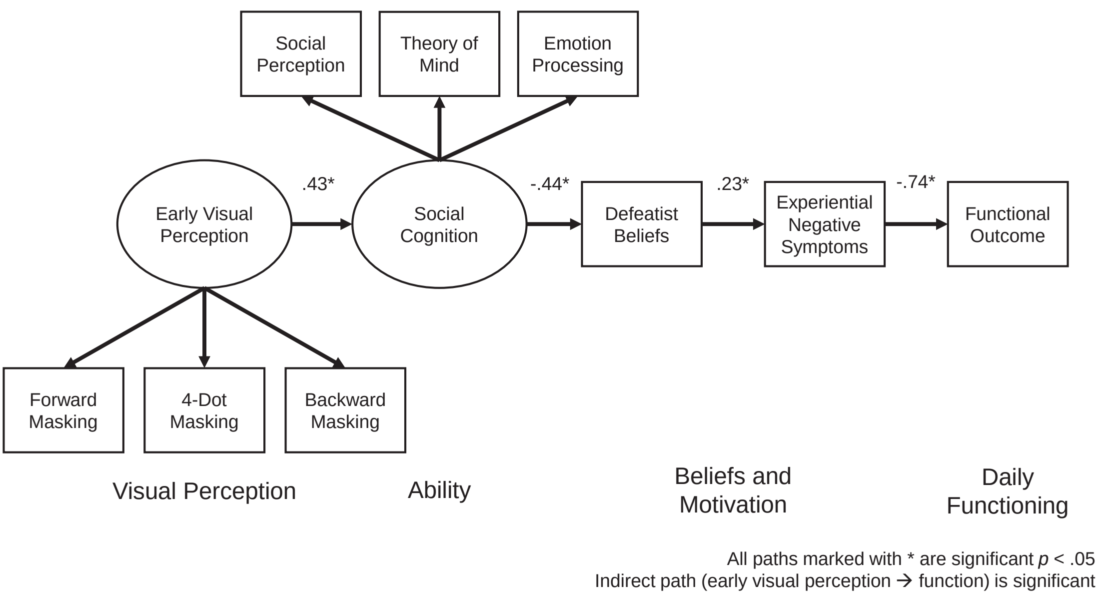

FIGURE 21.1. Mapping pathways to functional outcome: linking abilities with motivation. Adapted with permission from Green et al. (2012).

consensus regarding the appropriate design of clinical trials. For example, subject selection criteria, phase of illness, length of the trials, and ways to manage potential drug–drug interactions all required consensus before the FDA was willing to move forward. Other obstacles involved the prioritization of neuropharmacological targets (e.g., which receptor targets are the most promising) and criteria to evaluate promising compounds. Given the overriding ambiguity involving methods and measurements, together with the absence of any pathway for FDA approval, the pharmaceutical industry was understandably reluctant to make a substantial investment in developing cognition-enhancing drugs for schizophrenia.

To resolve this situation and to stimulate the development of new drugs for cognition enhancement in schizophrenia, the National Institute of Mental Health (NIMH) launched the MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) initiative (Marder & Fenton, 2004). The mandate of MATRICS was to address the barriers to drug approval by holding a series of consensus meetings (with representatives of industry, academia, and government). This initiative was charged with building a pathway for drug approval by reaching consensus on the methods and measures that would be used to evaluate promising new cognition-enhancing drugs for schizophrenia. The expectation was that once a pathway for drug approval was created, it would motivate the pharmaceutical industry to invest their resources and develop drugs for cognitive enhancement in schizophrenia—and this happened to some extent.

An essential product of the NIMH-MATRICS initiative was a consensus cognitive battery that would be the standard outcome measure for clinical trials of cognition-enhancing drugs for schizophrenia. Selection of the consensus cognitive battery involved a thorough, multistep process consisting of several consensus meetings, evaluation, discussion, and finally a data collection component (Green, Nuechterlein, et al., 2004). Essential criteria for the final selection of tests included (1) high test–retest reliability, (2) high utility as a repeated measure, (3) demonstrated relationship to functional outcome, and (4) demonstrated tolerability (acceptable to patients) and practicality (acceptable to testers). A relationship to functioning was selected as one of the essential criteria because part of the rationale of MATRICS was the linkage between cognitive and community functioning. The components of the MATRICS Consensus Cognitive Battery (MCCB) are shown in Table 21.1. As a group, individuals with schizophrenia exhibit marked impairment across all MCCB domains, with performance ranging from about 1–2 *SD* below that of the healthy adult normative sample (Kern et al., 2011; McCleery et al., 2014).

