DEMENTIA, DIABETES, AND DEPRESSION: RELATIONSHIP TO COGNITIVE FUNCTIONING

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The number of adults in the United States who are age 65 or older is rapidly increasing. With longer lifespan comes an increase in chronic diseases such as dementia, diabetes, and depression. This study used archival data from a larger study conducted at the Memory Clinic at John Peter Smith County Hospital in Ft. Worth, Texas to examine several hypotheses and research questions related to the influence of type of dementia, presence of Type II diabetes, and presence of depression on neuropsychological test performance. First, this study attempted to identify specific patterns of performance on neuropsychological measures for those with Alzheimer's dementia (AD), vascular dementia (VaD), or mild cognitive impairment (MCI). The results indicated that those with MCI perform better than those with AD or VaD on all neuropsychological measures, and that those with VaD perform better than those with AD on a measure of verbal memory. Another purpose of the study was to determine how the presence of Type II diabetes affects this pattern of functioning; the overall finding in this study was that the presence or absence of diabetes did not affect performance on measures of cognitive functioning. Additionally, the study attempted to add to literature examining the influence of depression on older adults with diabetes and/or dementia; no significant differences emerged.

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INTRODUCTION

The number of adults in the United States who are age 65 or older is projected to increase from approximately 35 million (12.4%) in 2000 to approximately 71 million (19.6%) in 2030 (Chapman, Williams, Strine, Anda, & Moore, 2006). This increase in older adults is partly due to more effective public health measures that lead to improved health for older adults (Goulding & Rogers, 2003). However, in addition to improved healthcare and increased age, there has become an increase in chronic disease. In the recent past, infectious disease and acute illness were the leading cause of death; with increased lifespan, chronic disease and degenerative illnesses (such as cardiovascular disease and cancer) have become the leading cause of death (Goulding & Rogers). This increase in chronic conditions will ultimately lead to increased disability and health-care costs. According to one report (Goulding & Rogers), the health-care costs for people age 65 years and older is three to five times greater than the health-care costs for people under age 65.

Aging can create a multitude of unique issues that include a complex interaction of physical health and mental health. This study will explore three illnesses that frequently affect older adults: dementia, diabetes, and depression. Health officials state that it is important to understand and treat both physical and psychiatric illnesses in older adults (Chapman et al., 2006). According to public health reports, one of the most common physical illnesses that affect older adults is diabetes (Goulding & Rogers, 2003). One of the most common psychiatric disorders that afflict older adults is dementia (Chapman et al.), and depression in older adults increases with other illnesses (National Institute of Mental Health [NIMH], 2007). By treating and possibly

preventing these illnesses, older adults can improve their quality of life by decreasing disability and increasing functional independence.

Dementia affects approximately 6% to 10% of people 65 years or older (Chapman et al., 2006), and this prevalence rate increases with age. It is estimated that 30% of those aged 85 years or older suffer from dementia, 40% of those aged 90 to 94 years, and 58% of people over age 94 years suffer from dementia. Due to the associated memory impairment and cognitive decline, these increased rates of dementia create decreased independence and increased health-care costs.

There are many causes of dementia, including head trauma, substance abuse, and diseases such as Alzheimer's, Pick's, HIV, and vascular disease. The two most common causes of dementia are Alzheimer's disease and vascular dementia. Alzheimer's disease (AD), which is the most common cause of dementia in the United States, affects around 4.5 million Americans (National Institute on Aging [NIA], 2006). Approximately 75% of people with dementia suffer from Alzheimer's disease (Chapman et al., 2006). Impairments related to AD include poor judgment, difficulty with calculation (and therefore having difficulty managing finances), and getting lost while driving (Chapman et al.). These impairments will eventually interfere with a person's ability to live and function independently. AD is a major problem for public health because of the loss of memory, cognitive functions, and activities of daily living. The annual treatment cost for AD in the United States is $100 billion ($18,408 for mild AD/per patient, $30,096 for moderate AD/per patient, and $36,132 for severe AD/per patient) (Desai & Grossberg, 2005).

The second most common type of dementia, vascular dementia (VaD), affects approximately 15% to 20% of people suffering from dementia (Chapman et al., 2006). Vascular dementia is the result of cerebrovascular disease, such as infarctions. Impairments associated with vascular dementia include confusion, problems with recent memory, loss of bladder or bowel control, laughing or crying inappropriately, problems handling money, wandering, getting lost in familiar places, difficulty following instructions (NIH, 2003).

Mild cognitive impairment (MCI) is a term that encompasses individuals who experience memory or cognitive impairment but who do not meet criteria for dementia. MCI is an important disorder to understand because research has shown that between 23% and 47% of people with MCI eventually develop dementia (Chapman et al., 2006). It is important to monitor patients with MCI, both through clinical evaluation and neuropsychological testing (Chapman et al). In turn, researchers can better understand the progression of MCI to dementia and develop more effective treatments to prevent more pronounced cognitive decline.

AD and VaD can have similar clinical presentations (Kramer et al., 2004), and both AD and VaD can occur simultaneously within the same patient. These factors can make differential diagnosis complicated. Recent research (Golden et al., 2005; Kramer et al., 2004; Graham, Emery, & Hodges, 2004; Onyike, 2006) has provided evidence that neuropsychological testing produces different profiles for patients with AD compared to patients with VaD. This evidence suggests that patients with different types of dementia have different patterns of cognitive deficits. Therefore, it appears that

neuropsychological testing can be a useful tool in making differential diagnoses of dementia.

Sano (2006) discusses the role of neuropsychological testing in making dementia diagnoses. She says that neuropsychological testing is important in providing confirmation of cognitive deficits that may otherwise be difficult to find in the early stages of the disease. Normative data from these tests allow comparisons to specific groups; when normative data fail, comparisons of relative strengths and weaknesses can help determine possible cognitive deficits in the early stages of disease. Testing can also help to document specific neuropsychological deficits important in determining functional limitations. For example, someone with memory impairment may need supervision with medication management, while visual-spatial impairment may impact a person's ability to drive. Sano believes that neuropsychological testing can provide additional certainty to dementia diagnoses. This is due increasing research in this area which provides more normative samples from different populations. Practitioners are in turn beginning to identify patterns of deficits among different diagnostic groups. For example, patients with vascular dementia have a different pattern of performance than patients with normal performance or other types of dementia (Sano). Therefore, the first purpose of this study is to identify disparities in performance on neuropsychological measures within three prevalent subgroups of cognitive impairment: Alzheimer's disease, vascular dementia, and mild cognitive impairment.

Ecological validity is considered an important component of neuropsychological testing, but only limited research exists on this component of neuropsychological tests. Ecological validity refers to the extent to which a measure can predict everyday

functioning in real-world settings (Spooner & Pachana, 2006). The role of neuropsychological testing is changing because of the increasing demand to draw conclusions from assessments about patients' abilities to function independently. Specifically, one role of neuropsychologists in assessments of neurologically-impaired individuals is to explain changes in patients' ability to perform daily activities (Spooner & Pachana). The role of ecological validity in the assessment of older adults is important in understanding a patient's ability to function independently and can aid in treatment planning. In the current study, the Pillbox Test will be examined to add to the research on ecological validity and neuropsychological tests.

Diabetes, a chronic metabolic condition, affects one in five people over the age of 65 years (Goulding & Rogers, 2003). As of 2005, 10.3 million (20.9%) of Americans age 60 years or older had diabetes (CDC National Diabetes Fact Sheet). As of 2002, the total estimated diabetes cost in the United States (including direct medical costs and indirect costs due to disability, work loss, and premature mortality) was $132 billion (Centers for Disease Control and Prevention [CDC], 2005). Diabetes increases the risk of several other conditions. For example, people with diabetes have two to four times higher risk for stroke than adults without diabetes. Those who suffer from diabetes are also at greater risk for high blood pressure, blindness, amputation and many other diseases including heart disease, kidney disease, nervous system disease, and dental disease. Due to the increased risk of cerebrovascular disease in patients with diabetes (Clark & Asimakopoulou, 2005), researchers (Ryan, 2001b; National Institutes of Health [NIH], 2003; Biessels, van der Heide, Kamal, Bleys, & Gispen, 2002) are linking diabetes with cognitive impairment and dementia. Therefore, a second goal of this study

is to determine if the presence of Type II diabetes further diminishes the performance on these measures of cognitive functioning.

Depression, another common psychiatric disorder in older adults, has been estimated to affect 1% to 5% of community-dwelling older adults and 11.5% to 13.5% of those who require home healthcare or who are hospital patients (NIMH, 2007). Depression frequently affects older adults with chronic illness, cognitive impairment, or disability (Alexopoulos, 2005). Depression in older adults is under-diagnosed and under-treated, partly because many healthcare professionals and older adults themselves attribute depressive symptoms to symptoms of other medical conditions or to other hardships associated with aging (NIMH). However, left untreated, depression can delay recovery, worsen the outcome of many medical conditions, and promote disability (Alexopoulos; NIMH). The final two goals of the study will examine the effects of depression on this sample. One goal is to compare the severity of depression in people with and without Type II diabetes. The next goal is to determine the effect of depression on neuropsychological performance in people with and without Type II diabetes.

Increasing numbers of older adults, along with increased risk of chronic illnesses such as diabetes, dementia, and depression confirm the need for continued research in these areas. Although research is available on the independent constructs of dementia as well as on diabetes and depression, there is limited evidence of how depression and diabetes affect the neuropsychological profiles of individuals with specific subtypes of dementia. The current study examines these issues and attempts to determine similarities and discrepancies in the patterns of neuropsychological functioning in six

groups: individuals diagnosed with Alzheimer's disease, with and without Type II diabetes, those diagnosed with vascular dementia, with and without Type II diabetes, and individuals diagnosed with mild cognitive impairment, with and without Type II diabetes. Additionally, the influence of depression on performance on measures of cognitive functioning will be explored in relationship to diabetes.

Operational Definitions and Terminology

Dementia in Older Adults

As mentioned previously, dementia affects approximately 6% to 10% of people 65 years or older (Chapman et al., 2006). The prevalence of dementia will continue to increase with the rapidly expanding population of older adults. Dementia is clearly a public health concern.

Most simply, dementia is defined as the combination of memory decline and the decline of other cognitive functions (McKhann et al., 1984). The *Diagnostic and Statistical Manual of Mental Disorders, Text Revision* (*DSM-IV-TR*, 2000) states that memory impairment must be evident to make a diagnosis of dementia. The person must also exhibit one of the following cognitive disturbances: aphasia, apraxia, agnosia, or impairment in executive functioning. This decline in memory and cognitive abilities must be significant enough to cause impaired functioning in daily living (Roman, Tatemichi, Erkinjuntti, Cummings, Masdeu, & Garcia, et al., 1993). The *DSM-IV-TR* describes several causes of dementia, including dementia of the Alzheimer's type, vascular dementia, dementia due to head trauma, and dementia due to Parkinson's disease, to name a few. Although the clinical presentations of these disorders are similar, they are distinguished based on their etiologies (*DSM-IV-TR*). The current study focuses on the

two most common causes of dementia: Alzheimer's disease and vascular dementia. Additionally, the current study examines a group of individuals with mild cognitive impairment. These individuals complain of memory impairment or cognitive disturbances, but they do not meet criteria for dementia.

Alzheimer's Disease

Prevalence. Approximately 5% of Americans between the ages of 65 and 74 have been diagnosed with AD, while nearly half of Americans age 85 and older may suffer from AD. Patients with AD typically live eight to ten years after being diagnosed, but may live as many as 20 years after diagnosis (NIA, 2006). AD accounts for approximately 60% to 70% of all cases of late-onset dementia (Askin-Edgar, White, & Cummings, 2004), and it is the most common cause of dementia (Desai & Grossberg, 2005). Researchers project that by 2050, AD will affect 13.2 million Americans (Desai & Grossberg).

Neuropathology. AD is a progressive degenerative disorder (Askin-Edgar et al., 2004) that is characterized by several neuropathologic and neurotransmitter changes. The neuropathologic changes include neurofibrillary tangles, neuritic plaques, and synaptic and neuronal loss. It has been proposed that the accumulation of amyloid leads to formation of plaques and nerve cell death. Once the synaptic loss occurs, it is almost impossible to interfere with disease process and cognitive decline is imminent (Desai & Grossberg, 2005). MRI reveals atrophy of hippocampus early in the disease. The frontal lobes are affected as disease progresses while subcortical structures and primary motor and sensory structures are usually spared (Askin-Edgar et al.).

Neurotransmitters. Neurotransmitter changes occur when cell death occurs in transmitter-related nuclei. Cholinergic abnormalities are the most prominent (Desai & Grossberg, 2005). Acetylcholine is involved in memory function. Loss of acetylcholine contributes to cognitive deficits and behavioral changes (Askin-Edgar et al., 2004), and loss of this neurotransmitter is also associated with severity of AD (Desai & Grossberg).

Research has shown that cholinesterase inhibitors improve cognitive functions and are the approved treatment for AD. There is also some evidence that pathologic stimulation of glutamatergic receptors, such as N-methyl-D-aspartate (NMDA), can lead to cell death. Therefore, there has been increased use of memantine, which is an NMDA receptor antagonist. These pharmacologic therapies usually delay the onset of psychological and behavioral symptoms by one year (Desai & Grossberg).

Neuropsychiatric aspects. Neuropsychiatric aspects affect nearly every patient with AD, and they are the primary cause of caregiver burden (Askin-Edgar et al., 2004). Personality alterations are common in patients with AD. The most common personality alteration is passivity or disengagement, and this is characterized by diminished energy and initiative. Apathy, irritability, disinhibition, disturbances of sleep and appetite, and altered sexual behavior are also common (Askin-Edgar et al.).

