CALIFORNIA STATE UNIVERSITY, NORTHRIDGE

FUNCTIONAL DEFICITS IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER’S DISEASE

A thesis submitted in partial fulfillment of the requirements
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by
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DEDICATION

I want to inspire people. I want someone to look at me and say, “Because of you, I didn't give up.”

—Anonymous

First and foremost, this thesis is dedicated to the individuals and their families fighting with the debilitating disease of Alzheimer’s. We will not give up the fight until a cure is found. This is also dedicated to all of the individuals who have believed in my journey thus far. My mother and father, Belizean immigrants, who came the U.S. to live a better life and who have supported me in everything I set out to do, thank you. Furthermore, I would also like to dedicate this to all of my loved ones and friends who have motivated me to get this far on my academic journey. This is for you!
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ABSTRACT

FUNCTIONAL DEFICITS IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER’S DISEASE

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Alzheimer’s disease (AD) is a chronic neurocognitive degenerative disease affecting millions of individuals every day. Mild Cognitive Impairment (MCI) represents a prodromal gray-area state between normal aging and cognitive impairment. MCI is frequently a precursor to several forms of neurocognitive deficits, most commonly Alzheimer’s disease. Research suggests that early detection of the inability to carry out activities of daily living (ADL) may aid in identifying those at greatest risk for additional decline. Nonetheless, the severity of ADL functioning in MCI and mild stages of AD remains unclear. The purpose of this study was to characterize impairment in various domains of ADL functioning in MCI relative to AD and normal elderly controls.

Participants were recruited from various medical and health centers in the greater Los Angeles area. The sample consisted of 59 AD patients, 38 MCI patients, and 64 normal controls. All participants were administered the Direct Assessment of Functional Status (DAFS), and the following 5 domains will be analyzed: 1) time orientation (Orientation); 2) communication abilities (Communication); 3) transportation knowledge (Transportation); 4) financial skills (Financial); and 5) shopping skills (Shopping). A multivariate analysis of variance was conducted to characterize and assess differences among groups. Results revealed significant differences among all three groups on DAFS overall performance. Post hoc analysis revealed
that normal controls performed best, followed by MCI, and then the AD group on most of the DAFS subscales. This information can provide an understanding of the course of functional change and hopefully support the imperative need for the development of methods for treatment plans in functional deficits.
CHAPTER I
INTRODUCTION

Dementia and Cognitive Impairment

Dementia is a clinical syndrome characterized by a cluster of symptoms manifested by deficits in several different cognitive domains (Prince, Bryce, Albanese Wimo & Ribeiro, 2013). This term is a general idiom used to encompass cognitive deficits that are a direct result of various neurodegenerative diseases. It is still the most widely used to signify these deficits, although it is important to note that this customary name is currently transitioning to neurocognitive disorder in order to include individuals of all ages and to better describe the deficits occurring within affected individuals (American Psychiatric Association, 2013). According to the Alzheimer’s Association, National estimates of the prevalence of all forms of dementia are not available, but many population-based studies, including the Aging, Demographics, and Memory Study (ADAMS), have provided estimates (Alzheimer’s Association, 2014). In the United States, 13.9 percent of people ages 71 and older are currently afflicted with some form of dementia (Plassman, et al., 2007). Deficits in dementia range from a steady or fast progressing inability to perform activities that require a substantial amount of memory, spatial ability, executive functioning, disturbances in language, psychological changes, and impairments in activities of daily living (Burns, 2009). All individuals with dementia present with cognitive deficits, but the etiology of these deficits varies. AD, vascular, frontotemporal, and Lewy Body dementia are some of the most common types.

As the numbers of individuals affected by these various types of neurocognitive disorders increase, early detection has become a watchword in dementia research and clinical practice (Smith & Bondi, 2013). It has thus become increasingly important to detect dementia in its very early stages.

Neuropsychological test batteries, evidence of genetic mutations, and different brain scans are
all testing modalities developed to aid in the diagnosis of various forms of dementia. Although these recent technological advances have provided ways to measure cognitive functioning, neuropsychological tests remain invaluable in the diagnosis of these conditions (Chaytor & Schmitter-Edfecombe, 2003). More importantly, neuropsychological test measures (1) serve as biomarkers for illness; (2) can be potent predictors for the development of AD and other dementias; (3) can dynamically capture countervailing influences on disease trajectory; and (4) are proxies for etiology and examination of accompanying functional deficits (Fields, Freenab, Boeve, & Smith, 2011). Due to its primary influence in diagnosis, in order for these results to be useful in predictive ability, we need to better understand their ability to determine patients’ everyday functional limitations.
CHAPTER II
REVIEW OF LITERATURE

Alzheimer’s Disease Epidemiology

The most common type of dementia is AD, accounting for 60%–80% of all dementia cases (Alzheimer’s Association, 2014). Estimates vary, depending upon the source, but currently AD is estimated to affect 5.4 million Americans worldwide. These numbers are expected to increase to about 16 million in the United States by 2030 (Alzheimer’s Association, 2013). As a result of this, by 2050 the number of people with AD may nearly triple from 5 million to 13.8 million (Alzheimer’s Association, 2014). Currently, there is a 2:1 ratio in female to male AD cases, and roughly 17% of women versus 9% of men living to age 65 whom are suffering with AD (Smith & Bondi, 2013). Therefore, of the 5 million with AD, 3.2 million women are affected, as compared to 1.8 million men (Herbert, Weuve, Scherr, & Evans, 2013). Moreover, AD is the sixth leading cause of death in the U.S. Following a diagnosis of AD, a person’s risk of death is double that of the normal aging population (Obuodiyat, Glazer, Seifan, Greer, & Isaacson, 2013). Risk factors for this disease include age and genetic components, i.e., chromosomes 21, 19, and 14I, and the APOE gene. Additional risk factors that make an individual more susceptible to this diagnosis may include a history of head trauma, substance abuse, low educational and occupational attainment, diabetes, and malnutrition (Castellani, Rolston, & Smith, 2012; Oboudiyat, Glazer, Seifan, Greer, & Isaacson, 2013). These numbers are staggering and clearly represent the imperative need for treatment, interventions, and diagnostic accuracy.