The results of clinical trials for cognitive-enhancing pharmaceutical agents have been inconsistent thus far. A recent meta-analysis found evidence for a small ($g = 0.10$) but significant effect of cognitive enhancers on overall neurocognition but no significant effects on individual neurocognitive domains (Sinkeviciute et al., 2018). However, it is important to note that many of the pharmaceutical studies conducted so far have been insufficiently powered to detect small to medium effect sizes, and the duration of treatment was typically brief (Keefe et al., 2013). Based on preclinical and clinical evidence, some studies have posited that pharmaceutical agents combined with psychosocial interventions, such as a cognitive training regimen, may yield greater benefits for cognition than either intervention alone (Michalopoulou, Lewis, Wykes, Jaeger, & Kapur, 2013).

Cognitive training, also called cognitive remediation, aims to alleviate cognitive

TABLE 21.1. MATRICS Consensus Cognitive Battery

Domain	Test
Speed of processing	Brief Assessment of Cognition in Schizophrenia (BACS)—Symbol-Coding Category Fluency (Animal Naming) Trail Making Part A
Attention/vigilance	Continuous Performance Test-Identical Pairs
Working memory (nonverbal)	Wechsler Memory Scale (WMS)-III—Spatial Span
Working memory (verbal)	University of Maryland—Letter–Number Span
Verbal learning	Hopkins Verbal Learning Test—Revised
Visual learning	Brief Visuospatial Memory Test—Revised
Reasoning and problem solving	Neuropsychological Assessment Battery (NAB)—Mazes
Social cognition	Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT)—Managing Emotions

impairment through repeated practice to retrain the targeted cognitive domain(s) (i.e., "drill and practice" restorative approach) or to compensate for impairment through cognitive strategies and/or implementing environmental accommodations or supports (i.e., compensatory approach) (Medalia & Choi, 2009). Increasingly, training is delivered individually via computerized programs, which may be accompanied by group discussions aimed toward bridging the skills trained in the laboratory to activities of daily life (i.e., "bridging groups"; Bowie & Medalia, 2016). Although cognitive training interventions are based on learning principles, they may differ with regard to their relative emphasis on either higher-level or lower-level cognitive processes (Medalia & Choi, 2009; Reddy, Horan, Jahshan, & Green, 2014).

The results of cognitive training intervention trials have been promising regarding improvement in functioning in trained, and in some cases, untrained cognitive domains, as well as improved functional outcome in schizophrenia (Chan, Hirai, & Tsoi, 2015; Grynszpan et al., 2011; Kambeitz-Ilankovic et al., 2019; McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Reddy, Horan, Jahshan, & Green, 2014; Twamley, Jeste, & Bellack, 2003; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). However, some clinical trials reporting positive effects of cognitive training were methodologically limited (e.g., outcome assessors not blind to treatment condition; Chan et al., 2015). Moreover, some rigorously controlled trials found little evidence for generalization of treatment gains beyond improvement on the trained tasks (Dickinson et al., 2009; Gomar et al., 2015). Clearly, more work is needed to identify characteristics of effective cognitive training programs, as well as factors that enhance generalization of gains to untrained cognitive domains and community functioning.

Training interventions have also been developed to target social cognitive impairment.

These interventions may include live instruction (individual or group-based) or computerized programs geared toward skills training in domains such as emotion and social perception (e.g., identifying emotional states of others using facial emotion and tone of voice) and theory of mind (e.g., identifying sarcasm and jokes, understanding the intentions and motivations of others; (Horan et al., 2009; Nahum et al., 2014). These interventions show promise for improving social cognitive abilities in patients (Horan et al., 2009, 2011; Nahum et al., 2014). A preliminary randomized controlled trial from our group found encouraging results for the combined effect of social cognition training and pharmacological agents. Intranasal administration of oxytocin, a neuropeptide posited to increase the salience of social information (Averbeck, 2010; Prehn et al., 2013), immediately prior to social cognition training yielded enhanced training effects on a test of empathy, a higher-order social cognitive ability (Davis et al., 2014). These gains were evident at one week and one-month post-training. These results cannot be attributed to the acute effects of the drug, but rather suggest that oxytocin facilitated learning during the intervention. A follow-up randomized controlled trial is currently underway.