Mood changes may include depression, which has been estimated to affect 20% to 40% of patients, and anxiety, which is found in about 40% of patients. The anxiety is usually in regards to anticipating upcoming events or being separated from caregiver. Disturbances of psychomotor activity include wandering and pacing, restlessness, assaultive behavior. Wandering typically occurs in the middle to late stages of the disease, and this behavior creates challenges for caregivers. Research suggests that

60% of patients with AD experience restlessness and 60% of patients engage in assaultive behavior (Askin-Edgar et al., 2004). Delusions affect 30% to 50% of AD patients and are usually about theft, spousal infidelity, or abandonment. Hallucinations affect 9% to 27% of patients and are generally visual and include visions of people from the patient's past (Askin-Edgar et al.). Clearly, the neuropsychiatric aspects of AD can create challenges and burdens for both the patients and the caregivers. Diagnosis of AD is important so that treatment and support can be provided to the patients and families.

Diagnostic criteria. In 1984, the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) proposed criteria for the diagnosis of AD (Romàn et al., 1993). Specific criteria were needed because at that time, 20% or more of cases that were diagnosed as AD were found at autopsy to have other diseases and not AD (McKhann et al., 1984).

The NINCDS-ADRDA proposed three levels of diagnostic certainty for AD: it is diagnosed based on criteria for probable AD, possible AD, or definite AD (Askin-Edgar et al., 2004). Possible AD is diagnosed when the course of the dementia is atypical, or when other significant diseases are present, but AD appears to be the main cause of the progressive dementia (McKhann et al., 1984). Definite AD can only be diagnosed with postmortem autopsy (Desai & Grossberg, 2005). Probable AD can be diagnosed when there is evidence of insidious onset, progressive worsening of memory and other cognitive deficits, and when there are no systemic disorders or other brain diseases that could account for the memory and cognitive deficits (e.g., Parkinson's disease, vascular

dementia, drug intoxication). Research suggests that the NINCDS-ADRDA criteria for probable dementia are generally accurate in diagnosing AD. The criteria have an average sensitivity of 81% and an average specificity of 70% when compared to neuropathological confirmation (Patterson & Clarfield, 2003).

The NINCDS-ADRDA state that in order to make a diagnosis, several methods of examination are needed: medical history, clinical examination, neuropsychological testing, and laboratory testing (e.g., computerized tomography, positron emission tomography, magnetic resonance imaging) (McKhann et al., 1984). Neuropsychological tests are not only useful in confirming the diagnosis of dementia, but they can also provide evidence for patterns of impairment, and they can be valuable in tracking changes in impairment over time.

Vascular Dementia

Prevalence. Reports on the prevalence of vascular dementia (VaD) vary due to diverse clinical presentations and challenges in making diagnoses (Onyike, 2006). However, most studies report that VaD is either the most common or the second most common cause of dementia worldwide. Onyike reported that VaD is the most common form of dementia after AD, accounting for 2.8% of Americans with dementia and 6.7% of Japanese with dementia. Other authors state that VaD is the most prevalent form of dementia worldwide because it is the most common form of dementia in countries with larger populations, such as Asian countries (Looi & Sachdev, 1999).

Neuropathology. Vascular dementia (VaD) can be defined as any dementia associated with cerebrovascular disease (O'Brien & Lilienfeld, 2002). Cerebrovascular disease may be the most common risk factor for dementia worldwide (Romàn et al.,

1993). Unlike AD, where it is known that more neurofibrillary tangles are associated with more severe cognitive impairment, there is not a simple indicator in VaD (Chui, 2005). For example, a large infarct may create severe impairment, but a relatively small infarct may also cause as much if not more damage/deficits.

VaD is a syndrome with various etiologies (Erkinjuntti, 1999). VaD includes dementias that result from ischemic and hemorrhagic brain lesions (Romàn et al., 1993). The two main syndromes of VaD are cortical VaD and subcortical VaD (Erkinjuntti, 1999). Cortical VaD typically presents with abrupt cognitive impairments and aphasia (Erkinjuntti). An example of cortical VaD is multi-infarct dementia, which refers to several large complete infarcts that result from blockage of large vessels. Subcortical dementia is characterized by pure motor hemiparesis, bulbar signs and dysarthria, and emotional lability (Erkinjuntti). Small-vessel disease with dementia is an example of subcortical dementia, and it is characterized by multiple lacunes and white matter lesions. Other causes of VaD are cerebral ischemic-hypoxic lesions (e.g., from cardiac arrest), and strategic single-infarct. Strategic single-infarct dementia involves small, localized lesions (Romàn et al.). The location of the lesion is related to the cognitive symptoms or types of impairment (Erkinjuntti).

Risk factors. Because VaD is associated with stroke, it is important to understand and reduce the risk factors for stroke. The majority of VaD cases are associated with hypertension. (Onyike, 2006).Other risk factors include age, hypertension, diabetes, smoking high cholesterol, and chronic heart disease. Although it is not possible to reverse brain damage from stroke, it is possible to prevent future strokes. Preventing

future strokes is important in preventing worsening dementia. Patients may do this through controlling blood pressure, cholesterol, and diabetes (NIH, 2003).

Diagnostic criteria and neuropsychiatric aspects. There are several theories regarding the diagnosis of VaD; however, researchers have not reached a consensus on the definition. These theories include DSM criteria, Hachinski Ischemia Score, and the NINDS-AIREN, which is the most widely used set of criteria (Onyike, 2006).

The National Institute of Neurological Disorders and Stroke (NINDS) and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) held an international workshop for vascular dementia. The purpose of the workshop was to define VaD for research purposes and develop diagnostic criteria (Romàn et al., 1993); the result of the workshop was a set of diagnostic criteria, theories of etiology, and treatment recommendations for VaD known as NINDS-AIREN criteria.

NINDS-AIREN criteria contain three levels of diagnostic certainty: probable, possible, and definite VaD (Erkinjuntti, 1999). To receive a diagnosis of probable VaD, three criteria must be met (Romàn et al., 1993). First, the patient must be demented (as defined by decline in memory and a decline in at least two cognitive abilities; these declines must create impairment in daily living). Secondly, the patient must also have either a history of cerebrovascular disease (CVD) or results that suggest CVD from clinical examination and brain imaging. CVD is defined as the presence of "focal neurologic signs consistent with stroke, with or without history of stroke" (Romàn et al., p. 254). Finally, it must be concluded that the dementia and CVD are reasonably related (i.e., with onset of dementia within three months following a stroke).

There are several clinical features that are typical of or consistent with the diagnosis of probable VaD. There is usually an abrupt decline in cognitive abilities within three months following a stroke. After the abrupt decline, patients usually experience a fluctuating pattern of impairment. Patients with VaD typically experience unsteady gait or frequent falls, urinary incontinence, depression or other mood changes, and several neurologic symptoms. Neurologic symptoms may include hemiparesis, sensory loss, weakness of facial muscles, swallowing difficulties, and emotional lability (Romàn et al., 1993).

Possible VaD refers to cases in which one of the three criteria for probable VaD is not met. Definite VaD refers to cases of probable VaD that have been confirmed by biopsy or autopsy, and lack evidence of neurofibrillary tangles, neuritic plaques, and other disorders that may cause dementia (Romàn et al., 1993).

Mild Cognitive Impairment

MCI is a term used to describe patients who experience decline in cognitive functioning that is greater than would be expected for their age, yet they don't meet criteria for dementia and they do not have a significant decline in activities of daily living (Luis, Lowenstein, Acevedo, Barker, & Duara, 2003). People with MCI could be entering the preclinical phase of dementia (Crowell, Luis, Vanderploeg, Schinka, & Mullan, 2002).

Prevalence. There is considerable variability in the prevalence of MCI due to differences in definitions/diagnostic criteria of MCI as well as differences in the methodology (i.e., tests used to diagnose MCI) (Luis et al., 2003). Studies reviewed by Luis et al. found prevalence rates that ranged from 3% to 85% dependent upon the

criteria used to define MCI. However, researchers agree that patients with mild cognitive impairment have an increased risk for developing dementia, especially AD (Lopez et al., 2003). It has been estimated that each year, 12% of MCI cases turn into AD (Desai & Grossberg, 2005; Ames et al., 2006) compared to age-matched normal subjects who develop AD at 1-2% per year (Crowell et al., 2002 and Luis et al., 2003). It is important to identify those with MCI so that clinicians can detect the early signs of AD. By detecting the early signs of AD, patients can start treatment and delay the onset of AD. Treatment can thereby increase the patients' quality of life and save billions of healthcare dollars (Crowell et al., 2002).

Diagnostic criteria. According to Ames et al. (2006), the criteria for MCI include "memory complaint preferably corroborated by an informant, memory impairment for age, largely intact general cognitive function, essentially preserved activities of daily living, and not demented." Other terms that have been used to describe this particular set of characteristics are age-associated cognitive decline, cognitive impairment not otherwise specified, and age-associated memory impairment (Ames et al.).

Risk factors. Several studies have attempted to identify risk factors of MCI. Lopez et al. (2003) looked at risk factors for MCI in a longitudinal study called the Cardiovascular Health Study. They compared people with MCI to healthy participants and found that those with MCI were significantly older than healthy controls. These researchers stated that other risk factors for MCI include being African American, lower levels of education, diabetes mellitus, heart disease, hypertension, and low mental status exam scores, and depression. To reduce the risk of MCI, it is recommended that patients engage in risk reduction strategies such as mental and physical exercise, social

activities, stress reduction, proper nutrition, treatment of cardiovascular risk factors, and incorporation of antioxidants in their diet (Desai & Grossberg, 2005).

Predicting conversion of MCI to dementia. There are several signs that may mark the progression of MCI and may also predict the conversion of MCI to dementia. Desai & Grossberg (2005) reported several factors that best predict the conversion from MCI to AD. These factors include patients' level of functioning in situations that require judgment and problem solving. Other factors that may predict conversion to dementia are level of depression and extent of hippocampal atrophy. In a review of several studies, Luis et al. (2003) found that some researchers found hippocampal atrophy to be the best indicator of progression, while others found elevated levels of tau protein in cerebrospinal fluid be the best predictors of conversion to dementia.

Crowell et al. (2002) reported that several assessment methods, such as genotyping and neuroimaging, have been used in an attempt to predict the conversion of MCI to AD. Additionally, neuropsychological testing can help identify very early cases of dementia (Arnàiz & Almkvist, 2003). Because neuropsychological testing can detect subtle changes in memory, this assessment method has been particularly useful in predicting the change from MCI to AD. The authors cited previous research that found the best indicators of this conversion were measures of memory acquisition and delayed recall. It is important to recognize the patterns of cognitive functioning in patients with MCI to better understand the relationship and conversion of MCI to dementia. It is important to note that not every case of MCI progresses to dementia; some cases improve and some cases stabilize (Luis et al., 2003 and Crowell et al., 2002).

Differentiating between Types of Cognitive Impairment

Recent research suggests that distinguishing between AD and VaD is becoming increasingly difficult (Patterson & Clarfield, 2003; Tierney et al., 2001; Looi & Sachdev, 1999). This is due to research that reveals considerable overlap in the risk factors and symptomatology between VaD and AD. Some research suggests that both conditions can occur together (O'Brien & Lilienfeld, 2002). Researchers have suggested that comorbidity between AD and VaD is an issue (Kramer et al., 2004). Vascular disease is common in patients with AD (up to 30% of AD patients have cerebrovascular pathology) and one third of patients diagnosed with vascular dementia will have AD pathology at autopsy (Kramer et al.).

Adding to the difficulty in making differential diagnosis, patients with vascular dementia may not have stepwise progression; instead their decline may be smooth, and this mimics AD (Onyike, 2006). Many researchers have attempted to define clear distinctions between AD and VaD. For example, one speculation is that VaD is a subcortical dementia, while AD is a cortical dementia; cortical dementias are associated with complete losses of cognitive functions, while subcortical dementias are associated with impairments in cognitive functions. For example, a patient with AD (cortical dementia) cannot learn/encode new information whereas a patient with VaD (a subcortical dementia) will learn the information, but may have difficulty retrieving the information (Onyike, 2006).

NINCDS-ADRDA and NINDS-AIREN, the formal criteria for AD and VaD respectively, state that autopsy is the only method to definitively confirm the presence of either type of dementia. Other methods of diagnosis include neuroimaging techniques

such as computed tomography (CT) and magnetic resonance imaging (MRI) (Howieson & Lezak, 2004). Neuroimaging has increased the accuracy of diagnosis of both AD and VaD, and neuroimaging is a criterion that is required by both the NINCDS-ADRDA and NINDS-AIREN for probable diagnoses of AD and VaD (McKhann et al., 1984; Romàn et al., 1993).

As mentioned before, neuropsychological testing can provide additional certainty to dementia diagnoses due to increasing research that attempts to identify patterns of deficits that distinguish between different diagnostic groups such as AD and VaD (Sano, 2006). Additionally, a neuropsychological evaluation can provide specific information about a patient's cognition and personality, as well as identify the nature of related behavioral and emotional problems. This information can be beneficial in treatment planning, competency evaluations, and in providing counseling and support to both patients and their families (Howieson & Lezak, 2004). The NINCDS-ADRDA state that in order to make a diagnosis of AD, several methods of examination are needed, including neuropsychological testing (McKhann et al., 1984).

Researchers and clinicians have understood the necessity of neuropsychological assessment in diagnosing and treating patients with dementia. Several researchers have attempted to determine precise patterns of performance on neuropsychological measures to aid in differential diagnosis of dementia.

In a study by Cherrier, Mendez, Dave, & Perryman (1999), the researchers compared performance of patients diagnosed with AD and VaD to normal controls. They found that patients with AD and VaD performed worse than normal controls on all scoring categories. In comparing patients with AD to patients with VaD, the results

indicated that those with AD performed significantly worse on the left category of the ROCF, which reflects left hemispatial inattention. The authors highlighted the functional pertinence of this information: inattention and visual scanning difficulties could result in poor driving abilities and increased risk for falls. The authors proposed that the lack of a unique pattern of performance in VaD patients could be due to the heterogeneity of VaD pathology.