Diagnosis and Alzheimer’s Disease

There are various definitions and specific criteria that have been developed to establish what constitutes a diagnosis of AD, but there is currently no definitive measure that represents a true
presence of this disease. At present, AD can only be definitively diagnosed post mortem, although earlier diagnosis may be possible with improved diagnostic techniques (Perry, et al., 2012). For decades, the medical and research community predominately used two diagnostic criteria: The National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA), and the Diagnostic and Statistical Manual of Mental Disorders (DSM). These criteria now follow the AD pathophysiological process, which begins years, and perhaps decades, before the onset of clinical symptoms and dementia (Budson & Solomon, 2012). Furthermore, associated genes and biomarkers have been studied meticulously, resulting in a clearer understanding of the processes in the AD formulation. Ultimately, the purpose of finding different biomarkers, genetic predispositions, and neuropsychological test profiles is to enable healthcare professionals to identify and treat this disease as early as possible (Budson & Solomon, 2012).

In light of these developments, The National Institutes on Aging and the Alzheimer’s Association workgroup changed their 1984 criteria in 2011 to reflect this accompanied knowledge. Briefly stated, the workgroup added new guidelines to recognize the pre-clinical stage of AD. They enhanced the assessment of AD to include amyloid accumulation as well as neurofibrillary plaques; established protocols for the neuropathologic assessment of Lewy body disease, vascular brain injury, and hippocampal sclerosis; and recommended standard approaches for the workup of cases (McKhann, et al., 2011). They proposed the following terminology for classifying individuals with dementia caused by AD to: 1) Probable AD dementia, Possible AD Dementia, and Probable or possible AD dementia with evidence of the AD pathophysiological process. The first two types of AD diagnoses were intended for use in clinical settings, while the third was established for research purposes (McKhann, et al., 2011). The new criteria proposed a four-step approach to diagnosing
dementia due to AD. Biomarkers enable the diagnosis of probable AD dementia with evidence of the AD pathophysiological processes. If one of the two-biomarker categories is positive, the biomarker probability of AD etiology rises to intermediate, and if both categories are positive, the probability is increased to high. Possible AD is used instead of probable AD if the cognitive deficits look like AD but there is an atypical course (either sudden onset, no definite decline or mixed etiology). Thus, the patient might meet the criteria for probable AD dementia, but there is also evidence of significant vascular disease, Lewy bodies, or other condition that could be contributing to the patient’s dementia. The next diagnosis is pathophysiologically proven AD, consisting simply of the unchanged criteria of patients meeting both the clinical and neuropathological criteria for AD. Finally, the criteria established for dementia unlikely due to AD is given (Budson & Solomon, 2012).

**Neuropathology of Alzheimer’s disease**

Brain changes in AD may begin 20 or more years before symptoms appear (Villemagne, et al., 2013). The core pathological hallmarks of AD include an excessive amount of amyloid plaques, neurofibrillary tangles, and neuronal loss, which is seen particularly in the parietal and temporal lobes of the brain (Oboudiyat, Glazer, Seifan, Greer, & Isaacson, 2013). The amyloid hypothesis is currently the most widely accepted model for explaining the neuropathological development of AD (Smith & Bondi, 2013). This model emphasizes the idea that misprocessing of the amyloid precursor protein leads to amyloid fragments that are insoluble in the brain. These fragments begin to aggregate to form plaques in the extracellular space in the brain, producing an inflammatory response. The plaques and inflammation are neurotoxic and cause neurons to die, which in turn causes neurofibrillary tangles to develop. As previously mentioned, these brain changes usually begin several years before actual cognitive deficits appear. Further along this continuum, the brain can no
longer compensate for the neuronal damage that has occurred, and the individual shows subtle decline in cognitive function. Later, the damage to, and death of, neurons are so significant that the individual shows obvious cognitive decline. Afterward, individuals affected even begin to lose basic bodily functions such as chewing and swallowing (Smith & Bondi, 2013). These neuropathology deficits are evident in their effects on functional ability in AD.

**Alzheimer’s Disease Presentation**

Neuropsychological test profiles of AD are distinguished from other forms of neurodegenerative diseases by the symptoms presented that correspond to the neuropathological hallmarks affected. The pattern and progression of cognitive deficits fit well with the proposed distribution and spread of neurodegeneration. Given that the earliest neurofibrillary changes occur in the medial temporal lobe structures, which are critical for learning and recall of new information, a wealth of neuropsychological evidence supports that episodic memory impairment is usually the first and most salient cognitive manifestation (Weintraub, Wicklund, & Salmon, 2012). As the neuropathology of Alzheimer’s disease spreads past the medial temporal lobes to the adjacent lateral temporal cortex, individuals affected usually lose semantic memory (which encompasses a general knowledge of facts, concepts, and the meanings of words that support knowledge (Weintraub et al., 2012). Later, there is also documented executive dysfunction, which entails the ability to perform activities that require mental manipulation, concept formation, problem solving, and planning (Smith & Bondi, 2013; Weintraub et al., 2012). Later in the course of the disease, deficits in visuospatial skills and constructional ability commonly begin to occur. This involves an increasing inability for individuals to carry out tasks which involve the skills needed to copy complex figures, mentally rotating representations of objects, and identifying commonly used objects (Weintraub et al., 2012).
As AD progresses virtually all areas of cognition are affected. Individuals eventually become incapable of caring for oneself, oftentimes living their final months and sometimes years in a vegetative bed bound state (Holtzman, Morris & Goate, 2011). Essentially, the neuropsychological profile of AD heavily translates and matches accompanied functional deficit.

**Mild Cognitive Impairment (MCI) Definition and Diagnosis/Changes That Have Been Made**

There has been growing interest in the pre-cognitive impairment phase of dementia in the hopes of being able to identify early clinical features so that the disease process can be stopped, slowed, or even reversed (Petersen, et al., 2009). Ideally, there has been a push to establish ways to prevent or postpone the disease process by intervening early. It is still unclear why some individuals revert to their previous cognitive state, and others do not. Many have proposed that this is a result of a pre-neurocognitive state, which matches their proceeding form of dementia. In turn, the construct of MCI serves a useful purpose as a clinical stage in which meaningful interventions can take place.

