NEUROCOGNITIVE IMPLICATIONS OF DIABETES ON DEMENTIA AS MEASURED BY AN EXTENSIVE NEUROPSYCHOLOGICAL BATTERY

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Diabetes is a disease with a deleterious pathology that currently impacts 4.5 million individuals within the United States. This study examined the ability of a specific neuropsychological battery to identify and classify dementia type, investigated the impact of diabetes on cognition and analyzed the ability of the memory measures of the 7 Minute Screen (7MS) and the Rey-Osterrieth Recall to correctly categorize dementia type when not used in combination with a full battery. The battery in addition to exhaustive patient history, medical chart review and pertinent tests were used in initial diagnosis. Results indicated the battery was sufficient in the identification and classification of dementia type. Within the sample, diabetes did not appear to significantly impact overall battery results whereby only two measures were minimally affected by diabetes. Finally, the memory measures of the 7MS and the Rey-Osterrieth Recall were sufficient to predict membership into the Alzheimer's (AD) and vascular dementia (VD) groups with 86.4% accuracy. The classification percentage dropped to 68.3% with addition of the mild cognitive impairment category. The full battery correctly classified AD and VD dementia 87.5% and appeared to be the most robust.

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INTRODUCTION

Overview

Dementia is a serious diagnosis with a propensity to complicate and alter an individual's life. Not only is the individual impacted, but family members and loved ones struggle to accept the accompanying cognitive and personality changes and dread the eventual deterioration and loss of their loved one. Within the United States, approximately 4.5 million people are diagnosed with Alzheimer's Disease and millions of others carry a diagnosis of Vascular Dementia, Lewy Body disease or Frontotemporal dementia (Grossman, Bergmann & Parker, 2006). This estimation is on the conservative side and given the United States ever growing elderly population, these numbers are set to increase exponentially.

With regards to the ever increasing elderly population, it is pertinent to be cognizant of variables that potentially impact cognitive health. With age, the accumulation of lifelong habits and disease presence wrecks havoc on an individual's health. A sedentary lifestyle, unhealthy food choices, stress, hypertension and diabetes are some of these common variables impacting older Americans. Of these variables, diabetes is an influential disease that impacts health and maintains a strong potential to alter cognitive capacities after years of assault. Fluctuations in blood sugar produce complications that lead to significant alterations of the vasculature and compromise overall vascular integrity. With continued vascular insults, necrosis, or death of vasculature and the surrounding tissue, ensues. This death is not only manifested in the peripheral tissue but affects the organs with notable changes manifested in the brain.

Current research exists to support and to rebut the consequences of diabetes on cognitive health; however a substantial amount of literature identifies the vascular complications of diabetes as contributors to the dementia process (Elias, Elias, D'Agostina, Silbershatz & Wolf, 1999; Launer, Feskens, Kalmijn & Kronhout, 1996; Ryan, Vega & Drash, 1985; Verhaeghen, Borchelt & Smith, 2003). The study of the direct implications of diabetes on cognitive decline is pertinent for comprehension of the etiology and to identify the areas of the brain most susceptible to diabetic vascular change (Tariot, Ogden, Cox & Williams, 1999). Specifically, additional research is imperative because the demarcation of etiological differences between Alzheimer's Disease and Vascular Dementia is steadily becoming less defined as researchers uncover particular similarities in the pathogenesis process. The below study seeks to identify areas of the brain most affected by vascular change associated with diabetes and classify any significant differences between those with dementia and diabetes and those with only a dementia diagnosis. With greater understanding of this process, it may be possible to inhibit further decline via appropriate medications and lifestyle adaptations and perhaps, in the future, prevent cognitive decline. The diabetes and dementia processes as well as current research on these and potential implications are outlined below.

Diabetes Mellitus

Diabetes mellitus is a metabolic disorder in which perturbations are seen in the body's ability to produce normal glucose output, to effectively utilize insulin or to produce sufficient insulin. Insulin is a crucial hormone needed by the body in order to metabolize carbohydrates efficiently (Fujimoto, 2000; Golay, Felber, Jequier, DeFronzo & Ferrannini, 1988; Liu, Liberzon, Kong, Lai, Park, Kohane, & Kasif, 2007). Numerous

factors such as genetics, environment, a possible interaction of these, along with obesity and lack of exercise may influence the manifestation of diabetes (Adeghate, Schattner & Dunn, 2006). Currently, the American Diabetes Association (2005) estimates 20.8 million children and adults in the United States, or 7 percent of the population, have diabetes. Of these, approximately 14.6 million have been diagnosed with diabetes; however, nearly one-third or 6.2 million people are unaware that they have the disease (National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 2005). Other sources estimate the above numbers to be on the conservative side where the true number of diabetics is closer to 9.3 percent of the United States population whereby 19.3 million adults have diabetes (Norris, Kansagara, Bougatsos & Fu, 2008). To better illuminate the impact diabetes has on the American population, in 2005 alone, approximately 1.5 million people aged 20 or older were diagnosed with diabetes (NIDDK, 2005). Worldwide estimates of diabetes (i.e., Type 2) have reached epidemic proportions whereby approximately 150 to 170 million people or roughly 6 percent of the world's population are affected (Adeghate, Schattner & Dunn, 2006; Hattersley, 2006). Projected estimates figure a doubling of the current rates by the year 2030 (Adeghate, Schattner & Dunn, 2006; Kasuga, 2006; Liu et al., 2007).

Complications of Type 2 Diabetes include atherosclerotic vascular disease, heart disease, retinopathy, kidney failure and cognitive deficits (Douaihy, 2005; Kang & Grodstein, 2004; Kasuga, 2006; MacLeod, Hepburn, Deary, Goodwin, Dougall, Ebmeier & Frier, 2004; Monnier, 2000; Ryan, 2004; Warren & Frier, 2004). These complications are typically compounded when the diabetes is not well managed; however, a lifetime of blood sugar fluctuations in an individual who adequately manages the diabetes is still

shown to cause vascular complications (Fabre, Balant, Dayer, Fox & Vernet, 1982; Gaede, Lund-Anderson, Parving & Pedersen, 2008; Gu, Cowie & Harris, 1999; Wredling, Levander, Adamson & Lins, 1990). With research that clearly connects a detrimental relationship between diabetes and health, early identification and maintenance is necessary. For research purposes, the focus of this paper is on Type 2 diabetes, however because the fundamental processes of Type 1 give insight to the etiology and are similar to later dysfunction of Type 2 diabetes, these processes will be discussed as well.

Epidemiology and Etiology

Diabetes mellitus is a term liberally applied to metabolic disorders that produce chronically high blood glucose levels or hyperglycemia (Roden, 2004; Xeqiri, Ylli & Zeqiri, 2007). Diabetes mellitus is currently the most common endocrine disease within the world and was first identified as a disease associated with "sweet urine" and excessive muscle loss in the ancient world. The term sweet urine is used to describe spillage of glucose into the urine; this spillage is a way to reduce the elevated levels of glucose within the blood (Gutteridge, 1999; Steffes & Sacks, 2005; Xeqiri et al., 2007).

Diabetes is broken into two groups distinguished by insulin production within the pancreas and the groups are as follows: Type 1 or insulin-dependent diabetes is noted by the body's inability to secrete insulin and Type 2 or non-insulin-dependent is distinguished by insulin resistance with progressing impairment of beta cell function (Atkinson & Maclaren, 1994; Roden, 2004; Williams, Clouse, Rubin & Lustman, 2004).

Epidemiology of Type 1 diabetes within the United States varies with age yet rarely occurs prior to six months of age (Melton, Palumbo & Chu, 1983). Incidence rises

at 9 months of age and continues until ages 12 to 14 years of age (Christau, Kromann, Christy, Andersen & Nerup, 1979). Studies indicate the incidence of Type 1 diabetes occurs in most ethnic and racial groups with the highest risk being linked to the Caucasian population (Patrick, Moy & LaPorte, 1989). Contrasting is the epidemiology of Type 2 diabetes in which the number of the United States' population affected, ranges from 20 to 74 years of age with a greater prevalence seen in women than in men. Of interest, African Americans have a higher prevalence of Type 2 diabetes when compared to other races (Warram, Rich & Kroleswki, 1994).

The specific etiology of diabetes is not clearly understood; however specialist best conceptualize diabetes as multifactorial, linking environmental and genetic factors as contributors. Examples of possible environmental factors include physical inactivity, obesity, viral infection, location, drugs and toxic agents (Adeghate, Schattner & Dunn 2006). Genetic makeup is shown to increase one's propensity to develop Type 1 diabetes and is documented to play a crucial part in the etiology of Type 2 diabetes. The concordance in monozygotic twins approaches 100 percent for Type 2 diabetes (Kumar, Clark, 1999). Familial linkage is well documented from ancient Hindu physicians to current day with a frequency from 25 to 50 percent (Frank, 1957; Pincus & White, 1933; Vadheim, Rimoin & Rotter, 1991; Trevisan, Vedovato & Tiengo, 1998).

Type 1 diabetes. The precise etiology behind Type 1 diabetes is not fully understood, however researchers hypothesize Type 1 diabetes is resultant from an immune-mediated cause or an idiopathic cause (Tomky, 1997). These immune-mediated or autoimmune causes are the best understood and buttressed via research. Current research suggests that with autoimmune assault, comes destruction of the beta cells or a

defect in beta cell function within the pancreas (Atkinson & Maclaren, 1994; Hart, Bilo, Redekop, Stolk, Assink & Jong, 2003; Tomky, 1997). Beta cells are primarily responsible for release of insulin into the bloodstream; within the bloodstream, the insulin binds with cell membrane receptors to promote intracellular glucose movement. Without normal beta cell function, an insulin deficiency is manifested. This resultant deficit of insulin prohibits efficient carbohydrate metabolism. With inadequate metabolism, glucose levels dangerously rise within the bloodstream (Tomky, 1997). Glucose levels will continue to rise unless insulin is supplied exogenously. This pattern is typical of Type 1 diabetes, a disease typically marked by excessive thirst, or polydipsia and excessive urination, or polyuria. In addition, Type 1 is accompanied by unexplained rapid weight loss and overwhelming fatigue (Bohannon, 2001; Tomky, 1997). If not recognized and treated properly, severe dehydration and ketoacidosis or even diabetic coma and death may result (Roden, 2004; Williams, Clouse, Rubin & Lustman, 2004). Due to the lack of endogenous insulin, an individual with Type 1 diabetes must obtain exogenous insulin; regulate his diet and exercise to assist the body in normalization of carbohydrate metabolism (Tomky, 1997).

Type 2 diabetes. The etiology of non-insulin-dependent or Type 2 diabetes may be contributed to genetic and environmental factors or interplay of the two (Kahn, Vicent & Doria, 1996). The onset of Type 2 diabetes is rarely signaled by a clinically obvious medical crisis. Oftentimes, non-insulin-dependent diabetes will be noticed only after culmination of medical complications such as a cardiovascular event (Clement et al., 2004; Douaihy, 2005; Kalofoutis et al., 2006). Ryan and colleagues (1985) outline two different metabolic events in the occurrence of Type 2 diabetes. These are as follows: the

development of insulin resistance and resistance followed by progressive impairment of beta cell function. The combination of these changes will effectively decrease bioavailability of insulin and therefore lead to chronic hyperglycemia (Robertson, 1989; Ryan, 1985; Tomky, 1997). Insulin resistance is a loss in sensitivity to insulin at the peripheral cell receptor sites of muscles and within the liver (Robertson, 1989). The loss in sensitivity is hypothesized to be triggered in genetically susceptible individuals through overeating, inactivity and smoking (Ryan, 1985). Additional research reiterates this premise and states that most patients with Type 2 diabetes are obese with an increased percentage of abdominal or visceral body fat (Bosello, Armellini, Zamboni & Fitchet, 1997; Kahn, 2004; Tomky, 1997).

Complications of Diabetes

Hyperglycemia or high blood sugar concentration results from inadequate insulin or excessive carbohydrate consumption (Clement et al., 2004). Chronic hyperglycemia is associated with microvascular and vascular damage that ultimately increases the likelihood of developing serious medical complications which affect the entire body (Di Carli, Janisse, Grunberger & Ager, 2003; Jansson, 2007; Laakso & Lehto, 1997; Monnier, 2000; Williams, Clouse, Rubin & Lustman, 2004). Hyperglycemia damages vasculature via a resultant cascade of biochemical event that leads to vascular dysfunction and early structural changes of the vasculature (i.e., abnormalities in blood flow, increased vascular permeability and endothelial dysfunction; Andreani, 1995; Brownlee, 2001; Ceriello, 1993; Gargiulo et al., 1999; Lusis, 2000). Medical complications ensue and include microvascular damage within the retina resulting in impaired vision or blindness (Clement et al., 2004). Microangiopathy within the

glomerular loops of the kidneys is also seen; this damage increases the possibility of end-stage renal disease. Damage to microvasculature may lead to peripheral neuropathy in which fine motor control is impaired and pain or reduced sensation within the extremities is felt (Laakso & Lehto, 1997). Microvascular damage may also perturb sexual function (Romeo, Seftel, Madhum & Aron, 2000). In addition, cardiac arrhythmias or loss of urinary bladder sensation results from autonomic neuropathy (Monnier, 2000). Increased risk of heart attacks, stroke and gangrene of the feet are resultant of atherosclerosis in the large arteries of the heart, brain and legs (Di Carli et al., 2003; Khaw et al., 2004; Roden, 2004). Not only are vasculature changes noted in the peripheral and organ systems but vasculature integrity is compromised in the brain's vasculature system (Arvind, Pradeepa, Deepa & Mohan, 2002; Biessels, van der Heide, Kamal, Bleys & Gipson, 2002). Resulting insults cause damage to the surrounding tissue and overall cognition thus causing Vascular dementia (Biessels et al., 2002; Biessels, Staekenborg, Brunner, Brayne & Scheltens, 2006; Tariot, Ogden, Cox & Williams, 1999).

On the opposite end on the continuum is hypoglycemia or low blood glucose. Hypoglycemia is noted when excessive insulin exists or there is a failure to balance exogenous insulin with food intake and exercise (Bohannon, 2001; Tomky, 1997). Hypoglycemia produces an overall sense of discomfort noticeable by sweating, weakness, anxiety, fine motor tremors, irritability, mental confusion and motor incoordination (Roden, 2004). If left untreated, blood glucose levels will continue to fall and hypoglycemic seizures, loss of consciousness, permanent brain damage and increased risk of death may ensue (Cranston, Lomas, Maran, Macdonald & Amiel, 1994; Ryan 2004; Warren & Frier, 2004).

A balance between hyperglycemia and hypoglycemia is orchestrated via the pancreatic beta cells. These cells function to provide the precise balance of insulin to the body tissues and maintain plasma glucose levels within a narrow range. The beta cell secretes insulin in a highly transcribed manner to meet the composition and rate of meals as well as balance tissue needs (Ferrannini & Mari, 2004). Dysfunction within this relationship usually results from a combination of acquired and genetic factors (Marchetti, Dotta, Lauro & Purrello, 2008). Current research acknowledges a dual approach to the dysfunction whereby beta-cells are impaired and tissue insulin sensitivity is compromised (Ferrannini & Mari, 2004; Hattersley, 2006; Kahn, 2003; Marchetti et al., 2008). Although research exists on this relationship, it is unclear of the direct mechanism of beta-cell malfunction. One current hypothesis suggests a feedback loop mediates the interaction of insulin-sensitive tissues and beta cells. Another hypothesis reports insulin resistance is the primary occurrence with the resultant beta-cell dysfunction due to a prolonged and increased secretory demand on the beta-cell. In regards to the last hypothesis, an individual's pancreas is initially able to balance the increased circulating blood glucose levels with secretion of more insulin. Over time, the constant bombardment of insulin results in a deterioration in beta cell function and a concomitant reduction in insulin secretion (Hattersley, 2006; Kahn, 2004; Wollheim, 2000). Though a reduction of insulin secretion is noted, beta cells maintain moderate secretion capacities thereby allowing numerous individuals to function without daily insulin injections.

Oscillations in blood sugar play a deleterious role in laying the foundation of and progressing microvascular and macrovascular complications (Dailey, 2007; Dall et al.,

2008; Monnier, 2000). Due to the injurious nature of uncontrolled blood sugar, maintenance of glycemic control is the primary therapeutic goal to prevent these sequelae. According to the American Diabetes Association (2002), prospective randomized clinical trials have shown achievement of glycemic control is associated with decreased rates of retinopathy, nephropathy and neuropathy; epidemiological studies support the potential of intensive glycemic control in the reduction of cardiovascular disease.

Measurement of hemoglobin A1c (HbA1c) to assess chronic glycemic control is a crucial component of diabetes management (Alam, Weintraub & Weinreb, 2005; Dailey, 2007). The HbA1c test reflects a mean glycemic exposure over the preceding two to three months, whereby measurement every three months is required to determine whether a patient's metabolic control has been reached and maintained within the targeted range (American Diabetes Association, 1987, 1994, 2002; Dailey, 2007; Khaw, Wareham, Bingham et al., 2004). Duration of increased HbA1c levels as well as greater fluctuations of chronic hyperglycemia is shown through increased percentage of HbA1c levels. The American Diabetes Association recommends achievement of an HbA1c level at or below seven percent. Doctors and health professionals encourage patients to maintain control and keep blood glucose levels within little variance from the normal range through frequent monitoring of blood glucose levels, multiple daily injections of insulin when needed and adjustment of insulin dosage to meet needs (DCCT Research Group, 1993).

Type 2 diabetes is characterized via impairment in beta-cell function and tissue insulin sensitivity (Wollheim, 2000). A reduced islet of Langerhans or beta-cell mass exemplifies the development and progression of Type 2 diabetes. Studies consistently

illustrate quantitative and qualitative defects in glucose-stimulated insulin secretion (Buchanan, 2003; Del Prato, Marchetti & Bonadonna, 2002; Ferrannini & Mari, 2004; Kahn, 2003; Marchetti, Dotta, Lauro & Purrello, 2008). Although damage is sustained, the plasticity of the body is noted through an ability to control hyperglycemia with sustained weight loss and modification of diet. If improvement is not seen with weight reduction and diet, oral drugs may be of benefit with a mechanism of action that stimulates insulin secretion (e.g., sulfonlureas) or via enhancement of insulin action in muscle and liver tissues (e.g., metformin; Jones & Gil, 1997; Kenny, Aubert & Geiss, 1995; Ryan et al., 1985). With regards to the aforementioned, it is pertinent to remember beta cell dysfunction is central to the development of diabetes (Hattersley, 2006; Marchetti et al., 2008).

Population

According to the World Health Organization (WHO), the estimate of diabetes prevalence in 2000 was approximately 171 million people worldwide (2006). In 2006, WHO projected this conservative number would increase to 366 million people worldwide by 2030. No distinction was made between Type 1 and Type 2 diabetes within the WHO report, however, research by Chiu and Permutt (1997) alludes to a growing trend of Type 2 diabetes in the late 1990's. Specifically research suggests Type 2 diabetes to be most common in individuals age 40 and older with a body mass index greater than 25 (Chui & Permutt, 1997; Holbrook, Barrett-Connor & Wingard, 1989; Schienkiewitz, Schulze, Hoffman, Kroke & Boeing, 2006; Wilson, Anderson & Kannel, 1986). Contrary to the conservative ages reported in 1997 by Chiu and Permutt (1997), 2005 diabetes statistics plot an alarming trend in decreasing ages of Type 2 diabetes onset (Diabetes

Association of Greater Cleveland, 2007; National Diabetes Information Clearinghouse, 2005). Prevalence rates of diabetes within the United States in 2005 indicated approximately 20.8 million people or 7 percent of the population at that time had diabetes. Stunningly, 6.2 million people of this estimate represent undiagnosed cases. To better illustrate group distinctions, in 2005, 20.6 million people age 20 years and older or 9.6 percent of all people contained within this group had a diabetes diagnosis. Approximately 10.3 million or 20.9 percent of all people age 60 years and older had a diabetes diagnosis. Differences between men and woman in 2005 were as noted: 10.9 million men or 10.5 percent of men aged 20 years and older had diabetes; 9.7 million women or 8.8 percent of women aged 20 years or older had diabetes (National Diabetes Information Clearinghouse, 2005).

