Chapter 10

Applications of Neurocognitive Assessment in Behavioral Medicine

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1 Introduction

Neuropsychology is defined as the study of brain–behavior relations. Assessment of neurocognitive (or cognitive) function focuses more specifically on information processing abilities that can be grouped according to major domains of performance such as attention, learning and memory, executive functions, visuospatial and visuoconstructional skills, psychomotor abilities, perceptual skills, and language (see Lezak et al, 2004). These domains are assessed most thoroughly by a battery of neuropsychological tests, although under select circumstances such as initial dementia assessment, gross estimates can be derived from screening tests such as mental status exams.

Cognitive function is an important dimension of quality of life. Frank cognitive deficit, and even smaller decrements in cognitive performance, can be disruptive to well-being and daily functioning. A large literature has documented adverse effects of various chronic, non-neurological diseases and associated risk factors on cognitive function, and brain structure and function, across the life span (see Armstrong and Morrow, in press; Tarter et al, 2001; Waldstein, 2000; Waldstein and Elias, 2001). Interestingly, these are the very diseases and risk factors commonly studied in the field of behavioral medicine. Inter-individual variability in cognitive performance has for decades been used as an important outcome variable in medical and behavioral medicine research. Indeed, the brain is increasingly recognized as a target organ of chronic disease. More recently, cognitive function has been examined as a predictor of other important endpoints in behavioral medicine such as quality of life, medical decision making, and treatment outcomes. Furthermore, recent data suggest that decreased cognitive function is a predictor of mortality in the context of clinical disease (e.g., Lee et al, 2006). Among older adults, chronic disease is known to increase risk for dementia, disability, and frailty.

In the present chapter, we will discuss several applications of cognitive assessment in behavioral medicine. We will first provide a brief overview of the major domains of cognitive function and provide select examples of commonly used tests. Next, we will briefly describe a spectrum of risk factors and chronic diseases with known relations to cognitive function. Lastly, we will examine use of cognitive performance to predict select outcomes in behavioral medicine research.

2 Neurocognition and Its Assessment

It is important to evaluate cognitive function in the behavioral medicine setting because such

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A. Steptoe (ed.), *Handbook of Behavioral Medicine*, DOI 10.1007/978-0-387-09488-5_10,

function is apt to change in the face of medical illness or brain insult. Neurocognitive assessment is particularly complex in the field of behavioral medicine where patients can experience any number of health-related cognitive disruptions. Evaluation of cognitive function in patients or research participants in behavioral medicine is best accomplished by assessing each major domain of cognitive function.

Cognitive function can be categorized into multiple domains including (1) orientation, (2) perceptual processes, (3) attention and concentration, (4) executive function, (5) reasoning, (6) learning and memory, (7) visuospatial and visuoconstructional abilities, (8) psychomotor function, and (9) verbal or language function (Lezak et al, 2004). Making matters more complicated, tests rarely assess just one domain. In that regard, the nature of brain–behavior relations is such that several brain structures and functions are needed to complete even simple tasks. Furthermore, researchers and practitioners use differing terminology to describe similar constructs. Despite these challenges, neuropsychologists seek to accurately assess cognitive impairments in behavioral medicine populations and to make important recommendations to assist patients with these difficulties.

Patients who undergo neurocognitive testing may display a range of minor impairments across or even within any particular domain of function. Some patients may experience subtle decrements in cognitive function that are not of sufficient magnitude to qualify for diagnosis of a cognitive disorder. However, it is possible that these decrements remain noticeable or distressing to the patient. In contrast, other patients may experience declines that reach greater levels of clinical significance. For example, the diagnosis of mild cognitive impairment (MCI) is characterized as the presence of a significant deficit in one or more domains, though these impairments may not interfere with activities of daily living. However, more severe cognitive impairments, typically associated with pronounced functional limitations (e.g., caregiver dependence), may be indicative of a dementia diagnosis such as Alzheimer's disease (AD). Varying levels of dementia and impairment exist along the continuum between MCI and AD, and MCI and AD are among a myriad of possible cognitive disturbances that patients may experience.

In the behavioral medicine setting, certain medical conditions are characterized by typical patterns of cognitive impairment, and neuropsychological batteries may be designed accordingly to target these patterns. For example, individuals with vascular disease often show decrements in the domains of attention and executive function (O'Brien, 2006). However, although it is important to emphasize patterns of impairment, individual findings from a neurocognitive assessment are rarely, if ever, pathognomonic for a particular diagnosis.