This clinical stage is thought to be a prodromal stage, which lies in between expected cognitive decline accompanying aging and the serious decline of cognitive abilities attributed to neurodegenerative diseases. When originally presented, Petersen and colleagues (1999) adopted the term *mild cognitive impairment* to describe an epoch in the longitudinal course of neurodegenerative disease where cognition is no longer normal relative to age expectations, but also where daily function is not sufficiently disrupted to warrant the diagnosis of dementia (Smith & Bondi, 2013; Petersen, 2011). The original Mayo criteria for MCI (Petersen, et al., 1999) stated that a subjective complaint of a memory disturbance (preferably supported by an informant) must be present to base a diagnosis. With the current understanding of the types of impairments associated with different forms of dementia, it is now apparent that not all neurocognitive disorders begin with memory impairments.
For example, individuals with frontotemporal dementia typically present symptoms related to changes in behavior and personality, and speech and language, in the early stages, due to the area affected. Different etiological neurodegenerative disorders lead to the distinction proposed to include different subtypes of MCI.

MCI now includes two different subtypes: amnestic and non-amnestic. Briefly stated, amnestic encompasses cognitive deficits, which include individuals who have revealed impairment in memory that is not severe enough to meet criteria for a neurocognitive disorder. Furthermore, individuals affected are aware of this subtle, yet increasing, inability to remember. However, in the amnestic subtype of MCI, the abilities such as executive functioning, use of language, and visuospatial skills remain relatively intact despite minor deficiencies (Petersen, 2011). On the contrary, the non-amnestic subtype is characterized by subtle decline in functions not related to memory, such as attention, use of language, and executive functioning skills (Petersen, 2011).

**Epidemiology: Mild Cognitive Impairment**

During the last decade, an increasing number of studies have been conducted in an attempt to estimate the prevalence of MCI in the general population. At the inception of this diagnostic entity, the frequency of MCI in the population was underestimated (Petersen, et al., 2014). Furthermore, during the first round of epidemiological studies of MCI, the original Mayo Clinic criteria were adopted, which restricted MCI to memory impairment only. In more recent studies, the expanded MCI criteria have been used, producing considerably higher estimates. From the major population-based studies using the expanded Mayo Clinic criteria (Petersen et al., 2014), the average prevalence of MCI was found to be 18.9%, which is almost three times higher than the prevalence of 7% derived from the population-based studies of MCI using the old criteria.

The incidence and prevalence rates of MCI have also been varied due to different diagnostic
definitions and methods, making it difficult to assess. As a set of diagnostic principles is agreed on, clearer estimates will be provided.

Moreover, work from the Mayo Clinic suggests that about 12% of MCI patients will progress to dementia per year and that 7%–10% of MCI patients will not ultimately have a progressive neuropathology at autopsy (Smith & Bondi, 2013). In fact, Smith and Bondi, (2013) propose an estimate of 9%–18% of all individuals with various forms of dementia passed through the MCI state prior to the dementia diagnosis. In contrast, they also found that, unlike the Mayo Clinic studies, the literature suggests that as few as 3% to as many as 63% of MCI patients will progress to dementia (Smith, & Bondi, 2013).

Studies have also examined rates of conversion amongst MCI subtypes. For example, Smith and Bond, (2013) found that upon examination of 41 studies, individuals diagnosed with amnestic MCI had a conversion to dementia rate of about 12% per a year following a seven-year follow up. Also, (Petersen et al., 2009) concluded that MCI amnestic type made up the majority of cases of the condition. Although these rates of prevalence and conversion rates differ among studies, it is evident that these individuals are highly susceptible to future cognitive impairments and functional deficit. Furthermore, the scatter and inconsistency of epidemiology point to the future need of study among this group in order to understand these deficits better.

**Pathology and Mild Cognitive Impairment**

In an attempt to identify early pathological changes that can be predictive of a neurocognitive disorder, efforts have moved toward utilizing several neuroimaging and neuropsychological testing modalities (Smith & Bondi, 2013). As a result of these studies, MCI has shown no single pathological explanation because it represents multiple substrates, whether in its amnestic or non-amnestic form (Petersen, et al., 2014). Several studies have been conducted using neuro-imaging devices, which
have been able to examine the brains of individuals diagnosed before and after death. For example, after the assessment of 15 Mayo Clinic AD patient registry cases that were examined post-mortem while their clinical diagnoses were still amnestic MCI, eight of the cases did not meet the criteria for AD, although their pathology suggested a transitional state of evolving AD (Petersen, et al., 2006; Smith, & Bondi, 2013). Additionally, these cases revealed a significant amount of argyrophilic grain disease, hippocampal sclerosis, and vascular lesions, while one case did not meet any neuropathological neurocognitive disease criteria (Petersen et al., 2006). Another study, which examined individuals upon autopsy who had been diagnosed with MCI, included 483 autopsied participants from the Religious Orders Study and the Rush Memory and Aging Project with probable AD (National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association criteria), who had been diagnosed with MCI or no cognitive impairment. They found that out of the 134 persons who died with their final diagnoses being MCI, around over half of them met pathological criteria for AD. Additionally, those who met pathologic criteria for AD were divided somewhat equally between amnestic and non-amnestic subtypes, and another 20% had mixed pathologies, again with similar proportions of amnestic (22.7%) and non-amnestic (15.2%) post-mortem diagnoses (Smith, & Bondi, 2013; Schneider, Arvanitakis, Leurgans, & Bennett, 2009). Overall, these findings suggest that the MCI pathology, including the amnestic subtype, is not always consistent with the AD pathology profile. Rather, this cognitive state is pathologically heterogeneous, with many persons exhibiting mixed pathologies (Smith, & Bondi, 2013). These mixed pathologies show that the literature has still not proven a clear picture of the trajectory and state of MCI. Furthermore, it is imperative to understand not only the causes of MCI but also how these mixed cognitive profiles present in the ability to perform functional everyday tasks.
Neuropsychology and Mild Cognitive Impairment