The aforementioned sampled United States diabetes rates in 2005, the below make a distinction of 2007 and how the prevalence of Type 2 diabetes is continuously increased. The American Diabetes Association, in 2007, reported the prevalence of diabetes continues to grow with estimates in the United States reaching 17.5 million diagnosed individuals. Dall and colleagues (2008) reported a truer estimate of United States diabetes prevalence is derived by combination of prevalence rates for the noninstitutionalized population (i.e., general public) with those individuals in long-term resident facilities (i.e., nursing homes). Rates, when viewed from this combinatory approach, reach 24 million individuals with diabetes in the United States. Noteworthy, African Americans and Hispanics have a higher prevalence of diabetes within each age group; an upward trend is seen in the younger populations of these groups when compared to Caucasian counterparts (2008).

The alarming trends are of concern for several factors. First, the United States population is aging due to improvements in health care. These improvements allow people to survive longer and expire from chronic versus acute illnesses. Secondly, although life expectancy is increasing, the manifestations of chronic diseases such as diabetes compound as the individual ages. Specifically, microvascular health is compromised and damage (e.g., retinopathy, nephropathy and neuropathy) is noted. Associated macrovascular complications (e.g., ischemic heart disease, stroke and peripheral vascular disease) ensue. As mentioned previously, vascular insult is not specific but yields an overall affect on the vasculature system (Biessels et al., 2002; Biessels et al., 2006). Detrimental effects are seen in the brain and these changes lay the foundations for the progression of Vascular and Alzheimer's dementia (Biessels et al., 2006; Ott et al., 1999; Tariot, Ogden, Cox & Williams, 1999). The mounting prevalence rates of diabetes coupled with an increasing life expectancy call for attention and drastic intervention (Arvind, Pradeepa, Deepa & Mohan, 2002; Dall et al., 2008; Di Carli et al., 2003; Khaw et al., 2004).

Cognitive Complications

To expound on the above, as individuals age, similar aging processes are revealed in their cognitive aptitude and intelligence test performance (Verhaeghen, Marcoen & Goossens, 1993; Verhaeghen & Salthouse, 1997). Some cognitive decline is normal with age (Celsis, 2000; Park, Connell & Thomson, 2003); however, the addition of certain diseases (i.e., diabetes) along with increasing age will expedite the cognitive decline and eventually lead to dementia (Kannel & Belanger, 1991; Verhaeghen, Borchelt & Smith, 2003). The demarcations between Alzheimer's Disease and Vascular Dementia are

becoming increasingly vague as similar underlying etiologies are noted (Dede et al., 2007; Humpel & Marksteiner, 2005; Knopman, 2006). Currently, within the United States, approximately 4.5 million people are diagnosed with Alzheimer's Disease and millions of others carry a type of dementia diagnosis (e.g., Vascular Dementia, Lewy Body Disease, Frontotemporal Dementia; Grossman, Bergmann & Parker, 2006). With the aforementioned diabetes information (i.e., vascular insult), it is intuitive to study the process of dementia, similarities and differences of Alzheimer's and Vascular Dementia and how diabetes expedites or influences this process.

To best comprehend what constitutes cognitive health, it is pertinent to have an understanding of dementia. Dementia was noted in the Greco-Roman period by Pythagoras and Hippocrates via their depictions of symptoms they referred to as senile dementia (Román, 1999). In 1290, Roger Bacon expounded upon the premise of senile dementia through his explanation of aging as a developmental process (Román, 1999). Some years later, advancements were made to define the neurological foundation of dementia; in 1549 Jaso de Pratis wrote the first textbook of neurology which contained a chapter on dementia. Dementia definitions and research continued into the 17th century, when Thomas Willis acknowledged intellectual deficits were associated with aging (Román, 1999, 2003). In the 19th century, Philippe Pinel's student, Jean-Étienne Dominique Esquirol, wrote the first modern classification of mental disease and included senile dementia. Developments in the understanding of dementia were seen in 1860, when Morel associated aging with brain atrophy and later when Otto Binswanger and Alois Alzheimer differentiated between ateriosclerotic brain lesions from senile dementia and from neurosyphilitic general paresis within the insane. In 1896 when Emil Kraepelin

expounded upon the work of Binswanger and Alzheimer and penned a chapter on "ateriosclerotic dementia;" this chapter consequently classified Vascular Dementia (Román, 1999, 2003).

Although dementia has been recognized as deterioration in one's cognition during later years for many centuries, true comprehension of the etiology has arisen only in the past three decades (Grossman et al., 2006). The medical field defines dementia as a chronic deterioration of one's intellectual functions whereby deficits are noted in learning and remembering, verbal facility, numerical skill, visual-spatial perception and the capacity to properly deduce, analyze and solve problems (Adams & Victor, 1994). The Diagnostic and Statistical Manuel of Mental Disorders-Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000) went a step further and clarified dementia as a term to refer to a pattern of cognitive deficits with no regard to prognosis. The DSM-IV-TR acknowledges dementia to be progressive, static or remitting and characterizes the disorders in the Dementia section via the development of multiple cognitive deficits due to direct physiological manifestations of a general medical condition, to the persisting effects of a substance or multiple etiologies. Similarly, designating features of dementia include the development of multiple cognitive deficits that perturb memory and at least one of the following: aphasia, apraxia, agnosia or an overall disturbance in executive functioning. These deficits must be of a severity to cause impairment in either occupational or social functioning and must be a noticeable decline from previous functioning (American Psychiatric Association, 2000).

Furthermore, the DSM-IV-TR specifies memory impairment to be a determinant of dementia wherein which the individual is impaired in the ability to acquire new

material and/or has a propensity to forget previously learned materials (American Psychiatric Association, 2000). Deterioration of language function or aphasia is most often seen in one's ability to generate names of people and objects; this inability to formulate words is termed anomia (Braaten, Parsons, McCue, Sellers & Burns, 2006; Mendez & Cummings, 2003). Speech formation of individuals with aphasia has a noticeable deterioration in which the content becomes vague, circumlocutory phrases are used and repetition of indefinite references such as "thing" and "it" are utilized (American Psychiatric Association, 2000; Braaten et al., 2006; Kramer & Duffy, 1996; Mendez & Cummings, 2003).

Additional impairments may be seen in an individual's ability to execute motor activities, or apraxia (Cormack, Aarsland, Ballard & Tove, 2004). Apraxia is defined as a difficulty in making voluntary gestures regardless of intact sensory functions, motor abilities and overall comprehension of the request (Della Sala, Lucchelli & Spinnler, 1989; Edwards, Deuel, Baum & Morris, 1991; Sjogren, Sjogren & Lindgren, 1952). Moreover, individuals with apraxia frequently are unable to pantomime object uses (i.e., toothbrush use) or execute known motor acts (e.g., waving hello). Disturbances are also noted in the complex goal-directed activities of dressing, cooking and drawing (Knopman, 2006; Luchelli, Lopez, Faglioni & Boller, 1993).

Not only are the aforementioned a concern, but dementia may obliterate one's ability to recognize or identify objects although intact sensory function is present (Huber & Paulson, 1985). The term agnosia is used to denote impairment in one's recognition abilities (Tranel & Damasio, 2000). Agnosia presence is typified when an individual demonstrates normal visual acuity but loses the ability to identify familiar objects (e.g.,

table, chairs, and keys). The phenomenon of agnosia involves a normal percept that is devoid of meaning to the individual (Teuber, 1968). Eventually, cognitive deterioration will increase and potentially perturb one's ability to recognize familiar others and eventually the self (i.e., prosopagnosia; Damasio, Tranel & Demasio, 1990; De Renzi, 1997; Tranel & Demasio, 2000).

Finally, executive function loss is a common feature of dementia usually seen with disorders of the frontal lobe or associated subcortical regions (Buckner, 2004). Executive function is a term used to categorize a set of seemingly related cognitive and behavioral capabilities. These capabilities include the complex procedures of judgment, planning, decision making and social conduct (Tranel & Demasio, 2000). When considering executive function, we attribute these abilities to the frontal lobe region of the brain (Tranel, Anderson & Benton, 1994). One crucial aspect is that this executive functional ability is the apex of functioning and pulls from all other cognitive faculties such as perception, memory and emotion (Tranel & Demasio, 2000). Any associated perturbation has the capacity to influence one's ability to think abstractly and plan, initiate, sequence, monitor and cease complex behaviors. Impairments in executive function would be best illustrated through an increased difficulty associated with novel tasks and decreased ability to process new and complex information (Szameitat, Schubert, Muller & von Cramon, 2002). Examples of task difficulty associated with executive function impairment include finding similarities or differences between objects (Szameitat et al., 2002). Individuals with executive function impairment have a reduced ability to shift mental sets, generate novel verbal/nonverbal information and to execute

serial motor activities (American Psychiatric Association, 2000; Badgaiyan, 2000; Szameitat et al., 2002).

Not only are the above cognitive changes a concern, but dementia has the propensity to cause malfunctions in spatial orientation and visuospatial functioning. Spatial and visuospatial disorders encompass a variety of cognitive functions with diverse neuroanatomical mechanisms (Freeman et al., 2000). Dementia potentially impacts the visuoperceptual, visuospatial and visuoconstructive areas (Benton & Tranel, 1996). For example, a deficit in the visuospatial functioning that includes visuoconstructional ability is characterized by discrepancies in one's ability to copy or construct two or three dimensional figures or objects when presented with a copy (Benton & Tranel, 1996; Freeman et al., 2000). Additionally, poor judgment and insight may arise and the individual may have little or no awareness of deficits (Adams & Victor, 1994; American Psychiatric Association, 2000). Without knowledge of one's deficits, unrealistic expectations of abilities and an underestimation of risky activities may ensue. Although not commonly labeled as a risky venture, driving, for an individual with dementia, is considered a risky activity (Adler & Kuskowski, 2003; Dobbs, 1997). A driver with dementia may not be cognizant of any deficits in motor control, visuospatial acumen and reaction time abilities (Marieke, Wouter, Koek & Dautzenberg, 2006). Furthermore, with dementia progression, occasional violent behaviors are manifested and suicidal ideation may be seen (Osvath, Kovacs, Voros & Fekete, 2005; Peisah, Snowdon & Kril, 2007). Disinhibited behaviors such as negligence of personal hygiene and disregarding of societal rules are often seen with further dementia progression (Adams & Victor, 1994; American Psychiatric Association, 2000).

Mild Cognitive Impairment

The dementia process is not typically defined as an immediate deficit in cognition but rather by a slow transitory phase imposed between normal aging and dementia. Attempts to identify and describe cognitive alterations between normal aging and dementia were undertaken by Kral in 1962 when he described the changes with his term "benign senescent forgetfulness" (Ellison, 2008; Gauthier et al., 2006; Kral, 1962). Kral's work was expounded upon in 1986 when a workgroup of the National Institute of Mental Health met and formulated the term "age-associated memory impairment" (AAMI) to identify cognitive changes outside the normal aging process (Petersen & Negash, 2008). This newly coined term referred to memory changes that varied from normal aging. The specified diagnostic criteria of AAMI had some shortcomings in that impairments were restricted to the memory domain and incompatible comparisons were made between memory function of older adults to young adults. With these standards, AAMI failed to pinpoint individuals at risk of developing deleterious cognitive decline outside the normal aging process (Petersen & Negash, 2008). To counteract the failures of AAMI, the International Psychogeriatric Association developed the term "age-associated cognitive decline" (Levy, 1994; Petersen & Nagash, 2008). This novel term incorporated a system that applied a graded system to the cognitive domains thought to decline in normal aging as well as made norm adjustments for education and age. At approximately the same time, the Canadian Study of Health and Aging derived the term "cognitive impairment-no dementia" (CIND) in an attempt to describe individuals with impaired cognitive function of a lesser degree than dementia (Graham et al., 1997). Although the Canadians

attempted to classify individuals between normal aging and dementia, their inclusion criteria were broad and oftentimes over-inclusive.

The above attempts laid the foundation for a more concise and well-defined term, Mild Cognitive Impairment (MCI), which was introduced by Reisberg and colleagues in the early 1980s (Flicker, Ferris & Reisberg, 1991; Petersen & Negash, 2008; Reisberg, Ferris, de Leon & Crook, 1982; Reisberg et al., 1988). These researchers ranked individuals with MCI on the Global Deterioration Scale (GDS) and thus placed cognitive health on a continuum (Gauthier et al., 2006; Petersen & Negash, 2008). The GDS is a scale used to identify seven clinical stages of dementia; four of these range from normal to mild dementia (i.e., stage 4) to very severe cognitive decline (i.e., stage 7; Gauthier et al., 2006). The above dedicated researchers encouraged the emergence of MCI as a stage of impairment greater than what is considered normal for age, but of a lesser extent than to warrant a classification of dementia (Petersen, 2003).

In 1999, the first major study of MCI was conducted and primarily focused on characterizing the stage as well as observing outcomes of MCI (Petersen et al., 2001). This seminal study acknowledged individuals with MCI had a greater propensity to experience additional cognitive decline and even develop Alzheimer's Disease (Petersen et al., 2001). From this study and similar studies that ensued, the following were designated as MCI criteria: a basic memory complaint; memory impairment for age-matched and education-matched people; preservation of one's general cognitive function; intact ability to carry out activities of daily living; and not being demented (Gauthier et al., 2006; Petersen & Negash, 2008).

As noted above, the terminology to conceptualize the transition between normal aging and dementia has evolved in a manner similar to our understanding of MCI. Contemporary literature does refer to the transition phase as MCI and distinguishes MCI into the main categories of amnestic MCI (aMCI; MCI with memory deficits) and non-amnestic MCI (naMCI; MCI without memory deficits; Petersen, 2000; Petersen et al., 2001; Sepe-Monti et al., 2007). Amnestic MCI is typified by an isolated memory decline in perspective of otherwise normal cognition and daily functioning (Broder, Herwig, Teipel & Fast, 2008; Petersen, 2004). Contrary, Non-amnestic MCI is noted when an individual has intact memory yet demonstrates deficits in non-memory domains such as executive function, visuospatial skills or language (Petersen & Negash, 2008).

Although MCI appears well defined, a debate, fueled via research, exists on whether these individuals with MCI represent a preclinical stage of Alzheimer's Disease or if they form a distinct group of cognitive decline (Broder et al., 2008; Ellison, 2008; Feldman & Kandiah, 2008; Petersen & Negash, 2008). Although some skepticism exists on all cases of MCI, research indicates a diagnosis of aMCI denotes a greater predisposition to develop Alzheimer's Disease. In fact, the prodromal period of Alzheimer's Disease is referred to in some literature as MCI (Small, Gagnon & Robinson, 2007). During this preclinical period, episodic memory, or memory that involves remembering verbal or visual material is disturbed but other cognitive functions such as language, praxis and executive function remains intact (Broder et al., 2008). Individuals with episodic memory deficits have difficulties with recalling lists of words, have delays in facial recognition and have troubles recalling personal events (Belleville, Chertkow & Gauthier, 2007; Small, Herlitz & Backman, 2004; Small et al., 2007).

Current research pinpoints that aMCI individuals typically progress into the diagnosis of Alzheimer's Disease within three to six years (Fisk, Merry & Rockwood, 2003; Petersen, 2004). Other progression rate estimates suggest aMCI individuals deteriorate to Alzheimer's Disease at 10 percent to 15 percent per year (Gauthier et al., 2006; Petersen et al., 1999). Intriguingly, Petersen and colleagues followed a group of MCI individuals over 6 years and identified a conversion rate up to 80 percent at an annual rate of 10 to 15 percent (Petersen et al., 1999, 2001). This observed progression rate is approximately ten times greater than the conversion rate for a normal population (i.e., 1% to 5%; Belleville et al., 2007; Gauthier et al., 2006; Petersen & Negash, 2008). To this day, research continues to uncover the facets of MCI, to delineate the stage of transition between normal aging and dementia and to study conversion rates and differences (Ellison, 2008; Petersen & Negash, 2008).

Causes of Mild Cognitive Impairment Pathogenesis of MCI is thought to involve cerebrovascular disease and/or neurondegeneration (Bennett, Schneider, Bienias, Evans & Wilson, 2005; Mufson et al., 1999). Although the precise etiologies are uncertain, research has found that individuals with MCI demonstrate white-matter lesions and small lacunar infarcts (i.e., similar to Vascular Dementia) and/or neurofibrillary tangles, amyloid deposition and tau-positive tangles (i.e., comparable to Alzheimer's Disease; Bennett et al., 2005; Chertkow et al., 2008; Morris et al., 2001; Mufson et al., 1999; O'Brien et al., 2003). Researchers also identify MCI to be heterogeneous and suggest the disease is promoted via individual variables (e.g., physiological, genetic) and external variables (e.g., environmental; Ganguli, Hiroki, Changyu, Dekosky, 2004; Richie, Artero & Touchon, 2001).

Although MCI represents a heterogeneous population, researchers have acknowledged those with aMCI deteriorate to a greater extent than naMCI individuals. Due to this increased propensity, the majority of studies focus on aMCI and the cognitive areas affected. Findings indicate aMCI individuals have increased atrophy or brain volume loss that typically occurs in the hippocampus and entrohinal cortex of the medial temporal lobes (Du et al., 2001; Masdeu, Zubieta & Arbizu, 2005; Pennanen et al., 2004; Tapiola et al., 2008). Additionally, MCI individuals have increased cortical grey matter loss and ventricular enlargement when compared to normal age-matched individuals; these areas are similarly affected in Alzheimer's Disease (Du et al., 2001; Pennanen et al., 2004). Although the focus remains on the aMCI group, researchers do know that the severity of MCI is directly related to the rate of progression. Specifically individuals with greater memory impairment are more apt to progress to Alzheimer's disease as compared to those with less memory impairment (Petersen & Negash, 2008).

Alzheimer's Dementia

Given the propensity for aMCI individuals to progress on the continuum from normal cognition to dementia, it is pertinent to understand the next stage or Alzheimer's Disease and the associated ramifications. These ramifications were first identified approximately 100 years ago by Alois Alzheimer. Alzheimer studied individuals and depicted a combination of memory impairments and behavioral disturbances that accompanied neuropathological changes such as the development of military bodies (i.e., plaques) and dense bundles of fibrils (i.e., tangles; Gershon & Herman, 1982; Moller & Graeber, 1998). His seminal research identified the trademark impairments and neurological changes and laid the foundation for dementia study (Blennow, de Leon &

Zetterberg, 2006). Interestingly, the precise etiology of Alzheimer's Disease (AD) is still a mystery; however, research has made vast strides in uncovering predisposing and contributing factors as well as identifying the areas of the brain affected by this disease process (Au, Chan & Chiu, 2003; Blennow, de Leon & Zetterberg, 2006; Braaten et al., 2005; Cummings & Benson, 1984; Dede, 2007).

Approximately 4.5 million individuals were living with AD in the United States in 2000; researchers and doctors estimate this number will almost triple to 13 million within the next 50 years (Herbert, Scherr, Bienias, Bennett & Evans, 2003). These projected estimates strike terror in the hearts of Americans as noted on a survey by the MetLife foundation. This survey documented that Americans fear the diagnosis of AD more than stroke, diabetes and heart disease (MetLife Foundation, 2006). This diagnosis is terrifying because of the insidious and incurable nature that causes early and noticeable deficits (American Psychiatric Association, 2000). Alzheimer's disease is the most common form of dementia and comprises approximately 50 to 60 percent of all dementia cases (Blennow et al., 2006; Dede et al., 2007). Furthermore, AD is defined via early-onset, in which the symptoms emerge prior to age 65 or late-onset whereby symptom presentation is after age 65 (Golde, 2003; Toyota et al., 2007). These symptoms encompass a broad and heterogeneous spectrum whereby initial symptoms include progressive loss of memory, cognitive and language impairments (i.e., aphasia, apraxia and agnosia) and later behavioral disturbances (Braaten et al., 2005; Grazina et al., 2006). Deficits and cognitive changes are resultant of neurological insult and correspond with the impacted areas (Au et al., 2003; Bondi, Salmon & Kaszniak, 1996; Braaten et al., 2006; Storey, Slavin & Kinsella, 2002).