Looi & Sachdev (1999) conducted a review of existing literature on the comparison of VaD and AD on neuropsychological test functioning. The studies were conducted within the timeframe of 1966 to 1997. One purpose of the study was to determine whether neuropsychological tests could be used to differentiate between VaD and AD. They found that in general, VaD patients performed significantly better on verbal subtests of intelligence. Most of the assessments of language function did not find any significant differences between AD and VaD participants on this language domain. There were also no significant differences in attention/immediate memory, arithmetic, constructional abilities, motor speed, or nonverbal memory. VaD patients generally performed significantly better on verbal learning and memory as well as on measures of orientation. The majority of studies indicated that AD patients demonstrated superior performance on measures of executive functioning (Looi & Sachdev). The authors stated that limitations in their review include the fact that in the studies they reviewed, different researchers used different diagnostic criteria for VaD and AD. Looi and Sachdev also mention that most of the studies did not use neuropathologic data to confirm their diagnoses.

Golden et al. (2005) also examined differences in neuropsychological test performance between patients with AD and patients with VaD to determine if this test performance could help differentiate between the two groups of dementia. Patients were diagnosed as having either AD or VaD based on results from neuroradiological tests. They found that those in the vascular group performed better than those in the AD group on Mathematics, Information, Similarities, and Picture Completion portions of WAIS-R. The VaD group also exhibited better performance on the Boston Naming Test and auditory and visual tests of immediate and delayed memory. Both groups performed equally poorly on more complex tests, such as the Rey Complex Figure Test. In a similar study, Graham, Emery, & Hodges (2004) found that AD group was more impaired than VaD group on delayed recall portions of episodic memory tests, and performance was equally impaired on recognition tests. They also found that the VaD group was more impaired on all six tests of executive functioning, while the AD group was impaired on three tests. This suggests that impaired executive functioning is associated with VaD.

Other studies (Tierney et al., 2001; Kramer et al., 2004) have limited generalizability because of their focus on one subtype of VaD, subcortical ischemic vascular dementia (SIVD). SIVD is a subtype of vascular disease that is most likely seen at dementia clinics. SIVD presents like AD with gradual onset and progression and lacking obvious focal neurologic symptoms (Kramer et al., 2004). The purpose of one study by Tierney et al. was to compare neuropsychological test performance of AD patients and SIVD patients. The authors used NINCDS-ADRDA guidelines to diagnose probable AD. They used the NINDS-AIREN criteria to diagnose probable VaD, but the

criteria were narrowed to include only those with neuroimaging evidence of a subcortical ischemic infarct. Results suggest that poor recognition memory on Rey Auditory Verbal Learning Test, better oral fluency scores on Controlled Oral Word Association Test, and higher education increased the probability of having AD (Tierney et al., 2001). Similar to the findings of Looi and Sachdev (1999) and Graham et al. (2004), Kramer et al. (2004) found that patients with AD performed better on tests of executive functioning. They also found that patients with SIVD performed better on the delayed recall portion of a list-learning test, which is consistent with results reported by Looi and Sachdev, Golden et al. (2005), and Graham et al. A summary of these results can be found in Table 1.

The studies mentioned above examined the differences in cognitive profiles between patients with AD and VaD or SIVD. The studies generally used a comprehensive battery that assessed numerous cognitive domains including verbal and visual memory, executive functioning, and visuospatial and perceptual skills. The majority of studies have found that patients with VaD tend to perform better than those with AD on measures of verbal learning and delayed recall. In general, when compared to patients with VaD, patients with AD demonstrate superior performance on measures of executive functioning. These results suggest that differences in the patterns of neuropsychological test performance may help differentiate between VaD and AD.

Limitations to these studies include the use of different diagnostic criteria, lack of neuropathologic data, and limited generalizability due to narrow inclusion criteria. None of these studies compared performance of patients with MCI to those with AD or VaD.

Diabetes Mellitus

Prevalence

Diabetes mellitus (DM) refers to group of metabolic disorders that are characterized by chronically high glucose levels (Ryan, 2001b). Type I diabetes (also known as insulin-dependent or juvenile-onset diabetes) is typically diagnosed in childhood or adolescence. Type I diabetes is due to an autoimmune destruction of the islet beta cells in the pancreas which creates an inability to secrete insulin. Therefore, patients must administer insulin exogenously (Ryan, 2001b). Type I diabetes affects approximately one million Americans. Type II diabetes (also known as non-insulin-dependent or maturity-onset diabetes) affects about 14 million Americans. It is typically diagnosed in adulthood because it usually affects overweight middle-age and elderly adults (Ryan, 2001b).

Type I diabetes accounts for 5% to 10% of all cases of diabetes, while Type II diabetes accounts for about 90-95% of all cases (CDC, 2005). Because of the greater proportion of Type II diabetics, both in general and especially in the older adult population, along with a growing literature that suggests different etiologies between Type I and Type II diabetes in older adults (CDC, 2005), this study will only address Type II diabetes.

Onset and Risk Factors

The onset of Type II diabetes is often gradual. In fact, many older adults are not aware that they have developed diabetes because of the gradual accumulation of symptoms that are more subtle than in Type I diabetes and they may attribute their symptoms to normal aging (Clark & Asimakopoulou, 2005). This lack of awareness often leads to a delay in diagnosis and treatment of the disease. Symptoms of Type II

diabetes include fatigue, thirst, frequent urination, weight loss, blurred vision, skin infections, or healing slowly from cuts and bruises (NIH, 2004).

In Type II diabetes, the pancreas continues to produce insulin, but patients develop insulin resistance (decreased sensitivity to the effects of insulin). Risk factors for insulin resistance (and subsequent development of Type II diabetes) include obesity, inactivity, and smoking. Type II diabetes can generally be controlled without daily insulin injections; instead, Type II diabetes can be controlled by modifying diet, exercising, or taking oral medications. However, poorly controlled Type II diabetes can lead to increased risk of stroke, heart attack, kidney disease (Ryan, 2001b). Compared to people without diabetes, individuals with diabetes are at a much higher risk for the development of coronary artery disease, peripheral vascular disease, and cerebrovascular disease (Clark & Asimakopoulou, 2005).

Diabetes and Cognitive Functioning in Later Life

As mentioned previously (Clark & Asimkopoulou, 2005; NIH, 2003), Type II diabetes is associated with a higher likelihood of vascular problems including increased risk of heart disease, stroke, and vascular impairments, all of which affect cognitive functioning. The majority of previous research on diabetes has focused on the negative effects of diabetes on cardiovascular health. Only recently have researchers gained an interest in the effects of diabetes on brain function (Hendrickx, McEwen, & van der Ouderaa, 2005).

Clark & Asimakopoulou (2005) reported that is difficult to come up with consistent results regarding diabetes and cognitive decline in older adults. Older adults may have other medical disorders that could affect cognitive functioning such as hypertension and

cardiovascular disease. The authors also mentioned that in their review of studies on the relationship between diabetes and cognitive functioning, no two studies have used the same test battery. Other complicating factors in determining the effects of diabetes on cognitive functioning include age, duration of diabetes, and diabetes complications. Older age, longer duration of diabetes, and more complications are associated with more severe cognitive decline (Clark & Asimakopoulou, 2005).

Other authors (Hendrickx et al., 2005; Hassing et al., 2004) also acknowledge a need for more research because of the difficulty ascertaining which processes are responsible for the association between diabetes and cognitive functioning. They explain that Type II diabetes usually develops in the context of metabolic syndrome. Metabolic syndrome includes obesity, hypertension, and hypercholesterolemia, and these factors could play a role (in addition to hyperglycemia) in the relationship between glucose regulation and cognition (Hendrickx et al., 2005). Hassing et al. (2004) report that diabetes is associated with other medical conditions such as hypertension and stroke, and these in turn are risk factors for dementia. They also report that diabetes is associated with an increased risk of vascular dementia in particular.

Several studies and reviews of previous research have revealed theories regarding the relationship between diabetes and cognitive functioning. Hassing et al. (2004) conducted a longitudinal study comparing cognitive decline across several cognitive domains among elderly patients with and without diabetes. At the end of their six year study they found that of those with diabetes, 25% had dementia diagnosis. Those without diabetes had rate of diagnosis at 12%. The authors propose that this is evidence that diabetes is a significant risk factor of dementia.

One theory regarding the relationship between diabetes and cognitive functioning is that Type II diabetes causes accelerated brain aging (Biessels et al., 2002). These changes in the brain can be seen at the structural and neuropsychological levels. At the structural level, neuroimaging techniques have revealed cerebral atrophy and increased white matter hyperintensities. Cognitive impairment, especially in areas assessing verbal memory or complex information processing, is often seen at the neuropsychological level (Biessels et al.).

In a review of literature, Ryan (2001a) found that diabetes is associated with modest cognitive impairment, and that this only applies to certain subgroups of patients with diabetes. In Ryan's review of 20 case control studies, the best predictor of cognitive dysfunction was chronic hyperglycemia (elevated glycosylated hemoglobin values or diabetes-related complications). He also found that older diabetic patients appear to have a higher risk of developing cognitive impairment. Based on results from three studies, Ryan reports that there is some evidence that suggests that patients may experience improved cognitive functioning when they improve metabolic control. In a review of larger, community-based studies, Ryan also found an association between diabetes and significantly increased risk of cognitive impairment, even when controlling for other medical, psychosocial, and demographic variables. Ryan reports that researchers still don't completely understand pathophysiological mechanism linking Type II diabetes with cognitive dysfunction. However, researchers agree that cognitive dysfunction is probably a direct consequence of chronic hyperglycemia, hypoglycemia, or hyperinsulinemia (that damages CNS) rather than as a secondary effect of comorbid cardiovascular disorders (Ryan, 2001a).

Other studies have attempted to determine specific cognitive domains that are affected by diabetes. In a meta-analysis of existing literature, Awad, Gagnon, & Messier (2004) found that in patients who were being treated for Type II diabetes, the most sensitive measures of performance decrements were measures of verbal memory, processing speed, and brief cognitive screening measures. Hendrickx et al. (2005) provide a summary of conclusions from a workshop that examined how poor glucose control may affect brain function. They explain that Type II diabetes is associated with chronic high levels of blood glucose (chronic hyperglycemia). Glycemic control is associated with cognitive tasks that are dependent on the hippocampus. Therefore, tasks, such as the ability to recall a word list, that rely on hippocampal function are often impaired in people with diabetes.

Kuo et al. (2005) examined the cross-sectional and longitudinal effects of hypertension and diabetes on cognitive and physical functions of participants. Participants included 2802 independent-living older adults between the ages of 65 and 94. Participants were excluded if they were under age 65, had known diagnosis of AD, or indication of cognitive impairment (under 23 on MMSE). The researchers found that diabetes was associated with impairments on memory, speed of processing, and global cognition. Longitudinally, they found that performance on speed of processing measures declined at an accelerated rate for those with a history of diabetes, but there were no changes in other cognitive domains.

There are several theories regarding the relationship between diabetes and cognitive functioning, and research suggests that diabetes affects certain cognitive domains more than others. Based on evidence from previous studies, it appears that

diabetes is most obviously associated with decreased performance on tasks involving verbal memory and processing speed.

Depression in Older Adults

Late-life Depression

Depression is one of the most common psychiatric disorders in the older adult population, and it is often under-diagnosed and under-treated in older adults. (Beekman et al., 1995; Williams, Clouse, Rubin, & Lustman, 2004). There are several theories regarding the development of depression in older adults. For example, the cognitive theory of depression suggests that a person (regardless of age) can have negative views of oneself, experience, and the future. The person can also develop negative underlying beliefs, or the person may develop cognitive errors (Blazer, 2002). Another etiological theory is the social theory of depression. While social factors can be protective factors for depressive disorders, loss of social roles (e.g., due to retirement and/or declining physical health) can be a risk factor for depression (Blazer, 2002).

Some researchers (Williams et al., 2004; Alexopoulos, 2005) report that depression is a risk factor for illnesses, while other researchers (Blazer, 2002) speculate that illness and declining physical health is a risk factor for depression. Depressive symptoms in older adults often occur with co-morbid medical and neurological disorders (Alexopoulos, 2005). Depression can exacerbate medical illnesses and can even be a risk factor for dementia (Alexopoulos, 2005). Effective treatments are available for depression in older adults (Alexopoulos, 2005), and it is imperative that treatment be implemented in older adult care to improve the outcome of co-morbid medical

conditions and prevent further disability. This study will explore the role of depression in both diabetes and dementia.

Depression and Dementia

Depressive symptoms are common in patients with AD and VaD, and some have estimated that 20%-40% of AD patients experience elements of a depressive syndrome, while up to 60% of VaD patients report symptoms of a depressive syndrome (Askin-Edgar et al., 2004). Several researchers have reported high prevalence rates of depression in patients with MCI, AD, and VaD. For example, Gabryelewicz et al. (2004) found that both minor and major depression are common in patients with MCI. Additionally, if the depression was not appropriately treated, the patients were likely to be diagnosed with dementia at a follow-up visit. Lopez, Becker, & Sweet (2005) found that similar to patients with AD, patients with MCI can present with major depression, disruptive behaviors, and psychosis. Bowirrat, Oscar-Berman, and Logroscino (2006) found depressive symptoms in both patients with VaD and AD.