Several neuropsychological exams are incorporated into the evaluation of cognitive functioning in the assessment of MCI. Some have revealed that cognitive performance is heterogeneous among individuals diagnosed. Other studies reveal that cognitive assessment results of different subtypes of MCI have followed the pattern of diagnosis. For example, Libon, et al., 2011) revealed that the results of a delayed free recall and recognition test of an amnestic group revealed low scores along with a tendency for intrusions and false positive errors (Smith & Bondi, 2013). In contrast, the MCI non-amnestic group presented higher scores on the same recognition relative test in relation to a free-recall task (Libon et al., 2011). This reveals that a deficit in memory performance is often associated with individuals characterized in cortical disorders (e.g., AD) versus sub-cortical neurocognitive disorders (e.g., Huntington’s disease) (Smith & Bondi, 2013). Furthermore, as previously stated, prior work has also shown that MCI presents with more diverse cognitive profiles more often than a restricted loss of memory. This idea has been supported by difficulties with complex executive control tasks or semantic memory in addition to episodic memory where they have been seen more often than not in individuals previously diagnosed with MCI (Delano-Wood, et al., 2010; Bondi et al., 1999). As more sophisticated and set cognitive impairment diagnostic criteria are set, optimal clustering of test performance patterns may improve cognitive characterizations and may ultimately be as valuable as biomarkers in disease detection and future functional deficit (Smith, & Bondi, 2013).

Defining Activities of Daily Living (ADL)

Disability, characterized by the loss of ability to perform activities of daily living (ADL), is a defining feature of neurocognitive deficits that results in growing caregiver burden and the eventual need for alternative care. This decline in functional ability is one of the most troubling aspects of
neurocognitive disorders. ADL’s are defined as typical day-to-day tasks and basic functions necessary to live independently and sustain, and care for oneself (Warner, 2000). These include things as simple as eating, dressing, bathing, toileting, and walking. These types of tasks are often referred to as basic ADL’s. Secondary tasks that are not necessary for survival, such as cooking, housekeeping, paying bills, banking, and laundry (Warner, 2000), are often referred to as instrumental ADL tasks. In the early stages of neurocognitive deficits, individuals affected are still able to perform many ADL and family responsibilities despite occasional accidents or episodes of forgetfulness. However, as time progresses, more of these everyday activities begin to require assistance (Warner, 2000).

Over the years, several different modalities have been used to measure an individual’s ability to carry out ADL tasks. The most common include self-reports, informant reports, and performance-based measures. Problems with these measures have resulted in various inaccurate reports of functional ability. Informant reports of individuals who are family or friends tend to misjudge the general functional abilities of patients relative to their performance on objective measures (Wadley, Harrell, & Marson, 2003). This may be due to a lack of insight about their family member or denial as to actual ability of the individual they are reporting on. Self-reports tend to be inaccurate as well. This may be a result of the impact of the neurocognitive disorder, which calls into question the accuracy of their reports. Research has shown that patients often overestimate or exaggerate their functional abilities in relation to their performance on objective measures as well. For example, Zanetti, Geroldi, and Frisoni (1999), found that caregivers had a tendency to underestimate functional deficits in individuals affected with AD. In contrast, an alternative study found that caregivers overestimated the functional deficits of individuals with AD (Loewenstein, Arguelles, & Bravo, 2001). This raises the fact that although caregiver reports can still be beneficial measures of ADL’s
considering that they have the chance to observe patients everyday, researchers and clinicians must be mindful of their tendency to provide inaccurate results (Wadley, et al., 2003).

**Alzheimer’s Disease and Activities of Daily Living**

Functional status has been shown to be an important determinant of the quality of life, mood, and behavior in patients with AD (Albert, et al., 2011). Previous research has demonstrated different areas of decline in the ability to perform ADL tasks in individuals with AD more than any other form of dementia, due to the high prevalence seen within this disease. There is a general consensus that measures of functional disability form an essential part of the diagnosis process and care planning for individuals who have these functional deficits (Gauthier, et al., 2009). Most functional changes seen in AD seem to be strongly associated with basic neurological changes in the brain (Gauthier, et al., 2009). A wide range of deficits in perception and cognition such as memory, attention, and executive function can affect the ability to perform ADL tasks. Previous research has shown that in the beginning, individuals with AD show decline in their ability to perform the more complex ADL’s (instrumental ADL’s) and that as time goes on and decline in cognitive functioning occurs, individuals begin having trouble performing simple activities such as eating and drinking, and even become incontinent. For example, an examination of ADL tasks in mild AD in comparison to normal controls revealed that individuals with AD performed worse on all 14 ADL tasks on the Direct Assessment of Functional Status (DAFS). More specifically, individuals with AD demonstrated worst performance on finance- and shopping-related tasks, which require substantial memory skills (Razani, et al., 2011). Another study, which examined ADL deficits in AD, revealed that patients with moderate to severe AD showed a decline on the ADL Cooperative Study over a short span of 6–12 months (Galasko, et al., 2005). Furthermore, several studies have linked the executive function deficits seen in AD with the inability to carry out ADL tasks. For example Martyr and Clare, (2012)
found that following a meta-analysis of associations between ADL ability and executive functioning tasks of 49 studies, the analysis suggested a consistent moderate association between ADL ability and executive functioning. Furthermore, another study, which examined the correlation between executive functioning deficits with functional ability on the DAFS, found a strong correlation between functional abilities and executive functioning scores (Razani, et al., 2007). Although there are several studies that assess the functional deficits seen in AD, there is currently a lack of performance-based measures used to assess these deficits. Furthermore, these deficits are not clearly defined in AD.

**Activities of Daily Living Deficits in the Literature Presented**

Measures of functional disability are crucial in monitoring disease progression, assessing the benefit of interventions, and making decisions on legal issues such as guardianship. Therefore, it is essential to use accurate tools to measure functional ability to obtain accurate information. Author’s caution that these measures should be ideal for the specific cognitively impaired populations (Gauthier, et, al., 2009). However, several scales have been established to measure ADL’s in individuals with neurocognitive disorders, such as the Basic Activities of Daily Living Scale, the Disability Assessment for Dementia, and the Progressive Deterioration Scale (Gauthier, et al., 2009). These measures may improve its diagnostic accuracy by being observation-based instead of obtained by the individuals themselves (self-report) and individuals’ caregivers and family members (informant-based reports). The amount of knowledge we have on how AD functions as a disease physiologically must match the knowledge we have on how this impairment translates into everyday functioning in order to improve diagnostic accuracy.