One of the first noticeable cognitive deficits with AD, as well as a prominent feature of the disease, is a disproportionate decline in memory function in relation to the individual's other cognitive capacities (Braaten et al., 2006; Cummings & Benson, 1992). During this early stage or the mild stage of AD, an individual may display a progressive difficulty in naming objects or express word-finding deficits (Au et al., 2003; Braaten, 2006; Cummings & Benson, 1992). These deficits, or anomic aphasia, are evident regardless of an individual's intact speech fluency, auditory comprehension, articulation, prosody and repetition (Bouchard, 2007; Braaten et al., 2006; Cummings & Benson, 1992). As mentioned prior, impaired word finding leads to circumlocution (American Psychiatric Association, 2000; Mendez & Cummings, 2003). In this mild stage of AD there is little cognitive loss demonstrated, however an impact on one's functional abilities are seen, specifically in regards to a loss of instrumental activities of daily living (IADL; i.e., balancing a checkbook). Although minimal IADL disturbances emerge, the individual's self-care is not affected within this stage and negligible neruopsychiatric symptoms such as depression and irritability are recognized (Bouchard, 2007; Braaten, 2006; Rabheru, 2007). As AD progresses to the moderate stage, a rapid cognitive decline ensues. This decline is noted by an observable reduction on performance of IADL and self-care ADL (i.e., maintenance of hygiene). Within the moderate AD stage, additional neuropsychiatric symptoms may arise (i.e., depression, anxiety; Rabheru, 2007). Furthermore, personality alterations may also coincide with the disease progression (American Psychiatric Association, 2000; Braaten, 2006). The transition into severe AD is punctuated via culminations of motor deficits (e.g., gait disturbances), additional cognitive decline and oftentimes, incontinence (American Psychiatric Association, 2000;

Braaten et al., 2006; Gershon & Herman, 1982; Rabheru, 2007). During this severe stage, aggressive behaviors may become prevalent and take the form of verbal aggression (i.e., most common), aggressive resistance and physical aggression (Rabheru, 2007). Additionally, within the severe stage, continued and rapid cognitive decline may give rise to hallucinations and paranoia. Eventually mutism, bed confinement, loss of consciousness and death result (American Psychiatric Association, 2000; Braaten, 2006; Gershon & Herman, 1982). Generally, individuals with AD are alert and transitioning levels of consciousness are only prominent within the end disease stages (Gershon & Herman, 1982; Katzman, 1981).

Alois Alzheimer was on target when he portrayed the combination of memory impairments and behavioral disturbances that accompanied neuropathological changes (Gershon & Herman, 1982; Moller & Graeber, 1998). Currently AD has been pinpointed to involve generalized cerebral atrophy, enlargement of the ventricles, hippocampal atrophy, amyloid beta deposits, abnormal tau protein, hyperphosphorylation, granulovacuolar degeneration and neurotransmitter deficiencies (Cummings, 2004; Dede et al., 2007; Petrella, Coleman & Doraiswamy, 2003; Yavuz et al., 2006).

Causes of Alzheimer's Dementia Pathogenesis is via deposits of senile or neuritic plaques and neurofibrillary tangles in the medial temporal lobe structures and cortical areas (Blennow et al., 2006; Braak & Braak, 1991; Golde, 2003). Pathology research converges and identifies that prior to AD diagnosis, amyloid beta protein accumulates within the brain and is deposited via plaques and neurofibrillary tangles; some accumulation is present within the cerebral vessels (Golde, 2003; Golde, Eckman & Younkin, 2000). These deposits may agitate stations responsible for input to and output

from the hippocampus (Hyman, Damasio, Van Hoesen & Barnes, 1984; Van Hoesen & Damasio, 1987). At the same time this foundation is being laid, the brain's neurons and synapses are also being targeted and show some degeneration (Blennow et al., 2006; Golde, 2003). Research supports the hypothesis of amyloid beta deposits, which trigger a chain effect thereby leading to neuronal degeneration (Cummings, 2004; Dede et al., 2007; Humpel & Marksteiner, 2005). High concentrations of neuritic plaques and neurofibrillary tangles are typically seen within the hippocampus, amygdala and surrounding cortical structures, therefore, these areas are the most affected by AD (Horinek et al., 2006). In addition to the above chain reaction, one's genotype may promote the deleterious disease (Bondi, Houston, Eyler & Brown, 2005). Specifically, occurrence of the ApoE 4 allelle is linked to cause structural and functional changes and is documented to cause neuropsychologic deficits (Bondi et al., 2005). Again, AD tends to be more global in its manifestations on cognitive decline and perturbations are noted when brain structures are assaulted and altered (Bondi, Salmon & Kaszniak, 1996; Braaten et al., 2006; Storey et al., 2002). These specific alterations lead to cognitive deficits that are readily diagnosed as AD with a high degree of accuracy (Berg, McKeel, Miller, Storandt, Rubin, 1998; Herholz, Perani, & Morris, 2006; Jellinger, 2007; Khachaturian, 2006).

Vascular Dementia

In the 17th century, Thomas Willis first described intellectual loss with aging and laid the foundation for future studies of Vascular Dementia (VD) when he attributed the observed symptoms to atherosclerotic disease (Aalten, de Vugt, Jaspers, Jolles & Verhey, 2005; Román, 1999, 2003; Onyike, 2006). Otto Binswanter and Alois Alzheimer

expounded upon Willis's purported disease and clarified the pathology to be an atherosclerotic process within VD (Aalten et al., 2005; Onyike, 2006). During the 1970s, the atherosclerotic process was collectively called multi-infarct dementia to reflect the view that cumulative processes of recurrent infarctions were crucial in the dementia progression (Gershon & Herman, 1982; Hachinski, Lassen & Marshall, 1974). Terminology has evolved throughout the past 20 years to encapsulate the multi-infarct etiology as well as to include cases with a single strategic infarct or cases where extensive white matter lesions are present (Bouchard, 2007; Onyike, 2006). In general, the term VD embodies a large span of diseases with heterogeneous manifestations attributable to a vascular origin (Bouchard, 2007). This disease process or dementia secondary to cerebrovascular pathology (i.e., vascular dementia) is currently the second most common type of dementia (Bouchard, 2007; Erkinjuntti, 2002; Gershon & Herman, 1982; Onyike, 2006). Approximately 8 to 20 percent of dementia cases are VD (Gershon & Herman, 1982; Jellinger, 2007; Martinez-Vila, Murie-Fernandez, Perez-Larraya & Irimia, 2006; Onyike, 2006; Stewart, 2006).

Although VD is purported to be the second most common form of dementia, the ability to correctly diagnosis VD is highly difficult (Black, 2007). Vascular dementia etiology potentially overlaps with other dementias such as AD and is not as selective in the exact causal pathway (Black, 2007; Jellinger, 2007). Concerning diagnostic criteria, the required cognitive impairments for VD include impaired memory and any deficits involving aphasia, apraxia, agnosia or a disturbance in executive functioning (American Psychiatric Association, 2000; Onyike, 2006). Additionally, impairments in psychosocial functioning must be ascribed to dementia and laboratory evidence of cerebrovascular

disease and/or focal neurological signs and symptoms present (i.e., sensory, motor impairments; American Psychiatric Association, 2000; Onyike, 2006). In some extreme cases of VD, disturbance are noted in the form of hypokinesia, rigidity, balance, gait and incontinence (i.e., usually resultant from lacunar infarcts; Onyike, 2006). The evidence of cerebrovascular disease may be primarily cortical, primarily subcortical or a combination of these (Braaten et al., 2006; Jellinger, 2007; Onyike, 2006; Stewart, 2006).

Though the above diagnostic criteria seem straight forward, they are eerily similar to the diagnostic criteria for AD with an added vascular component (American Psychiatric Association, 2000). Contrary to the global deficits common in AD, there are no identified seminal deficits, cognitive impairments or even neuropsychological profiles indicative of a vascular dementia profile (Black, 2007; Jellinger, 2007). In fact cerebral vascular insults may transpire without resulting dementia (Bouchard, 2007). Although difficult to diagnose, one characteristic is heavily relied upon to parse out VD cases from AD; this characteristic is onset differences. The characteristic onset of AD is typically slow and insidious with steady progression whereas the onset of VD is typically rapid with a stepwise and fluctuating progression (Badgio & Worden, 2007; Onyike, 2006). Vascular dementia oftentimes develops in the age range from late 60s to 70s and is closely associated with a discrete stroke or a series of strokes (Onyike, 2006). Similar to AD, the location and nature of the insulted neuroanatomical areas will determine the displayed deficits and behavioral manifestations (Roman et al., 2004). Contrary to AD progression, with VD, emotional and personality disturbances may appear prior to other cognitive impairments. In some cases, the neuropsychiatric symptoms of depression and anxiety result and additional impairments are evident are common (Onyike, 2006).

Causes of vascular dementia The pathology of VD is supported through research that identified the following: interactions between vascular etiologies (i.e., cerebrovascular disease, vascular risk factors); alterations in the brain (e.g., infarcts, white matter lesions, atrophy); and an individual's personal variables (i.e., age, vascular risk factors; Borchelt & Smith, 2003; Elias, Elias, D'Agostina, Silbershatz & Wolf, 1999; Erkinjuntti, 2002; Leys, Pasquier & Parnetti, 1998; Verhaeghen, Launer, Feskens, Kalmijn & Kronhout, 1996). Individuals with VD generally suffer from large-vessel disease (i.e., multi-infarct dementia), small-vessel disease (i.e., Binswanger's disease, lacunar state) or a combination of these (Jellinger, 2007; Roman, 2003; Stewart, 2006). Research reinforces this relationship and suggests the presence of heart disease, diabetes, hypercholesterolemia or hypertension to be associated with decreased cognitive performance frequently seen in VD (Elias & Elias, 1993; Schaie, 1996; Stewart, 2006; Waldstein & Elias, 2001). The mechanism of action associated with decreases in cognitive performance is a corresponding insult to one's vasculature (e.g., atherosclerosis; Vingerhoets, 2001). To give an example of the complexity of VD, the associated variable of atherosclerosis is linked to abnormalities in hemodynamic structures (i.e., calcification, rupture, hemorrhage), in one's genotype (i.e., ApoE 4 allelle) and in metabolic function (i.e., impaired insulin metabolism; Hachinski, 1990; Verhaeghen et al., 2003; Vingerhoets, 2001). Current methods to assess for the presence of VD include a comprehensive medical history in conjunction with computed tomography (CT) and magnetic resonance imaging (MRI); these instruments are beneficial in diagnosing the topography and severity of vascular changes (i.e., white matter lesions; American Psychiatric Association, 2000; Guermazi et al., 2007;

Hentschel, Damian, Krumm & Froelich, 2007). Although AD is diagnosed with high accuracy, precise diagnosis of VD is more complex and as times, not as accurate (Black, 2007; Jellinger, 2007).

Similarities between AD and VD

Research acknowledges the comorbid presence of AD and VD, typically referred to as mixed type (Black 2007; Martinez-Vila, Murie-Fernandez, Perez-Larraya & Irimia, 2006; Onyike, 2006). Cases of pure Alzheimer's or Vascular dementias are not as common as previously believed (Martinez-Vila et al., 2006). For example, an individual may express a history positive for infarcts or stroke, however research suggests it is premature to automatically rule out the presence of Alzheimer's disease (Martinez-Vila et al., 2006; Zekry et al., 2002). Research has also identified that approximately half of the individuals diagnosed with VD have some type of Alzheimer's pathology; autopsy results indicate that 30 percent of individuals with an AD have significant cerebrovascular lesions (Kalaria & Ballard, 1999; Martinez-Vila, et al., 2006; Zekry et al., 2002). This relationship may be attributed to similar underlying etiologies involving amyloid proteins, white matter changes and compromised vasculature (Haglund, Kalaria, Slade & Englund, 2006; Lind, Jonsson, Karlsson, Sjogren & Wallin, 2006; Martinez-Vila et al., 2006).

To further convolute the argument, some researchers developed the purported linkage and suggested AD to be an expression of VD (Onyike, 2006; Snowden et al., 1997). This hypothesis is supported via research which suggests cerebrovascular disease disrupts amyloid homeostasis thereby activating a cascade of events which leads to deposition of amyloid via senile plaques, aggregation of tau, formation of neurofibrillary

tangles and possible neuronal dysfunction and consequent neuronal death (Casserly & Topol, 2004; de la Torre, 2002, 2004; Onyike, 2006). Additionally, cerebral infarcts may amplify the effects of the AD progression (Onyike, 2006; Roman & Royall, 2004).

Research

With continued research the demarcation of etiological differences between AD and VD fades however, the pathogenesis continues to destroy cognitive capacities and remains an area of great concern. Researchers are persistent in identifying methods to stop this process as well as understand how comorbid diseases (e.g., diabetes) compound the progression. Some current hypotheses purport cognitive decline to be directly dependent on the individual's overall somatic health and educational level (De Ronchi et al., 1998; Lindenberger & Baltes, 1994, 1997; Salthouse & Czaja, 2000); whereas other research suggests the brain's reserve capacity is drained and decreased neuronal plasticity allows for detrimental changes (Baltes & Kliegl, 1992; De Ronchi et al., 1998; Singer, Lindenberger & Baltes, 2000). Although research proven, these hypotheses are only pieces of the overall relationship puzzle.

Diabetes research and cognitive implications

The relationship between diabetes and cognitive health has been a topic of interest for numerous years. Research exists to support and to refute the ramifications of diabetes on cognitive health; however, more evidence exists in support of this detrimental relationship than to refute it (Biessels, Koffeman & Scheltens, 2006; Convit, Wolf, Tarshish & de Leon, 2003; Croxson & Jagger, 1995; Logroscino, Kang & Grodstein, 2004; Ryan, Vega & Drash, 1985; Verhaeghen, Borchelt & Smith, 2003). Findings from the articles that included Type 1 diabetes indicated neuroanatomical changes along with

impairments in mental flexibility and mental speed (i.e., slowing) with learning and memory typically unaffected (Brands, Biessels, De Haan, Kappelle, & Kessels, 2005; Brands et al., 2007).

In comparison, Type 2 research findings demonstrated that diabetes presence is linked to neuroanatomical changes and to impairments in information processing speed, memory and attention functions and executive function (Awad, Gagnon & Messier, 2004; Brands et al., 2007; Manschot et al., 2006; Stewart & Liolitsa, 1999; Verhaeghen, Borchelt & Smith, 2003). The impact of diabetes on cognition and dementia (i.e., Alzheimer's and Vascular) will be outlined and summated in the following text.

Between groups comparison Initial studies on differences between diabetics and nondiabetics commenced in the 1920s (Miles & Root, 1922). Miles and Root sought to answer why their diabetic patients complained of memory loss and concentration difficulties. Tests of mental efficiency were administered to 40 diabetic patients and 14 nondiabetic patients (i.e., control group). Upon comparison, results for diabetic patients indicated modest decline in mental efficiency by approximately 15 to 20 percent. Additionally, in comparison to nondiabetic controls, deficits were demonstrated for diabetics in immediate memory span for numbers and letters. Individuals with diabetes also manifested a reduction in performance speed without deficits in accuracy (i.e., on tasks requiring sustained attention; digit cancellation). Furthermore, tasks measuring over learned mental operations (e.g., rapid addition of single digit numbers) did not show deficits (Miles & Root, 1922).

Additional comparative studies have investigated the contribution of diabetes on cognition (Convit et al., 2003). Convit and colleagues (2003) compared diabetic and

nondiabetic, nondemented middle-aged and elderly individuals. Findings revealed peripheral glucose regulation was associated with a general decrease in cognitive performance and memory impairments (Convit et al., 2003). Between groups differences were also noted for neuroanatomical structures. Specifically, when compared to their nondiabetic counterparts, individuals with diabetes had hippocampal atrophy. This atrophy is hypothesized to be related to severe, recurrent hypoglycemia levels (Convit et al., 2003). Additional studies have identified the presence of hippocampal atrophy as well as amygdalar atrophy in individuals with Type 2 diabetes (Heijer et al., 2003).

A similar study looked at differences between individuals with dementia in comparison to individuals with comorbid diagnoses of dementia and diabetes (Biessels et al., 2006). Interestingly, the studies outlined diagnostic criteria did not reflect increased cerebrovascular pathology in diabetic patients; however when imaging assessments were utilized, significant cerebrovascular incidents were identified for 38 percent of the diabetic patients and 17 percent of non-diabetic patients. Findings also indicated diabetic patients presented with greater cortical atrophy in comparison to their non-diabetic counterparts (Biessels et al., 2006).

Hypoglycemia and Cognitive Dysfunction

Recurrent hypoglycemia exposure has the potential to negatively impact neurological sequelae in a transient and permanent manner (Wallis, Donaldson, Scott & Wilson, 1985). This study utilized a cross-sectional method to examine the influence of repeated episodes of hypoglycemia (i.e., severe) on the development of neurological dysfunction. Findings indicated that diabetics with five or more lifetime episodes of severe hypoglycemia tended to perform worse on measures of mental efficiency and fluid

intelligence when compared to counterparts without severe hypoglycemia episodes (Wallis et al., 1985). Additionally, repeated severe hypoglycemia episodes may impede one's ability to perform on vocabulary tests (Bale, 1973). Psychomotor slowing and perturbations on visuospatial tests have been noted for patients with hypoglycemic episodes (Wredling, Levander, Adamson & Lins, 1990). Interestingly, mixed results were noted for declarative memory processes in patients who had experienced several episodes of hypoglycemia (Sacho et al., 1992). Hypoglycemia also has been linked to deficits in fluid intelligence (Deary et al., 1993; Langan, Deary, Heburn & Frier, 1991).

Contrary to the above listed, an 18 year longitudinal study followed Type 1 diabetics and found no evidence in support of substantial long-term cognitive declines even with high rates of recurrent severe hypoglycemia (Jacobson et al., 2007). Additional research by Ryan and colleagues (1991) sought to disprove the purported relationship between hypoglycemia and corresponding cognitive deficits. They designed a Diabetes Control and Complications Trial (DCCT) to test the postulation that intensive metabolic therapy, outlined by multiple daily injections of insulin, would reduce diabetes-related complications. The neuropsychological state of patients was monitored with an extensive battery of cognitive tests (Ryan et al., 1991). Data was collected from 1441 patients over an average of 6.5 years. Results indicated that regardless of severe hypoglycemic episodes, no evidence of clinically significant cognitive impairments was noted on the neuropsychological measures (DCCT Research Group, 1996). The Stockholm Diabetes Intervention Study group came to similar conclusions (Reichard, Berglund, Britz, Levander & Rosenqvist, 1991; Reichard, Nilsson & Rosenqvist, 1993). As indicated

above, research is divided on the ability for hypoglycemic states to permanently influence cognitive capacities.

Hyperglycemia and Cognitive Dysfunction

Not only does hypoglycemia influence cognitive health but hyperglycemia is associated with cognitive deficits as well (Brands et al., 2007; Skundric & Lisak, 2003). Hyperglycemia is the primary contributor to diabetic microvascular damage and resultant neuropathy. The manifestations of hyperglycemia are well documented and are demonstrated in Type 1 and Type 2 diabetes (Sheetz & King, 2002; Skundric & Lisak, 2003; Williams, Van Gaal & Lucioni, 2002). Hyperglycemic complications affect peripheral, central and visceral sensorimotor and motor nerves (Skundric & Lisak, 2003). In 1984, the first large scale neuropsychological study to evaluate learning and memory skills in Type 2 diabetic was conducted (Perlmuter et al., 1984). Findings indicated diabetic patients learned fewer words on successive trials. When compared to demographically similar and nondiabetic controls, diabetics showed significant decreases in the ability to master word lists. Between groups differences such as mood, educational level, intelligence, immediate memory span and reaction time were eliminated through matching with healthy controls. Within group comparisons of the diabetic population yielded less efficient learning for those with poor metabolic control (i.e., hyperglycemia) and/or peripheral neuropathy as compared to diabetic counterparts who utilized good glucose control (Perlmuter et al., 1984). Additional studies have reinforced the relationship between hyperglycemia and decreased cognitive performance on learning and memory tasks (Elias & Elias, 1993; Schaie, 1996; Strachan, Deary, Ewing & Frier, 2000). Noteworthy, the relationship between chronic hyperglycemia and brain

dysfunction is supported by electrophysiological and neuroimaging studies. Results documented that diabetic adults have significantly slower brain stem auditory evoked potential latencies and have MRI scan abnormalities (Khardori et al., 1986; Pozzessere et al., 1988).