Summary

This chapter has briefly summarized several topics related to cognitive performance in schizophrenia. The evidence that cognitive performance is a core feature of schizophrenia was reviewed, and it was established that cognitive deficits are part of the illness and not secondary to clinical symptoms or to medications. A summary of the literature on the relationship of cognitive performance to functioning in schizophrenia showed that this literature is quite large and highly consistent in showing relationships between cognitive performance and community functioning. The strengths of the relationships are medium for individual domains and large for summary scores, which indicate that much of the variance in functional outcome lies beyond cognition.

Once such relationships have been demonstrated, other questions start to emerge. One question involves the mechanisms for such relationships. It is important, for both scientific and intervention reasons, to identify key mediators that act between cognition and community functioning. So far, several promising mediators have been suggested, including: social cognition, defeatist beliefs, and motivational negative symptoms. These constructs have been shown to be related to both cognitive performance and functioning; both reduce (or eliminate) the direct connection, and both add to the goodness of fit when added to models of outcome.

The final question to consider is whether cognition can be a target for intervention. The NIMH MATRICS initiative was charged with building a pathway for drug approval through a series of consensus meetings and through development of a consensus battery, the MCCB. The MCCB has provided the field with a common metric for assessing cognitive domains in schizophrenia treatment trials, facilitating interpretation of findings and comparison of results across studies. In this chapter we have focused on the efforts to develop promising new psychosocial treatments for cognitive enhancement in schizophrenia, such as cognitive remediation and social cognition skills training. It is plausible that significant advances in community outcome for patients with schizophrenia will occur when psychosocial approaches are combined with cognition-enhancing drugs.

Practice Guidelines

General Guidelines

- Although cognitive impairment is not included in the diagnostic criteria for schizophrenia, clinically meaningful cognitive impairment is very common in the disorder and it is linked to daily functioning.
- When working with individuals with schizophrenia, we encourage clinicians to evaluate cognitive functioning and to facilitate referral to supportive services if appropriate (e.g., disability services for academic or work accommodations).

Assessment of Cognition for Clinical Research

- The MATRICS Consensus Cognitive Battery has provided the field with a common metric for assessing cognitive domains in schizophrenia treatment trials, facilitating interpretation of findings and comparison of results across studies.

Targets for Intervention

- Improving cognitive performance with pharmacological agents and cognitive remediation is an energetic area of research. In addition, key mediators that act between cognition and community functioning, including social cognition, defeatist beliefs, and motivational negative symptoms, are potential therapeutic targets.
- It is plausible that significant advances in community outcome for patients with schizophrenia will occur when psychosocial approaches are combined with cognition-enhancing drugs.

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CHAPTER 22

Future Directions in the Assessment of Everyday Functioning

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It has been a decade since the first edition of this book was issued. In the ensuing years, technological advances have opened up new opportunities for improving the assessment of everyday functioning and capturing performance in the real-world environment. As noted throughout this volume, the neuropsychological approach to predicting everyday functioning has many advantages, including a legacy of developing standardized measures that are well characterized with respect to reliability and validity, and a rich literature addressing the relationships between brain function and real-world performance. But, as also summarized in numerous chapters, this approach still has limitations. As aptly stated in Chapter 17, neuropsychological assessment provides only an indirect link to everyday, real-world functioning. Here, we review our recommendations for future work from the first edition, reflect upon the progress made, and provide suggestions for the work still needed in order to better link brain function to real-world functioning.

1. ***Improve methods for directly measuring "real-world" outcomes.*** In the first edition, we noted that the operationalization of "real-world outcomes" is not necessarily any more advanced than the predictors being used to predict such outcomes. To develop useful laboratory-based measures, we need gold standards regarding what defines functioning in the real world. To establish how individuals are functioning in their daily lives, investigators/clinicians often rely on reports from patients and informants, which, though very important, have limitations, as noted throughout this volume. We predicted that developing technology would provide new opportunities for recording behavior as it occurs in the wild, improving our ability to observe and measure an individual's performance under common demands and distractions.

Thanks to the maturing of sensor design, machine learning, and pervasive computing, in the past decade, we have seen a number of new technologies begin to be used in the field to capture real-world information about a person's behavior. As discussed in several chapters (Chapters 10 and 11), to capture naturalistic data (e.g., sleep, activity level, location, eating, medications, driving behavior) sensors can be placed within the environment (e.g., infrared sensor), attached to the person (e.g., smartwatch) or connected to equipment that the person uses (e.g., car). One recent study that used a variety of different sensor types (e.g., pill, bed, motion, wearable) to track everyday behaviors found that, in comparison to cognitively healthy older adults, individuals with MCI were less active, had more sleep interruptions, and forgot their medications more frequently (Rawtaer et al., 2020). These types of studies remain rare but are beginning to improve understanding of how neurologic conditions impact real-world behaviors, and as the technologies become more available, and data analytics more accessible, they will contribute valuable information regarding real-world behaviors in the decade to come.