**Mild Cognitive Impairment and Activities of Daily Living**

In the diagnostic process of MCI, following the period where deficits in two or more areas of
cognition are identified, the clinician is faced with the challenge of determining whether an individual’s cognitive disturbance is also associated with a decline in the ability to perform ADL tasks (Smith & Bondi, 2013). While there are studies indicating that basic function of ADL’s is relatively well preserved, there is no agreement regarding the type or degree of impairment found in complex ADL’s for individuals with MCI (Nygard, 2003). Additionally, there is no set diagnostic formula for measuring these functional deficits. Depending upon the individual clinician or researcher, self-informant, informant reports, or observational tasks may be used to assess functional limitations. Due to individual variation in measuring ADL’s in this population, functional assessment processes vary by diagnosis. Unfortunately, this imperative aspect of diagnosis that may qualify or disqualify an individual for diagnosis also has generally scattered literature that has not been very helpful. (Smith & Bondi, 2013). Moreover, several studies have found that individuals with MCI do underperform, compared to normal elderly individuals. For example a meta-analytic study found that of the 37 studies examined all but two found differences between normal controls and MCI in at least one domain of functional ability (Jekel et al., 2015). Other studies not included in this analysis also found similar results. For example, (Ahn et al., 2009) found that individuals with MCI performed significantly worse on instrumental ADL tasks according to the Seoul-Activities of Daily Living informant-based scale, compared to normal controls. In contrast, other studies, like Bangen, et al., (2010), using performance-based instrumental ADL measure (The Independent Living Scales), found results that provided significantly lower scores in MCI-affected individuals, compared to normal controls as well. However, the MCI individuals were still considered to have normal ADL deficits (i.e., T-scores greater than or equal to 40) on this scale (Bangen et al., 2010). These conflicting results and many more support the need for better delineation using reliable diagnostic measures.

Examination of functional assessment of MCI individuals may also pose a benefit of predicting
conversion to various forms of neurocognitive disorders. For example, upon examination following a two-year period, a study done by Chang and colleagues, (2011) found that individuals with impaired instrumental ADL’s revealed widespread patterns of gray matter loss involving frontal and parietal regions, worse episodic memory and executive functions, and a higher percentage rate of progression to AD, relative to the intact ADL’s MCI group (Chang, McEvoy, & Fennema-Notestine, 2001; Salmon, et al., 2011). Results such as these furthermore demonstrate the importance of MCI as a clinical entity that not only predicts progression to neurocognitive disorders but also predicts anticipated functional decline.

**Gaps in the Literature and Goals of the Current Study**

MCI is an evolving diagnostic construct. It is imperative that we better understand impairments in daily activities. As previously mentioned, early research criteria stated that those with MCI must exhibit memory impairment beyond that of normal aging, but have relatively preserved daily functional abilities (Petersen, 2004). These criteria have now been refined to include mild daily functional impairments that do not interfere with the ability to work and carry out life activities. While the recognition that mild daily functional impairment is important, this revision allows considerable latitude as to what represents mild ADL impairment and the modalities of ADL that are affected in MCI (Morris, et al., 2001; Nygard, 2003). Given that the majority of those characterized as having MCI progress to AD, it is more imperative than ever to clearly define, characterize, and distinguish ADL impairments in MCI from those of AD.

The overall goal of the current study is to use an observation-based measure of ADL to characterize differences and similarities of functioning in MCI and AD individuals in relation to normal, age-matched controls.
Specific Aims of the Current Study

Aim 1: Differentiate the overall ADL performance of MCI, AD, and normal controls using an observation-based ADL task, (Direct Assessment of Functional Status).

Hypothesis 1: The MCI group will present subtle deficits on their overall ADL score in comparison to normal controls, but will perform better than the AD group.

Aim 2: Differentiate patterns of ADL performance between the MCI and NC group.

Hypothesis 2: Compared to healthy controls, the MCI group will demonstrate impairments in tasks requiring memory and higher order cognitive processing (i.e., DAFS subscales shopping, and finance) but relatively preserved ADL functions in others areas (i.e., DAFS orientation and transportation).

Aim 3: Differentiate patterns of ADL performance between the MCI and AD group.

Hypothesis 3: Compared to the MCI group, the AD group will demonstrate impairments in almost all ADL domains, but will perform relatively the same as the MCI group on tasks, which are heavily dependent on memory functioning (i.e., DAFS finance and shopping).
CHAPTER III

METHODOLOGY

Participants

Thirty-eight individuals with the research diagnosis of MCI were recruited from the University of California, Los Angeles (UCLA) Alzheimer’s Disease Research Center (ADRC). The MCI classification was based on a multi-disciplinary evaluation conducted at the UCLA ADRC and the modified Petersen criteria (Petersen, 2004) which stated that individuals included must have: 1) a subjective cognitive complaint, 2) reports of essentially intact activities of daily living, 3) objective cognitive impairment, and 4) individuals could not meet the clinical criteria for dementia. Individuals were excluded if: 1) They were under the age of 50, 2) had any significant neurological disease other than MCI, 3) MRI or CT of the brain demonstrated any major focal lesions except for (mild to moderate microvascular ischemic changes, which were permitted), 4) they had abnormal vitamin B\textsubscript{12} or thyroid function tests, 5) they had pre-morbid history of DSM-IV Axis I psychiatric disorders (American Psychiatric Association, 1994) or 6) significant systemic illnesses or unstable medical conditions that could contribute to impaired cognition. Given the relatively small sample size of this study, the MCI data were not separated into subtypes.

Fifty-nine AD patients, who were matched in age and education with the MCI participants, were recruited from the following four sites, The Veterans Affairs Hospital in the Greater Los Angeles area, the Alzheimer’s Disease Center (ADC) at the University of California Medical Center, and the regional Alzheimer’s Disease Association (ADA) at the California State University, Northridge campus. They all had a predetermined diagnosis of probable AD provided by a neurologist using the criteria set forth by the National Institute of Neurological and Communicative
Diseases and Stroke-Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA; McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984).