Glycemic control

When considering the above, if poor metabolic control adversely impacts cognition, then any type of intervention to improve metabolic control should abate the cognitive decline process. Two small studies found weak support for this hypothesis (Gradman, Laws, Thompson & Reaven, 1993; Meneilly, Cheung, Tessier, Yakura & Tuokko, 1993). Gradman and colleagues (1993) assessed neuropsyhological functioning in 30 older Type 2 diabetic adults pre and post intervention. Intervention targeted metabolic control in the form of an oral hypoglycemic agent, Glipizide. Treatment was found to be associated with significant metabolic control (e.g., declines in fasting blood glucose and glycosylated hemoglobin levels) and improved performance on measures of verbal learning and memory. Measures of attention and information-processing efficiency did not show improvement. Meneilly and associated (1993) followed the aforementioned experimental design and also found significant improvement in metabolic control and performance on tests of attention. Improvements were also documented on tests of learning and memory performance; however, improvement was not statistically significance. If true, these studies highlight that metabolic control may improve presence of the attention, learning and memory disorders.

The following hypotheses and research questions were formulated based on extensive work with the dementia populations and elaborated on via a thorough literature review:

Hypotheses

1. Overall individuals with AD will score worse on all neuropsychological test items as compared to individuals with VD. This prediction is based on the above literature review that indicates more severe and globalized deficits for AD (Au et al., 2003; Bondi et al., 1996; Bouchard, 2007; Braaten et al., 2006; Cummings & Benson, 1992; Gershon & Herman, 1982; Rabheru, 2007; Storey et al., 2002). Specifically those with AD when compared to VD counterparts will perform more poorly on the following neuropsychological tests:
    a. Pillbox test
    b. Western Aphasia Battery
        i. Fluency
        ii. Species
    c. Rey-Osterrieth
        i. Rey Copy
        ii. Rey Recall
    d. 7-Minute Screen
        i. Uncued
        ii. Cued
        iii. Forgotten
    e. Clock Drawing Test

f. DAFS Check Writing

g. Peabody Picture Vocabulary Test

2. The second hypothesis centered on the comorbid affect of diabetes and maintained that individuals with diabetes and dementia will perform more poorly than individuals with a dementia diagnosis only. This hypothesis is considered given that diabetic changes disrupt vascular homeostasis and causes detrimental alterations (Biessels et al., 2006; Ott et al., 1999; Tariot et al., 1999). These diabetic changes are hypothesized to expedite the present AD and VD processes, therefore, individuals with a comorbid diagnosis will show decreased performances on neuropsychological tests (Kannel & Belanger, 1991; Verhaeghen et al., 2003). It is predicted that on all tests, as listed below, individuals with diabetes will score worst on all measures as compared to those without diabetes.

    a. Pillbox test

    b. Western Aphasia Battery

        i. Fluency

        ii. Species

    c. Rey-Osterrieth

        i. Rey Copy

        ii. Rey Recall

    d. 7-Minute Screen

        i. Uncued

        ii. Cued

iii. Forgotten

e. Clock Drawing Test

f. DAFS Check Writing

g. Peabody Picture Vocabulary Test

3. The third prediction suggests that the scores on the specific memory measures of Rey-Osterrieth Recall and the 7MS variables of Uncued, Cued and Forgotten will be sensitive to predict group membership of AD and VD. This hypothesis was formulated based on prior research that indicated individuals with AD show significant decreased memory test performance in comparison to VD counterparts (Braaten et al., 2005; Grazina et al., 2006).

    a. Rey-Osterrieth Recall

    b. 7MS Uncued

    c. 7MS Cued

    d. 7MS Forgotten

4. The last hypothesis built upon the previous and asserted the above memory tests to be sufficient to classify MCI individuals. This hypothesis was formulated based on the literature that alleged individuals with MCI have memory deterioration similar to the AD group but different from the VD group. Specifically, individuals with MCI will have the same profile (e.g., memory impairments) as AD but not be as impaired as VD individuals. As research indicated, MCI individuals have episodic memory deficits and therefore an increased difficulty with recalling verbal and visual material (Belleville et al., 2007; Broder et al., 2008; Small et al., 2004; Small et al., 2007). On the following tests, the individuals with MCI will

have lower scores than VD individuals but higher scores than AD individuals, therefore these tests will be able to correctly predict MCI group membership.

a. Rey-Osterrieth Recall
b. 7MS Uncued
c. 7MS Cued
d. 7MS Forgotten

Research Questions

After an extensive review of the literature and acknowledgment of different clinical experiences, the below questions were formulated in an attempt to understand this population to a greater extent and to identify any unique differences. Noteworthy, the nature of this sample may not be adequate to acknowledge differences.

1. Are there significant neuropsychological test performance differences between males and females within this population?
2. Are there significant test performance differences between right-handed and left-handed individuals on any of the measures?
3. Does higher education (i.e., college) provide a buffer against cognitive decline? Specifically, do individuals with higher education score better on test measurements than those without a college education?
4. Will there be significant neuropsychological test performance differences between races/ethnicities?

CHAPTER II

METHOD

Participants

Participant demographic information and test data were obtained from an existing archival database comprised of outpatients referred to the John Peter Smith (JPS) County Hospital Memory Clinic in Fort Worth, Texas for neuropsychological testing. John Peter Smith hospital is a publicly funded county hospital that receives frequent neuropsychological referrals; all referrals that meet the inclusion criteria will be included within this study. The current study is in adjunct to larger studies implemented by Dr. Andrew Houtz, a neuropsychologist. At the time of proposal, Dr. Houtz was a neuropsychologist at JPS; he has since left JPS for private practice.

John Peter Smith county hospital typically serves ethnic and/or racial minority individuals of lower socioeconomic standing and from lower educational and occupational achievement. Included individuals in the database are of age 50 and older, have at least a second grade educational level and are English speaking. Assessment protocol limitations (i.e., English protocols, norm groups) and interpreter restrictions severely impeded the ability to include participants with other primary languages. Specifically, first-generation, non-English speaking Hispanics were excluded from the sample used for this study. In addition, included participants were individuals without significant auditory and visual impairments (i.e., impairments that could not be corrected via glasses or hearing aids). Participants were only included if they expressed an adequate verbal ability as established by the Peabody Picture Vocabulary Test-Third Edition. The last inclusion criteria asserted that only first time referrals were to be included and those

who were actively taking medications specified for dementia were excluded. This criterion was established to control for any perceived dementia medication affects.

Adherence to the aforementioned criteria, allowed for 231 participants within the studied sample. Of the 231 participants, 84 (36.4%) were male and 147 (63.6%) were female. Participants ranged in age from a minimum of 50 years to a maximum of 90 years (M = 70.6; SD = 9.3). In addition, race/ethnicity was also recorded and identified group memberships are as follows: 174 (75.3%) Caucasians, 30 (13%) African Americans, 26 (11.3%) Hispanics and 1 (0.4%) individuals chose a different group membership that was classified as Other.

A diabetes diagnosis was established via the patients' self-report of using exogenous insulin or oral hypoglycemic medications for diabetes and/or stating a history positive for diabetes. The patients' self-report was then confirmed via consultation with the treating physician, a reference to medication use and a chart review. Included participants were receiving treatment for diabetes within the JPS hospital system. Patient characteristics for diabetes included 86 (37.2%) with diabetes and 145 (62.8%) without diabetes.

Group assignments for dementia type and presence were specified via specific inclusion criteria. A diagnosis of AD was based on NINCDS-ADRDA criteria. A diagnosis of Vascular Dementia was given when the participant met NINDS-AIREN criteria. A Mild Cognitive Impairment diagnosis was established on DSM-IV criteria. Multimodalities were used in determination of diagnostic criteria and included a consensus of the following: extensive neuropsychological battery, geriatrician assessment, computed tomography (CT) scan, laboratory tests and a history and physical

performed by a geriatrician. With inclusion of these modalities, the division of diagnosis is as follows: 63 (27.3%) had AD, 114 (49.4%) were classified with VD and 54 (23.4%) were considered to have MCI.

An additional variable, Dementia/Diabetes, was formulated to compare groups with dementia and no diabetes to groups with comorbid diagnoses of diabetes and dementia. With the combinatory approach, participants comprised the following six groups: Alzheimer's Disease with diabetes (AD & Diabetes), Alzheimer's Disease without diabetes (AD & No Diabetes), Vascular Dementia with diabetes (VD & Diabetes), Vascular Dementia without diabetes (VD & No Diabetes), Mild Cognitive Impairment with diabetes (MCI & Diabetes) and Mild Cognitive Impairment without diabetes (MCI & No Diabetes). The following depicts the group compositions: 20 (8.7%) had AD & Diabetes; 43 (18.6%) with AD & No Diabetes; 46 (19.9%) were classified with VD & Diabetes; 68 (29.4%) had VD & No Diabetes; 20 (8.7%) with MCI & Diabetes; 34 (14.7%) of the population had MCI & No Diabetes.

Other variables such as handedness and educational level were garnered through patient self-report. Statistical analyses revealed 217 (93.9%) of the participants were right-handed whereas 14 (6.1%) of the participants were left-handed. Educational level ranged from 2 years of education to a maximum of 18 years of education (M = 12.6; SD = 2.6). The aforementioned descriptive statistics for the categorical variables are noted below in Tables 1 and 2.

Table 1

Descriptive Statistics for Categorical Demographic Variables

		N	%
Gender			
	Male	84	36.4
	Female	147	63.6
	Missing Data	0	0
Race/Ethnicity			
	Caucasian	174	75.3
	African American	30	13.0
	Hispanic	26	11.3
	Other	1	0.4
	Missing Data	0	0
Diabetes			
	Present	86	37.2
	Absent	145	62.8
	Missing Data	0	0
Diagnosis			
	Alzheimer	63	27.3
	Vascular	114	49.4
	MCI	54	23.4
	Missing Data	0	
Handedness			
	Right	217	93.9
	Left	14	6.1
	Missing Data	0	0

Table 1 Continued

Dementia/Diabetes			
	AD & Diabetes	20	8.7
	AD & No Diabetes	43	18.6
	VD & Diabetes	46	19.9
	VD & No Diabetes	68	29.4
	MCI & Diabetes	20	8.7
	MCI & No Diabetes	34	14.7

Table 2

Descriptive Statistics for Continuous Demographic Variables

	N	*M*	*SD*	Range	Skewness	*SE* Skew	Skew / *SE* Skew	Kurtosis	*SE* Kurt	Kurt / *SE* Kurt
Age (yrs)	231	70.6	9.3	50-90	-.20	.16	-1.2	-.80	.32	-2.4
Education (yrs)	226	12.6	2.6	2-18	-.42	.16	-2.6	1.6	.32	5.1

For the purpose of this study only data from the following measures will be analyzed: Rey-Osterrieth Complex Figure Test Copy and Rey-Osterrieth Complex Figure Test Recall, 7-Minute Screen (i.e., Uncued, Cued and Forgotten), Pillbox Test (Pass/Fail), portions of the Western Aphasia Battery (e.g., Fluency, Species), Check Writing Test (Pass/Fail), the Clock Drawing Test and the Peabody Picture Vocabulary Test-Third Edition. These tests were chosen because of the surplus of supporting research that buttressed their ability to distinguish and identify specific neurological deficits; the measures and supporting research are discussed below. Additionally, these tests were utilized as measures within a larger neuropsychological battery; all measures were outlined in the later text.

Measures

Rey-Osterrieth complex figure test The Rey-Osterrieth Complex Figure Test (ROCF; Rey 1941) is a common neuropsychological test used to assess for deficits in an individual's visuospatial organization, planning and memory (Brauer-Boone, Ponton, Gorsuch, Gonzalez & Miller, 1998; Caffarra, Vezzandini, Dieci, Zonato & Venneri, 2002; Corwin & Bylsma, 1993; Kasai et al., 2006; Osterrieth, 1944; Weinstein, Kaplan, Casey & Hurwitz, 1990). The ROCF was originally developed by Rey in 1941 and later elaborated by Osterrieth in 1944. Osterrieth expounded upon Rey's original figure and developed a supplementary system for scoring various components of the complex figure (Osterrieth, 1944); his method of analysis is the most frequently utilized in clinical practice (Rapport, Charter, Dutra, Farchione & Kingsley, 1997). The test assesses visuospatial organization, planning and memory via a complex drawing that requires the individual to plan, use organizational skills and implement problem-solving strategies

when copying the complex bidimensional figure (Caffarra et al., 2002). In addition, this test requires individuals to engage their non-verbal short-term memory as well as perceptual and motor skills when copying and recalling the complex figure (Grossman et al., 1993; Strauss, Sherman & Spreen, 2006).

The ROCF is a timed paper and pencil test with a maximum time limit of five minutes for the Copy portion and a minimum time limit of two minutes on the Recall portion. The patient is asked to copy the complex design on a plain sheet of 8 ½ x 11-inch paper and approximately 20 to 30 minutes later, recall and reproduce the design. The complex figure is evaluated on the Lezak-Osterrieth scoring system (Lezak, 1995). This system divides the complex figure into 18 components; each component is awarded a maximum score of 2 points, with a possible range from 0 to 2 points (Lezak, 1995; Rapport et al., 1997). The Lezak-Osterrieth scoring system requires the scorer to make subjective judgments for each item based on the component placement and accuracy of reproduction (Rapport et al., 1997; Strauss et al., 2006). The designated score depends on the overall quality of reproduction. For example, components with accurate reproduction and correct placement are scored as a 2 whereas items with only one of these variables are given 1 point. The components are allotted 0.5 points when inaccurate and misplaced and 0 points when missing (Rapport et al., 1997). This scoring system is implemented for the Copy and Recall portions and overall scores range from a maximum of 36 points to a minimum of 0 points (Lezak, 1995; Rapport et al., 1997).

Various researchers have used the ROCF to identify the relationship between age and performance deterioration (Boone, Lesser, Hill-Gutierrez, Berman & D'Elia, 1993; Chiulli, Haaland, LaRue & Garry, 1995). Findings from this research suggest a

progressive, yet steady, decline in visuospatial memory which begins in middle adulthood or ages 40 to 50 (Boone et al., 1993; Chiulli et al., 1995; Gallagher & Burke, 2007). This decline progresses until around age 70 when dramatic drops in composite scores are noted. Specifically, tested individuals had an increased number of omitted detail items that resulted in decreased visuospatial performance in normal aging individuals. These visuospatial deficits were distinct and did not assume the typical dementia profile of overall distortion of elements (Boone et al., 1993; Spreen & Strauss, 2006). In fact the authors purport this omission pattern is indicative of impaired storage commonly associated with the normal aging process (Boone et al., 1993).

In addition to age related performances, research findings suggest significant correlations between visuospatial performance on the ROCF and the additional factors of gender, education and overall intelligence (Boone et al., 1993; Fastenau, Denburg & Hufford, 1999; Gallagher & Burke, 2007). Specifically, one study recorded that higher scores on the ROCF correlated with higher scores on intelligence measures (Boone et al., 1993). Although the literature is robust in support of the above relationships, a study by Strauss and colleagues (2006) did not find a significant relationship between visuospatial performance and gender, education or ethnicity. Another study also dismissed the relationship between education and ROCF performance (Meguro et al., 2001).

In regards to test-retest reliability, estimates are low for elderly individuals after a one-year lapse between testing; coefficients range from 0.57 to 0.68 for immediate Copy and coefficients range from 0.57 to 0.77 for delayed Recall. No exact figures were provided within this study, however the researchers did find good to excellent convergent

and discriminant validities for normal older controls and patients with dementia (Strauss et al., 2006).

Not only has the relationship between normal aging and visuospatial performance been examined but researchers have diligently studied the visuospatial deficits associated with dementia. For example, researchers utilized between groups comparison of visuospatial performance for Alzheimer's and Vascular dementia individuals as compared to normal controls (Cherrier, Mendez, Dave & Perryman, 1999; Freeman et al., 2000). Findings revealed individuals with a dementia diagnosis had poorer visuospatial performance as compared to normal controls. Of interest, Freeman et al. (2000) noted individuals with Alzheimer's Dementia performed better in comparison to those with Vascular Dementia on the Copy portion. However, on the Recall portion, those with Vascular Dementia were able to recall more details of the figure as compared to participants with Alzheimer's Dementia (Freeman et al., 2000). Cherrier and colleagues (1999) found individuals with Alzheimer's disease performed significantly worse on the left category of the ROCF. This decreased performance suggests left hemispatial inattention. These findings are instrumental and left hemispatial deficits not only affect attention but visual scanning abilities; both tasks are essential in the completion of many activities such as driving, gait faculties and complex tasks (Cherrier et al., 1999). As mentioned in Chapter I, Vascular Dementia stems from complex interactions between vascular etiologies, alterations in the brain and an individual's personal variables; therefore, the destruction of these factors is highly variable and may impact any brain area (Elias et al., 1999; Erkinjuntti, 2002; Launer et al., 1996; Leys, Pasquier & Parnetti, 1998; Verhaeghen, Borchelt & Smith, 2003). With the variable impact of the vascular

pathology, it is not out of the ordinary the researchers did not find a specific area of deficit. The current study will use the raw Copy score and the raw Recall score for the analyses.

7 minute neurocognitive screening battery The 7 Minute Neurocognitive Screening Battery (7MS), or 7 Minute Screen™ (Janssen Pharmaceutica & Research Foundation, Titusville, New Jersey, www.janssen.com), is a test for cognitive impairment used to differentiate between patients with AD and those without (Solomon et al., 1998). This test was devised with the premises of being rapidly administered and of not requiring extensive training or clinical judgment (Solomon et al., 1998). The 7 Minute Screen is purported to take approximately 7 minutes and 42 seconds to administer and is useful in primary care settings and long term care facilities (Langbart, 2002; Solomon et al., 1998). Contrary to the test name and assertions of Solomon and colleagues (1998), the actual administration required a range from 6 to 11 minutes and depended on variables such as participant and administrator characteristics.

This 7 Minute Screen is comprised of four tests specifically designed to test the corresponding cognitive areas most frequently affected in Alzheimer's Disease; these areas are as follows: memory, verbal fluency, visuospatial and visuoconstruction and orientation for time (Solomon et al., 1998). This study was particularly interested in the ability of the Memory portion to distinguish between those with dementia and those without. In particular, response pattern differences will be examined to determine if any differences are noted between groups (i.e., MCI, AD and VD). The Memory assessment portion required the patient to correctly identify 4 pages of 16 pictures (i.e., 4 pictures per

page) after the examiner provided a semantic cue for each picture (e.g., There is a bird on this page, what is it?). The patient is next tested for immediate recall (e.g., I just showed you a picture of a bird, what was it?). After a distracter task, the patient is asked to recall the items again; if needed the same semantic cues are given as in the learning portion. These cues provide a verbal stimulus to help prompt the individual to recall additional items.

This study will specifically look at score differences on the Total Raw Recall (i.e., a combination of Uncued and Cued responses) as well as differences on the Uncued recall score and the Cued recall score. A possible total of 16 points may be accrued within the Total Raw Recall (i.e., Uncued plus the Cued responses). Similar to the name, the Uncued Recall is a score derived from the number of items the individual is able to freely recall without any verbal prompts. The Cued recall is given immediately after the Uncued and during this portion, the examiner provides the individual with a verbal cue (e.g., I showed you a picture of a bird earlier, what was it?). The Cued and Uncued recall enable the examiner to assess the individual's long-term episodic memory (Del Ser, Sanchez-Sanchez, de Yebenes, Otero & Munoz, 2006).

Although this test provided a measurement for visuospatial deficits (i.e., Clock Drawing test), the Clock Drawing test was administered later within the battery and implemented a different scoring system whereby one point was assigned for the following variables: click circle, clock numbers, clock hands and specific time (i.e., Solomon et al., 1998, used a raw score with a maximum of 7 points). This information will be discussed later within the methods section.

According to researchers, age, sex and education do not appear to influence one's performance on the 7MS (Solomon et al., 1998; Solomon & Pendlebury, 1998; Tsolaki et al., 2002). Contrary to the above research, a different study revealed a relatively modest influence of age, education and gender was documented on the 7MS performance (Skjerve et al., 2007).