We next describe the major domains of cognitive function and several representative tests according to Lezak and colleagues (2004) who offer one of the most commonly used classification systems in neuropsychology. The interested reader is referred to her text for more detail. Further information about specific cognitive tests reflecting the different domains of function can also be found in Mitrushina et al (2005) and Strauss et al (2006).

2.1 Orientation

Prior to testing specific domains of function, an examiner may choose to include a general mental status measure that tests orientation, or the awareness of self relevant to time, place, and person. Screening measures such as the Mini-Mental State Examination accomplish this goal, or the investigator may simply ask questions regarding personal data and/or current events. Barring suspected dementia, particularly poor orientation may indicate the presence of a delirium. Postponement of neuropsychological testing is preferable until the delirium clears and the examinee is able to perform more optimally.

2.2 Perception

Performance on most cognitive tests is affected by perceptual processes, but certain tests better isolate basic perception by limiting physical interaction with test materials. As an example, the Judgment of Line Orientation (JLO) test is a commonly administered test of visual perception. The JLO is presented in flip-book style; two lines appear on the top page, and a standard fan-shaped array of 11 lines appears on the bottom page. Examinees must identify the lines from the bottom page that match the angles of the two lines at the top page. Depending on the examinee's presentation, tests are available for a variety of other basic perceptual processes, including visual neglect, color perception, auditory perception, tactile perception, and olfaction.

2.3 Attention and Concentration

Similar to perception, attentional processes are tapped by numerous neurocognitive tests, but select tests disproportionately target attention. Basic attention refers to the ability to focus on, or perceive, specific information. Complex attention (including working memory) tasks require the examinee to hold information in mind while manipulating it in some way. Concentration (or vigilance) refers to the ability to maintain basic or complex attention over a period of time. Attentional deficits may occur at one, some, or all of these levels, and neurocognitive testing helps to distinguish among these respective functions. For example, the Digits Forward portion of the Digit Span test of the Wechsler Adult Intelligence Scales (WAIS) assesses basic attention. Examinees are asked to immediately recall strings of digits spoken by the examiner at an approximate rate of one digit per second. The digit sequences increase in length until participants fail two trials of a particular length. In contrast, the Digits Backward portion of the test, which taps more complex attentional and working memory processes, requires examinees to immediately recall additional strings of digits and repeat them to the examiner in reverse order.

2.4 Executive Functions

The executive functions are integral to the completion of the most complex human behaviors, particularly (a) adapting to novel situations, (b) engaging in social interactions, (c) abstract reasoning, and (d) regulating cognition and emotion. Executive functioning is a multi-component construct with dimensions that are generally defined as (a) volition, (b) purposive action, and (c) effective performance. Executive functions include the ability to sustain or flexibly redirect attention, the inhibition of inappropriate behavioral or emotional responses, the planning of strategies for future behavior, the initiation and execution of these strategies, and the ability to switch among problem-solving strategies. There are several multi-step tests designed to assess select executive functions. For example, the Trail Making Test Part B is a test easily administered in a behavioral medicine setting. To complete the test, patients draw lines connecting alternating numbers and letters in sequence (i.e., 1 to A, A to 2, 2 to B). The number of errors and task completion time are recorded and used to evaluate performance. There are also longer, more complex tests, such as the Wisconsin Card Sorting Test, that have the potential to yield more detailed information.

2.5 Reasoning

Like executive function, reasoning is usually characterized by a person's ability to integrate multiple facts or stimuli. Reasoning is distinguished from executive function in that an examinee must make a conscious effort to make rational judgments or to reach a conclusion about related stimuli. Tests intended to assess this

domain usually involve reasoning about verbal or visually presented stimuli. An example of such a test is Comprehension, a subtest of the various versions of the WAIS. This test presents the examinee with increasingly difficult open-ended questions that assess social competence and practical reasoning.

2.6 Learning and Memory

Learning refers to the process of acquiring new information, whereas memory involves the encoding, retention, and later retrieval of that information. Tests of learning and memory are classified according to the modality of administration (e.g., verbal versus visual). Verbal learning and memory tests frequently take one of two forms: (a) list recall or (b) story recall. The California Verbal Learning Test is an example of the former. Examinees are asked to recall a 16-item list across five learning trials after a short delay and a longer 20-min delay. The Logical Memory subtest of the Wechsler Memory Scales is an example of story recall. Examinees hear simple stories of a few lines and are asked to repeat as much information as possible from each story. In contrast, the Benton Visual Retention Test assesses visual memory; examiners show examinees 10 consecutive cards, each containing three geometric figures of varying sizes and shapes. Following a 10-s exposure period, examiners remove the card from view, and examinees immediately reproduce the figures from memory on a blank sheet of paper.