Technology-enabled assessment methods are also beginning to improve understanding of how person, task and environmental factors can interact to impact cognition and function. For example, using ecological momentary assessment (EMA), associations have been captured between fluctuations in cognition and symptom expression, including the side effects of antiepileptic medications (Frings et al., 2008) and fatigue (Small et al., 2019). Combining continuous data collection with EMA offers opportunities for unraveling the complex array of factors (e.g., physical, neuropsychiatric, environmental, compensation) that, along with cognition, play an important role in supporting everyday functioning. Work in this area is also being propelled forward by newer statistical methods that can examine temporally and at a time lag both between-person and within-person relationships among behaviors (e.g., cognition and mood).

In addition to improving understanding of how multideterminant factors impact everyday behaviors, technology-enabled methods have the potential to augment traditional clinic-based assessment of everyday abilities. For example, continuous data collected from a smartwatch or from environmental sensors could be used to capture variability and trends over time, augmenting absolute values that are collected in the clinic at one or more time points. An opportunity to have access to such continuous data may be especially useful when tracking recovery after injury or progression of neurological disorders, as such data may provide a more ecologically valid means for capturing changes that occur across time in everyday activities.

We expect that some of the sensor and data challenges that currently impact technology-enabled data collection (e.g., battery life limitations, data privacy and security concerns, big data analyses) will continue to see advancements. We also expect a continued explosion of novel methods that utilize technology to gather information about real-world functioning. These newer methods will require psychometric analyses to demonstrate reliability and validity. For many of these measures, rather than group normative data, comparisons will likely be made with respect to an individual's own performances over time. This presents a challenge in a climate in which clinicians are asked to determine whether a patient has experienced cognitive or functional decline based upon a single assessment, or evaluations in close proximity. However, as monitoring becomes less obtrusive and more practical, we foresee a time when such follow-ups become routine practice. Regardless, validating these new measures, which are expected to be more objective measures of real-world behaviors, will likely require an approach different from that used with traditional models and tests. In addition, if such methods are to be used to augment clinical evaluation, then incremental validity or value-added must be demonstrated. Alternately, if such methods come to replace more traditional methods, their efficacy and cost-effectiveness will need to be demonstrated. Identification of a "gold standard" functional measure would also facilitate comparisons across studies.

2. ***Foster development and implementation of new measures with greater ecological validity.*** This call has gone out for over four decades (Heaton & Pendleton, 1981). In the first edition of the book we noted that, rather than starting with circumscribed behaviors that have been well delineated in the controlled laboratory and trying to extrapolate findings to real-world scenarios, it might prove fruitful to develop new measures whose design begins with observations of human behavior in the real world, in all of its complexity (Burgess et al., 2006; Kingstone, Smilek, & Eastwood, 2008). Such approaches may ultimately lead to new constructs regarding how we attend to, prioritize, and manage our complex lives, and may also give us a better understanding of the component processes that are at work during complicated activities. In addition, newer technologies, such as virtual reality, might provide interesting opportunities for studying behaviors in a seminaturalistic manner.

Following the lead of the Multiple Errands Test (Shallice & Burgess, 1991), in the last decade some clinic-based tests have been developed with a more function-led approach. As described throughout this volume, these tasks are open-ended and require the use of multiple cognitive abilities for completion, including planning, problem solving, prospective memory, temporal order memory, and multitasking. As individuals complete these tasks, examiners observe and code for aspects of performance, such as strategy use (e.g., midtask planning, double-checking) and types of errors committed (e.g., rule breaks, omissions, off-task behaviors). This information can then be used to clarify the nature of the functional difficulties and target interventions. Recent technological advances have also improved the efficiency and accuracy with which more nuanced information about performance can be coded. As one example, a recent tablet-based app for the Night Out Task allows the examiner to time-stamp activities as they are being completed and easily code multiple process-related variables (e.g., self-corrections, preplanning) and specific error types (Schmitter-Edgecombe, Cunningham, McAlister, Arrota, & Weakley, 2020). One enduring challenge for any task completed in the laboratory, no matter how complex, is that the laboratory environment may be devoid of typical distractors or of contextual cues and supports that can assist task completion in the real-world environment.