Although documentation exists on both sides in regard to other variable influence, authors agree that the 7 Minute Screen has a strong test-retest reliability for the different subtests (i.e., $r = 0.92$, Memory subtest). Solomon and his contemporaries (1998) analyzed a sample that involved an older community-dwelling adult population. They utilized a logistic regression to assess inter-rater reliability and found a reliability of 0.93. Each of the four tests were able to detect patients with Alzheimer's disease within the 92 percent accuracy and able to detect normal patients within 96 percent accuracy. For AD, the 7MS has demonstrated 92.9 percent sensitivity for identification of AD with a specificity of 96 percent for non-demented older adults (Meulen et al., 2004; Scinto & Daffner, 2000; Solomon & Pendlebury, 1998; Solomon et al., 1998; Tsolaki et al., 2002;). Meulen and colleagues (2004) also found a sensitivity of 89.4 percent with a specificity of 93.5 percent for other dementias.

Due to this instrument's ability to identify Alzheimer's disease, some individuals prefer this instrument over the Mini Mental State Exam (MMSE; Folstein et al., 1975) specifically because the 7MS assesses visuospatial skills and verbal fluency to a greater extent than the MMSE (Meulen et al., 2004; Shores et al., 2004; Sobow et al., 2001). Authors do suggest the entire battery to be a better predictor than any individual scale (Solomon et al., 1998).

Interestingly, the validity of the 7MS appears to hold when translated into different languages. Specifically, Del Ser and coworkers (2006) found the 7MS to be a valid assessment for the presence of dementia within the Spanish population.

The pillbox test The Pillbox test was designed by Houtz (2003) as a method to measure one's functioning within the environment. The Pillbox test was formulated as a method to measure executive function via replicating an instrumental activity of daily living (i.e., medication administration; Zartman, 2006). Houtz utilized current hypotheses that emphasized ecologically valid measures to be the most beneficial in providing current patient function information to physicians, healthcare providers, patients and families. Ecologically valid measures not only measure real-world function but enable formation of a concrete treatment plan that accounts for real-world tasks. Brose and Houtz (2003) believe the Pillbox Test encompasses four domains of executive function as outlined in Lezak's model of the Executive Function construct.

Houtz identified a "real-world" task that oftentimes present as a problem for geriatric patients and result in over medicating or under medicating complications. With this knowledge he utilized a standard weekly pillbox and five pill containers with specific administration instructions. The weekly pillbox contained 4 rows (i.e., breakfast, lunch, dinner and bedtime) and seven columns, each one representing a day of the week. Each pillbox compartment was labeled for time of day and was accessed via an open/close snap lid. Each pill container held an unspecified number of the same colored pills (i.e., beads) with a different color in each container. Printed pharmacy administration

instructions were placed on the container's label and followed typical pill administration protocols (Houtz, 2003).

The Pillbox Test examined an individual's Executive Function via the expectations that the patient will inhibit knowledge of their current medication regimen in regards to pill color and/or similar instruction and successfully follow test instructions. With this premise, the Pillbox test required the patient to have intact volition and inhibition. The test also commanded the patient to formulate an appropriate plan to complete this task as well as sustain attention throughout the task; both of which incorporated elements of the Planning and Attention Executive Function domain. Additionally, the patient must understand when to stop placement of pills into the pillbox (i.e., based on administration directions) and the patient should self-monitor behavior (Brose & Houtz, 2003; Houtz, 2003). The aforementioned required the individual to utilize elements of the Effective Performance and Self-Monitoring Executive Function domain. Abilities within the Purposive Action and Self-Regulation Executive Function domain were also noted, as the test necessitated a patient to make inferences from the medication instructions, reason alternative solutions, mentally shift between medication instructions, demonstrate working memory and demonstrate motor programming. Therefore, the Pillbox Test is expected to provide a more encompassing and sensitive measure in comparison to previous measures of Executive Function (Brose & Houtz, 2003; Houtz, 2003; Zartman, 2006).

Houtz (2003) considers the Pillbox Test to be a more effective measure of Executive Function due to the test's ability to compensate for some weaknesses typically seen in other tests of Executive Function. Primarily, the Pillbox Test is a more effective

measure as it utilizes a typical instrumental activity of daily living and does not invent or rely on completion of a set of steps or patterns for success. Given the test design and use of a familiar activity, the Pillbox Test is expected to have greater test-retest reliability estimates as compared to other standardized measures of Executive Function. Additionally, the test directions are ambiguous and the examiner does not interfere with the patient's activity or placement once the test has begun. Utilization of this format inhibited the examiner from assisting and/or assuming the role of the patient's frontal lobes (Brose & Houtz, 2003; Houtz, 2003).

The Pillbox Test is presented to the individual in the following yet precise manner. First, the examiner placed the pillbox (i.e., with compartments in the open position) and the pill containers in front of the individual. The individual is then instructed to place the medication in the pillbox via specified pill bottle label instructions for the week. Next, the individual is allotted approximately five minutes to complete the task. The examiner will record the number and placement of the beads within each compartment on a separate sheet of paper. Numbers of commissions, or extra included pills, and omissions are then assessed.

A pilot study, conducted at JPS county hospital, was used to set the number of pills and administration directions (Brose & Houtz, 2003). A chart review of 50 memory clinic patients (i.e., referred to JPS) established that on average, referred individuals took five daily medications; this finding was congruent with other research (Burdick et al., 2005). The pill administration procedures (i.e., found on the pill bottles) are as follows: one tablet every other day (i.e., red pills); one tablet daily in the morning (i.e., blue pills); one tablet three times a day (i.e., yellow pills); one tablet twice a day with breakfast and

dinner (i.e., green pills); and one tablet daily at bedtime (i.e., orange pills; Brose & Houtz, 2003; Houtz, 2003). These obscure directions forced the individual to make conclusions. Inferences based upon obscure labels are known to influence daily consumed medications via commissions and omissions (Willis, Dolan & Bertrand, 1999). Brose and Houtz (2003) chose the bead colors to coordinate with commonly prescribed medications (i.e., aspirin, anti-hypertensive and arthritis medications).

Not only did this pilot study identify the aforementioned, but the pilot recognized a significant correlation between the Pillbox Test and the presence of organic pathology on a Computed Tomography (CT) scan. Organic pathology as measured by a CT scan is indicative of a neurological insult (Brose & Houtz, 2003). The pilot study also compared individuals' scores on the Pillbox Test to their scores on the Mini Mental State Examination (MMSE), a highly utilized measurement for cognitive impairment. Comparisons of these tests identified that the Pillbox Test demonstrated higher sensitivity for Executive Function (Brose & Houtz, 2003). Interestingly, 15 individuals who scored above the normal cutoff of 25 on the MMSE obtained complete failures on the Pillbox Test. Data from the pilot study supported the assertion that the Pillbox Test may be an ecologically valid performance based measure of medication planning and medication adherence as a whole (Brose & Houtz, 2003).

For the purpose of this design, the overall Pillbox Test score was classified as pass or fail and used in comparison of group differences. The pass or fail designation was given based upon the total number of errors which is the sum of three specific error types. The first error type was total omission errors, or the number of pills omitted from the pillbox. The next error reflected the number of misplaced pills; this error represents a

correct number of pills for the day but with incorrect placement (e.g., a morning pill misplaced in the lunch compartment). The final error recognized any commissions or additional pills beyond the original requirements (Brose & Houtz, 2003). Although the main focus of this study was on the Pillbox test pass/fail, examination of the total pills used and the total errors will also be analyzed (i.e., to better conceptualize group differences).

Direct assessment of functional status The Direct Assessment of Functional Status (DAFS; Loewenstein et al., 1989) is an assessment designed to provide a behaviorally oriented measurement of instrumental activities of daily living. Lowenstein and colleagues (1989) recognized the need for a direct assessment of functional status. This instrument was designed with the intent to examine functional competence, an area of functioning which often becomes impaired in Alzheimer's disease and other states of cognitive decline (Arguelles, Loewenstein, Eisdorfer & Arguelles, 2001). The DAFS is comprised of seven different domains that test an individual's ability in the domains of communication (e.g., look up a telephone number, dial a telephone), financial skills (e.g., count currency, balance a checkbook, write a check), transportation (e.g., response to traffic signs), shopping skills (e.g., prepare a grocery list, obtain the items), orientation (e.g., date, day, month), dressing/grooming skills (e.g., teeth brushing, buttoning a coat) and feeding (e.g., cutting up food, pouring water; Loewenstein et al., 1989; Tomaszewski, Farias, Harrell, Neumann & Houtz, 2003; Zanetti, Frisoni, Rozzini, Bianchetti & Trabucchi, 1998). Research emphasized these activities were integral aspects of daily living and allowed for a safe living environment (Loewenstein et al.,

1989; Willis, Dolan & Bertrand, 1999; Zanetti et al., 1998). According to research by Loewenstein and colleagues (1989), the DAFS had high inter-rater and test-retest reliabilities. In addition, convergent validity was documented via significant correlations between the scale and established measures of functional status.

The current study utilized only the check-writing portion of the assessment; this subtest is similar to the Pillbox Test in that it was an ecologically valid assessment that measured an individual's ability to perform the real-world function of writing a check for a purchase. With this subtest, individuals were asked to write a check to a specific store (i.e., any store they choose) for any amount desired. Upon completion, the individual was given a pass/fail score which was based on correct completion of the following: date, store name, amount in numbers, written amount and the total score (Loewenstein et al., 1989). For the purposes of this study, only the total pass/fail score from the total score was used.

Western aphasia battery The Western Aphasia Battery (WAB; Kertesz, 1982; Kertesz & Poole, 1974) is a test designed to measure the clinical aspects of language function. Specifically, the originators of the WAB were interested in measuring the following facets of language function: content, fluency, auditory comprehension, repetition and naming, reading, writing and calculation (Bakheit, Carrington, Griffiths & Searle, 2005; Kertesz, 1982). In addition to these areas, the WAB sought to measure the individual's nonverbal skills of drawing, block design and praxis. The WAB is a validated test that is easily administered in approximately 60 to 90 minutes (Bakheit et al., 2005). The administration may be divided into sections and given at different times.

Of interest, the WAB may be administered as independent units (i.e., oral portion, reading, writing, calculation and praxis) and the nonverbal tests are optional (Kertesz, 1982). Each subtest was scored on a numerical scale and summed to obtain an overall score that represented the aphasia quotient (AQ; i.e., oral portion of language assessment) and/or the cortical quotient (CQ; i.e., nonverbal scores; Bakheit et al., 2005). A taxonomic table was then used to allow a practical classification of the patient (Kertesz, 1979).

Since its development, the WAB has been extensively standardized (Kertesz, 1979; Shewan and Kertesz, 1980). The independent oral language portion (i.e., summarized as the Aphasia Quotient) was designed to elicit conversational speech from the individual in response to questions asked in the context of an interview and a picture description. Some leniency was allowed during this portion where alterations of the wording and encouraging comments were permitted. The information content measured functional communication ability. Repetition was tested by high frequency single words of increasing length, composite words, numbers, number-word combinations, high and low probability sentences and sentences of increasing length and grammatical complexity (Kertesz, 1982).

The naming of objects on visual confrontation constituted 60 percent of the naming score and consisted of 20 familiar prototypical objects commonly available. These objects were individually shown to the individual and included common items such as a fork, a ball and a paperclip. The patient was presented the object and asked to name the object upon visual presentation. If the individual was unable to name the object or if the incorrect response was given, the individual was allowed to palpate the object.

After palpation, if the object name was not readily given, the examiner provided a phoneme of the word as a clue. If the presented object was a compound word, the first half was given as a semantic prompt. The patient had twenty seconds to identify the object with the above described if necessary (Kertesz, 1982). Responses were recorded and scored via a standardized format. The examiner was encouraged to ignore minor articulatory errors; however phonemic paraphasias received two points versus a total of three points. Responses to tactile or phonemic cues were only given a partial score of one point (Kertesz, 1979; Kertesz & Poole, 1974; Shewan & Kertesz, 1980).

Next, word fluency was measured by requesting the patient to name as many animals as possible within one minute. Previous studies have shown this test to be highly sensitive to any present brain damage and studies demonstrated that even nonaphasics may score low (Kertesz, 1979; Shewan & Kertesz, 1980). Noteworthy, individual variation in performance among normal populations was seen particularly if the individual was anxious or easily distractible. Upon administration, the patient was prompted with examples at the beginning and at 30 seconds if no response was forthcoming (Kertesz, 1982; Kertesz & Poole, 1974). Sentence completion and responsive speech are an automatic variety of speech function but each involve the process of word finding in a specific context and should be considered along with naming (Kertesz, 1982). Although typically interpreted in its entirety, for the purpose of this study, the animal naming or word fluency will be analyzed. The numbers of named animals in addition to the number of different named species will be analyzed to determine any significant group differences.

Clock drawing test The Clock Drawing Test (CDT) is an easily administered test designed to measure frontal and temporo-parietal functions. The CDT was designed to enable the neuropsychologist, neurologist or other medical professional to measure for cognitive dysfunction secondary to dementia, delirium or a range of neurological and psychiatric illness. Oftentimes, the CDT was administered in conjunction with other screening tests such as the Mini Mental State Examination and was an included component of the 7 Minute Neurocognitive Screening Battery (Solomon et al., 1998). The CDT was originally formulated to be administered as follows. The patient was given a sheet of paper and prompted to adhere to oral instructions which asked him to draw a clock face, mark the hours and then place the hands to indicate a specified time. Researchers noted that a potential dissociation based on task demand may have transpired with the above directions. To counteract any dissociation, patients were next asked to draw a clock or copy a clock (Kaplan, 1980). Kaplan explained the potential dissociation and stated that if a patient with right parietal lesion was asked to draw a clock, potential deficits such as inattention for the lower left quadrant may have gone unnoticed. Contrary, if the same patient was only asked to copy a clock, deficits such as the absence of global contour and left upper inattention may have been missed.

When originally formulated, the patient was asked to set the hands of the clock to 20 after 8. Kaplan (1980) believed a precise time setting was important and suggested appropriately placed hands (i.e., in each parietal hemifield) would thereby measure for potential neglect. Kaplan's research (1980) prevailed and she opted for the time placement of 10 after 11 because this hand placement would increase task demand for patients with right frontal lesions (i.e., these patients are drawn to the sensory perceptual

features of a stimulus). Additional research suggests this particular requirement required inhibition of one's frontal pull response (Riegel et al., 2002; Senanarong et al., 2005; Strauss, Sherman & Spreen, 2006).

Researchers believe the CDT utilized a number of cognitive, motor and perceptual functions which were required simultaneously for successful completion (Lam, Fung & Ng, 1998). Additionally, orientation, conceptualization of time, visual spatial organization, memory and executive function, auditory comprehension, visual memory, motor programming, numerical knowledge, semantic instruction, inhibition of distracting stimuli, concentration and frustration tolerance have been identified as contributing to successful completion of the CDT (Estaban-Santillan, Praditsuwan, Ueda & Geldmacher, 1998; Lam et al., 1998; Royall, 1996; Shulman, 2000). Interestingly, Royall (1996) believed the executive function necessary for clock-drawing, required a patient to control functions which would guide her complex goal-directed behavior with novel and ambiguous cues. Royall (1996) considered the above similar demands to be an integral part of independent living skills; results may indicate how a patient is currently functions within her environment.

With regards to the above, a normal clock was considered indicative of intact functions and provided evidence that the patient may have capabilities to continue independent living (Royall, 1996). Contrary, an abnormal clock may indicate the presence of cognitive problems that would warrant further investigation and/or resource allocation (Royall, 1996; Shulman, 2000). Furthermore, while a grossly abnormal clock demands immediate attention, mild errors may also require further investigation. Shulman (2000) believed the use of serial clock drawings could be a valuable tool for

following the progressive dementia process. Minor errors may suggest early presence of dementia and arm placement an indicator of early onset (Esteban-Santillan et al., 1998).

Clock errors are best conceptualized in the following categories: visuo-spatial, perseveration and grossly disorganized. Patients with Alzheimer's Disease manifested common errors with perseveration, counter-clockwise numbering, absence of numbers and irrelevant spatial arrangement. Errors which followed a stroke may reflect spatial neglect, hemianopsia and sensory loss (Freidman, 1991). In their study, Lam and colleagues (1998) were unable to differentiate Alzheimer's Disease and Multi-infarct Dementia via clock errors.

Contrary to the above, Shulman (2000) reports sensitivity and specificity, likelihood ratio and positive predictive value for the CDT. These advantages have been used to measure the potential value of the clock-drawing test as a screening tool. According to Shulman (2000) sensitivity (i.e. few false negatives) to dementia across many studies range from 75 percent to 92 percent with an average of 85 percent and is dependent on the population being assessed. Whereas specificity (i.e., few false positives) ranges from 65 percent to 96 percent with an average of 85 percent, however clock errors may predict many conditions in addition to dementia. Therefore, Shulman (2000) suggested it to be pertinent for healthcare professionals to maintain a wide differential diagnosis with clock errors.

Typically, the Clock Drawing Test was scored based the following variables: intact circle, numbers, hands and correct time. Each of these items was given a point when correct with a possible total of four points. The total score was utilized within this

study; acquisition of four points was deemed as a pass and any deviations were considered a fail.

Peabody picture vocabulary test-third edition Dunn and Dunn (1981, 1997) developed the Peabody Picture Vocabulary Test-Third Edition (PPVT-III) to assess receptive vocabulary abilities. Standardization of the PPVT-III was on a carefully selected population that matched the demographic composition for the 1994 United States census. Specifically, matched factors included age, sex, socioeconomic status, ethnicity and overall geographical distributions (Smith, 1997). This standardization allowed for the age range to be extended to encompass ages 2 ½ to 90 plus years (i.e., the prior revised form only assessed ages from 2 ½ to 40 years; Dunn & Dunn, 1981; Smith, 1997).

The PPVT-III is often administered to determine an individual's premorbid intelligence and overall general mental abilities (Lezak, 2004). Given the premise that vocabulary is crystallized intelligence, vocabulary is thought to remain intact through the beginning stages of dementia. Contrary, researchers urge the use of the PPVT-III as only a screening tool and not as a primary diagnostic tool (Strauss, Sherman & Spreen, 2006).

The PPVT-III is available in two forms, A and B, and is arranged in order of increasing difficulty. For example, a simple word such as bed will come early within the test whereas a more difficult word like dromedary will come towards the end. Analysis of the PPVT-III indicated receptive vocabulary continued to increase until age 60 and manifested a minimal decline in the 61 to 90 plus group (i.e., demonstrated on form A and B). Furthermore, expressive vocabulary yielded a decline in the 51 to 60 year old

group with a significant decline in the 61 to 90 plus group (i.e., form A and B; Dunn & Dunn, 1997; Smith, 1997).

Administration of the test involved the examiner showing four illustrated pictures contained on a page. The examiner then stated a particular word and waited for the individual to point to the corresponding picture. Research demonstrated the PPVT-III was a solid instrument that had a high internal reliability (0.95), high test-retest reliability (0.91-0.94) and a high inter-rater reliability at 99.5 percent (Strauss et al., 2006). The PPVT-III was initially used within the neuropsychological battery to assess individuals' verbal abilities and to approximate premorbid functioning. This study was interested in the overall intelligence score and any significant differences between groups.

Design and Procedure

IRB approval was obtained first from John Peter Smith (JPS) and secondly from The University of North Texas, Denton. Data will be archival and taken from patients referred to the Memory Clinic at JPS for neuropsychological data. The database does not contain any identifying information and all identification (i.e., from original protocols) will be kept confidential in a separate database. All testing sessions were held in the morning to control for time of day effects on cognitive abilities, for this effect was a concern for elderly and neurological populations (Salthouse, Atkinson & Berish, 2003).