It is important to differentiate between patients with dementia who have comorbid depression and those patients that have cognitive impairment resulting from depression (a.k.a., depressive dementia, pseudodementia, reversible dementia). Some older adults appear to have a dementia syndrome, but this syndrome disappears when depressive symptoms have been treated (Alexopoulos, 2003). Most researchers agree that it is not difficult to differentiate between depression and dementia because older depressed patients perform better overall on neuropsychological tests than older patients with dementia. Older patients with cognitive impairment due to depression typically show more impairment in the domains of attention, memory, and psychomotor speed

compared to the profiles of older patients with dementia (Mayberg, Keightley, & Mahurin, 2004). In addition, depressed patients often present with specific symptoms of depression, such as sadness (Mayberg et al.). Regardless of the direction of the relationship, it is important to recognize the co-morbidity of depression and dementia.

Diabetes and Depression

Many researchers have reported higher rates of depression in people with diabetes compared to the general population (Watari et al., 2006; Sacco et al., 2005; Mast, Yochim, MacNeill, & Lichtenberg, 2004). Some estimate that depression affects 15%-20% of patients with diabetes (Clark & Asimakopoulou, 2005).

There appears to be some debate as to whether diabetes or depression starts first. However, most agree (Williams et al., 2004; Sacco et al., 2005; Clark & Asimakopoulou, 2005) that depression appears to increase diabetes symptoms by interfering with patients' self-care ability. Williams et al. (2004) report that depression is a risk-factor for depression, and that depression is frequently diagnosed years before diabetes is diagnosed. Some researchers have found that depression is associated with worsening symptoms of diabetes (Sacco et al., 2005). One explanation is that depression may lead to a failure to adhere to strict self-care regimens (e.g., diet, exercise, and medication management), which then leads to higher blood glucose levels and exacerbated diabetes-related health problems (Sacco et al.; Williams et al., 2004). Clark & Asimakpoulou (2005) report that depressive symptoms interfere with self-care by diminishing overall quality of life, reducing physical activity levels, and impairing the ability of effectively communicate with health care professionals. Clearly, there is a need

to further explore the relationship between depression and diabetes to prevent worsening symptoms of either disease.

Summary

Estimates of a rapidly-expanding older adult population along with the staggering estimates regarding an increase in the prevalence of dementia provide clear evidence of the need for more research on dementia in the older adult population. Studies that have attempted to examine cognitive patterns of patients with AD and VaD have produced conflicting results; this supports the need for more studies to help identify unique patterns on neuropsychological measures that can potentially aid in differential diagnosis of AD and VaD. It is also important to identify and treat MCI in the hopes of preventing the development of dementia. In the past, research regarding diabetes has focused on the disease's negative impact on cardiovascular health. Researchers have recently begun to explore the effects of diabetes on cerebrovascular health. It is important to bolster this new research with more evidence of the relationship between diabetes and cognitive functioning. Previous research has begun to investigate the relationship between depression and medical conditions such as diabetes and dementia. Additional research is needed to help understand this relationship. The role of neuropsychology is expanding due to the increasing demand to draw conclusions from assessments about patients' abilities to function independently. The final objective of this study is to add to the research on ecological validity of certain neuropsychological measures.

This study will attempt to: 1) identify specific patterns of performance on measures of neuropsychological functioning between those with Alzheimer's dementia,

vascular dementia, and mild cognitive impairment, 2) determine how the presence of Type II diabetes affects this pattern of functioning, 3) add to the existing literature by examining the effect of Type II diabetes on people who have been diagnosed with AD, VaD, or MCI, 4) add to literature examining the influence of depression on older adults with diabetes and/or dementia, and 5) add to existing literature on ecological validity and neuropsychological test performance.

Hypotheses

1. Based on previous literature regarding differential diagnosis of AD and VaD (Graham et al., 2004; Kramer et al., 2004; Golden et al., 2005), it is predicted that those with VaD will demonstrate better performance on verbal tests compared to those with AD.

2. It is also hypothesized from the work of several researchers (Graham et al., 2004; Kramer et al., 2004) that compared to those with VaD, those with AD will demonstrate better performance on tests of executive functioning.

3. Based on previous literature (Awad et al., 2004; Hassing et al., 2004; Ryan, 2001a) that suggests that Type II diabetes is associated with worse cognitive functioning, and in particular with verbal memory, it is hypothesized that those with Type II diabetes will have diminished performance on the measure of verbal delayed recall compared to those without Type II diabetes.

4. From the findings of Watari et al. (2006), Sacco et al. (2005), Mast et al. (2004), and Clark & Asimakopoulou (2005), it is predicted that those with Type II diabetes will have greater depression compared to those without diabetes, controlling for the various levels of cognitive function.

Research Questions

1. The presence of a relationship between depression and individual cognitive functioning will be investigated both for linear and non-linear trends.
2. Related to Hypotheses 1 and 2, and adding MCI as a separate diagnostic category, the influence of each of the measures of cognitive functioning will be tested as to how these measures are patterned in their relationship to diagnosis of VaD versus AD versus MCI.
3. Related to Hypothesis 3, the influence of each of the measures of cognitive functioning will be tested as to how these measures are patterned in their relationship to the presence or absence of a diagnosis of Type II diabetes.
4. Related to Hypothesis 4 above, the influence of each measure of cognitive functioning will be tested as to how performance on these measures are patterned in their relationship of diabetes to depression.
5. To add to literature on ecological validity and neuropsychological measures, performance on the Pillbox Test will be compared to performance on other standardized measures of executive functioning that are proposed to be ecologically-valid.

METHOD

Participants

The source for participants was an outpatient memory clinic within John Peter Smith (JPS) hospital, a large publicly funded county hospital in Fort Worth, Texas. This memory clinic receives consecutive neuropsychological referrals, and the referrals that meet inclusion criteria will be included in the current study. Participants were referred within the JPS system. Patients were initially seen in the geriatric unit of JPS; if there was a concern about a patient's memory, they were referred to the memory clinic. The current study is part of larger study conducted by a neuropsychologist at JPS.

JPS hospital generally treats ethnic/racial minority individuals of lower socioeconomic status and lower educational achievement. However, due to the requirement for participants to speak English as their primary language, first-generation Hispanics were eliminated from the sample for the current study. Participants for this study included individuals from one of six groups: a group with Alzheimer's disease without diabetes (*n* = 43), a group with Alzheimer's disease with diabetes (*n* = 20), a group with vascular dementia without diabetes (*n* = 68), a group with vascular dementia with diabetes (*n* = 46), a group with mild cognitive impairment without diabetes (*n* = 34), and a group with mild cognitive impairment with diabetes (*n* = 20). Alzheimer's disease diagnoses were based on the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable Alzheimer's disease, vascular dementia diagnoses were based on The National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en

Neurosciences (NINDS-AIREN) criteria, and mild cognitive impairment diagnoses were based on *DSM-IV-TR* criteria. Determination of whether the patients met specific criteria for Alzheimer's disease, vascular dementia, or mild cognitive impairment were based on a consensus reached after a geriatrician examines a CT scan, laboratory tests, integrative neuropsychological report, and a history and physical performed by a geriatrician.

Diabetes diagnoses were based on patients' self-report to the question, "are you taking medication for diabetes?" These diabetes diagnoses were then confirmed by the patient's physician. All patients in this study were receiving treatment for diabetes at JPS hospital. All participants demonstrated adequate verbal ability (participants with VIQ under 55 were excluded) determined by the Peabody Picture Vocabulary Test. Only patients for whom this was a first referral were included in this study (people who were actively taking medication for dementia were excluded). Participants included in this study were at least 50 years of age and had at least a second grade education level. Specific participant demographics can be found in Tables 2 and 3.

Procedure

As part of the larger study initialized by the principal investigator, a neuropsychologist who at the time was on JPS hospital staff, participants were administered the following neuropsychological tests by trained masters- and doctoral-level examiners in compliance with published instructions: Rey Complex Figure Test Copy, 7 Minute Screen, Trail Making Test, Pillbox Test, WAIS-III Similarities subtest, portions of the Western Aphasia Battery, Check Writing test, 7 Minute Screen Recall, Rey Complex Figure Test Recall, Clock Drawing Test, Peabody Picture Vocabulary

Test, Use of Objects Test, Tinkertoy Test, Controlled Oral Word Test, Reitan-Indiana Aphasia Battery, Test of Nonverbal Intelligence – 2nd edition, Penny Pickup Test, and the Geriatric Depression Scale. It is important to note that the administration of these tests was completed over a period of time, and therefore, the protocol changed over the course of administrations. For the purpose of this study, it is important to note that the GDS was added later, which resulted in some missing data. After the evaluation was over, the examiner placed the informed consent into a file separate from the participants' test data. The protocols were photocopied and assigned a code number. No identifying information was placed on the original protocols until the code number had been assigned. The code number was cross-referenced to a separate list containing only code number and name. This list is kept in possession of the principle investigator, and only the principal investigator has access to this identifying information. The code number was then cross-referenced to a SPSS database where the participant's age, race, gender, education, and diagnosis were recorded along with raw scores for all measures. For the purpose of this study, data from the following measures were analyzed: Peabody Picture Vocabulary Test, Rey Complex Figure Test Copy, 7-Minute Screen, Pillbox Test, verbal fluency from Western Aphasia Battery, Check Writing test, 7 Minute Screen Recall, Rey Complex Figure Test Recall, Clock Drawing Test, and the Geriatric Depression Scale. This comprehensive battery was chosen to measure several cognitive domains. According to previous studies, these tests have utility in identifying neurological deficits, including dementia.

Measures

Standardized Neuropsychological Tests

Peabody Picture Vocabulary Test (PPVT-III). The PPVT-III was developed by Dunn & Dunn to assess receptive vocabulary. It is often administered to determine pre-morbid intelligence/general mental abilities (Lezak, Howieson, & Loring, 2004), but the test authors warn that it should be used only as a screening tool and not for diagnostic purposes (Strauss, Sherman, & Spreen, 2006). To administer the test, the examiner says a word and the examinee must point to the correct picture out of a set of four illustrations. Research has shown that the PPVT-III has high internal reliability (0.95), high test-retest reliability (0.91-0.94), and high interrater reliability (99.5% agreement) (Strauss, Sherman, & Spreen, 2006). For the purpose of the current study, the PPVT-III was administered to determine if participants met the required verbal ability to be included in the study. All participants with a score below 55 were excluded from this study. Cutoff scores used for the PPVT are low average (80-100), average (100-120), and high average (120+).

Rey-Osterrieth Complex Figure Test (ROCF). The ROCF was developed by Rey in 1941 and elaborated by Osterrieth in 1944 to assess visuospatial abilities and memory. This test also requires planning, organizational skills, and problem-solving strategies (Strauss, Sherman & Spreen, 2006). The patient is instructed to copy the design on a plain sheet of 8 ½ x 11-inch paper. The patient has a five-minute maximum time limit to complete the copy portion. After a 30-minute delay, the patient is then asked to draw the figure from memory. The scoring procedure involves assessing the accuracy of eighteen components of the design (Strauss, Sherman & Spreen, 2006). Each component is given a score from 0 to 2 depending on the accuracy of reproduction, resulting in a potential maximum of 36 points for both the copy and the

recall portions (Zartman, 2006). The current study used the raw copy score and the raw recall score.

Seven Minute Screen (7MS). The 7MS was developed by Solomon et al. (1998) as a mental status screening instrument that could be rapidly administered, required no clinical judgment and little training, and could differentiate between AD and normal aging.

No age, sex, or education effects have been noted to influence performance on the 7MS (Solomon et al., 1998). The test authors reported a high degree of overall test-retest reliability (r = 0.91) and interrater reliability (r = 0.93). This screen appears to have a high ability to discriminate between patients with AD and healthy controls as demonstrated by the 92.9% sensitivity for AD with a specificity of 96% for non-demented older adults (Solomon et al., 1998).

The 7MS is comprised of four tests including memory, verbal fluency, visuospatial and visuoconstruction, and orientation for time. The current study used the memory subtest of the 7MS.

The memory subtest requires the participant to identify a total of 16 items (four pages with four items on each page) after the examiner provides a semantic cue for each picture (e.g., “There is a piece of fruit on this page, what is it?”). The participant is then tested for immediate recall. After a distracter exercise the patient is asked to recall the items again and is then given the same semantic cues given in the learning portion (Zartman, 2006). The memory subtest score that was used in this study is the Total Raw Recall score (maximum = 16). The Total Raw Recall includes the combined total of uncued and cued responses.

Clock Draw Test. The Clock Draw Test (CDT) is believed to be useful as a screening instrument or as an aspect of a neuropsychological assessment in the differentiation of AD patients and healthy controls (Shulman, Gold, Cohen, & Zucchero, 1993; Cahn et al., 1996; Tuokko, Hadjistavropoulos, Miller, & Beattie, 1992). The CDT requires the use of many cognitive skills including auditory comprehension, planning, visual memory and reconstruction, visuospatial abilities, motor programming and execution, numerical knowledge, abstract thinking, concentration, and frustration tolerance (Shulman, 2000). In an analysis of multiple studies, Strauss, Sherman, and Spreen (2006) found that researchers agree that that the CDT is a measure of executive functioning. They also found several studies which stated that the CDT was related to functional impairment. In the diagnosis of dementia, Shulman found the CDT to have a sensitivity of 75% to 92% and a specificity of 65% to 96%. Individuals are asked to draw the face of a clock with the time at “10 after 11.” The requirement of “10 after 11” requires patients to inhibit the tendency to draw the hands to “10” in “10 after 11” (Shulman, 2000). There are several scoring methods available to use with the CDT (Tuokko et al., 1992). The scoring method in this study implemented a four-point scoring system for the following variables: circle quality, correct placement of numbers, correctly drawing the lengths of the minute and hour hands, and the correct placement of the clock hands to “10 after 11.” In this study, four points is considered passing; any score below four is considered failing.