As discussed in detail in Chapter 13, computerized assessment methods like virtual reality allow one to capture automatically, and on a continuous time scale, detailed information as an individual performs a task. Virtual reality assessments, which have become increasingly sophisticated and less costly, typically simulate the real world. These methods have been used in the assessment of driving abilities, where other approaches (e.g., on-road assessments) are time consuming, costly, and dangerous. Although several studies have found correlations between virtual reality cooking tasks and analogous cooking tasks performed in the laboratory or kitchen (Allain et al., 2014; Giovannetti et al., 2019), others have not (Tanguay, Davidson, Nunuez, & Ferland, 2014). As "virtual" is not synonymous with "ecologically valid," such instruments should be held to the same standards of reliability and validity as traditional paper-and-pencil and computerized tests. This brings us back to our first recommendation related to the selection of outcome measures that best represent real-world performance.

In addition to virtual reality, we have seen the development of computerized tests that assess more advanced, yet increasingly ubiquitous, activities of daily living by testing computer/technology use skills (e.g., Goverover, O'Brien, Moore, & DeLuca, 2010). For example, such tasks may require individuals to use the internet to perform actual everyday tasks, such as purchasing an airline ticket or shopping online. As individuals complete these tasks, data is automatically collected and the clinician can observe in real time where the breakdown in performance occurs. A recent comprehensive review of 17 internet navigation skills revealed associations with self-reported internet behavior and performance-based tests but not with global manifest functional status, described as what people actually do in their everyday lives (vs. capacity) and quality of life (Woods, Kordovski, Tierney, & Babicz, 2019). These tests also remind us that in order to keep up with changes in technology and modern living (e.g., automated bill pay), instruments assessing activities of daily living will need to be revised periodically.

Given that functional outcomes are to play a key role in evaluating the efficacy of pharmaceutical and behavioral treatments, how can development and implementation of new measures be facilitated? As was the case a decade ago, newer measures are often investigated by only a few researchers and are studied in select labs. This approach of relying on individual investigators/research teams to develop, refine, and apply new everyday functioning instruments to multiple populations continues to be inefficient. As noted in the last edition, it is difficult to lay a foundation for industry standards when careers rely on external funding and publishing, activities that almost universally require "novel" experiments and findings. As a result, although a few measures have developed a wider following (e.g., Rivermead Behavioral Memory Test, Test of Everyday Attention, Six Elements Test), in many cases there is limited understanding of how measures designed to predict real-world functioning perform across different clinical groups and, importantly, few studies aim to replicate previous findings. Confidence in such measures would be greater if findings were examined repeatedly within similar patient groups and across different patient groups. And the continuing question of how to best validate these measures as representative of real-world functioning remains.

In addition to the single "investigator-initiated" approach (which admittedly may best promote creativity), research can also be significantly advanced by developing common methodologies that yield predictor or outcome measures that serve as standards to which other approaches can be compared. The variability in current methods makes it difficult to provide recommendations for evidenced-based practice. If there were commonly accepted, valid instruments that predicted real-world functioning across different samples and studies, one would be able to compare the value of different interventions, as well as the relationship between brain function and everyday performance between these groups. Such a step is likely only to occur with institutional support, given the challenges involved in developing ecologically valid measures discussed earlier.

As in the first edition, we continue to recommend that potential stakeholders, such as the National Institutes of Health (NIH), convene expert panels to advance the development of standardized measures for assessing everyday functioning abilities. Such an initiative has yet to take place. One potential high-impact focus would be developing a consensus everyday functioning battery for use in clinical trials. The NIH took a rigorous approach to developing cognitive and other assessments as part of the NIH Toolbox (*www.nihtoolbox.gov*) in which experts were formally surveyed, and investigators then selected or developed measures that constituted a brief battery usable in clinical trials and other research. This effort does not include functional measures. In schizophrenia research, the National Institute of Mental Health supported a project that involved surveys of experts and focused conferences to define a standard cognitive battery for use in clinical trials (MATRICS; Nuechterlein et al., 2008). This effort also included the identification of "co-primary" measures that would be functionally meaningful (Green et al., 2008). While time will tell whether these efforts advance clinical research and treatment, a similar approach, perhaps on a more modest scale, might be undertaken to carefully identify, modify, or even develop everyday functioning measures that are appropriate for multiple research and clinical situations. This would likely result in more widespread use of such instruments, and facilitate comparisons across different treatments. This approach has its limitations—"consensus" does not always equate to "best"—and not all investigators would be pleased with the selected approaches and measures, but it would likely provide a needed impetus to further the cause of addressing functional outcomes in research.