Sixty-four healthy controls, matched in age and education with the MCI and AD participants, were recruited via advertisements, flyers and word of mouth. A thorough medical history was gathered on these individuals to screen out those with major medical illnesses known to affect cognition such as a history of head injuries, major affective or psychotic disorders, seizures or other neurological disorders and substance abuse. Additionally, participants with major issues with mobility that would interfere with task performance were excluded from the study (Razani, et al, 2010). All individuals were participating in a larger National Institutes of Health (NIH)-funded research study comparing functional status among older people with dementia and without dementia. Prepared signed consent forms were completed prior to administration of test battery. The Institutional Review Boards (IRB) at the Veterans Affairs Hospital in the Greater Los Angeles area, UCLA ADC, and California State University Northridge, approved research methods and procedures.

As part of the larger study, participants completed approximately 3 hours of testing. Tests included a neuropsychological battery that included tests of attention, concentration, abstract reasoning, and visual spatial skills. For the purposes of this study, the only task that will be examined is the Direct Assessment of Functional Status in order to analyze functional deficits among groups.

**Demographic Information**

The demographic information for the participants, including age, educational level, and Mini-Mental State Examination (MMSE) scores can be found in Table 1. As can be seen from this table, the normal control participants were on average in their 8th decade of life and no significant differences were found among the groups on age \((F (2, 155) = 2.40, p < .05)\). There were also no significant differences among groups on years of education attained \((F (2, 155) = 2.696, p < .05)\). As
expected, however, the groups differed on the Mini-Mental State Examination (MMSE) scores. Patients with AD scored on average (23.30) lower than the MCI (26.82), and normal control (29.21), and the normal controls scored relatively higher than the MCI group \((F(2, 155) = 37.76, p < .05)\).

**Direct Assessment of Functional Status**

The Direct Assessment of Functional Status (DAFS) is a direct observation-based test designed to assess the daily functional abilities of those with dementia (Loewenstein, et. al 1989). The test has been found to have high inter-rater and test re-test reliability, and has been found to be a valid measure in distinguishing different forms of dementia (McDougall, Becker, Vaughan, Acee & Delville, 2009; Zanetti, Frisoni, Rozzini, Bianchetti & Trabucchi, 1998). The DAFS has demonstrated inter-rater reliabilities in the mid .9 ranges, with the lowest subscale being .91. This test also shows high-test retest reliability ranging from .57 to .92 for the individual subscales (Razani, et al., 2011).

The DAFS provides an overall score of 92 which is derived from the sum of scores on the following subscales:

1) *Time orientation* assesses (a) ability to tell time using a clock (0 -8 points), and (b) orientation to person, places, and dates. (0-8 points).

2) *Communication* skills assess (a) the ability to use a telephone (0-8 points) and (b) the ability to prepare and mail a letter (0-6 points).

3) *Transportation* skills assesses (a) the ability to identify road signs (0-10 points) and (b) knowledge of driving rules (0-3 points).

4) *Financial* skills assess (a) the ability to identify currency (0-7 points), (b) the ability to count currency (0-4 points), (c) the ability to write a check, (0-4 points) (d) the ability to balance a checkbook (0-4 points).
5) *Shopping* skills assesses (a) the ability to “shop” from a mock grocery store by freely recalling shopping items, (0-6 points), (b) “shop” by recognizing items, (0-6 points) and (c) “shop” with a list (0-4 points). The ability to make correct change (0 -1 point) is also included on the shopping skills subscale, but for the purposes of this study and analyses it was separated as its own subscale.

6) *Grooming* skills assess (a) the ability to use everyday grooming materials such as brushing hair, brushing teeth, and using a washcloth.

7) Eating assesses (a) the ability to pour a glass of water, and use utensils such as a knife, spoon, and fork.

While the total DAFS scores is derived from the sum of all subscales, for the purpose of this study, the last two DAFS subscales (grooming and eating abilities) will not be individually computed and analyzed due to ceiling effects for all groups.

**Procedure**

The DAFS was administered by a trained research assistant at the patient’s home, or on the campus of California State University, Northridge as part of a larger test battery. Administration of this test usually took approximately 30-45 minutes depending upon the participant’s level of cognitive impairment. All participants were paid $100 for their involvement in the study.

**Analyses**

In order to assess the three hypotheses, a Multivariate Analysis of Variance (MANOVA) was used to examine differences among MCI, AD, and normal controls on the overall, and 5 subscale scores of the DAFS. To further assess hypotheses two and three, individual analysis of variance and post-hoc analysis were used to examine differences among the groups on each individual subscale of the DAFS.
Due to the multiple comparisons, the p-value required for statistical significance was lowered to .01 rather than the standard .05 values. Significance values for the follow-up analyses were set at the standard .05 level. While we recognize that this may not entirely protect against Type I error, a more stringent criterion would increase Type II error due to the small sample size.
CHAPTER III
RESULTS

Overall group comparisons

Results from the MANOVA revealed a significant difference between all three groups overall performance on the DAFS, (Wilk's $\Lambda = .305$, $F (40, 266) = 5.395, p < .01$).

Given the significance of the overall test, univariate analyses were performed. The analysis revealed significant differences between all three groups on all but 2 of 14 subscales. Groups did not differ on the shopping with a list task, ($F (2, 152) = 2.54, p > .01$), or the ability to identify currency ($F (2, 152) = 4.27, p > .01$).

Groups, however, differed on the orientation to time ($F (2, 152) = 10.18, p < .01$), orientation to date ($F (2, 152) = 28.17, p < .01$), ability to use a telephone ($F (2, 152) = 8.47, p < .01$), ability to mail a letter ($F (2, 152) = 14.95, p < .01$), ability to identify traffic signs ($F (2, 152) = 7.67, p < .01$), knowledge of driving rules ($F (2, 152) = 10.51, p < .01$), ability to count currency ($F (2, 152) = 4.27; p < .01$), ability to write a check ($F (2, 152) = 10.89, p < .01$), balance a checkbook ($F (2, 152) = 17.74, p < .01$), shopping free recall ($F (2, 152) = 58.3, p < .01$), and shopping recognition ($F (2, 152) = 46.0, p < .01$).

Pairwise group comparisons

A series of post-hoc analyses were performed on the overall DAFS scores and the DAFS subscales on which groups differed and the following results were observed. Means and standard deviations of the subscales for each group are presented in Table 2. The analyses revealed that the AD group performed significantly worse than the normal controls on all subscales ($p < .01$), with the exception of the shopping with a list task ($p = .306$).