Western Aphasia Battery. The WAB was designed by Kertesz & Poole (1974) to measure clinical aspects of language function. The WAB was based on the Boston Diagnostic Aphasia Examination (BDAE), which is considered to be the standard in

aphasia tests (Pirozzolo, 2004). The WAB and BDAE were designed for both diagnostic and research purposes, but the advantage of the WAB is shorter administration time (Pirozzolo; Lezak, et al., 2004). The four oral language subtests of the WAB include spontaneous speech, auditory comprehension, repetition, and naming. Other subtests are tests of reading, writing, gestural praxis, construction, and Raven's Progressive Matrices (Lezak et al.). The subtests can be administered and scored individually or summed as an overall score. For the purpose of this study, only verbal fluency was administered.

The purpose of verbal fluency tests is to assess the ability to spontaneously produce words under certain circumstances (e.g., a given category or letter of the alphabet). There are several versions of verbal fluency tests, some assessing only phonemic fluency, some assessing only semantic fluency, and some assessing both phonemic and category/semantic fluency. Test versions vary in the letters used to test phonemic fluency and the categories used in semantic fluency (e.g., animals, food names, things that get you from one place to another, etc.). The category/semantic fluency test used in the current study requires participants to spontaneously name as many animal names as possible in a one-minute time period. Total administration time is generally around five minutes. Research has shown a steady decline in number of animal names produced from about age 20 on, and that poorer performance is associated with increasing age (Strauss, Sherman, & Spreen, 2006). Education and IQ also influence fluency scores, with higher education and IQ being associated with higher fluency scores. Gender does not appear to significantly impact scores of semantic fluency (Strauss, Sherman, & Spreen). Strauss, Sherman, & Spreen report that

semantic fluency is useful in the detection of dementia, and is often significantly impaired in patients with Alzheimer's disease. Lezak et al. (2004) also report that lower fluency scores have been shown to distinguish patients with AD from patients with left hemisphere stroke. Total number of generated words will be the score used in the current study. The following cutoff scores were used: mild impairment (10-14 generated words), moderate impairment (5-9 words), and severe impairment (0-4 words).

Geriatric Depression Scale (GDS). The GDS was created by Yesavage et al. (1983) as a screen for depression in the older adult population, and it assesses both affective and behavioral symptoms of depression. The GDS is composed of 30 items with a yes/no response format. Total scores can range from 0 (no depression) to 30 (severe depression). Yesavage et al. suggested the following cutoff scores for the 30-item GDS: scores between zero and nine are considered to be in the normal range, scores between 10 and 19 are considered to be in the mild range, and scores between 20 and 30 are considered to be in the severe range (Strauss, Sherman, & Spreen, 2006). Yesavage et al. (1983) suggested that the cutoff score of 11 resulted in an 84% sensitivity rate and a 95% specificity rate. Total score will be used in the current study.

Age and gender do not appear to affect GDS scores. However, lower education is linked to higher depression scores (Strauss, Sherman, & Spreen, 2006). It has also been noted that GDS scores may underestimate depression in African American individuals because this group is less likely to endorse depression symptoms than older Caucasians (Strauss, Sherman, & Spreen). The GDS has a high degree of internal consistency of items (α = 0.94) and test-retest reliability (r = 0.85) (Yesavage et al., 1983).

Performance-Based Measures/Ecological Validity

Functional assessment is important in the diagnosis of dementia (i.e., NINCDS-ADRDA and DSM-IV criteria require the presence of functional impairment in the diagnosis of dementia), monitoring the progression of dementia, and in determining the effectiveness of treatment (Zanetti et al., 1998; Arguelles, Loewenstein, Eisdorfer, & Arguelles, 2001). The most common measures of functional ability are in activities of daily living (ADL) and instrumental activities of daily living (IADL) scales. Three methods of measuring functional ability are reported in past research: self-report rating scales, care-giver report rating scales, and performance-based measures. Past researchers have found that use of self-report measures in the geriatric population can be problematic due to low agreement between self-reports and other measures. Similarly, caregiver reports tend to result in low agreement with other measures because caregivers may underestimate or overestimate the patient's abilities (Tomaszewski, 2000).

A solution to the problematic self- and proxy-reports is performance-based measures. These measures require researchers or clinicians to directly observe patients in standardized situations that closely resemble situations in everyday life (Tomaszewski, 2000). The Pillbox Test and Check-writing test are two examples of performance-based measures.

Pillbox Test. The Pillbox Test was created by Houtz in 2003 as a performance-based measure of executive function. Executive function refers to higher cognitive skills such as planning, organization, volition, and attention, and researchers have suggested that declines in executive function may be an initial indicator of cognitive decline

(Zartman, 2006). Medication management is considered to be an instrumental activity of daily living (IADL), along with other tasks such as managing a checkbook. IADLs are important because in addition to activities of daily living (ADLs; e.g., bathing, eating, and toileting), they are necessary for independent living. IADLs and executive functioning appear to be associated because researchers have found that deficits in executive functioning impair a person's ability to complete IADLs (Zartman, 2006). Therefore, by creating a scenario that mimics medication management, this test measures several aspects of executive function, as well as providing a way to measure a person's ability to function independently. The pilot study (Brose & Houtz, 2003) proposes that the Pillbox Test may be an ecologically-valid measure of medication planning and management. One goal of this study is to add to the data on the ecological validity of the Pillbox Test.

In the administration of this test, participants are given a pillbox that contains four rows (morning, noon, evening, bedtime) and seven columns (each column representing one day of the week, Sunday through Saturday). The Pillbox compartments are labeled for time of day and are opened and closed by a snap closure. Participants are provided with five medication bottles. Based on information gathered about commonly-used medications in the pilot study (Brose & Houtz, 2003), it was decided that each bottle would contain colored beads which are the approximate size and contour of common aspirin, anti-hypertensive, and arthritis medications.

Each bottle contains a pharmacy label with standardized administration directions. The directions on the labels read: one tablet daily at bedtime (orange pills), one tablet daily in the morning (blue pills), one tablet three times a day (yellow pills),

one tablet twice a day with breakfast and dinner (green pills), one tablet every other day (red pills). The participant is first asked to read each medication bottle out-loud to verify the literacy level of the person. The only direction that is provided to the participant is to organize the medication in the pillbox as they normally would for one week. The examiner does not provide any additional feedback or intervention for the rest of the test, and the participant is allowed five minutes to complete this test. Throughout the test, the examiner notes the order in which the participant places the pills into the pillbox (Zartman, 2006). The following scores were used in the data analysis: Pillbox Pass or Fail, Number of total pills used, and Total number of errors. The total number of errors is the sum of Omission Errors (i.e., the number of pills omitted from the Pillbox) and the sum of Commission errors (i.e., the number of extra pills added to the Pillbox).

Check-Writing Test. The check-writing test is part of the performance-based assessment procedure called the Direct Assessment of Functional Status (DAFS; Loewenstein et al., 1989). The purpose of the DAFS is to assess memory-impaired patients' performance on a variety of activities of daily living, which are integral in living safely and independently (Arguelles et al., 2001). The original version of the DAFS assessed seven domains: Time Orientation, Communication Abilities, Transportation, Financial Skills (check-writing), Shopping Skills, Eating Skills, and Dressing/Grooming (Tomaszewski, 2000). Research has shown that the DAFS is a valid tool for the assessment of dementia (Tomaszewski; Zanetti et al., 1998). The current study assessed performance on the check-writing domain of the DAFS. In this task, participants are asked to write a check for a specific party (a fictional store). Participants are given a pass/fail score for each component of the check: total score, date, store

name, amount in numbers, and written amount. The current study used the pass/fail score from the total score.

RESULTS

Descriptive Statistics

First, descriptives and/or frequencies were calculated for all demographic and medical diagnosis variables. For all categorical variables (gender, ethnicity, presence of diabetes, and type of dementia diagnosis), frequencies and percentages were calculated. For all continuous variables (age and years of education) means, standard deviations, skewness, and kurtosis were calculated. These results can be found in Table 2.

Chi-square analyses were performed to determine any association between presence of diabetes and type of cognitive impairment. The first chi-square analysis was performed for all three types of cognitive impairment, and the results were non-significant. A second chi-square analysis was performed comparing only two of the three cognitive impairment diagnoses: AD and VaD. Again, results were non-significant for type of dementia and presence or absence of diabetes. These analyses suggest that there is no association between dementia and diabetes. Complete results can be found in Tables 2 and 3.

Additional chi-square analyses were performed to determine any associations between diabetes, type of dementia diagnosis (again using both a three dementia group and a two dementia group analysis), and two demographic variables. No significant associations were found for the presence of diabetes or type of dementia diagnosis for gender. These results can be found in Table 2. The relation between race/ethnicity and diabetes was significant, $\chi^2 (3, N = 231) = 23.92, p < .001$. In this sample, fewer than

expected Caucasians were diabetic. Specific results for this chi-square can be found in Table 4.

Next, descriptives and frequencies were calculated for all measures of cognitive functioning. Again, sample sizes and percentages were obtained for categorical variables (pass/fail on both the Pillbox Test and the check-writing test), while means, standard deviations, skewness, and kurtosis were calculated for the continuous measures of cognitive functioning (word fluency; copy and recall portions of the ROCF; clock-drawing score; PPVT IQ score; total memory from 7MS; total pills and total errors on the Pillbox Test; total for Geriatric Depression Scale). These statistics were computed for each variable and are presented in Table 5. These results were utilized in exploring descriptive data pertaining to the sample.

In a final analysis, the presence of a relationship between type of dementia diagnosis (i.e., AD, VaD, MCI) and several demographic factors was explored. The purpose of these analyses was to understand the current sample. First, the relationship of age to type of dementia diagnosis was explored with an Oneway ANOVA comparing age between the three diagnostic groups using a Tukey HSD range test. A significant difference between diagnostic groups was found, F (2, 228) = 17.21, $p < .001$, with those in the MCI being significantly younger than those in the AD and VaD groups. Specific results can be found in Table 6. Secondly, the relationship of race/ethnicity to type of dementia diagnosis was explored using a chi-squared analysis. No significant difference was found. Finally, the relationship of years of education to type of dementia diagnosis was explored in the same way as age using an One-way ANOVA with a

Tukey HSD range test. No significant differences were found. These results can also be found in Table 6.

Inferential Statistics

A series of independent sample *t*-tests were run to test the first three hypotheses. The first *t*-test was to determine if those with VaD demonstrated better performance on verbal tests (i.e., word fluency and PPVT) than those with AD. Results (Table 7) indicated no significant difference between these cognitive impairment groups for verbal IQ, t (144) = 0.44, p = 0.66, or for word fluency, t (175) = -1.85, p = 0.07. Those with VaD (n = 114) had an average score of 11.61 (SD = 4.50) on word fluency, while participants with AD (n = 63) had an average score of 10.30 (SD = 4.54).

The second hypothesis stated that those with AD would perform better than those with VaD on measures of executive functioning as measured by the Pillbox Test and Clock-drawing test. For the continuous variables, Pillbox Test total errors and total pills and the clock-drawing test), *t*-tests were used. As the details in Table 8 show, these results indicated no significant group differences for type of cognitive impairment and performance on these measures of executive functioning. A chi-square analysis was used to determine group differences for the categorical variable, Pillbox Test pass/fail. The percentage of participants that passed the Pillbox Test did not differ by type of dementia diagnosis, χ^2 (1, N = 177) = 3.34, p = 0.07.

The final independent *t*-test was performed to test the prediction (hypothesis 3) that those with Type II diabetes would have lower scores on tests of verbal memory than those without Type II diabetes. None of the group differences reached significance.

The fourth hypothesis stated that those with Type II diabetes would have greater total depression compared to those without diabetes, controlling for various measures of levels of cognitive functioning. An analysis of covariance (ANCOVA) was planned to test this hypothesis. Measures of cognitive functioning were entered as covariates because based on previous research regarding diabetes and cognitive functioning (Biessels et al., 2002; Hassing et al., 2004), cognitive functioning may be different for people with diabetes as compared to those without. Entering measures of cognitive functioning as covariates ensured that cognitive functioning would not obscure the results. One assumption of ANCOVA is that the covariates (measures of cognitive functioning) have a linear relationship with the dependent variable (depression). Another assumption of ANCOVA is that the covariates should not correlate highly with other covariates. Therefore, a correlation matrix was first run to determine if there was collinearity among the measures of cognitive functioning or if the measures of cognitive functioning correlated with depression. Correlations for the measures of cognitive functioning revealed that none of these variables were inter-correlated (see Table 11). This correlation matrix also determined that the GDS is not correlated with the measures of cognitive functioning.

The originally-planned ANCOVA was then used to test the prediction that those with Type II diabetes would have greater total depression compared to those without diabetes, controlling for various levels of cognitive functioning. This ANCOVA was a 1 (depression score) X 2 (diabetes: present/absent) with 8 covariates (continuous test scores of cognitive functioning). It should be noted that in actuality this has the characteristics of a *t*-test but was run as an ANCOVA to include covariates. Results

indicated that there was not a significant effect of diabetes on depression after controlling for the effects of cognitive functioning, F (1, 110) = 0.30, p = 0.59. Please refer to Table 12.

Exploratory/Post-hoc Analyses for Hypothesis 4

Given that the planned analyses as directed by the hypotheses did not show hoped-for results, a series of exploratory/post-hoc analyses were conducted to engage in data exploration.

First, the test of Hypothesis 4 was done more directly, where a *t*-test was run to check for group differences (in GDS scores between those with and without Type II diabetes) without the use of covariates. A significant difference in depression scores for factor one of the GDS (dysphoria) was found t (112.87) = 1.99, $p < .05$. Those with diabetes (n = 60, M = 4.25, SD = 3.61) reported more symptoms of depression on this factor than those without diabetes (n = 72, M = 3.10, SD = 2.91). Table 13 shows these differences.