2.7 Visuospatial and Visuoconstructional Abilities

Tests of visuospatial and visuoconstructional abilities go beyond tests of simple perception to assess an individual's ability to organize visual information, orient objects in two- or three-dimensional space, and perform construction via drawing, building, or assembling test materials. In the Hooper Visual Organization Test examinees are presented with line drawings of objects that have been divided into multiple "puzzle" pieces. The examinee must correctly identify the object presented by mentally rotating the pieces to form a coherent picture. Commonly used examples of constructional tasks include the Copy trial of the Rey Complex Figure Test and the Block Design subtest of the WAIS. In the Rey Complex Figure Test, examinees are presented with a two-dimensional complex drawing and are asked to copy the figure. Copies are then systematically scored for accuracy using a 36-point scale. For Block Design, examinees are presented with red and white blocks, each with two red sides, two white sides, and two half-red half-white sides. Examinees must assemble the blocks to replicate a two-dimensional target stimulus within a specified amount of time. The number of blocks utilized increases with increasing item difficulty.

2.8 Psychomotor Function

In neuropsychology, two facets of psychomotor function are typically assessed – speed and strength. The examiner is typically interested in centrally mediated deficit, rather than fatigue or damage to the extremities. The Finger Tapping Test is an example of a test of psychomotor speed. Examinees are asked to use their index finger to tap a key that is connected to a counter as quickly as they can for a specified period of time. Several trials are typically completed and then averaged. Higher counts are associated with better performance. The Grip Strength Test (or Hand Dynamometer) is designed to test hand strength. Examinees are instructed to squeeze the device as hard as they can. Performance is measured in the amount of pressure the examinee is able to apply to the device. Two trials per

hand are completed, usually alternating hands between trials, and the trials are averaged by hand.

2.9 Verbal and Language Function

Neurocognitive assessment of verbal and language function is aimed at assessing (a) verbal production (e.g., articulation and sound sequence), (b) fluency (e.g., the ability to produce spontaneous speech or to name objects), and (c) reading and writing abilities. The Boston Naming Test is a common test of naming abilities. Examinees are presented with ink drawings that range in familiarity and are asked to name the object in the picture. Verbal fluency, another facet of verbal and language function, is commonly assessed with the Controlled Oral Word Association Test. In this test, examinees are given 1 min to name as many words as they can that begin with a particular letter of the alphabet. The first (and still most common) set of letters used is F-A-S. Importantly, verbal fluency also assesses aspects of executive function, so conclusions regarding performance on this test should take into account this overlap of assessed domains.

2.10 General Assessment Issues

It is apparent that cognitive function is not a unitary construct and cannot be assessed as such. Indeed, adequate assessment of cognitive performance typically depends on at least brief evaluation of all or almost all major domains of performance (or a hypothesis-driven focus on fewer domains). Use of composite scores is discouraged because they can mask understanding of specific cognitive processes. Importantly, cognitive screening measures such as the Mini-Mental State Examination are grossly inadequate to evaluate cognitive abilities, their prospective change, or response to treatment (Tombaugh and McIntyre, 1992). Concerns about floor or ceiling effects must be considered when working with those of considerably low or high levels of cognitive ability. In research and clinical contexts, it is necessary to consider known sociodemographic influences on performance such as age, sex, education, race/ethnicity, and socioeconomic status. Emotional status (e.g., symptoms of anxiety or depression), psychiatric disorders, sleep, and acute ingestive behaviors (e.g., smoking, caffeine, alcohol) are also highly relevant. Testers must be sure to make participants feel comfortable and promote motivation. For more detailed discussion see Lezak et al (2004). As we discuss below, a host of chronic diseases and their risk factors also influence cognitive performance.