3. ***Develop algorithms for predicting everyday performance based on the contributions of neuropsychological and non-neuropsychological factors.*** In the first edition, we noted that factors such as personality/temperament, psychiatric conditions (especially depression), licit and illicit substance use, medications, disease, psychosocial factors, environmental conditions, literacy, idiosyncratic approaches to daily life, and so on, no doubt explain different amounts of variance regarding performance of everyday tasks. Predictions will have better validity (and real-life meaning) if the major contributors to everyday functioning can be given appropriate weight as to their likely importance in a particular situation. For example, a prospective memory difficulty may predict everyday performance in particular areas, but in some circumstances there may be "higher-order" cognitive–dispositional–motivational complexes that determine even more of the variation in functioning and the extent to which prospective memory problems matter. Thus, some people have trouble initiating behaviors (e.g., due to obsessional traits or basal ganglia pathology, such as in Parkinson's disease), others may have disinhibition, some have decisional difficulties, and still others may have altered reward contingencies that affect their motivation. Attitudinal (e.g., sense of optimism) and coping (e.g., problem-solving approach, sense of mastery) variables may be powerful moderators of the path from cognitive changes to successful real-world performance.

Over the course of the past decade, there has been increasing progress in examining ways in which factors beyond "pure" cognitive functioning can individually, and in concert with cognitive deficits, impact everyday functioning. Throughout the chapters, many person, task, and environmental factors that can affect everyday performance were discussed. Chapter 8 detailed how stronger adherence to medications was related to numerous factors, including greater stability in lifestyle, more structured schedules/routines, less drug and alcohol abuse, better financial status, and higher disease-related knowledge among other variables. As discussed in several chapters (Chapters 18, 20, 21), studies have also begun to investigate factors that may mediate the relationship between cognition and functional outcome, including social cognition and depression. Although our understanding of the impact of other factors on everyday activities has improved, there is still a lot that we do not understand. Given the combination of factors that may impact everyday performances, as stated in Chapter 6, neuropsychological testing alone may be insufficient in many cases to make judgments about a person's ability to perform specific tasks in the real-world environment. Clearly, the more we understand about these multideterminant factors and their interactions, the better we will be at predicting everyday behaviors.

Over the past decade, the development of algorithms to support assessment of everyday behavior and intervention has progressed in a number of different ways. In Chapter 7, we saw an example of how instrumented vehicles that capture real-world driving data are being used to create collision warning algorithms. In Chapter 8, a study was referenced demonstrating that reinforcement learning algorithms could be used to improve medication adherence rates by matching patients with the type of text message reminder that works best for them (Piette et al., 2014). In Chapter 10, although more work is needed, data suggesting that machine learning algorithms could be applied to smart home data to create group and individualized normative data and to monitor and detect meaningful changes from baseline behaviors was discussed. And, in Chapter 16, machine learning methods were applied to magnetic imaging data to characterize diverse vascular pathologies, with results demonstrating correspondence with cognitive measures (Jokinen et al., 2020). Collectively, this work suggests that algorithms can be developed to assess and detect changes in cognitive and functional health status at the earliest stages, perhaps before individuals become aware of the changes themselves, leading to more proactive interventions and improved quality of life. For example, algorithms might detect a subtle shift in driving behaviors or increasing variability in the speed and temporal order of everyday activities being completed within the home. In addition, algorithms could be created to improve diagnosis, support everyday activity completion, and deliver real-time interventions. Opportunities await, facilitated now by both continuous and in-the-moment data collection, to develop algorithms that utilize both cognitive and non-neuropsychological factors in the prediction of everyday functioning.

4. ***Address cultural issues when developing and interpreting everyday functioning measures.*** As discussed in Chapter 5, although many everyday tasks are universal and are required for successful functioning in most societies, these tasks can also differ substantially from culture to culture. In order to determine the real-world effects of diseases and brain dysfunction across cultures, it would be ideal to standardize instruments as much as possible; however, this may be neither easy nor appropriate. For example, an activity that is important for functional independence in one culture (e.g., independence in medication management) may hold less meaning in another. Akin to assessing whether culture-specific norms are needed for neuropsychological tests, the field may need to develop culture-specific norms for everyday functioning measures. This is true even within societies. For example, Spanish speakers in the United States may have different methods of money management and cooking than native English speakers. In some cases, particularly when individuals have little or no education, measures of functional ability may prove to be the best way to determine whether cognitive decline has occurred.