Additional exploratory *t*-tests were also computed to determine differences in the measures of cognitive functioning for those with and without Type II diabetes. There were significant differences for the PPVT, ROCF copy portion, and total number of pills used on the Pillbox Test. Specifically, those with Type II diabetes scored lower on the PPVT and ROCF copy portion, and they used fewer pills on the Pillbox Test. Specific results can also be found in Table 13. These *t*-test results prompted an additional ANCOVA controlling for only these three measures of cognitive functioning, but no significant differences were found.

Finally, because of the significant difference in depression scores for factor 1 of the GDS, separate ANCOVAs were run to examine each factor of the GDS, controlling for the PPVT, ROCF copy, and total number of pills for the Pillbox Test. The ANCOVAs remained non-significant. In summary, no significant results were found in these exploratory analyses. It appears that in general the presence of diabetes does not influence depression scores, even when controlling for level of cognitive function.

Research Questions

The goal of the first research question was to investigate the presence of a relationship between depression and individual cognitive functioning both for linear and non-linear trends. It was predicted that a curvilinear relationship would exist. Specifically, as cognitive impairment initially increased, depression would increase. However, as the level of cognitive impairment continued to increase (thus causing a decrease in level of insight), it was predicted that depression would decrease. The first step in answering this research question was to examine correlations between the 10 measures of cognitive functioning and the factors of the GDS. The four correlations that were found to be significant had small magnitude and were not theoretically meaningful. See Table 14. Next, scatterplots were computed and examined to look for the predicted curvilinear relationship. No meaningful relationships between cognitive impairment and depression were found.

The goal of the second research question was to determine the patterns of each of the measures of cognitive functioning in their relationship to diagnosis of VaD versus AD versus MCI. A MANOVA was used with three diagnostic groups (AD, VaD, and MCI) and the eight continuous components of cognitive functioning as the dependent

variables. The Wilks-Lambda multivariate test for overall differences among groups was statistically significant, F (16, 362) = 12.50, $p < .001$. Univariate between-subjects tests showed significant results for seven out of the eight continuous measures of cognitive functioning, with the exception of Total Pills used on Pillbox Test. One-way analyses of variance (ANOVA) were then performed to determine the specific group differences for each of the seven significant continuous measures of cognitive functioning. A significant relationship was found for dementia diagnosis and scores on Peabody Picture Vocabulary Test, F (2,190) = 4.58, $p = .01$. Post-hoc Tukey HSD range test indicated group differences existed, as the mild cognitive impairment group scored significantly higher than the group with vascular dementia. Specific group differences can be found in Table 15. Significant relationships were also found for dementia diagnosis and scores on the: ROCF Copy Portion, F (2, 225) = 9.04, $p < .01$; ROCF Recall Portion, F (2, 227) = 34.03, $p < .01$; Clock-drawing test, F (2,228) = 7.95, $p < .01$, with group MCI scoring significantly higher than groups AD and VaD; Total Memory on 7MS, F (2, 228) = 99.66, $p < .01$; word fluency from WAB, F (2, 228) = 15.86, $p < .01$; total error on Pillbox Test, F (2, 228) = 12.43, $p < .01$. For each of these tests, those in the MCI group scored significantly better than those in the AD and VaD groups. Additionally, for ROCF Recall Portion and Total Memory from the 7MS, those in the VaD group scored significantly better than those in the AD group. Complete results can also be found in Table 15.

For the two categorical variables of cognitive functioning, two 3 X 2 chi square tests were used ((AD, VaD, and MCI) X (pass/fail on Pillbox) and (AD, VaD, and MCI) X (pass/fail on check-writing test)). As seen in Table 16, chi-square analyses indicated

significant diagnostic group differences for pass/fail on the Pillbox Test, but not for pass/fail on the Check-writing test.

The purpose of research question 3 was to investigate how each of the measures of cognitive functioning are patterned in their relationship to the presence or absence of a diagnosis of Type II diabetes. This was also tested as a MANOVA with 2 diagnostic groups (Diabetes, yes/no) and 8 components of cognitive functioning as the dependent variables. The Wilks-Lambda multivariate test for overall differences among groups was statistically significant, F (8, 182) = 2.52, $p < .01$. Univariate between-subjects tests revealed that only one test of cognitive functioning (PPVT) was significantly related to the presence/absence of diabetes, F (1,189) = 10.60, $p < .001$. An ANOVA was run to determine specific group differences for the PPVT. A significant group difference for diabetes and PPVT was found, F (1, 191) = 10.63, $p = .001$, with those without diabetes scoring higher than those with diabetes.

Again, to test the categorical variables, two chi square analyses were conducted. This time, two 2 (diabetes yes/no) x 2 (pass/fail on check-writing test and pass/fail on Pillbox Test) chi squares were used. No significant differences for either chi-square were found.

The purpose of the fourth research question was to determine differences in depression scores for those with diabetes on the categorical tests (Pillbox Test and check-writing test). Two separate 2 (diabetes, yes/no) x 2 (pass/fail on Pillbox Test and pass/fail on check-writing test) ANOVAs were used for the categorical Pillbox Test and check-writing test, with depression as the dependent variable. Neither ANOVA was significant as noted by interactions for diabetes and check-writing, F (1, 128) = 0.003, p

= 0.96, and for diabetes and Pillbox Test, F (1, 128) = 0.05, p = 0.83. Complete results can be found in Table 17.

The purpose of the final research question was to address issues of ecological validity and neuropsychological measures. In the current study, the Pillbox Test was proposed to be ecologically-valid. To explore whether this test can be considered ecologically-valid, tests of veridicality were used. Veridicality refers to the extent to which results on a traditional assessment are related to scores on other measures (Spooner & Pachana, 2006). This was determined using correlations. Specifically, correlations were run between the three Pillbox measures (Total Pills, Total Errors, and Pass/Fail) and two neuropsychological measures that are thought to be ecologically-valid, the Clock-drawing test and the check-writing test. The correlations were first run for all participants and then again for each diagnostic category (AD, VaD, and MCI). For all participants as well as for the three separate diagnostic groups, greater number of total errors on the Pillbox Test was associated with failing on the check-writing test (2 = fail, 1 = pass) and a lower score on the clock-drawing test (higher score is better performance). Additionally, passing on the Pillbox Test (2 = fail, 1 = pass) was associated with a higher score on the clock-drawing test. For all participants and those with a diagnosis of VaD, the more pills used on the Pillbox Test was associated with higher score on the clock-drawing test, (r = 0.31, p < .001; r = 0.35, p < .001) and passing on the check-writing test (r = -0.17, p < .01; r = -0.27, p < .01). Correlations did not reach significance for those with MCI or AD. For all participants as well as for those with AD and VaD, passing on the Pillbox Test was associated with passing on the

check-writing test (r = 0.43, p < .001; r = 0.26, p < .01). Correlations did not reach significance for those with MCI. See Tables 18-20 for complete results.

As a final step, the relationship between Total Errors on the Pillbox Test and all other neuropsychological measures was investigated. Total Errors was chosen as the Pillbox Test scale to investigate because it provides a more detailed account of performance than Pass/Fail. All correlations were significant, and the check-writing test was among the lowest correlations. Among reviewing these seven measures with Pillbox Total Errors, the correlations of ecological validity are as follows: Clock Draw Test (r = -0.51, p < .001), ROCF Copy (r = -0.50, p < .001), ROCF Recall (r = -0.46, p < .001), Fluency (r = -0.36, p < .001), Total Memory from 7MS (r = -0.35, p < .001), Check-writing test (r = -0.35, p < .001), and PPVT (r = -0.34, p < .001). Z-tests for differences in correlations were run to investigate the significance of the differences between the largest correlation (Clock Draw Test and Total Errors on Pillbox Test) and the correlations of the other neuropsychological measures with Total Errors on Pillbox Test. The correlation between the Clock Draw Test and Total Errors on Pillbox Test was significantly larger than those between Total Errors and the PPVT, check-writing test, Total Memory from 7MS, and Fluency. See Table 21 for complete results.

DISCUSSION

Purpose of Study

There were four objectives to this study. The first was to identify specific patterns of performance on measures of neuropsychological functioning between those with Alzheimer's dementia (AD), vascular dementia (VaD), and mild cognitive impairment (MCI). Based on a review of previous literature, it was predicted that those with VaD would demonstrate better performance on verbal tests than those with AD, while those with AD would demonstrate better performance on tests of executive functioning than those with VaD. MCI was then added as a separate diagnostic category, and performance on each measure of cognitive functioning was tested and compared to the performance from participants in the AD and VaD diagnostic categories.

The second objective was to determine how the presence of Type II diabetes affects this pattern of performance on neuropsychological measures. It was predicted that those with Type II diabetes would have diminished performance on a measured of verbal delayed recall compared to those without Type II diabetes. Performance on all measures of cognitive functioning was then compared for those with and without Type II diabetes to determine if the presence of diabetes has an impact on cognitive functioning.

The third objective was to examine the influence of depression on older adults with diabetes and/or dementia. It was predicted that those with Type II diabetes would have greater depression compared to those without diabetes. Then, the presence of a relationship between depression and individual cognitive functioning was investigated. Finally, the influence of each measure of cognitive functioning was tested to determine

how performance on each of these measures was patterned in their relationship of diabetes to depression.

The final objective was to add to existing literature on ecological validity and neuropsychological test performance. Specifically, performance on the Pillbox Test was compared to performance on standardized neuropsychological measures that are traditionally thought of as ecologically-valid.

Demographics

Chi-square tests were performed to determine if any significant categorical differences existed between groups. No significant associations were found for type of dementia diagnosis and diabetes. Research from previous studies (Clark & Asimakopoulou, 2005; Ryan, 2001b) found that compared to people without diabetes, those with diabetes are at a much higher risk for the development of cerebrovascular disease, which is in turn related to vascular dementia. However, other research has shown conflicting reports on the relationship between dementia and diabetes. Hendrickx et al. (2005) and Hassing et al. (2004) reported that it is difficult to determine exactly which processes are responsible for the association between diabetes and cognitive functioning. It may be the case that to make a more accurate judgment of this relationship between diabetes and dementia, a population probability sample must be used rather than a convenience sample.

The relationship between diabetes and two demographic factors was explored. No significant relationship was found for diabetes and gender. However, the relationship between race/ethnicity and diabetes was significant, with a greater percentage of African American and Hispanic participants reporting presence of diabetes than

expected. This is consistent with research that states that African Americans and Hispanic/Latino Americans are at particularly high risk for Type II diabetes (CDC, 2005).

Next, the relationship between dementia diagnosis and several demographic factors was explored. Using chi-square analysis, no significant relationships were found between race/ethnicity or gender and dementia diagnosis. Oneway ANOVAs were used to determine the relationship of age and years of education to type of dementia diagnosis. No significant differences were found for years of education and type of dementia diagnosis. However, a significant difference was found between types of dementia diagnosis for age, with those with MCI being significantly younger than those in the AD and VaD groups. This would be expected, given that literature states that MCI is often a precursor for later dementia (Desai & Grossberg, 2005; Ames et al., 2006), and that prevalence of dementia such as AD increases dramatically with age (Askin-Edgar et al., 2004; NIA, 2006).

Hypothesis Testing

For the first hypothesis, it was expected that those with VaD would perform better on word fluency and PPVT than those with AD. In fact, no significant difference was found between groups on PPVT. This could be due to the fact that PPVT is a measure of receptive vocabulary, and other studies used tests that relied more on expressive language (e.g., Boston Naming Test). No significant difference was found on word fluency, but there was a trend toward significance with VaD performing better on this measure. Although not reaching significance, this trend that appears on word fluency does support the literature stating that those with VaD perform better on verbal tests than those with AD. For example, this finding is consistent with results from Looi &

Sachdev (1999) that states that those with VaD typically perform better on verbal subtests.

This particular finding may not have reached significance due to the characteristics of this sample. All participants in the sample have some sort of cognitive impairment, but because this is data from their first visit to a memory clinic, they are not institutionalized. Therefore, we would not yet expect word fluency scores to have decremented too much.

For the second hypothesis, it was predicted that those with AD would perform better on executive functioning measures than those with VaD. However, there were no significant differences on Pillbox Test or clock-draw test. Previous studies found that the CDT was useful in the differentiation of AD patients and healthy controls (Cahn et al., 1996; Shulman, Gold, Cohen, & Zucchero, 1993; Tuokko, Hadjistavropoulos, Miller, & Beattie, 1992). However, in these previous studies, the CDT was used to compare those with AD to healthy controls, and therefore the CDT may not be a good discriminator between AD and those with VaD or another type of dementia. Limited research has been completed on the Pillbox Test, and one goal of this study was to add to literature on the Pillbox Test. The previous research that does exist (Zartman, 2006) found that performance on the Pillbox Test did show group disparities between those with dementia and community controls. Again, these differences could be due to the comparison of demented participants with healthy controls instead of with participants with other types of dementia.

For the third prediction, it was expected that those with diabetes would have poorer performance on verbal memory than those without diabetes. In fact, there was a

possible trend in the opposite direction (but no significant group differences). There are several possible factors that may have contributed to this result. In this sample, there was not information available regarding patients' medication management or how long they have had diabetes. Also, only one measure (total score from 7MS) was used to test verbal memory. It would be interesting to see patterns of performance across various measures of verbal memory.