3 Chronic Diseases, Risk Factors, and Neurocognition

An increasingly broad spectrum of chronic diseases and their risk factors have been associated with decrements in cognitive function across the life span (Armstrong and Morrow, in press; Tarter et al, 2001; Waldstein and Elias, 2001; Waldstein et al, in press). Here we will briefly overview a sample of relevant areas of investigation, beginning with several known and putative risk factors for chronic diseases, followed by select diseases and their treatments. Space limitations preclude us from describing specific patterns of cognitive difficulties associated with any particular risk factor or disease. However, data suggest that almost all major domains of function are affected, with measures of attention, executive functions, learning and memory, and psychomotor abilities showing particular vulnerability to various conditions. The interested reader is referred to the above reviews for further detail and for reference to the extensive and growing literature documenting potential underlying neurobiological mediators of risk factor/disease – neurocognition associations.

3.1 Risk Factors and Neurocognition

A host of behavioral, biomedical, psychosocial, and psychophysiological risk factors can influence cognitive performance. Importantly, relations of these risk factors (and diseases) to cognitive outcomes may be moderated by select genotypes. For example, the apolipoprotein E (APOE) ε4 allele is associated with AD, cognitive decline (Farrer et al, 1997), cardiovascular disease, and stroke (Eichner et al, 2002). Haan and colleagues (1999) noted that among individuals with cardiovascular and metabolic diseases, those who had an APOE ε4 allele experienced a significantly greater rate of cognitive decline than those without.

Numerous lifestyle factors that promote or reduce risk for chronic disease have known a impact on cognitive function and its decline. Various health-compromising behaviors exert a negative influence on cognitive function, whereas health-enhancing behaviors are associated with higher levels of performance or potential improvement with intervention. Lifestyle factors can influence cognitive performance by impacting the brain directly or by promoting or reducing the development of chronic diseases that in turn affect the brain. Examples of health-compromising behaviors that are associated with lower levels of cognitive function include smoking (Swan and Lessov-Schlaggar, 2007), heavy alcohol consumption (Oscar-Berman and Marinkovic, 2007), dietary insufficiencies (Gillette et al, 2007), and physical inactivity (Colcombe et al, 2004). Health-enhancing behaviors such as greater intake of antioxidants including omega-3 fatty acids, and vitamins C and E have been associated with higher levels of cognitive performance (Del Parigi et al, 2006; Morris et al, 2004), although results of randomized clinical trials have been mixed. Greater levels of fitness or physical activity have also been related to better cognitive performance (Colcombe et al, 2004). Further, aerobic exercise has demonstrated exciting associations with cognitive improvements and even neuroplasticity in both animal models and humans (Dishman et al, 2006; Lautenschlager et al, 2008).

Various traditional biomedical risk factors for disease and newer biomarkers are associated with lower levels of cognitive function and decline. Examples include high levels of blood pressure (or hypertension; Waldstein and Katzel, 2001), cholesterol (Muldoon et al, 2001), glucose (even in a non-diabetic range; Taylor and MacQueen, 2007), insulin (Stolk et al, 1997), homocysteine (Elias et al, 2005), obesity (Gunstad et al, 2007), pro-inflammatory markers (e.g., interleukin-6; Yaffe et al, 2003), and indices of oxidative stress (Berr et al, 2000). Interestingly, both high and low levels of several of these risk factors (e.g. blood pressure, cholesterol, body mass index, alcohol consumption) have been related to poorer cognitive outcomes (see Waldstein et al, in press).

Various hormones are known to have a direct biological influence on the brain while potentially promoting diseases that affect cognitive function. In that regard, low levels of estrogen and androgens (Sherwin, 2003, 2006) and both low and high levels of thyroid hormones (Smith et al, 2002) have been related to poorer cognitive function. Hormone therapy in postmenopausal women may help prevent cognitive decline (Sherwin, 2003). Numerous studies have revealed associations between higher resting cortisol levels and lowered levels of cognitive performance, particularly on tests of learning and memory (Lupien et al, 2005). It has also been noted that stress-induced cortisol elevations are associated with decreased cognitive performance (Kirschbaum et al, 1996).

The latter findings reflect a larger literature on the negative relations of stress to cognitive performance and brain structure and function, at least in part via aberrations in cortisol (Sapolsky, 1999; McEwen, 2002). Stress-induced blood pressure responses have also been related to lower levels of cognitive function (Waldstein and Katzel, 2005). In addition to stress-related constructs, it is increasingly recognized that a number of psychosocial factors that may confer risk for chronic disease are related to cognitive function (see Waldstein et al, in

press). Depression is such a factor that has long been known to have negative relations to brain and cognition. Other psychosocial factors such as hostility and anxiety may confer a negative influence on cognitive function whereas social support – a factor usually associated with better health outcomes – may have a protective relation to cognitive function.