All participants were administered the below extensive neuropsychological battery as standard protocol. Trained masters and doctoral level examiners administered this battery and followed published administration instructions. The following assessments and measurements were given (i.e., tests are listed in administration order):

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-Third Edition; 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. In assure confidentiality, the examiner placed the participant's informed consent in a file separate from the test protocol. The protocol was then 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 then cross-referenced to a separate list that contained only the participant's code number and name (i.e., no scores or diagnoses were on this page). This list remained locked in a separate file cabinet in the possession of the principle investigator, Dr. Andrew Houtz. Dr. Houtz was the only individual permitted access to this identifying information. The assigned code number was entered into a SPSS database in conjunction with the participant's age, race, gender, handedness, education, diagnosis and raw assessment scores. Again, names and other identifying information were excluded from the SPSS database. The protocols were archived in the Department of Geriatrics/Memory Clinic at John Peter Smith County Hospital. Protocols were scored according to established test scoring criteria as outlined above and obtained raw scores as well as codes for pass/fail were entered into a database.

Limitations Potential limitations included a non-representative sample which accounted for some of the area demographics yet neglected others. Specifically, John Peter Smith county hospital typically served ethnic and/or racial minority individuals of

lower socioeconomic standing and the served individuals are typically from lower educational and occupational achievement. This study was able to sample individuals from lower socioeconomic standing, yet given the location and the fact this is a county hospital, individuals with moderate to high socioeconomic standing typically sought services from the surrounding area hospital facilities. In addition, this sample was over inclusive of Caucasians and under representative of African Americans, Hispanics and other race/ethnicities. This sample also excluded participants whom were unable to communicate in English. As previously mentioned, assessment protocol limitations (i.e., English protocols, norm groups) and interpreter restrictions severely impeded the ability to include participants with other primary languages. Noteworthy, Fort Worth, Texas has a concentration of first-generation, non-English speaking Hispanics; these individuals were excluded thereby further restricting the ability to generalize. In addition, necessary resources were not available to test individuals with significant auditory and visual impairments.

Lastly, the studied population was influenced by an over representation of females in comparison to males. Although limitations were present, the purpose of this study was to replicate findings from prior studies, study the influence of diabetes on cognition, to examine group differences within this county hospital served population and to analyze the effectiveness of the used neuropsychological battery.

Statistical analyses will be garnered via utilization of the Statistical Package for the Social Sciences (SPSS ver. 14.0). SPSS will be used to run descriptives, frequencies, correlations, parametric and essential nonparametric tests. A multivariate analysis of variance (MANOVA) will be employed to assess the influence of the dependent

variables, dementia and diabetes, on the neuropsychological tests. This test was deemed fundamental because MANOVA forms a linear combination of dependent variables for each main effect and interaction. Next, separate analyses of variance (ANOVA) will be run to determine whether mean differences among groups on a single dependent variable (e.g., dementia, diabetes) were to have occurred via chance. Furthermore, a discriminant function procedure will be utilized to determine which variables are related to the criterion variable (i.e., AD, VD and MCI) and furthermore predict values on the criterion variable when given values on the predictor variables. A discriminant function was chosen because it uses a weighted combination of those predictor variable values to classify an object into one of the criterion variable groups. Basically the discriminant function test will assign a value on the qualitative criterion variable. The parameters of weights and cutoff scores will be used to minimize the amount of classification errors (Kachigan, 1991). This study utilizes four discriminant functions to determine if dementia group membership can be predicted reliably from the neuropsychological measurements. The first discriminant function will attempt to predict group membership into either AD or VD via scores on all the neuropsychological tests. The second discriminant function will expound upon the first and determine if the test scores are able to reliably predict group membership to AD, VD or MCI. Two additional discriminant functions will be run in the same manner as above, however, only the test scores of Rey Recall, 7MS Uncued, 7MS Cued and 7MS Forgotten will be used in an attempt to predict group membership. Again, these measures are particularly sensitive to any memory deficits. Results will be considered significant if $p \leq 0.05$.

CHAPTER III

RESULTS

Descriptive Statistics

Basic descriptive statistics were used to analyze the variables and neuropsychological tests measurements and included the following: count, mean, standard deviation (*SD*), range, skewness, standard error of skewness (*SE* Skew), skewness divided by *SE* Skew, kurtosis, standard error of kurtosis (*SE* Kurt) and kurtosis divided by *SE* Kurt. A quick reference to Tables 1 and 2 revealed distributions were not equal for gender, race/ethnicity, diabetes and diagnosis. Additionally, the mean age was 70.6 years; an expected age given the presence of dementia is most often detected during later years with a demarcation at age 65. The age of 65 is employed by professionals to designate between early or late onset of AD (Golde, 2003; Toyota et al., 2007). Interestingly, the mean education within this study was 12.6 years thereby indicating a greater number of the participants completed high school with several of them pursuing additional education.

Due to a large sample size, the skewness and kurtosis divided by the standard error of skewness and kurtosis respectively for each test were used to compare the obtained value to the Z-value for the chosen alpha level. These analyses were run on continuous measurements. In addition, counts, percentages and valid percentages were used to analyze the dichotomous variables of Pillbox and Check Writing tests. The Rey-Osterrieth test was divided into two portions, Copy and Recall, and results were reported in terms of assigned points for design completion (i.e., 36 possible points). For the Copy portion, results ranged from 0 points (i.e., individuals whom were unable or refused to

draw the design) to 36 points (i.e., individuals whom drew a perfect design; *M* = 27.0; *SD* = 8.8). Analysis of the Recall portion revealed a decrease in points potentially due to a planned delayed which forced the individual to recall and produce the previously seen drawing. Difficulties with encoding and retrieving the information perturbed the individuals ability to perform at the same level on the Recall as compared to the Copy task; results ranged from 0 points to 33 points (*M* = 9.1; *SD* = 6.8).

Next the 7MS sections (i.e., Uncued, Cued and Forgotten) were analyzed; a total of 16 points was possible. Analysis of the Uncued section for 231 participants identified scores ranged from 0 points (i.e., essentially all shown pictures were forgotten) to 16 points (i.e., all pictures were recalled; *M* = 7.8; *SD* = 3.0). The 7MS Cued section, a section which the examiner gives prompts (e.g., "I showed you a piece of fruit earlier. Do you remember what it was?"), revealed a point range from 0 points to 13 points (*M* = 4.2; *SD* = 2.9). Lastly, the Forgotten 7MS results, a section measuring the number of items essentially forgotten, ranged from 0 points (i.e., none forgotten) to 16 points (i.e., all items were forgotten; *M* = 4.2; *SD* = 4.5). Possible permutations may consist of points in only one category (e.g., Uncued) or range from two to three of the categories (e.g., points in Uncued, Cued and Forgotten).

The Pillbox Test was examined on three different aspects as follows: Total Error, Total Pills and Pass/Fail. The Total Errors measurement consists of any commissions, or extra included pills, misplaced pills and omissions within the weekly Pillbox. Errors for 231 participants were analyzed and results ranged from 0 or perfect completion of the instructions to 139 errors (*M* = 24.6; *SD* = 24.4). Total Pills for 231 participants were also analyzed to determine and gross differences between groups. Total Pills accounts for all

correct medication administrations (i.e., 53 possible pills) as well as any commissions; results ranged from 0 pills (e.g., participants whom were unable or refused to complete the task) to 140 pills (M = 41.7; SD = 20.9). As previously stated in the Methods section, individuals are designated pass or fail based upon the total number of errors which is the sum of three error types (i.e., omission errors, misplaced pills, commission errors; Brose & Houtz, 2003). Of the 231 participants, 67 (29%) passed and 164 (71%) failed; loose interpretation of this ecologically valid instrument indicated that approximately 71 percent of the studied sample are not taking their medications as prescribed by their primary care physician. Given consideration to prior studies (Brose & Houtz, 2003) as well as current findings, it is most likely these individuals are over or under medicating on a frequent basis. With failure to adhere to a medication regimen, these individuals are apt to have greater deterioration in health. The possible ramifications of misuse of aspirin, anti-hypertensive, oral hypoglycemic medications, etc. may include progression of the medical illness, accidental overdose and/or potential adverse reactions.

The DAFS Check Writing test, another ecologically valid test, was also analyzed via obtained score. A score was designated upon completion, and was based on the following items: date, store name, amount in numbers, written amount and the total score (Loewenstein et al., 1989). Correct completion of these items earned a pass score whereby errors were given a fail score. Results from 231 participants revealed 113 (48.9%) passed and 118 (51.1%) failed. Although this test is considered an ecologically valid measurement, it does not appear to be as sensitive to dementia presence when compared to the Pillbox. Sensitivity may be limited because the Check Writing does not require the individual to deviate from a typical regimen (i.e., as encouraged in the Pillbox

test) but relies on a frequently reinforced skill without additional planning or excessive use of executive function (i.e., mentally shift tasks, make inferences).

The WAB Fluency and Species examined the ability of tested individuals to retrieve known animals without perseveration (e.g., naming cow repeatedly). Additionally, mental flexibility was predicted to be shown when the individual was able to name animals from different species (e.g., mammals, insects and amphibians). Analyses of 231 participants revealed scores on Fluency ranged from 2 named animals to 27 named animals (M = 12.0; SD = 4.9). In addition, categories of WAB Species ranged from 1 to 16 different species (M = 4.1; SD = 3.2). Again, studies have demonstrated the Fluency test to be highly sensitive to any brain damage (Kertesz, 1979; Shewan & Kertesz, 1980). However, this study did not find a significant correlation between performance on the Fluency and Species in relationship to dementia.

Analyses of the CDT for 231 participants revealed a range from 0 points, or an inability to complete task instructions or completion of task instructions without meeting score eligible criteria, to 4 points or receiving all criteria points (M = 3; SD = 1.2).

Lastly, the PPVT-III was administered to determine the individual's premorbid intelligence. Research indicates vocabulary to be crystallized; therefore vocabulary is thought to remain intact through the beginning stages of dementia (Lezak, 2004). Raw and IQ scores were determined to garner information about premorbid functioning. In some cases, the obtained score fell into the intellectual disabled category and was deemed misrepresentative of the individual's premorbid level of functioning. With these individuals, the dementia process had progressed beyond the initial stages whereby vocabulary abilities were severely perturbed. Raw scores were obtained for 194

participants and ranged from 12 points to 192 points (M = 125.4; SD = 27.9). Obtained IQ scores ranged from 59 points to 136 points (M = 104.5; SD = 19.4). The aforementioned are depicted below in Table 3.

Table 3

Descriptive Statistics for Neuropsychological Battery: Continuous Variables

Test	*N*	*M*	*SD*	Range	Skewness	*SE* Skew	Skew / *SE* Skew	Kurtosis	*SE* Kurt	Kurt / *SE* Kurt
Rey-Osterrieth										
Copy	228	27	8.80	0-36	-1.20	0.16	-7.50	0.68	0.32	2.13
Recall	230	9.10	6.80	0-33	0.65	0.16	4.06	0.29	0.32	0.91
7-Minute screen										
Uncued	231	4.20	2.90	0-13	0.31	0.16	1.94	-0.52	0.32	-1.63
Cued	231	7.80	3.00	0-16	-0.28	0.16	-1.75	0.07	0.32	0.22
Forgotten	231	4.20	4.50	0-16	1.04	0.16	6.50	0.00	0.32	0.00
Pillbox Test										
Total Error	231	24.60	24.40	0-139	1.04	0.16	6.50	1.92	0.32	6.00
Total Pills	231	41.7	20.90	0-140	0.44	0.16	2.75	3.33	0.32	10.41
Western Aphasia										
Fluency	231	12	4.90	2-27	0.46	0.16	2.88	-0.14	0.32	-0.44
Species	231	4.10	3.20	1-16	1.52	0.16	9.50	1.67	0.32	5.22
Clock Drawing										
Total	231	3	1.20	0-4	-0.98	0.16	-6.13	-0.13	0.32	-0.41
PPVT-III										
Raw	194	125.40	27.90	12-192	0.18	0.18	1.00	1.09	0.35	3.11
IQ	193	104.50	19.40	59-136	-0.10	0.18	-0.56	-0.91	0.35	-2.60

Table 3 continued

Descriptive Statistics for Neuropsychological Battery: Categorical Variables

	N	*P*
Pillbox Test		
Pass	67	29.0
Fail	164	71.0
Check Writing		
Pass	113	48.9
Fail	118	51.1

Next Pearson correlations were calculated to identify relationships among variables. Some of the significant findings are outlined below however, due to the great number of correlated variables, not all are mentioned within text. Please reference Table 4 for correlations between all continuous neuropsychological measurements as well as age and education.

A Pearson correlation coefficient was calculated for the relationships between the individual's age and the following variables: age, education, Pillbox total pill, WAB Fluency, WAB Species, Rey-Osterrieth Copy, Rey-Osterrieth Recall, 7MS Uncued, 7MS Cued, 7MS Forgotten, Clock Draw score and the PPVT-III. Given the population is older and referred for dementia screening, it is expected that age will highly correlate with most variables. Correlation findings for the relationship between the individual's age and education noted a weak positive correlation ($r(226) = 0.14$, $p < 0.05$). In addition, Pearson correlations were calculated to examine the relationship between individuals' ages and the neuropsychological measures; significant correlations were identified between age and each test excluding the 7MS Cued ($r(229) = -0.01$, $p > 0.05$) and the PPVT-III ($r(191) = 0.30$, $p > 0.05$). The significant correlations for age and the test variables are located below in Table 4.

Pearson correlations were calculated to examine any significant relationships between education and the stated variables. Strong and positive correlation were identified between education and the WAB Fluency ($r(226) = 0.18$, $p = 0.01$) and education and the Peabody Picture Vocabulary Test ($r(192) = 0.51$, $p < 0.01$. Non-significant correlations between education and the other neuropsychological tests are found in Table 4.

Pearson correlations were also employed to examine correlative strength and direction between the neuropsychological tests. The obtained results were utilized in exploration of descriptive data pertaining to the sample. It was expected these measurements would be correlated because they were formulated to measure cognitive function. Correlations revealed strong significant relationships between many of the measures. In addition, weak significant relationships were identified between a few measures. Pearson correlations also identified that some of the measurements were correlated at a non-significant level. The following table contains Pearson correlations for each of the studied continuous variables.

Table 4

Correlations

		Age	Education	Total pill	Fluency	Species	Rey copy	Rey recall	Uncued	Cued	Forgotten	Clock
Age	Pearson Correlation											
	Sig. (2-tailed)											
Education	Pearson Correlation	0.14*										
	Sig. (2-tailed)	0.04										
Total pill	Pearson Correlation	-0.24**	0.08									
	Sig. (2-tailed)	0.00	0.22									
Fuency	Pearson Correlation	-0.34**	0.18**	0.24**								
	Sig. (2-tailed)	0.00	0.01	0.00								
Species	Pearson Correlation	-0.26**	-0.09	0.07	0.24**							
	Sig. (2-tailed)	0.00	0.18	0.27	0.00							
Rey copy	Pearson Correlation	-0.27**	0.13	0.37**	0.39**	0.07						
	Sig. (2-tailed)	0.00	0.06	0.00	0.00	0.31						
Rey recall	Pearson Correlation	-0.47**	0.11	0.25**	0.44**	0.25**	0.53**					
	Sig. (2-tailed)	0.00	0.09	0.00	0.00	0.00	0.00					

Uncued	Pearson Correlation	-0.43**	-0.03	0.17*	0.27**	0.25**	.28**	0.57**					
	Sig. (2-tailed)	0.00	0.71	0.01	0.00	0.00	0.00	0.00					
Cued	Pearson Correlation	-0.01	0.00	0.02	0.19**	0.06	0.18**	0.23**	0.08				
	Sig. (2-tailed)	0.89	0.97	0.73	0.00	0.38	0.01	0.00	0.24				
Forgotten	Pearson Correlation	0.28**	0.03	-0.12	-0.36**	-0.23**	-0.31**	-0.52**	-0.66**	-0.72**			
	Sig. (2-tailed)	0.00	0.64	0.08	0.00	0.00	0.00	0.00	0.00	0.00			
Clock	Pearson Correlation	-0.27**	0.09	0.31**	0.49**	0.13	0.65**	0.44**	0.21**	0.24**	-0.34**		
	Sig. (2-tailed)	0.00	0.16	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00		
Peabody	Pearson Correlation	0.03	0.51**	0.20**	0.40**	-0.08	0.35**	0.17*	0.04	0.15*	-0.13	0.26**	
	Sig. (2-tailed)	0.68	0.00	0.00	0.00	0.26	0.00	0.02	0.60	0.03	0.07	0.00	

N varies between 193 and 231 depending on the missing data.

Inferential Statistics

Parametric tests Next parametric tests were implemented to compare scores on the different neuropsychological test variables and to determine group differences between individuals with AD and those with VD. An independent-samples *t* test was implemented to compare the mean scores of the AD and VD groups. No significant differences were found for the Pillbox Total Error as the means of individuals with AD were not significantly different from individuals with VD. Therefore, AD individuals did not have a greater tendency to make more errors on this ecological measure when compared to VD individuals.

With regards to the WAB, no significant differences for the Fluency subcategory were noted for those with AD when compared to VD counterparts. No significant differences were found in one group's ability to name more animals in the allotted time when compared to the other group. However, for the WAB Species test, a significant difference was found between individuals with AD and those with VD. Specifically, individuals with VD were able to name more Species than those with AD on this measure.

Next, *t* tests revealed no significant difference between AD and VD groups on Rey-Osterrieth Copy score. One group did not significantly outperform the other. Contrary, a significant difference was noted on the Rey-Osterrieth Recall portion whereby VD individuals were able to recall and draw from memory more of the complex figure than AD individuals.

Next, an independent-samples *t* test compared the mean scores of the AD and VD groups on 7MS sections and found significant differences between the group means for

Uncued, Cued and Forgotten. With regards to the Uncued section, those with VD were able to freely recall more of the previously seen items than AD individuals. Additionally, the VD group outperformed the AD group when given prompts for the previously seen items (i.e., Cued). Lastly, a distinct difference was pinpointed between group means on the Forgotten subtest. The AD individuals essentially forgot more of the previously seen items on the 7MS as evidenced by a greater score on the Forgotten subtest.

No significant differences on the Clock Score or the PPVT were noted for AD individuals when evaluated against VD individuals. Neither group was significantly different from the other on these measures. Independent-samples *t* test results for all variables are located in Table 5.

Table 5

T-Tests Results for Neuropsychological Battery

	AD (N = 63)		VD (N = 114)		t	df	Sig (2-tailed)
	M	*SD*	*M*	*SD*			
Pillbox Total Error	32.75	26.61	26.24	24.51	1.64	175	0.10
WAB Fluency	10.30	4.54	11.61	4.50	-1.85	175	0.07
WAB Species	2.86	1.84	3.91	3.00	-2.90	173.11	0.00
Rey Copy	25.89	8.94	25.56	9.55	0.22	172	0.83
Rey Recall	5.28	5.17	8.72	6.28	-3.91	149.99	0.00
7MS Uncued	2.03	2.47	4.25	2.61	-5.52	175	0.00
7MS Cued	5.16	2.79	9.01	2.53	-9.34	175	0.00
7MS Forgotten	9.03	4.22	2.95	3.15	10.02	100.77	0.00
Clock Score	2.81	1.27	2.88	1.21	-0.35	175	0.73
PPVT-III	103.02	19.43	101.59	18.82	0.44	144	0.66

*Levene's Tests for Equality of Variance was first reviewed so that the appropriate *t* was then used.

Nonparametric tests Next a chi-square test of independence was utilized to determine the frequency of Pass/Fail on the Pillbox and Check Writing measures for AD and VD. This test was chosen due to the dichotomous nature of these variables. Results for Pillbox Pass/Fail indicated no significant relationship differences between groups ($\chi^2(1) = 3.34$, $p > 0.05$). Given the high failure percentage on this test, this finding was unexpected yet indicated the Pillbox test identified dementia presence, but was not able to correctly distinguish between dementia groups. Neither AD nor VD individuals were more prone to pass or fail this ecological measure. In addition, Check Writing Pass/Fail also indicated no significant relationship with a group ($\chi^2(1) = 0.80$, $p > 0.05$). Therefore, AD individuals are not more apt to pass or fail as compared to VD counterparts on this measure.

Analysis of variance Analysis of variance (ANOVA) was next implemented to compare the three means of the dementia groups in order to determine if the MCI group was distinctly different from the other groups on the neuropsychological measures. The ANOVA was chosen over multiple *t* tests to control for inflation of the Type I error rate. Significant differences were found for each test with the exception of Check Writing pass/fail. The significant results are interpreted in the below paragraphs and Table 6 shows the specific results.