Additionally, post-hoc analysis revealed that the MCI group only performed poorer than the
normal controls on the overall DAFS total, shopping free-recall, and shopping recognition subscales ($p < .01$; see Table 2). There were no significant differences between the MCI and controls on any of the other DAFS subscales.

Finally, the MCI group outperformed the AD group on all subscales of the DAFS ($p < .01$), except the ability to identify currency, and shopping with a list.

Overall, it appears that with the exception of the shopping task, ADL functioning is relatively preserved during the non-diagnosable stages of dementia, but that all functioning is impaired in the early stages of probable AD.
CHAPTER V
DISCUSSION

The purpose of this study was to differentiate the overall ADL performance of MCI, AD, and normal controls using an observation based ADL task, (Direct Assessment of Functional Status), to determine patterns of ADL performance between the MCI and NC group, and to differentiate patterns of ADL performance between the MCI and AD group.

As predicted, there were group differences on the total DAFS score as well as the individual subscales. Furthermore, the AD group performed worse than both the MCI and control group. Moreover, the MCI group remained in an intermediate stage between AD and normal controls on tasks requiring memory mediation, but not on other tasks. These overall differences are consistent with the literature characterizing the cognitive characteristics of these groups.

Previous research has found that individuals diagnosed with AD have widespread cognitive deficiencies, which have been shown to be related to functional deficits. More specifically, research suggests that in addition to general cognitive abilities, executive functioning and memory abilities are the two cognitive domains most consistently related to everyday functioning in the AD population (e.g., Farias et al., 2006; Mariani et al., 2008; Rapp & Reishcies, 2005; Razani, et al., 2010). For example, a number of studies have found that executive functioning deficits account for a significant amount of functional ability in patients with mild AD and other forms of dementia on the DAFS (Farias, Harrell, & Neuman, 2003; and Razani et al., 2007; Razani, et al., 2010). These findings have also been demonstrated in studies that incorporated MCI, AD, and normal controls. For example, Rog et al., (2014), indicated that worse memory and executive function, were all independent and additive determinants of poorer functional abilities on the Everyday Cognition scale in MCI, AD, and normal controls.
Studies like these corroborate the findings that AD patients perform poorly on all of the DAFS subscales, since their level of cognitive impairment has advanced to a stage that affects widespread functional domains (Razani et al., 2010).

The MCI group performed significantly worse in comparison to normal controls on the overall DAFS subscale. Interestingly, however, it appears that this difference is due to the performance of MCI on the shopping subscales of the DAFS. The MCI group only significantly differed from the controls on the shopping free recall and shopping recognition tasks. These findings may be due to the fact that in comparison to other DAFS tasks (e.g., shopping with a list and telling time), these subscales require more complex cognitive processing skills. This is consistent with a study done by Perneczky and colleagues (2006), which found that individuals with MCI presented difficulty in comparison to normal controls on ADL activities that involved memory or complex reasoning, whereas more basic activities were unimpaired. These findings are also consistent with other research on ADL functioning of MCI and controls. In a recent meta-analytic study examining functional deficits in MCI, Jekel et al., (2015) found that out of the 35 studies reviewed, deficits on shopping tasks were consistently prominent. Pereira, and colleagues (2010) also found that normal controls outperformed MCI individuals on shopping tasks presented on the Brazilian version of the DAFS. Furthermore, Werner, Rabinowitz, Klinger, Korczyn, and Josman (2009) found shopping deficits in MCI in comparison to normal controls using a virtual action supermarket.

The shopping free-recall task on the DAFS requires individuals to verbally recall shopping items after a 10-minute delay. The shopping recognition task prompts individuals by presenting actual grocery items, and then asks individuals to select items previously given. Cognitively, these tasks require higher order processing abilities such as attention, organization of information, and proper encoding, and retrieval of shopping items. Given the early appearance of pathologic changes
in the brains of MCI, (Smith & Bondi, 2013) it is not surprising that this task is particularly problematic. More specifically, the medial temporal lobe, critical for learning and recall of new material (Salmon & Bondi, 2009), is one of the areas most affected in MCI (Smith et al, 2013). Our findings of poor memory for the shopping task is also in line with a wealth of neuropsychological studies which supports that episodic memory impairment is usually the first and most salient cognitive manifestation of MCI and AD (Smith et al, 2013). For example, Gifford, Liu, Damon, Chapman, and Romano (2015), found that self reported memory concern in individuals with MCI was specifically related to objective episodic memory deficits. Furthermore, Bennett et al., (2002) found that after a 4.5 year follow up of individuals with MCI, individual cognitive domains assessed revealed that subjects declined significantly faster on measures of episodic memory more than any other cognitive domain examined. Similar results were also found when individuals with MCI were examined, using the Face Place Test of episodic memory. This study found that individuals with MCI not only presented deficits in episodic memory, but when compared to individuals with AD, episodic memory deficits were matched (Dudas, Clague, Thompson, Graham, & Hodges, 2005).

Surprisingly and somewhat inconsistent with other studies, there were no differences found between MCI and normal controls on any of the financial tasks (i.e., identifying and counting currency, writing a check, balancing a checkbook, and making correct change) in the current study. Financial tasks on the DAFS require individuals to use several cognitive abilities such as working memory and executive functioning (Razani et al., 2007). As previously mentioned individuals with MCI start out presenting subtle cognitive deficits with specific areas affected depending upon the subtype. Individuals with amnestic MCI usually have a cardinal deficit in memory. Conversely, individuals with non-amnestic MCI usually pose deficits in other cognitive domains, such as executive functioning. The lack of significant differences found between groups on the finance
subscales in the present study may be explained by the variability or lack of subtype differentiation diagnosis in the MCI group. Previous research has found that individuals who pose deficits in financial performance appear to lack an ability to selectively attend, self-monitor, and temporally integrate information (Cook, & Marsiske, 2006). Compromised performance on cognitive measures of attention and executive function also constituted clinical markers of lower financial abilities (Oboudiyat, Glazer, Seifan, Greer & Isaacson, 2013). It is possible that the MCI individuals in the present study are primarily of the amnestic type with attention, working memory and executive skills relatively intact. With larger samples, we may have been able to separate participants based on subtypes in order to better characterize financial skills performance.