Finally, for the fourth hypothesis, it was predicted that those with diabetes would have greater depression compared to those without diabetes, controlling for measures of cognitive functioning. An ANCOVA was used, and it was found that there was not a significant effect of diabetes on depression after controlling for measures of cognitive functioning. Additional exploratory *t*-test analyses revealed that only one factor (dysphoria) of the GDS was significantly higher for those with diabetes. It was expected that there would be more differences in total depression score or other factors because previous research reports higher rates of depression in people with diabetes compared to the general population (Mast, Yochim, MacNeill, & Lichtenberg, 2004; Sacco et al., 2005; Watari et al., 2006; Williams, Clouse, Rubin, & Lustman, 2004). However, it is surprising that the significant difference was found on dysphoria factor. Some research has found that older depressed patients report more somatic and cognitive symptoms of depression compared to affective symptoms (Alexopoulos et al., 2002). There is little research on the specific symptoms of depression in those with diabetes in particular. These results may not be representative of the sample. The GDS was added to the protocol later in the study, so only 132 out of the possible 231 participants completed the GDS.

Additional exploratory *t*-tests were used to determine differences in the measures of cognitive functioning for those with and without diabetes. Differences were found for the PPVT, ROCF copy portion, and total number of pills on the Pillbox Test. These results are inconsistent with previous research which has primarily found diminished performance on verbal memory and speed of processing in patients with diabetes (Awad, Gagnon, & Messier, 2004; Biessels et al., 2002; Kuo et al., 2005). These additional analyses were done for exploratory reasons, so it is possible that the significant results (i.e., differences in factor one of GDS and performance on PPVT, ROCF copy, total number of pills) may have been a function of capitalization on chance.

Research Questions

Additional research questions were examined to explore characteristics of the current sample as well as to investigate the influence of type of dementia, presence of Type II diabetes, and presence of depression on neuropsychological test performance. The goal of the first research question was to investigate the presence of a relationship between depression and cognitive functioning. Correlations were first run with all measures of cognitive functioning and only the GDS total. No significant correlations were found. Because of this, correlations were run for measures of cognitive functioning with each of the four factors of the GDS, even though because multiple tests were used these results were highly likely due to capitalization on chance. The correlations that were significant (GDS, factor 1 with PPVT; GDS, factor 3 with Total Pills and Total Errors; GDS, factor 4 with Total Errors) had a range of variance between .03 and .05. This accounted for between three and five percent of the variance.

For the second research question, a MANOVA was used to determine any relationship between performance on neuropsychological tests and type of dementia diagnosis. The only test that was not significant was total number pills from Pillbox Test. This may be because Total Errors are a more accurate representation of performance (includes both omission and commission errors); total pills is simply the number of pills the person used to complete the test. A more meaningful index may be the absolute value of the difference between number of pills used and the number of correct pills (53 pills). All other neuropsychological tests resulted in significant differences among groups. Those with MCI performed better on the remaining tests than those with AD and VaD. This would be expected, given that MCI is a precursor for other dementias, but those with MCI do not yet meet full criteria for dementia. It is important to recognize that those with MCI scored better on seven out of the eight tests. These tests likely map on, to some degree, the differential criteria for MCI, which states that these patients report memory impairment for age, but have largely intact general cognitive function, and are not demented (Ames, 2006). These criteria are different from the criteria for AD and VaD that measure greater cognitive impairment.

Several other group differences existed. Those with VaD performed better than those with AD on ROCF Recall. This is inconsistent with previous literature which found that those both groups performed equally poorly on ROCF and other tests requiring constructional ability (Looi & Sachdev). Those with VaD also performed better than those with AD on Total Memory from the 7MS. This is very much in line with previous research that has found that those with VaD typically perform better than those with AD on tests of verbal learning/memory (Golden et al.; Kramer et al.; Looi & Sachdev;

Tierney et al.). For the categorical variables of cognitive functioning, there was a significant group difference for pass/fail on the Pillbox Test, but not for pass/fail on the Check-writing test. On the Pillbox Test, a significantly greater proportion of those with VaD failed the test compared to those with AD or MCI. This is in line with previous research stating that those with AD typically perform better on measures of executive functioning than those with VaD (Graham, Emery, & Hodges; Kramer et al.; Looi & Sachdev).

The purpose of the third research question was to investigate if there were differences in performance on measures of cognitive functioning for those with diabetes compared to those without diabetes. A MANOVA was used to look for differences in performance; only one test (PPVT) was significant. This is similar to the previous *t*-test finding that also found significant differences on the PPVT. Those without diabetes scored higher than those with diabetes. This is consistent with results from Kuo et al. (2005) which found that those with diabetes have decrements in global cognition.

The goal of the fourth research question was to explore differences in depression scores for those with and without diabetes on categorical tests (i.e., Pillbox Test and check-writing tests). However, no significant results were found. This provides further evidence to confirm that in this sample, depression, diabetes, and cognitive functioning are not related.

The fifth research question explored the ecological validity of Pillbox Test. This was initially explored by comparing each available score on the Pillbox Test (total number of pills, total number of errors, and pass/fail) to other measures that likely have high ecological validity (check-writing test and clock-draw test). Although the check-

writing test may be considered a more ecologically-valid test, the CDT appears to be a test that has real-world functionality. The results indicated that for all participants, passing on the Pillbox Test is associated with higher score on CDT and passing on check-writing test, more total pills on Pillbox Test is associated with passing on check-writing and with higher score on CDT, and more errors on the Pillbox Test is associated with lower score on CDT. No significant association between Total Errors and pass/fail on check-writing was found. Lack of significance may be because of the pass/fail nature of the check-writing test. Pass/fail measures tend to be more gross measures, whereas measures such as the CDT provide more detailed scores.

Finally, the relationship between Total Errors on the Pillbox Test and all other neuropsychological measures was investigated. It was predicted that the check-writing test and CDT would be among the highest correlations with Total Errors. As predicted, the CDT was the highest correlation, suggesting that Pillbox Total Errors may be an ecologically-valid measure. However, the check-writing test was among the lowest correlations, which again could be due to the pass/fail nature of this measure.

Overall Summary

Important results were found concerning the main objectives of the study. First of all, specific patterns of performance between dementia diagnosis groups were identified for two measures: ROCF Recall portion and 7MS Total Memory. For both of these measures, those with MCI performed better than those with VaD, and those with VaD performed better than those with AD. For all other measures of cognitive functioning, those with MCI performed better than those with VaD or AD, but specific patterns were not identified beyond that.

The second objective concerned determining how the presence of Type II diabetes affects performance on neuropsychological measures. It appears that in general in this sample, the presence of diabetes does not affect performance on neuropsychological measures.

The third objective was to examine the relationship of depression and several variables. There was no significant difference in depression for those with diabetes compared to those without diabetes. Also, it appears that there is no consistent relationship between depression and the individual measures of cognitive functioning.

The final objective was to explore ecological validity of the Pillbox Test by comparing Pillbox Test performance to performance on standardized neuropsychological measures. The Pillbox Test scores are moderately related to scores from other executive function measures, suggesting that the Pillbox Test is a valid performance-based measure.

General Limitations of Study and Future Directions

In general, this was a highly-selective sample from a memory clinic. Associations found or not found can only be interpreted within the context of this sample. Like most studies using a sample of older adults with dementia, this sample was derived from the clinic setting. More specifically, the sample was from a clinic in a county hospital. Therefore, this may result in a selection bias: the participants in this study might more accurately represent a lower SES population.

There are several limitations to the general methodology of this study. First of all, the geriatric population has multiple issues, and it is difficult to narrow research questions due to the many diseases (both physical and mental) that afflict this

population. Therefore, several complex issues were explored in this study, and it was difficult to detect meaningful relationships. Secondly, it is difficult to tease apart co-morbid issues in an archival dataset because of an inability to manipulate the variables.

In addition, there were limitations directly related to the specific variables explored in this study. First, there were multiple, heterogeneous dementia groups. Previous literature states difficulty differentiating between AD, VaD, and dementia of mixed type. It is difficult to determine if participants fit into only one diagnostic category or to know if participants may have co-morbid AD and VaD. Related to this issue, people with AD may be more homogeneous due to the relative homogeneity of the disease process; in contrast, the VaD group may have been more heterogeneous due to the heterogeneity of the disease (i.e., those with VaD most likely had a different presentation in each individual dependent on where the lesion/s occurred in the brain). Additionally, all participants in this sample had some sort of cognitive impairment, and because there was not a measure of severity or chronicity of dementia, there is not much variability in diagnosis. Data is based on participants' first visit to the memory clinic because of memory/cognitive impairment (and therefore the participants are most likely in an early stage of the dementia process), and no patients are institutionalized; this combination also leaves us with a narrow sample. It would be helpful for future studies to provide more information regarding the severity of level of dementia.

Secondly, limitations to the diabetes variable should be noted. The self-reported absence of diabetes could be inaccurate; the person may have diabetes that was not detected and not aware that they have it. There is no history of diabetes, and no record of medication management. Also, there were no variables of potential co-morbid

diseases, such as hypertension or obesity that could play a role in the relationship between diabetes and cognitive functioning.

Finally, there are limitations related to the depression variable. Depression was assessed with only one self-report measure, and there were no other questions about depression such as history of depression, use of medication. Given previous literature which states that depression and diabetes can affect cognitive functioning, it is important to continue research in this area by using more scales of depression, more clearly-defined criteria for diabetes, and perhaps longitudinal data (to determine is depression causes decreased cognitive functioning or if decreased cognitive functioning creates depression).

Table 1

Patterns of Performance on Neuropsychological Measures: VaD & AD

Study	VaD: Better Performance	AD: Better Performance	VaD & AD: Equal Performance
Looi & Sachdev, 1999	• Verbal Subtests on WAIS • Orientation • Verbal Learning	• Executive Functioning	• Language functioning • Attention • Immediate memory • Motor speed • Nonverbal memory • Arithmetic • Constructional ability
Golden et al., 2005	• Arithmetic, Information, Similarities, & Picture Completion (WAIS-R) • Boston Naming Test • Auditory & visual tests of memory	none reported	• Both VaD & AD performed poorly on complex tests such as the Rey Complex Figure Test and word fluency
Graham, Emery, & Hodges, 2004	• Delayed recall on Logical Memory	• Executive functioning • Visuospatial functioning	• Recognition tests
Kramer et al., 2004	• Delayed recall on list-learning task	• Executive functioning	none reported
Tierney et al., 2001	• Rey Auditory Verbal Learning	• Oral fluency on Controlled Oral Word Association Test • Higher education	none reported

Table 2

Demographics

Categorical Variables	*n*	*%*	*χ^2 Diff by Diabetes*		*χ^2 Diff by Dementia Diagnosis (AD, VaD, MCI)*		*χ^2 Diff by Dementia Diagnosis (AD, VaD)*		
			χ^2	*df*	*χ^2*	*df*	*χ^2*	*df*	
Gender									
Male	84	36.4	0.240	1	0.18	2	0.14	1	
Female	147	63.6							
Race/Ethnicity									
Caucasian	174	75.3							
Af Am	30	13.0	23.92***	3	8.80	6	6.94	3	
Hispanic	26	11.3							
Other	1	0.4							
Diabetes									
Present	86	37.2			1.29	2	1.29	1	
Absent	145	62.8							
Diagnosis									
AD	63	27.3							
VaD	114	49.4							
MCI	54	23.4							
						Skewness		*Kurtosis*	
Continuous Variables	*N*	*Min*	*Max*	*M*	*SD*	*Statistic*	*Std. Error*	*Statistic*	*Std. Error*
Age	231	50	90	70.56	9.32	-0.20	0.16	-0.75	0.32
Years of Education	226	2	18	12.62	2.58	-0.42	0.16	1.64	0.32

Table 3

Chi-square Differences for Type of Dementia and Diabetes

Group/ Variable	AD		VaD		MCI		Test for distributional differences	
	n	%	n	%	n	%	χ^2	df
Diabetes: Present	20	23.3	46	53.5	20	23.3	1.29	2
Absent	43	29.7	68	46.9	34	23.4		

Note: "%" is % within diabetes diagnosis.

Table 4

Chi-square Differences for Race/Ethnicity and Diabetes

Group/ Variable	Caucasian		African American		Hispanic		Other		Test for distributional differences	
	n	%	n	%	n	%	n	%	χ^2	df
Diabetes: Present	50	58.1	21	24.4	14	16.3	1	1.2	23.92***	3
Absent	124	85.5	9	6.2	12	8.3	0	0		

Note: "%" is % within diabetes diagnosis.