First, a significant difference was found among the three dementia groups on the Pillbox pass/fail. Tukey's *HSD* was used to determine the nature of the significant differences between the dementia groups. Interpretation revealed that more individuals with AD failed the Pillbox test than those with MCI. Also, more individuals with VD failed the Pillbox test than those with MCI. As previously discussed, no significant

differences in pass/fail were identified between AD and VD groups. In addition, a significant difference was also noted among the three dementia groups on the Pillbox Total Errors. Review of the Tukey's *HSD* revealed those with AD made significantly more errors than those with MCI. Similarly to the AD group, those with VD made significantly more errors on the Pillbox test than those with MCI. MCI individuals made fewer errors than AD and VD individuals. No significant group differences were noted for AD and VD individuals.

Significant differences were identified amongst the dementia groups on the WAB Fluency and the WAB Species. Tukey's *HSD* was used to determine the nature of the differences between the dementia groups on Fluency. Differences specifically occurred between the AD group and the MCI group whereby those with AD named significantly fewer animals. The MCI group also outperformed the VD group. No distinct differences were identified between the performance of the VD and AD groups. Basically those with MCI were able to recall more animals within the specified time as compared to the AD and VD groups. Similar findings were noted on the Species portion. Those with AD identified fewer species than MCI counterparts. MCI individuals also named more species than VD individuals. VD performed slightly better than AD counterparts but not as well as MCI individuals.

The Rey-Osterrieth Copy and Recall also demonstrated significant differences between the dementia groups. Tukey's *HSD* was utilized to determine the differences. On the Rey-Osterrieth Copy and Recall, those with AD respectively performed significantly worse than those with MCI correspondingly. MCI individuals also performed better on both measure than those with VD. No significant performance differences were

discovered between those with AD and VD on their ability to copy the design; however significant differences were noted on the recall. Specifically, those with VD were able to reproduce more of the design and receive a greater number of points on the recall portion than their AD counterparts.

Each of the 7MS subscales showed significant differences for each dementia group. Tukey's *HSD* was employed to determine the group differences. This analysis revealed that significant differences were identified between all groups on the Uncued and Forgotten subtests. First, for the Uncued test, those with AD were significantly different from those with VD; VD individuals were able to spontaneously recall a greater number of the previously shown pictures than AD individuals. Those with AD also recalled a fewer number of previously shown pictures than those with MCI. Furthermore, the MCI individuals were also able to recall a greater number of Uncued pictures than those with VD. On the Cued portion of the 7MS, individuals with AD were significantly different from VD and MCI. When presented with a cue, VD and MCI individuals recalled a greater number of the previously seen pictures than AD individuals. No significant difference was found between the Cued recall abilities of VD and MCI groups. Lastly, for the 7MS Forgotten, AD individuals essentially forgot more of the previously shown pictures than VD individuals and MCI individuals. Furthermore, significant differences were noted between VD and MCI groups whereby the MCI group demonstrated the least amount of forgotten pictures.

A significant difference was found among the dementia groups for the Clock Draw Test score. Tukey's *HSD* was employed to examine the differences between the groups. The AD group received a lower score on the Clock Draw Test as compared to the

MCI group. The MCI group also received a higher score on the Clock Draw Test when compared to the VD group. No significant differences were observed between the AD and VD groups on this measure. Results indicated the MCI group to be most able to adhere to instructions, to reproduce a specific clock and to receive the greatest amount of points.

No significant differences were noted between the groups on the Check Writing pass/fail measure. The means of the three groups are displayed in Table 6. Interpretation of these results indicated the three dementia groups did not differ significantly on their propensity to pass or fail the measure.

Significant differences were also identified between the groups on the PPVT-III. Tukey's *HSD* was implemented to ascertain the nature of the group differences. This analysis revealed that AD individuals did not score significantly different than VD individuals or MCI individuals. Contrary, MCI individuals scored significantly higher on the PPVT-III than VD individuals. The VD group scored the lowest on the PPVT-III, a test thought to measure one's premorbid level of functioning. Potential rationale for the above differences will be further elaborated within the discussion section.

Table 6

ANOVA Results for Neuropsychological Battery

	AD (N = 63)		VD (N = 114)		MCI (N = 54)		f	df	Sig (2-tailed)
	M	*SD*	*M*	*SD*	*M*	*SD*			
Pillbox P/F	1.84	0.37	1.72	0.45	1.54	0.50	6.89	2,228	0.01
Pillbox Total Error	32.75	26.61	26.24	24.51	11.70	14.89	12.43	2,228	0.01
WAB Fluency	10.30	4.54	11.61	4.50	14.98	4.97	15.86	2,228	0.01
WAB Species	2.86	1.84	3.91	3.00	5.81	3.99	14.29	2,228	0.01
Rey Copy	25.89	8.94	25.56	9.55	31.28	4.63	9.04	2,225	0.01
Rey Recall	5.28	5.17	8.72	6.28	14.44	6.31	34.30	2,227	0.01
7MS Uncued	2.03	2.47	4.25	2.61	6.48	2.20	46.78	2,228	0.01
7MS Cued	5.16	2.79	9.01	2.53	8.13	1.89	49.95	2,228	0.01
7MS Forgotten	9.03	4.22	2.95	3.15	1.37	2.37	94.31	2,228	0.01
Clock Score	2.81	1.27	2.88	1.21	3.56	0.74	7.95	2,228	0.01

Table 6 Continued

Check P/F	1.59	0.50	1.52	0.50	1.41	0.50	1.91	2,190	0.15
PPVT-III	103.02	19.43	101.59	18.82	111.70	19.04	4.58	2,190	0.01

Multivariate analysis of variance A multivariate analysis of variance (MANOVA) was next run to look at the dependent variables while minimizing Type I error inflation. A 2 x 3 between-subjects multivariate analysis of variance was performed on 12 dependent variables: Pillbox pass/fail, Pillbox total errors, WAB Fluency, WAB Species, Rey-Osterrieth Copy, Rey-Osterrieth Recall, 7MS Uncued, 7MS Cued, 7MS Forgotten, Clock Draw score, Check Writing pass/fail and PPVT-III. Results indicated diabetes had a marginal effect (*Lambda*(12, 174) = 0.89, $p = 0.052$). Follow-up univariate ANOVAs indicated that having diabetes significantly impacted scores on the 7MS Uncued ($F(1, 185) = 3.96$, $p < 0.05$) and the PPVT-III ($F(1, 185) = 10.32$, $p < 0.05$). These were the only measures that were significantly affected by diabetes.

Discriminant function Next four discriminant function analyses were performed to determine if the specified neuropsychological tests could reliably predict dementia group membership. The first discriminant function included the following tests as predictors of dementia group membership (i.e., AD or VD): Pillbox pass/fail, Pillbox total error, WAB Fluency, WAB Species, Rey-Osterrieth Copy, Rey-Osterrieth Recall, 7MS Uncued, 7MS Cued, 7MS Forgotten, Clock score, Check Writing pass/fail and PPVT-III. Of the original 231 initial cases, 33 (14.3%) cases were excluded because at least one discriminating variable was missing. Additionally, 54 (23.4%) cases were removed because they were classified as MCI. With removal of the above, 144 (62.3%) cases remained for analysis.

A discriminant function was calculated and revealed a strong association between groups and predictors $\chi^2 (12) = 91.83$, $p < 0.01$. The correlation matrix suggested the best predictors for identifying AD were the 7MS Forgotten and the 7MS Cued. Loadings of

less than 0.50 were not interpreted. With use of the discriminant function classification, approximately 87.5 percent of the original grouped cases were correctly classified. Of the 55 AD individuals, 46 (83.6%) cases were correctly categorized and 9 (16.4%) were misclassified as belonging to the VD group. As for the 89 VD individuals, 80 (89.9%) cases were correctly ordered and 9 (10.1%) were misclassified as AD cases.

The second discriminant function was run in a similar manner to the first, however the memory tests of Rey Recall, 7MS Uncued, 7MS Cued and 7MS Forgotten were used to predict membership into the AD or the VD group. Of the original 231 initial cases, 33 (14.3%) cases were excluded because at least one discriminating variable was missing. Additionally, 54 (23.4%) cases were removed because they were classified as MCI. With removal of the above, 144 (62.3%) cases remained for analysis.

A discriminant function was calculated and revealed a strong association between groups and predictors χ^2 (4) = 78.79, $p < 0.01$. The loading matrix of correlations between the four predictors and the discriminant function indicated the best predictors for distinguishing AD from VD were 7MS Forgotten, 7MS Cued and 7MS Uncued. Loadings of less than .50 were not interpreted. Classification results indicated that 86.4 percent of the original grouped cases were correctly classified. Specifically of the 63 AD cases, 49 (77.8%) were correctly classified as AD and 14 (22.2%) were incorrectly specified as VD cases. In regards to the 113 VD cases, 103 (91.2%) cases were correctly designated as VD and 10 (8.8%) cases were incorrectly classified as AD.

The third discriminant function further developed the first via inclusion of the MCI group; again all neuropsychological tests (i.e., 12 tests) were included within the analysis. With this analysis, 191 (82.7%) of the original 231 cases were considered valid

and therefore included; 40 (17.3 %) cases were excluded due to having at least one missing discriminating variable. Of the analyzed cases, 55 were in the AD group, 89 were members of the VD group and 47 comprised the MCI group. Two discriminant functions were calculated and revealed a combined χ^2 (24) = 198.40, $p < 0.01$. After removal of the first function, a strong association was still present between groups and predictors, χ^2 (11) = 63.54, $p < 0.01$. The two discriminant functions accounted for 72 percent and 28 percent of the between-group variability. The first discriminant function separates the AD individuals from the other two groups; the second discriminates the VD individuals from MCI individuals with AD individuals between these two groups.

The matrix of correlations between predictors and discriminant functions designated the best predictors for distinguishing between AD and the other two groups were as follows: 7MS Forgotten, 7MS Uncued and the Rey-Osterrieth Recall. Again, loadings of less than 0.50 were not interpreted. Classification results indicated that of the 191 cases, 143 (74.9%) cases were correctly identified. Of the 55 AD individuals, 45 (81.8%) were correctly classified; however 7 (12.7%) cases were misclassified as VD and 3 (5.5%) were misclassified as MCI. The classification table also revealed that VD had the lowest correct classification rate whereby 60 (67.4%) of the initial 89 cases were correctly classified; 10 (11.2%) were misclassified as belonging to the AD group and 19 (21.3%) were misclassified as MCI. Lastly, of the 47 MCI cases, 38 (80.9%) were classified correctly and 1 (2.1%) case and 8 (17.0%) cases were misclassified as AD and VD respectively.

Overall, when MCI is added, it is more difficult to correctly classify the VD individuals; this may transpire because the scores of the VD group are not as readily

distinguishable from those of the MCI group. Some overlap in test scores appears to emerge when comparing the two groups; specifically, 21.3 percent of the VD individuals appear to belong to the MCI group. Due to this overlap of VD and MCI, the discriminant function does predict AD group membership at a higher percentage.

The final discriminant function was formulated to match the second; again four test variables were used as predictors of membership in three groups. Predictors were the Rey-Osterrieth Recall, 7MS Uncued, 7MS Cued and 7MS Forgotten. Groups were AD, VD or MCI. Of the original 231, 1 case was excluded due to at least one missing discriminating variable. With exclusion 230 cases remained for the analysis with 63 individuals with AD, 113 with VD and 54 with MCI. Again, two discriminant functions were calculated with a combined χ^2 (8) = 169.09, $p < .01$. Removal of the first function still produced a significant association between the groups and predictors, χ^2 (3) = 49.52, $p < .01$. Respectively, the two discriminant functions accounted for 74.7% and 25.3% of the between-group variability. Within this analysis, the first discriminant function maximally separates the AD individuals from the other two groups; the second discriminant function distinguishes the MCI group from the VD individuals with AD aligning between the two groups.

The correlations between predictors and discriminant functions suggests the best predictors for distinguishing between AD and the other two groups are 7MS Forgotten, 7MS Uncued, Rey-Osterrieth Recall and 7MS Cued (i.e., all loadings were greater than 0.50). Classification results indicated that when four variables are predictors of membership in three dementia groups, the percentage of original grouped cases correctly classified dropped drastically to 68.3 percent. To better conceptualize why the correct

classification percentage dropped, it is pertinent to examine classification percentages within each dementia group. For those with AD, 48 (76.2%) of the cases were correctly assigned to the AD group, 9 (14.3%) were misclassified as VD and 6 (9.5%) were misclassified as MCI. Examination of the VD group revealed this group was the most difficult to predict correct membership via utilization of only the four test variables. Of the 113 VD cases, 67 (59.3%) were correctly classified as VD, however, 9 (8.0 %) and 37 (32.7%) were misclassified as AD and MCI respectively. Again, it appeared that correct classification of VD was more difficult based on these four variables. Lastly, of the 54 MCI cases, 42 (77.8%) were correctly classified, 1 (1.9%) case was misclassified in the AD group and 11 (20.4%) cases were misclassified in the VD group.

Overall comparisons revealed the last discriminant function which used four test variables as predictors of membership into the three dementia groups to be the poorest model for correct classification. Explicitly, the ability to parse out VD from the MCI group became increasingly difficult. Contrary, group membership appeared to be highly predictable when only two groups (i.e., AD, VD) were indicated and when all test variables were used as predictors of dementia group membership. Results and potential implications will be elaborated further within the discussion section.

CHAPTER IV

DISCUSSION

Purpose of this Study

This study had four outlined objectives. The primary purpose was to replicate previous research to determine if AD individuals scored poorer on the 12 neuropsychological measures as compared to VD individuals. Although previous research established a solid foundation of distinct cognitive protocols for the two groups, replication was deemed necessary to determine the utility of the chosen battery. Given the sample was taken from a county hospital, any distinct deviations in dementia presentation were also of interest. It was hypothesized that AD individuals would have more severe and globalized deficits when compared to VD counterparts.

The second objective was interested in the impact of diabetes on one's dementia. Basically this hypothesis stressed the comorbid affects of diabetes would compound and thereby make the dementia more profound as compared to those with only a dementia diagnosis. The detrimental affects of diabetes are thought to compound an individual's cognitive damage and intensify cognitive decline.

The third objective dealt with the ability of the Rey-Osterrieth Recall and the 7MS subtests of Uncued, Cued and Forgotten to predict group membership into the AD or VD group. It was hypothesized individuals with AD would demonstrate significant decreases in memory test performance on these measures and the use of these measures, dependent from the other battery measures, would accurately predict group membership.

The final objective centered on elaboration of hypothesis three and the ability of the specified neuropsychological memory measurements to identify and correctly predict

dementia group membership when MCI individuals were added to the equation. This objective was formulated based on literature that identified individuals with MCI demonstrated memory impairments similar to those with AD but distinct from the VD group. This hypothesis asserted that MCI individuals showed episodic memory deficits and impairments in recall of verbal and visual material; a similar impairment often noticed in AD individuals at a greater extent.

Research questions were formulated after extensive work with this population and a want to better understand the served individuals through recognition of any unique differences. The neuropsychological experience, in conjunction with a literature review, enabled the formulation of four research questions which explored sex, dominant hand, years of education and race/ethnicity differences.

Demographic Differences

Correlations and chi-square tests were performed to determine any significant categorical demographic differences between groups. Results indicated no significant differences for sex, handedness, years of education and race/ethnicity. These results are encouraged to be interpreted with caution due to the unequal sample sizes. For example, this study failed to replicate previous findings which identified sex differences on neuropsychological performance (Skjerve et al., 2007; Vincze et al., 2007). Failure to replicate previous findings was potentially linked to sample characteristics, whereby the sample was over representative of females at a rate of almost twice that of males.

In addition, no significant relationship was identified on neuropsychological test performance and dominant hand. Again, failure to identify differences in cognitive response and performance may be due to no actual differences existing between those

with dominant left hand versus those with dominant right hand. Again, the sample size is noteworthy because left-handed individuals were under sampled. Although left-handed estimates within the United States suggest that approximately 10 percent of the individuals are left-handed, this sampled population had only 6.1 percent with dominant left hand use (Ferrari, 2007). A truer and better estimate of dominant hand affects on cognition would be obtained from greater and equal groups. With a larger sample, comes the increased statistical power that would allow this study to better identify any real influences (Cohen, 1992).

Within this population years of education and one's ethnicity did not appear to influence neuropsychological test performance. A possible reason that no significant relationship was identified was prospectively due to unequal sample sizes and perhaps overall sample characteristics. The studied sample did not have equal distribution of education nor did the years of education have great enough membership to different groups (e.g., high school, associate degree, college) to reproduce previous findings (Skjerve et al., 2007). With regards to ethnicity, the majority of included individuals were Caucasian with few African American and Hispanic individuals. The sample further minimized diversity through exclusion of individuals whom were unable to communicate via English. Interestingly, the findings further convolute the research body and ad to the minimal research that refutes education and ethnicity influence (Meguro et al., 2001; Solomon et al., 1998; Solomon & Pendlebury, 1998; Strauss et al., 2006; Tsolaki et al., 2002). Again, these results should be interpreted with caution due to sample limitations.

Group Differences

Significant dementia group differences were recognized for AD and VD groups via statistical analyses. Specifically, group differences were pinpointed via *t*-tests and chi-square use. First, hypothesis 1a asserted that the Pillbox test results would indicate significant differences for AD and VD groups. Chi-square tests indicated this hypothesis was not supported within this population. Although a high percentage failure rate was recognized, AD individuals were not more likely to fail this test or to make statistically more errors when executing this test when compared to VD individuals. Loose interpretation of these results suggests that the Pillbox test is highly sensitive to dementia but does not display a great amount of specificity (Brose & Houtz, 2003). Currently, the breadth of research with the Pillbox test is sparse, therefore the ability of the Pillbox to correctly classify dementia group has not been thoroughly examined. This study provides one of the first in depth analysis of specificity; additional research within different populations may be beneficial to uncover any significant between groups differences.

Next, hypothesis 1b was examined; results indicated performance differences on the WAB Fluency and Species portions. In particular, hypothesis 1bi asserted that AD performance on the WAB Fluency portion would be significantly lower whereby this group was able to recall fewer animals than the VD group. Interestingly, no significant between groups differences were found within this sample, therefore this hypothesis was not supported. Hypothesis 1bii maintained the AD group would name fewer species than VD counterparts. This hypothesis was supported and AD individuals demonstrated significant differences on the WAB Species whereby they named fewer species than VD individuals. Identified results were intriguing because the WAB was designed to measure

facets of language function and research has indicated it to be an extremely sensitive measure of any present brain damage (Kertesz, 1979; Shewan & Kertesz, 1980; Kertesz, 1982; Bekheit et al., 2005). Given the sensitivity of the measure, those with greater damage as frequently manifested in AD should perform poorer. Acknowledgement to this premise would indicate AD performance to be lower on Fluency and Species. Possible deviations may be due to sample characteristics or outliers. Noteworthy, previous literature has not documented discrepancies between groups on the Fluency and Species portions.

Hypothesis 1c was formulated to examine the group differences on the Rey-Osterrieth Copy and Recall measures. First, hypothesis 1ci suggested that the AD group would score lower on the Rey-Osterrieth Copy when compared to the VD group. A *t*-test analysis revealed this hypothesis was not supported. In fact, closer examination revealed that although not significant, the AD group slightly outperformed VD individuals. Next, hypothesis 1cii was explored; this hypothesis suggested those with AD would perform significantly poorer on the Rey-Osterrieth Recall than VD individuals. This hypothesis was supported and significant differences between AD and VD performance were identified on the Rey-Osterrieth Recall portion.

Previous research has been utilized to examine distinct group differences on the Rey-Osterrieth measure. Previous findings acknowledged memory discrepancies for AD individuals were potentially caused by perturbations in their ability to engage non-verbal short-term memory with recall of the complex figure (Grossman et al., 1993; Strauss et al., 2006). As compared to VD individuals, those with AD in this sample were significantly worse in their ability to evoke short-term memory to recall the various

components of the figure. Interestingly, Freeman and colleagues (2000) compared AD to VD individuals and found those with AD performed better on the Copy but poorer on the Recall when compared to VD. The results of this study were similar in both regards whereby AD individuals performed somewhat better on the Copy (AD, *M* = 25.89; *SD* = 8.94; VD, *M* = 25.56; *SD* = 9.55) but significantly worse on the Recall (AD, *M* = 5.28; *SD* = 5.17; VD, *M* = 8.72; *SD* = 6.28). Additional studies are needed to examine why these differences are noted.