A number of the aforementioned risk factors such as less healthy lifestyles, psychosocial stressors, and an accumulation of biomedical risk factors may, in part, explain associations of low levels of education or socioeconomic status (SES) and race/ethnicity (e.g., African American) to cognitive performance (Waldstein, 2000). Those of lower SES may also be more likely to experience neurotoxic exposures that impact the brain and cognitive function negatively (Morrow et al, 2001) and are less likely to have access to adequate treatment of their medical conditions.

3.2 Chronic Diseases and Neurocognition

Disease of any physiological system can negatively impact the brain and cognitive function (see Armstrong and Morrow, in press; Tarter et al, 2001; Waldstein and Elias, 2001). Cardiovascular diseases have been studied fairly extensively, and a range of conditions are associated with cognitive decrements. These include cardiac arrythmias (Mead and Keir, 2001), clinical coronary disease or myocardial infarction (Vingerhoets et al, 1997), heart failure (Vogels et al, 2007), and peripheral arterial disease (Waldstein et al, 2003). Various indices of subclinical vascular disease such as carotid intimal-medial thickening (Wendell et al, 2009), pulse wave velocity (Waldstein et al, 2008), brachial flow-mediated dilation (Cohen et al, 2009), and left ventricular hypertrophy (Elias et al, 2007) are similarly associated with poor cognitive outcomes.

Negative cognitive outcomes are also associated with type I and type II diabetes mellitus, pulmonary diseases such as chronic obstructive pulmonary disease and asthma, hepatic diseases such as cirrhosis, kidney diseases, autoimmune diseases such as systemic lupus erythematosus, various cancers, sleep disorders such as obstructive sleep apnea, and the human immunodeficiency virus (HIV) and the acquired immunodeficiency syndrome (AIDS) (see Bellia et al, 2007; Biessels et al, 2008; Borson et al, 2008; Kurella et al, 2005; Tarter et al, 2001; Zhang et al, 2007).

Medical and surgical treatments for disease affect cognitive function though in inconsistent directions. For example, prospective investigations generally indicate better cognitive outcomes for those taking antihypertensive medication than untreated hypertensives (Murray et al, 2002). Yet, results of double-blind, placebo controlled trials of antihypertensive have yielded complex and conflicting findings. Statin use may also be related to lesser prospective decline in cognitive performance (Szwast et al, 2007), although results of investigations of statin administration are mixed. Treatments for asthma (e.g., corticosteroid, theophylline) have yielded similarly mixed findings. Acute improvements in cognitive function have been associated with oxygen-related treatments for chronic obstructive pulmonary disease and obstructive sleep apnea syndrome and with hemodialysis (see Tarter et al, 2001). Coronary artery bypass surgery – a major surgical intervention – has been associated with both short- and long-term cognitive difficulties, although long-term alterations in performance may be attributable to the underlying disease (Royter et al, 2005).

3.3 Summary

Identifying future needs for research, Waldstein (2000) has suggested a need for increased multidisciplinary collaboration to address research questions related to associations between health/disease and cognitive function

such as (a) understanding what domains of cognitive function are most affected by risk factors and diseases; (b) determining relevant effect modification variables (e.g., age, education, race/ethnicity, genetic polymorphisms, comorbidities) in order to identify vulnerability and resilience factors; (c) understanding the biological and/or psychological mechanisms intervening between health and cognition relations; (d) determining whether medical, surgical, or lifestyle interventions improve or further compromise cognitive performance; and (e) identifying whether changes in cognitive function associated with health status have an influence on quality of life, daily functioning, medical adherence, medical decision making, or treatment outcomes. Below we briefly consider aim (e).

4 Applications of Neuropsychology in Behavioral Medicine

Use of neurocognitive measures to predict outcomes in behavioral medicine research is, to date, less common than examining cognitive functions as outcome variables. Here we provide examples of several ways in which investigators are using cognitive performance measures in behavioral medicine research contexts.

4.1 Medical Decision Making

A primary application of neurocognitive assessment in behavioral medicine involves the role of certain cognitive functions in a patient's medical decision making. Here we conceptualize medical decision making broadly, including health behaviors and health behavior changes relevant to diet, exercise, substance use, and medical treatment adherence. We also focus on executive function, as this domain has been linked most often to patients' medical decision making.