Table 5

Measures of Cognitive Functioning

Continuous Variables						*Skewness*		*Kurtosis*	
	n	*Min*	*Max*	*M*	*SD*	*Statistic*	*Std. Error*	*Statistic*	*Std. Error*
Pillbox: Total Errors	231	0	139	24.61	24.41	1.04	0.16	1.92	.32
Pillbox: Total Pills	231	0	140	41.74	20.93	0.44	0.16	3.33	.32
7MS: Uncued	231	0	13	4.17	2.94	0.31	0.16	-0.52	0.32
7MS: Cued	231	0	16	7.75	2.95	-0.28	0.16	0.07	0.32
7MS: Total Recall	231	0	16	11.92	4.32	-1.07	0.16	0.11	0.32
PPVT IQ	193	59	136	104.47	19.40	-0.10	0.18	-0.91	0.35
Clock Draw Total	231	0	4	3.02	1.17	-0.98	0.16	-0.13	0.32
ROCF Copy	228	0	36	27.00	8.76	-1.20	0.16	0.68	0.32
ROCF Recall	230	0	33	9.12	6.82	0.65	0.16	0.29	0.32
Word Fluency	231	2	27.00	12.04	4.91	0.46	0.16	-0.14	0.32
GDS Total	132	0	29	10.01	7.35	0.64	0.21	-0.41	0.42
Categorical Variables	*n*	*%*							
Pillbox Test									
Pass	67	29.00							
Fail	164	71.00							
Check-Writing Test									
Pass	113	48.90							
Fail	118	51.10							

Table 6

ANOVA for Age, Education, and Dementia Diagnosis

Group/Variable	AD			VaD			MCI			F	Eta^2
	n	*m*	*sd*	*n*	*m*	*sd*	*n*	*m*	*sd*		
age	63	73.92_a	7.65	114	71.45_b	9.39	54	$64.76_{a,b}$	8.42	17.21***	0.13
years education	62	12.69	2.38	111	12.29	2.68	53	13.25	2.52	2.53	

Table 7

Hypothesis 1: Independent t-*Tests*

	AD			VaD			
	n	*m*	*sd*	*n*	*m*	*sd*	*t*-test
PPVT	56	103.02	19.43	90	101.59	18.82	0.44, ns
Fluency	63	10.30	4.54	114	11.61	4.50	-1.85

Table 8

Hypothesis 2: Independent t-*Tests*

	AD			VaD			
	n	*m*	*sd*	*n*	*m*	*sd*	*t*-test
Pillbox Test, Total Errors	63	32.75	26.61	114	26.24	24.51	1.64, ns
Pillbox Test, Total Pills	63	41.06	25.03	114	39.24	21.45	0.51, ns
Clock-Drawing Test	63	2.81	1.27	114	2.88	1.21	-0.35, ns

Table 9

Hypothesis 2: Chi-Square

	AD		VaD		Test for distributional differences	
	n	*%*	*n*	*%*	χ^2	*df*
Pillbox Test: Pass	10	5.6	32	18.1	3.34, ns	1
Fail	53	29.9	82	46.3		

Table 10

Hypothesis 3: Independent t-*Tests*

	Diabetes: Present			Diabetes: Absent			
	n	*m*	*sd*	*n*	*m*	*sd*	*t*-test
Memory Total	86	12.37	3.78	145	11.66	4.61	1.28, ns

Table 11

Hypothesis 4: Correlation Matrix

		PPVT	ROCF Copy	ROCF Recall	Memory	Clock	Fluency	GDS Total	Total Pills	Total Errors	Pillbox Pass/Fail	Check-writing
PPVT	Pearson r	1										
	Sig (2-tailed)	.										
	N	193										
ROCF Copy	Pearson r	(.352)*	1									
	Sig (2-tailed)	.000	.									
	N	191	228									
ROCF Recall	Pearson r	(.172)*	(.529)*	1								
	Sig (2-tailed)	.017	.000	.								
	N	192	228	230								
Memory Total	Pearson r	(.129)	(.309)*	(.541)*	1							
	Sig (2-tailed)	.075	.000	.000	.							
	N	193	228	230	231							
Clock-Drawing	Pearson r	(.261)*	(.650)*	(.440)*	(.311)*	1						
	Sig (2-tailed)	.000	.000	.000	.000	.						
	N	193	228	230	231	231						
Fluency	Pearson r	(.396)*	(.389)*	(.439)*	(.318)*	(.488)*	1					
	Sig (2-tailed)	.000	.000	.000	.000	.000	.					
	N	193	228	230	231	231	231					
GDS Total	Pearson r	(-.128)	(-.070)	(.075)	(.093)	(.025)	(.051)	1				
	Sig (2-tailed)	.160	.432	.396	.288	.780	.562	.				
	N	122	129	131	132	132	132	132				
Pillbox: Total Pills	Pearson r	(.204) *	(.368)*	(.247)*	(.128)	(.310)*	(.236)*	(.131)	1			
	Sig (2-tailed)	.004	.000	.000	.052	.000	.000	.134	.			
	N	193	228	230	231	231	231	132	231			
Pillbox: Total Errors	Pearson r	(-.344)*	(-.496)*	(-.464)*	(-.354)*	(-.513)*	(-.357)*	(-.146)	(-.234)*	1		
	Sig (2-tailed)	.000	.000	.000	.000	.000	.000	.094	.000	.		
	N	193	228	230	231	231	231	132	231	231		
Pillbox: Pass/Fail	Pearson r	(-.243)*	(-.354)*	(-.437)*	(-.241)*	(-.366)*	(-.352)*	(-.154)	(-.293)*	(.545)*	1	
	Sig (2-tailed)	.001	.000	.000	.000	.000	.000	.079	.000	.000	.	
	N	193	228	230	231	231	231	132	231	231	231	
Check-writing: Pass/Fail	Pearson r	(-.132)	(-.317)*	(-.360)*	(-.331)*	(-.378)*	(-.309)*	(.045)	(-.173)*	(.348)*	(.291)*	1
	Sig (2-tailed)	.066	.000	.000	.000	.000	.000	.606	.008	.000	.000	.
	N	193	228	230	231	231	231	132	231	231	231	231

Table 12

Hypothesis 4: Depression Score x Diabetes with 8 Covariates

Source	df	SS	MS	F	*p*	Eta^2
Covariates: Total Error	1	245.85	245.85	4.57*	0.04	0.009
Total Pills	1	155.13	155.13	2.88	0.09	
Fluency	1	15.82	15.82	0.29	0.59	
ROCF Copy	1	200.40	200.40	3.72	0.06	
ROCF Recall	1	12.90	12.90	0.24	0.63	
Memory Total	1	20.44	20.44	0.38	0.54	
Clock Score	1	4.88	4.88	0.09	0.76	
PPVT	1	132.46	132.46	2.46	0.12	
Diabetes	1	15.95	15.95	0.30	0.59	
Error	110	5922.28	53.84			

*$p < 0.05$.

Note: SS and MS are the same because this one-way ANCOVA only has two groups.

Table 13

Hypothesis 4: Group Differences for Those With and Without Diabetes

	Diabetes		No Diabetes				
Measures of Cognitive Function & Depression	*M*	*SD*	*M*	*SD*	*df*	*t*	Eta^2
GDS: Total	10.83	8.02	9.32	6.73	130	1.18	
Factor 1	4.25	3.61	3.10	2.91	112.87	1.99*	0.03
Factor 2	1.83	1.99	1.43	1.69	130	1.26	
Factor 3	2.13	1.75	2.00	1.67	130	0.45	
Factor 4	2.62	1.81	2.74	1.83	130	-0.38	
PPVT	98.37	20.03	107.71	18.33	191	-3.26**	0.05
ROCF: Copy	25.26	9.81	28.04	7.93	148.63	-2.22*	0.02
Recall	9.61	6.37	8.82	7.08	228	0.85	
Memory Total	12.37	3.78	11.66	4.61	206.32	1.28	
Clock Score	2.86	1.25	3.11	1.12	163.45	-1.53	
Fluency	11.79	4.40	12.19	5.20	229	-0.60	
Pillbox: Total Pills	37.64	19.30	44.18	21.54	229	-2.32*	0.02
Total Errors	26.29	21.97	23.62	25.77	229	0.80	
Pass/Fail	1.78	0.42	1.67	0.47	196.30	1.85	
Check-Writing	1.51	0.50	1.51	0.50	229	0.02	

Table 14

RQ 1: Correlations of Measures of Cognitive Functioning & Depression

		GDSTOT	GDSF1	GDSF2	GDSF3	GDSF4
PPVT	Pearson r	(-.128)	(-.222)	(-.133)	(.079)	(-.050)
	Sig. (2-tailed)	.160	.014	.143	.384	.587
	N	122	122	122	122	122
ROCF Copy	Pearson r	(-.070)	(-.076)	(-.105)	(-.008)	(-.027)
	Sig. (2-tailed)	.432	.393	.237	.929	.758
	N	129	129	129	129	129
ROCF Recall	Pearson r	(.075)	(.074)	(.037)	(.097)	(.046)
	Sig. (2-tailed)	.396	.398	.674	.272	.600
	N	131	131	131	131	131
Memory Total	Pearson r	(.093)	(.133)	(.000)	(.124)	(.031)
	Sig. (2-tailed)	.288	.127	1.000	.158	.725
	N	132	132	132	132	132
Clock Score	Pearson r	(.025)	(.022)	(.008)	(-.012)	(.050)
	Sig. (2-tailed)	.780	.803	.931	.891	.572
	N	132	132	132	132	132
Fluency	Pearson r	(.051)	(.006)	(.051)	(.078)	(.061)
	Sig. (2-tailed)	.562	.946	.562	.375	.489
	N	132	132	132	132	132
Pillbox: Total Pills	Pearson r	(.131)	(.060)	(.121)	(.194)	(.123)
	Sig. (2-tailed)	.134	.494	.168	.026	.160
	N	132	132	132	132	132
Pillbox: Total Errors	Pearson r	(-.146)	(-.058)	(-.141)	(-.179)	(-.174)
	Sig. (2-tailed)	.094	.507	.107	.040	.046
	N	132	132	132	132	132
Pillbox: Pass/Fail	Pearson r	(-.154)	(-.103)	(-.160)	(-.137)	(-.156)
	Sig. (2-tailed)	.079	.239	.068	.118	.074
	N	132	132	132	132	132
Check-writing: Pass/Fail	Pearson r	(.045)	(.030)	(.126)	(-.044)	(.030)
	Sig. (2-tailed)	.606	.734	.149	.614	.736
	N	132	132	132	132	132

Note: GDSF1 = dysphoria; GDSF2 = meaninglessness; GDSF3 = apathy; GDSF4 = cognitive impairment.

Table 15

RQ 2: One-way ANOVA Mean Differences

Group/Variable	AD			VaD			MCI			*F*	Eta^2
	n	*m*	*sd*	*n*	*m*	*sd*	*n*	*m*	*sd*		
PPVT	56	103.02	19.43	90	101.59_{a}	18.82	47	111.70_{a}	19.04	4.58*	.05
ROCF: Copy	62	25.89_{a}	8.94	112	25.56_{b}	9.55	54	$31.28_{a,b}$	4.63	9.04***	.07
Recall	63	$5.28_{a,b}$	5.17	113	$8.72_{a,c}$	6.28	54	$14.44_{b,c}$	6.31	34.30***	.23
Clock Score	63	2.81_{a}	1.27	114	2.88_{b}	1.21	54	$3.56_{a,b}$	0.74	7.95***	.07
Memory Total	63	$7.19_{a,b}$	4.25	114	$13.26_{a,c}$	2.79	54	$14.61_{b,c}$	2.36	99.66***	.47
Fluency	63	10.30_{a}	4.54	114	11.61_{b}	4.50	54	$14.98_{a,b}$	4.97	15.86***	.12
Pillbox: Errors	63	32.75_{a}	26.61	114	26.24_{b}	24.51	54	$11.70_{a,b}$	14.89	12.43***	.10

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Note: Groups with the same subscript are significantly different from one another using a Tukey HSD (Honestly Significantly Different) Range test, $p < 0.05$.

Table 16

RQ 2: Chi-Square

Group/Variable	AD		VaD		MCI		Test for distributional differences	
	n	*% within diagnosis*	*n*	*%*	*n*	*%*	χ^2	*df*
Pillbox Test: Pass	10	15.9	32	28.1	25	46.3	13.7**	2
Fail	53	84.1	82	71.9	29	53.7		
Check-writing:Pass	26	41.3	55	48.2	32	59.3	3.81	2
Fail	37	58.7	59	51.8	22	40.7		

Table 17

RQ 4: ANOVA for Diabetes, Check-writing, and Depression

Source	*df*	*SS*	*MS*	*F*
Diabetes	1	77.98	77.98	1.43
Check-writing	1	17.49	17.49	0.32
Diabetes x Check-writing	1	0.14	0.14	0.003
Within Cells	128	6986.36	54.58	
Total	131	7079.00		

Table 18

Correlations for Ecological Validity of Pillbox Test: AD

		Clock-drawing	Check-writing
Total Pills	Correlation	(0.29)	(0.23)
	Sig. (2-tailed)	0.10	0.86
	N	63	63
Total Errors	Correlation	(-0.39)	(0.32)
	Sig. (2-tailed)	0.002	0.01
	N	63	63
Pass/Fail	Correlation	(-0.31)	(0.43)
	Sig. (2-tailed)	0.01	0.00
	N	63	63

Table 19

Correlations for Ecological Validity of Pillbox Test: VaD

		Clock-drawing	Check-writing
Total Pills	Correlation	(0.35)	(-0.27)
	Sig. (2-tailed)	0.00	0.004
	N	114	114
Total Errors	Correlation	(-0.56)	(0.35)
	Sig. (2-tailed)	0.00	0.00
	N	114	114
Pass/Fail	Correlation	(-0.37)	(0.26)
	Sig. (2-tailed)	0.00	0.01
	N	114	114

Table 20

Correlations for Ecological Validity of Pillbox Test: MCI

		Clock-drawing	Check-writing
Total Pills	Correlation	(0.19)	(-0.22)
	Sig. (2-tailed)	0.18	0.11
	N	54	54
Total Errors	Correlation	(-0.27)	(0.30)
	Sig. (2-tailed)	0.05	0.03
	N	54	54
Pass/Fail	Correlation	(-0.31)	(0.17)
	Sig. (2-tailed)	0.02	0.23
	N	54	54

Table 21

Correlations Between Pillbox Test and All Other Measures for All Participants

		Pillbox P/F	Total Errors
PPVT	Correlation	(-0.24)	(-0.34)
	Sig. (2-tailed)	0.001	0.00
	N	193	193
ROCF Copy	Correlation	(-0.35)	(-0.50)
	Sig. (2-tailed)	0.000	0.00
	N	228	228
ROCF Recall	Correlation	(-0.44)	(-0.46)
	Sig. (2-tailed)	0.000	0.00
	N	230	230
7MS Total	Correlation	(-0.24)	(-0.35)
	Sig. (2-tailed)	0.00	0.00
	N	231	231
Clock	Correlation	(-0.37)	(-0.51)
	Sig. (2-tailed)	0.00	0.00
	N	231	231
Fluency	Correlation	(-0.35)	(-0.36)
	Sig. (2-tailed)	0.00	0.00
	N	231	231
Check-writing	Correlation	(0.29)	(0.35)
	Sig. (2-tailed)	0.00	0.00
	N	231	231

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