A decade later, as discussed in Chapter 16 with poignant examples of the impact of ethnic differences, most performance-based tests continue to be developed and normed in white populations. Moving forward, it will be important to make sure that our measures of functional health account for health disparities and are valid and reliable for diverse racial/ethnic groups. This also applies to algorithmic development. Chapter 11 provides several examples of how machine learning algorithms could end up containing implicit biases that are inequitable and even dangerous. Item-response theory (IRT) is a statistical technique that has been used in developing several newer activities of daily living questionnaires (e.g., Sikkes et al., 2012; Schmitter-Edgecombe, Parsey, & Lamb, 2014) and is also being applied to test development (Liu, Yin, Xin, Shao, & Yuan, 2019). This research method may be particularly valuable for reducing systematic differences due to culture (Bilder & Reise, 2019), as IRT-based approaches allow for examination of differential item functioning (DIF). Specifically, DIF allows for evaluation of whether items behave differently for members of different subgroups (e.g., gender, education, cultural background).

Despite the importance of culture to interpreting data gathered from neuropsychological evaluation, as argued in Chapter 5, greater attention still needs to be given to this topic in psychological assessment training. As discussed in several chapters in this book, clinicians need to learn to practice cultural awareness, cultural humility, and cultural competence (Greene-Moton & Minkler, 2020). This is especially important when data is being collected to make recommendations about ability to perform everyday activities of daily living, as this could have significant implications for an individual's autonomy and well-being (e.g., living arrangements, guardianship).

5. ***Pursue studies examining the neural basis of real-world functioning.*** In the first edition, we noted that attempts to relate real-world functioning directly to brain function were limited, and we primarily examined components of everyday functioning while individuals were in a scanner (e.g., Just, Keller, & Cynkar, 2008; Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006). The field of neuroergonomics (Parasuraman & Rizzo, 2006) focuses on using neuroimaging techniques (e.g., functional magnetic resonance imaging, electroencephalography) to capture real-time brain function during different activities; in some work-related studies, a high workload then initiates adaptive automation in which functions are distributed between human and machine. This work has been applied to military and clinical situations (Parasuraman & Wilson, 2008) and, as discussed in Chapter 3, has been used to improve task performance (Parasuraman & McKinley, 2014). Investigators have also begun to use portable EEG instrumentation to examine neurophysiological correlates of real-world activities, such as automobile driving (e.g., Rupp et al., 2019). However, such efforts to directly link brain function to everyday tasks remains largely nascent. It is hoped that advancing technology may provide the field with another tool for identifying individuals at risk for impaired functioning.

6. ***Translate research/clinical findings into results relevant to the individual.*** Most studies involve null hypothesis significance testing in order to determine if there is a statistically significant difference between groups with and without a given brain condition. To be most clinically useful, measures of everyday functioning should help clinicians and researchers identify *individuals* at risk for impaired real-world functioning. In the first edition, we recommended that whenever possible studies report classification accuracy statistics. This includes not only the more traditional measures of *sensitivity*, *specificity*, and *overall accuracy (hit rate)*, but even more clinically relevant measures such as *positive predictive value* (chance that someone who is impaired on a laboratory-based test also has impaired everyday functioning), *negative predictive value* (chance that if someone

was unimpaired on the laboratory-based measure, then he or she is also unimpaired in real-world functioning), and *risk ratios* (e.g., likelihood and odds ratios; Woods, Weinborn, & Lovejoy, 2003).

Many chapters in this book discuss the importance of going beyond simple statistical group differences to improve the empirical basis of our clinical practice. In the past decade, a few studies evaluating performance-based tests have reported positive and negative predictive values (e.g., Margolis, Hallowell, Davis, Kenney, & Tremont, 2021), and the present volume also included hypothetical prevalence rates, but there is still a long way to go. Real-world continuous data collection methods and repeated assessments will allow for examination of trends in performance as well variability, which may be an important marker of brain dysfunction (Gleason et al., 2018). As the availability of these different data types expand across many patient populations, the information will help us better understand the utility and universality of different approaches.