By definition, all health behaviors and health behavior changes involve executive functions (Williams and Thayer, 2009), as they require the planning of strategies for future behavior, the initiation and execution of these strategies, and the ability to troubleshoot ineffective strategies and implement new ones. Emotion regulation is also relevant to the maintenance of health behaviors and implementation of behavior changes. As an example, an obese individual interested in losing weight must initiate, execute, and maintain a weight loss plan in order to successfully achieve his or her goal. Furthermore, good problem-solving strategies and effective regulation of emotional reactions to this process may increase chances of success.

In their review of executive functions and changing substance use behavior, Blume and Marlatt (2009) point out that the conceptual relation between executive function and substance use behavior is reciprocal. That is, poor executive function contributes to poor substance-related decisions, such as excessive or illegal substance use. In turn, substance use behavior may result in further decrements in executive function through temporary or permanent damage to relevant brain circuits. Such deficits in executive function then become significant barriers to successful behavior change. Importantly, this cycle may be easily applied to the range of health behaviors described above, including diet and fitness. In fact, Sabia and colleagues (2009) show evidence of an association between a number of unhealthy behaviors (including smoking, alcohol abstinence, low physical activity, and low fruit and vegetable consumption) and likelihood of poor executive functioning. Specifically, individuals with three to four unhealthy behaviors were more likely to have poor executive function, and this association grew stronger with increasing age.

Similarly, executive functioning deserves consideration in the context of management of chronic illness and adherence to medical treatment regimens. As noted above, on average, individuals with obesity, diabetes, hypertension, peripheral vascular disease, renal dysfunction, pulmonary disease, HIV/AIDS, and other illnesses demonstrate poorer executive function than individuals without these diseases. Deficits in executive function may result

directly from disease or indirectly through treatments of disease (via mechanisms such as hypoperfusion of the brain or systemic inflammation). Moreover, these decrements in executive function are associated with poor treatment adherence, which may serve to perpetuate or exacerbate the disease processes. For example, executive function has been associated with poor adherence to medication regimens for cholesterol lowering (Stilley et al, 2004) and HIV/AIDS (Hinkin et al, 2003). Other cognitive functions, such as attention, prospective memory, and visuospatial-constructional ability, are also implicated in poor adherence to medication regimens (Hinkin et al, 2003; Stilley et al, 2004; Woods et al, 2008). Decisions to adhere poorly to prescribed treatments should therefore be understood as potential end-products of decrements in various cognitive functions.

Chronic pain, a common treatment target for behavioral medicine practitioners, provides a final example of the relevance of the neurocognitive examination to medical decision making. In their review of executive functions, self-regulation, and chronic pain, Solberg et al (2009) propose a model in which executive functions and associated decrements in self-regulation cause and maintain chronic pain disorders. Specifically, the cognitive, emotional, social, behavioral, and physiological challenges associated with chronic pain are more poorly managed in the context of poor executive function. Optimally designed chronic pain interventions may therefore require components aimed at improving executive functions and self-regulatory capacity, such as cognitive techniques and physical activity.

4.2 Quality of Life

Although the literature is limited, diminished cognitive function has been associated with decreases in health-related quality of life (HRQoL) in those with chronic disease. For example, patients with peripheral vascular disease and lower scores on measures of cognitive function exhibited diminished everyday adaptive functioning (Phillips, 2001) – itself a major predictor of HRQoL (Andersen et al, 2004). Cognitive difficulties have also been associated with lower levels of HRQoL in persons with chronic obstructive pulmonary disease (McSweeney and Labuhn, 1996), HIV (Tozzi et al, 2003), or those undergoing cancer treatments (O'Shaughnessy, 2002). Cognitive difficulties may also, in part, explain lower levels of HRQoL among those with hypertension (Thyrum and Blumenthal, 1995) or diabetes (Kuo et al, 2005).

5 Summary and Conclusions

Cognitive function has a long and extensive history as an important outcome variable in behavioral medicine research. There is a large available literature indicating that a multitude of chronic diseases and their risk factors can exert a negative impact on cognitive function. Despite an already impressive knowledge base, there remain as many questions as answers in terms of identifying the specific neurocognitive tests that are most sensitive to particular diseases and risk factors, understanding of relevant vulnerability and resilience factors, and study of underlying neurobiological mechanisms. Furthermore, there is a relative paucity of research on the daily life impact of cognitive difficulties related to chronic diseases and their risk factors, although work to date suggests associations with medical decision making, quality of life, physical and daily function, disability, and frailty. Improvements in our understanding of these areas will only strengthen the existing relevance of neurocognitive assessment to the practice of behavioral medicine.

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