The next hypotheses, 1d, focused on the 7MS and suggested the AD group would perform significantly poorer than the VD group on each subcomponent (Uncued, 1di; Cued, 1dii; Forgotten 1diii). These assertions were supported and significant group differences were noted for each of the subtests. Upon closer examination, the AD individuals were not able to remember (i.e., via Uncued or Cued) as many of the previously shown pictures when compared to VD individuals. Also, the AD individuals essentially forgot more of the pictures than VD counterparts. Hypotheses 1di, 1dii and 1diii were supported. These results were anticipated due to the original 7MS design that targeted the cognitive areas most frequently affected in AD (Solomon et al., 1998). Interpretation of results made it apparent that AD individuals had greater deficits in long-term episodic memory ability than VD individuals (Del Ser et al., 2006). Results replicated previous research and added to the robust literature that maintains this measurements sensitivity and specificity capabilities (Meulen et al., 2004; Scinto & Daffner, 2000; Solomon et al., 1998; Solomon & Pendlebury, 1998; Tsolaki et al., 2002).

Subsequently hypothesis, 1e, recommended AD individuals would have a lower score on Clock Drawing Test when compared against VD individuals. Results did not

support this hypothesis and no between group differences were identified. This finding buttressed research by Lam et al (1998) but refuted literature that found the CDT to be a good measure with moderately high sensitivity and specificity (Shulman, 2000). Failure to replicate the Shulman (2000) study is potentially from design error whereby the components were assigned a specific point value without inclusive interpretation of specific design variations. Research asserts analysis of clock errors to be pertinent. Specifically, analysis of design variation may have found that those with AD showed common perseveration errors, excluded numbers or utilized counterclockwise numbering and made irrelevant spatial arrangement errors (Freidman, 1991). Although, specific deviations were not analyzed in the above context, any deviation from normal was not given a point. Therefore, holding Shulman's (2000) assertion true, scores for AD should be lower than VD and if differences existed, assigned points would reflect discrepancies.

The penultimate hypothesis, 1f, focused on discrepancies between AD and VD scores on the Check Writing task. Analysis of this measure revealed no differences for AD and VD. Again, literature indicates the Check Writing to be part of a test that is able to measure functional competence, an area of functioning often compromised in AD (Arguelles, 2001). This sample did not manifest group differences and hypothesis 1f was refuted. Reasons for the inability of this measure to distinguish between dementia groups were potentially due to the use of this test without administration of the additional DAFS tests. Researchers formulated the Check Writing test to be used in conjunction with other measurements of instrumental activities of daily living (Lowenstein, 1989). Specificity is potentially reduced when this test is used outside of the other DAFS instruments.

Lastly, hypothesis 1g, focused on group differences on the Peabody Picture Vocabulary Test. Interpretation of the test results indicated no significant group differences on the Peabody intelligence score. A literature review revealed previous research had not explored the differences between dementia groups on this measure. Possible reasons for the lack of research is due to research that emphasized this test should be utilized as a screening tool and not as a diagnostic tool (Strauss et al., 2006). It is pertinent to recall the Peabody measure was employed to gage the individual's premorbid intelligence and overall general mental abilities (Lezak, 2004). Vocabulary is thought to remain intact throughout the initial stages of dementia. Given this premise, it is not a surprise to note no distinct between groups differences.

A multivariate analysis of variance was implemented to determine the influence of diabetes on neuropsychological test performance. Diabetic manifestations involve microvascular and macrovascular complications which are hypothesized to perturb cognition (Dailey, 2007; Dall et al., 2008; Monnier, 2000). This potential damage is an area of concern especially when an individual maintains a dementia diagnosis, for any addition vascular damage may further cognitive loss (Biessels et al., 2006; Convit et al., 2003; Croxson & Jagger, 1995; Ryan et al., 1985; Verhaeghen et al., 2003;). Thus far, cognitive areas involving processing speed, memory, attention and executive function are noted to be influenced via diabetes (Awad et al., 2004; Brands et al., 2007; Manschot et al., 2006; Stewart & Liolitsa, 1999; Verhaeghen et al., 2003).

With consideration to prior research, diabetics within this sample were hypothesized to have greater deficits than non-diabetics on the neuropsychological battery. Interestingly, the impact of diabetes on cognitive performance was not as great as

initially thought, as the MANOVA indicated diabetes had a marginal impact on test performance. Explicitly, univariate ANOVAs determined the addition of diabetes negatively impacted the diabetics' 7MS Uncued performance and the PPVT-III score. These results supported hypotheses 2di and 2g which suggested diabetes would significantly alter performance. The other neuropsychological tests were not significantly influenced by the presence of diabetes. Therefore the following hypotheses were refuted through univariate ANOVAs: 2a; 2bi, 2bii; 2ci, 2cii; 2dii, 2diii; 2e and 2f. Possible rationale for these findings was discussed below in terms of the cognitively affected areas.

An extensive literature review was conducted to determine if these findings were typical for individuals with diabetes. Research that examined diabetic implications on this study's neuropsychological tests was limited. Findings did not suggest the significant tests of the 7MS and the PPVT-III to be sensitive to diabetic influence on cognitive capabilities. Nonetheless, literature did recognize diabetes influenced cognition. Specifically, one test by Bale (1973) identified severe hypoglycemic episodes negatively impacted vocabulary test performance. Contrary, longitudinal research found hypoglycemic episodes did not result in significant cognitive impairments (DCCT Research Group, 1996; Reichard et al., 1991; Reichard et al., 1993). Hypoglycemia is documented to influence cognitive capabilities however hyperglycemia permanently alters vasculature via damage and resultant neuropathy (Sheetz & King, 2002; Skundric & Lisak, 2003; Williams et al., 2002). This alteration of vascular integrity and eventual neuropathy is more apt to explain significant cognitive differences. For example, research acknowledged that diabetic individuals with poor metabolic control and more frequent

hyperglycemic episodes were less efficient in learning and performance on memory tasks (Elias & Elias, 1993; Perlmuter et al., 1984; Schaie, 1996; Strachan et al., 2000).

Extrapolation of the above research would explain why the 7MS Uncued and the PPVT-III were affected; however these affects should be documented on additional memory test results. Possible explanations for this lack of differences on other tests may be related to sample characteristics whereby diabetic and non-diabetic groups were unequal. A more robust sample with equal group membership would increase power and clarify any misconceptions. In addition, this sample did not recognize diabetic history, metabolic control or differentiate between Type 1 and Type 2 individuals. Each of these variables potentially impacts the results. Although these issues pose a concern, additional research is encouraged to explore diabetic influence on cognitive function.

Next discriminant functions were run to determine if the specified neuropsychological tests could reliably predict AD and VD membership. The first discriminant function was run with all neuropsychological tests to examine the fundamental predictive ability of the battery. Results from this initial discriminant function indicated approximately 87.5 percent of the original group cases were correctly classified. The following tests were used as predictors of dementia group membership: Pillbox pass/fail, Pillbox Total Error, WAB Fluency, WAB Species, Rey-Osterrieth Copy, Rey-Osterrieth Recall, 7MS Uncued, 7MS Cued, 7MS Forgotten, Clock Score, Check Writing pass/fail and the PPVT-III. Overall, this discriminant function, with the above tests included, was pertinent in determining the dementia type based on test results alone. It is important to note that these test were a part of a greater neuropsychological battery and results from the entire battery in conjunction with patient self-report, family

report, medical history and available scans were included when assigning dementia type. It is reassuring that test scores are of a robust nature to predict group membership at a rate greater than 87 percent.

Although it was assumed the full neuropsychological battery was of a robust nature to accurately predict group membership, it was applicable to examine a shortened version. Due to the increased time constraints and pressure from insurance companies, shortened, less time consuming measurements with equal or greater sensitivity and specificity are in demand. The next discriminant function sought to answer hypothesis three via utilization of four specific test scores as predictors of dementia group membership. Given memory is most often affected in AD individuals, it was suggested that tests with memory components would be essential in differentiating between AD and VD (Grossman et al., 1993; Meulen at al., 2004; Solomon et al., 1998; Strauss et al., 2006). To test the ability of a shortened version to accurately predict AD or VD, another discriminant function was employed using the Rey-Osterrieth Recall, the 7MS Uncued, the 7MS Cued and the 7MS Forgotten as predictors. Results of this discriminant function determined 86.4 percent of the original cases were correctly classified based solely on score; this hypothesis was supported.

Interestingly, with the four measures as predictors, only approximately 1 percent of classification ability was lost. It does not appear the other neuropsychological tests were significantly adding to the prediction ability. Closer examination of the loading matrix of correlations revealed the best predictors for distinguishing AD from VD were the 7MS tests. The Rey-Osterrieth Recall had the least loading capabilities. These results confirm findings from prior research which indicated the entire 7MS to have the ability to

detect AD with about 90 percent accuracy (Meulen et al., 2004; Solomon et al., 1998; Solomon & Pendlebury, 1998; Tsolaki et al., 2002). Remarkably this study only used the memory portion of the 7MS. It is noteworthy that the 7MS memory portion alone was able to predict AD with a high percentage. Future research is encouraged to expound upon these findings and examine the predictive ability the 7MS memory components to predict group membership. Replication of these predictive abilities in other samples would be a crucial finding and perhaps enable shorter neuropsychological testing with equal or greater sensitivity and specificity.

Analysis of variance was utilized to ensure that distinct group differences existed between AD, VD and MCI. Results supported previous literature findings that asserted significant group differences on neuropsychological test performance (Drake et al., 2003; Freeman et al., 2000; Kasai at al., 2006; Meulen et al., 2004; Tsolaki et al., 2002; Wimberley, Herrera, Kidrowski, Brown & L'Esperance, 2003). The ANOVA results indicated significant dementia group differences on each neuropsychological test with the exception of the Check Writing pass/fail. The dementia groups did not differ on their ability to pass or fail this measure. The Check Writing was formulated to be used in conjunction with the additional DAFS measures. Deviations from the original design may inhibit the sensitivity of this test to classify significant dementia group differences. This knowledge was fundamental and necessary in order to determine distinct group differences; these differences were pertinent for laying the foundation of hypothesis four.

Lastly, a discriminant function was implemented to expound upon hypothesis three and determine group membership to AD, VD or MCI via inclusion of specified predictors. The demarcation between AD and VD is relatively well-defined with

abundant research extolling the memory differences (Del Ser et al., 2006; Freeman et al., 2000; Gershon & Herman, 1982; Kasai et al., 2006; Moller & Graeber, 1998; Solomon et al., 1998). With this distinction, the correct classification of AD and VD was done with a high percentage however the delineation became hazy with MCI classification added into the equation.

This distinction was difficult because research indicated MCI individuals represented a stage of impairment greater than what was considered normal for age, but of a lesser extent than to warrant a classification of dementia (Petersen, 2003). With this memory impairment, a debate was formulated which postulated MCI was either a preclinical stage of AD or a separate group (Broder et al., 2008; Ellison, 2008; Feldman & Kandiah, 2008; Petersen & Negash, 2008). Voluminous research has pinpointed those with MCI shown declines in episodic memory (Belleville et al., 2007; Broder et al., 2008; Small et al., 2004; Small et al., 2007). Contrary research existed to further convolute the picture and suggest that individuals with MCI have etiologies similar to VD and AD (Bennett et al., 2005; Chertkow et al., 2008; Morris et al., 2001; Mufson, 1999; O'Brien et al., 2003). Because MCI is heterogeneous, the ability to distinguish it from AD and VD may be difficult (Ganguli et al., 2004; Richie et al., 2001).

Similar to hypothesis three, a discriminant function was first run to determine if the neuropsychological battery could reliably predict AD, VD and MCI membership. Again, this discriminant function was run with all neuropsychological tests to examine the predictive ability of the battery. Results from this discriminant function indicated approximately 74.9 percent of the original group cases were correctly classified, a significantly lower percentage when compared to the classification ability with only two

dementia groups (i.e., AD and VD). The entire neuropsychological battery when used as predictors, correctly classified 81.8 percent of AD cases, 67.4 percent of VD cases and 80.9 percent of MCI cases. Interpretation of these results suggested MCI significantly influenced the predictive ability of the battery and more of the VD cases were misclassified as MCI (i.e., approximately 21.3 % of VD were given MCI classification). This misclassification was potentially due to MCI individuals performing similar to VD individuals on some measures; this similarity in score profile made classification more difficult. Contrary, the AD cases were of a significant degree to maintain correct classification (i.e., generalized, lower overall scores). Overall, this discriminant function, with all neuropsychological tests as predictors, did not classify dementia group as well when MCI was added into the equation. To reiterate, all test results in conjunction with patient self-report, family report, medical history and available scans are included when assigning dementia type.

Although predictive ability is greatly reduced with the addition of MCI, it was pertinent to determine the extent of the memory measures (i.e., Rey-Osterrieth Recall, 7MS Uncued, Cued and Forgotten) to be sensitive to dementia and to have the specificity to classify AD, VD and MCI. Given the classification ability was reduced when all measures were used as predictors, it did not bode well for the four memory measures to bolster classification capabilities. The resultant discriminant function indicated 68.3 percent of individuals were correctly classified when the memory measures were utilized as predictors. Specifically with the four predictors, 76.2 percent of AD, 59.3 percent of VD and 77.8 percent of MCI individuals were correctly assigned. Comparison of these results to the previous discriminant function (i.e., all neuropsychological measures as

predictors) illustrated significantly decreased classification abilities. These memory measures lost the ability to classify dementia groups when MCI individuals were added. With the AD and VD groups classification via the memory predictors was 86.4 percent, with addition of the MCI group, classification dropped to 68.3 percent. Addition of the MCI group reduced the classification abilities because the MCI group was not as distinct from the VD group as initially thought. Therefore, this hypothesis and the subcomponents (i.e., 4a, 4b, 4c and 4d) were not supported. Potential reasons for this lack of support may be linked to the MCI group having a heterogeneous presentation and having etiologies similar to VD and/or AD groups (Bennett et al., 2005; Chertkow et al., 2008; Ganguli et al., 2004; Morris et al., 2001; Mufson, 1999; Richie et al., 2001; O'Brien et al., 2003).

As of now, research identified MCI to represent a stage of impairment greater than what was considered normal for age, but of a lesser extent than to warrant a classification of dementia (Petersen, 2003). This definition of MCI does not identify seminal cognitive deficits but places MCI on the continuum from normal aging to dementia presence. The findings from this study demonstrated classification of the MCI group was not as clear or as readily identifiable on the continuum as classification of the AD or VD groups. Although MCI individuals did not have impairments as severe as AD individuals, this group did maintain similar memory impairments but to a lesser nature. In addition, scores on other tests were not as significantly different from those with VD. These findings reinforced previous literature and suggested MCI individuals had etiologies similar to VD and AD.

All in all, the findings from this study added valuable insight into classification abilities of common neuropsychological tests. The most robust way to assign group

membership was with the 12 neuropsychological measurements. These measurements were most useful when assigning membership into AD or VD groups. Interestingly, the memory measures as predictors were almost as vigorous in correct classification of AD or VD. Noteworthy, when MCI was added into the equation, the neuropsychological battery lost predictive ability and several VD individuals were misclassified as MCI. Furthermore, the memory measures severely failed as predictors when MCI was added. These results reinforced the importance of comprehensive interviews, medical history and neurological scans in conjunction with an extensive neuropsychological battery in order to increase correct classification.

Study Limitations

The possible limitations were listed before and summated again in the following paragraphs. First, this sample is a non-representative sample of the general population however this sample is thought to be partially representative of those typically served at the John Peter Smith county hospital. Specifically, this country hospital renders services to those of lower socioeconomic status and those without insurance. In addition, the majority of served individuals were typically from lower educational and occupational achievement. Those with additional education and higher occupational achievement were not adequately represented within this sample. Also, ethnic minorities were typically seen within this setting, however due to testing limitations (i.e., assessment protocol limitations, English tests, norm groups) and facility limitations (i.e., lack of interpreter availability) many individuals, whom were unable to communicate via English, were eliminated. Also, necessary resources were not available to test individuals with significant auditory and visual impairments.

Additionally, this sample did not have equal membership to studied groups. Specifically, the study was over inclusive of Caucasians and under representative of African Americans, Hispanics and other race/ethnicities. In addition, the studied population was influenced by an over representation of females and membership to the diabetic group was not as robust as initially thought. The lack of membership to these groups potentially impeded the power and the overall ability of this study to identify specific group differences.

In addition, the 7MS was utilized as an integral component for assigning dementia group. Results were potentially influenced by the use of this measurement in the process of designating a dementia classification. Although limitations were present, the purpose of this study was to replicate findings from prior studies, to examine the impact of diabetes on cognition, to determine group differences within this county hospital population and to seek the most efficacious measurements for classification of dementia groups.

Future Research

Future research is encouraged to build upon and clarify these findings. Given the sample limitations, it is foreseeable to utilize a similar battery with a more inclusive population in order to pinpoint any significant differences. Additionally, a larger sample size with greater group membership may enable study of demographic variables on the process of cognitive decline.

Noteworthy, the findings of this study reinforce a remarkably clear distinction between AD and VD individuals. Although significant differences between groups were noted within this sample, one must be concerned with the growing body of literature that

has identified similar etiologies between the two groups. Given similar etiologies, the presentation of a specific dementia may become unclear as deficits similar to both AD and VD emerge. With similar etiologies and presentation, acknowledgement of a mixed type dementia may be pertinent (Haglund et al., 2006; Martinez-Vila et al., 2006; Onyike, 2006; Black 2007). Research should delve into this possibility to help clarify differences, yet be open to recognizing a possible mixed type dementia diagnosis.

Additional research is encouraged to further explore any cognitive changes associated with diabetes. Specifically, research is urged to determine if hypoglycemic episodes or hyperglycemic episodes cause greater damage to cognition. As of now, research exists to support and refute the impact of diabetes on cognition (Elias et al., 1999; Launer et al., 1996; Ryan et al., 1985; Verhaeghen et al., 2003). Clarification is pertinent in order to identify the areas of the brain most susceptible to metabolic fluctuations, to educate diabetic individuals and to ensure optimal treatment. With greater understanding of the diabetic changes, it may be possible to inhibit further decline via appropriate medications and lifestyle adaptations.

Future studies would benefit from utilizing a battery exclusive of the 7MS measure to initially assign dementia group membership. In addition, this group will additionally be given the 7MS. Scores from the battery will be compared to the 7MS scores. This comparison will allow for independent examination of the 7MS's classification abilities.

Also, additional studies are encouraged to compare the abilities of the 7MS and the MMSE to identify and assign group membership. Currently the MMSE is the gold standard for quick identification of cognitive deficits within the clinic and hospital

settings (Folstein, Robins & Helzer, 1983). Abundant research has indicated the MMSE to be a poor measurement in regards to sensitivity and specificity (Escobar, Burnam, Karno, Forsythe, Landsverk & Golding, 1986). If given a preference, it is highly urged that medical professionals use the 7MS over the MMSE. Not only does the 7MS appear to be sensitive to AD and VD but it is easily administered within the primary care and long term care settings with little additional training (Solomon et al., 1998; Langbart, 2002). This study only examined the memory portion of the 7MS and found this measure to highly predict group membership to either AD or VD (i.e., 86.4 % correct classification ability). Other studies have shown the entire 7MS to detect AD presence within 92 percent accuracy (Solomon et al., 1998).

With the ever increasing time constraints and pressures from insurance companies, short yet effective measures are in high demand. The findings from this study support the 7MS memory portion to be an effective measure for determining AD and VD group membership. Although the 7MS does not maintain classification abilities when MCI is added, perhaps future research will identify a response pattern on the memory portion that is specific to MCI. As of now, it is encouraged that health professionals utilize this instrument over the MMSE while obtaining an extensive medical history before assigning a diagnosis. Future research is urged to continue pursuing effective means to identify dementia and to understand the dementia process. Perhaps one day, research will converge and discover a way to stop and treat cognitive decline.

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