7. ***Translate research/clinical findings into results relevant to rehabilitation.*** Even if neuropsychologists are not directly involved in treatment, recommendations provided to patients are a direct product of the data gathered during the assessment. Therefore, improvements in our understanding of the relationship between cognition and other multideterminants of everyday functioning should lead to better evidenced-based interventions. As highlighted in Chapter 21, factors such as insight and belief in the need and value of treatment may be more important than level of cognitive functioning when treating individuals with schizophrenia (Brain et al., 2013). Moreover, considering an individual's assets, skills, and abilities as opposed to focusing on deficits is also important. As an example, in a community-dwelling older adult population, compensatory strategy use was found to account for significant variance in quality of completion of a real-world prospective memory task even after controlling for cognitive and functional test performances (Weakley, Weakley, & Schmitter-Edgecombe, 2019). Depending on the activities under consideration, understanding of cognitive functioning alone might be considered necessary, but not sufficient, to predict how an individual will function in the real world.

In recent years, technology has played the role of a "cognitive prosthetic." For example, smartphones can be used to develop daily to-do lists, and automated time-based reminders can be sent to promote initiation and completion of activities. Technologies that allow for continuous and in-the-moment data collection also open up opportunities for real-time intervention, including prospects such as automated booster sessions to promote sustained engagement with treatment strategies. The success of such treatment-based algorithms will depend on their ability to accurately detect events that require intervention with a low degree of false positives. In addition, risks associated with not accurately recognizing a behavior (e.g., stove left on) must also be considered. Additional theoretical, computational, and ethical questions remain to be answered, including questions about best methods for capturing data and about the privacy and security of data and how to characterize anomalous data patterns that are suggestive of events requiring intervention. It is expected that advances will be made in these areas in the coming decades, which will have positive implications for the health and quality of life of neurological patients. An additional challenge for interventions targeting improvement in everyday functioning is demonstrating that the treatment meaningfully impacts real-world functional outcomes. This again returns to the challenging recommendation of identifying and establishing outcome measures that represent real-world outcomes.

8. ***Work across disciplines and embrace new ways of thinking and methods.*** Work in the area of neuropsychology and everyday functioning will surely advance as we continue to collaborate with other professions. As Chapters 2 and 4 on contemporary occupationally focused models remind us, everyday function arises from dynamic interactions between humans, their environments, and their occupations (everyday activities that people do that bring meaning and purpose to life). This means that performance may be influenced through change in any of these parameters. Occupational models also remind us that cognition is not static and can change as a result of contextual factors (e.g., fatigue) and the environment (e.g., distractions).

As discussed in Chapter 3, the basic tenet of human factors/ergonomics, which is to "know thy user," has important implications for developing appropriate rehabilitation tools. This includes understanding the cognitive and physical limitations and capabilities of the user as well as what functional abilities hold meaning and value to the user and are therefore important for rehabilitation. The corollaries are also to understand the technology/system and context of use. Consistent with this framework, research methods from human factors/ergonomic research, such as task analyses and usability testing, will improve efforts to develop efficacious, user-friendly cognitive aids (e.g., a digital memory notebook; Raganuth, Dahmen, Brown, Cook, & Schmitter-Edgecombe, 2020) for individuals with cognitive impairment.

As alluded to earlier, the field of neuropsychology and everyday functioning has much to gain by working with computer scientists and engineers. These colleagues provide expertise, ranging from sensor design to machine learning, which will complement the expertise of neuropsychologists in working toward new methods for assessing real-world behaviors and intervening. As also alluded to, data collection in naturalistic studies is typically immense and presents new statistical challenges for reducing and analyzing the data. It will be important to continue to work with statisticians to develop new methods for analyzing large amounts of data and for investigating mediators of everyday performance. The efficacy of tools available to neuropsychologists for predicting everyday functioning is expected to continue to advance thanks to the efforts of multidisciplinary teams and their openness to new ways of thinking about how to assess and validate measures of everyday functioning.

Clearly, technology has played an important role in advancing research in the area of everyday functioning in the last decade. The pervasive use of modern technology (e.g., automatic bill pay) also requires that we remain vigilant with our assessment instruments that may, for some people, be assessing outdated functional skills (e.g., writing checks). As noted in Chapter 13, to understand how individuals perform and make judgments in their everyday environments, a paradigm shift may be required that utilizes advances in modern technology. We expect that technology and technological advances will continue to play an important role in expanding knowledge in the neuropsychology of everyday functioning.

Yet technology alone will not solve the remaining challenges we have delineated throughout this book. The neuropsychologist will remain a critical actor in asking the right questions, guiding the development of new tools, interpreting findings in a manner that appreciates the breadth of factors that can affect everyday functioning, and helping patients and caregivers navigate through this ever-complex "real world."

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