It should be noted that our results were inconsistent with a few studies that have found deficits in financial ability in MCI. For example, Pereira and colleagues (2010), demonstrated that an MCI group in comparison to normal controls presented difficulty on all of the finance subscales of a Brazilian version of the DAFS. Furthermore, relative to controls, other studies have found that MCI participants demonstrated poor performance on the Financial Capacity Instrument, an observation based task intended solely for the measurement of financial ability (Griffith et al., 2003; Triebel et al., 2009). There may be a couple of reasons for the discrepancies found between the findings of the current study and that of the other studies. The previous studies may have found differences between MCI and controls on financial tasks (where the current study did not) because they had a sample primarily made up of MCI subtypes with executive/attention deficits. Most early studies of MCI did not differentiate between subtypes and/or domain specific deficits. Additionally, past studies examining financial abilities, used tests designed for that single domain, thus the task of managing may have been more detailed, involved and complex than those on the DAFS.
Not surprisingly, the MCI group did not present any deficits in comparison to normal controls on any of the communication or orientation subscales; i.e. using a telephone, mailing a letter, telling time and orientation to date. Results from the meta-analysis of studies that examined MCI functional deficits in comparison to normal controls found that of the 35 studies included, most of the results found no communication or orientation deficits (Jekel et. al, 2015). For example, (Binegar, Hynan, Lacritz, Weiner, & Cullum, 2009) found no deficits in communication on the Texas Functional Living Scale between MCI and normal controls. Moreover, (Brown, Devanand, Liu, & Caccappolo, 2011), found no differences in communication ability using the The Preffer Functional Activities Questionnaire. Nevertheless it is important to note that in other measures that solely do in depth ADL communication analyses, found that MCI individuals posed deficits in comparison to normal controls. For example, an analysis of 28 observational studies that solely comprised of communication ADL tasks, found generally impaired expressive and receptive communications skills in individuals with MCI, compared to their healthy counterparts (Johnson, & Lin, 2014).

Also not surprisingly, there were no differences found between normal controls and MCI on any of the transportation subscales (i.e., identifying road signs and driving rules). These two tasks generally require a substantial amount of long-term memory. As previously mentioned, individuals with MCI generally have preserved long-term memory, and thus for this task can draw on their knowledge of driving rules and meanings of road signs. The current findings are relatively consistent with previous research that investigated transportation capabilities in MCI. In fact, Wadley et al. (2009) found that when performance of MCI and normal controls were evaluated by a rehabilitation specialist on a driving task, the magnitude of difference between the MCI and control participants’ driving performance was so small that it did not warrant classifying MCI drivers’ ability as unsafe or unsatisfactory.
Finally, the current findings showed that the MCI group significantly outperformed the AD group on all DAFS subscales with the exception of identifying currency and shopping with a list. As previously mentioned both of these tasks did not require a substantial amount of cognitive ability, which could explain why they are relatively preserved in our sample of MCI and mild AD patients. Furthermore, identifying currency could be deemed as a task that requires relatively greater long-term memory components as opposed to short-term memory. People with MCI and mild AD tend to retain long-term memory skills but experience a significant short-term memory loss (Smith et al., 2013).

Overall, the current study showed that virtually all areas of ADL functioning are impaired in AD, but that in MCI, only tasks that heavily rely on short-term memory are affected. Given the large conversion rate from MCI to AD, it is clear that individuals with MCI need to be followed carefully to better understand the severity and specificity of the decline in ADL as the disease progresses.

Limitations

This study will add considerably to the understanding of functional deficits in MCI, AD, and normal controls however certain limitations exist. Sample sizes for the current study were relatively small. Some of the findings that were not significant may be due to lowered statistical power. Future studies should attempt to replicate the current study with larger samples, particularly in the MCI group where the effect sizes may be relatively small. Additionally, individuals with different subtypes of MCI were not studied. Examination of different subtypes may produce more detailed and distinct results in the MCI. Furthermore, the DAFS, although an observation-based measure, may lack the complexity needed to assess certain domains. Incorporating other performance-based measures, which contain more detailed assessment of specific domains (such as financial skills) may result in a clearer picture of functional deficits among cognitively impaired groups.
Future Studies

Future studies should incorporate subtypes of MCI into the comparison between groups on ADL tasks, which can allow for further distinguished and characterizing ADL deficits in this group. These studies should also include longitudinal follow up methods to examine the severity of decline in specific domains over time in MCI. This would help to better characterize daily dysfunction as these individuals transition to meeting criteria for dementia. Furthermore, longitudinal follow up functional studies can perhaps aid in predicting rates of conversion from MCI to dementia. Ideally, future studies should incorporate more than one performance based measure of ADL functioning in order to better characterize specific aspects of complex daily tasks. For example, the Financial Capacity Instrument (Marson, et al., 2000) and Virtual Action Planning Supermarket (Werner, Rabinowitz, Klinger, Korczyn, & Josman, 2009), provide an in depth analysis of functional deficits in areas of finance and shopping, and perhaps should be included in a more comprehensive ADL test battery.

Conclusion

Functional deficits are one of the hallmark features of neurocognitive disorders that pose significant problems in a patient and caregiver’s daily lives. It is estimated that in 2013 caregivers for individuals with dementia provided an estimated 17.7 billion hours of informal (that is, unpaid) care, valued at over $220.2 billion (Alzheimer’s, Association, 2014). The emotional and financial burden individuals have when losing their ability to perform functional tasks results in the imperative need to better understand these deficits to provide accurate and specific interventions. The current study adds to the growing literature on MCI in highlighting impairments in specific aspects of functioning. These findings along with others, can aid healthcare professionals to assist patients and their families in devising appropriate treatment plans for daily functioning.
REFERENCES


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APPENDIX A

Table 1: Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Normal Controls</th>
<th>MCI</th>
<th>AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>64</td>
<td>38</td>
<td>59</td>
</tr>
<tr>
<td>Males</td>
<td>13</td>
<td>20</td>
<td>41</td>
</tr>
<tr>
<td>Females</td>
<td>51</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Age</td>
<td>$M=70.55$</td>
<td>$M=73.12$</td>
<td>$M=74.31$</td>
</tr>
<tr>
<td></td>
<td>$sd\pm10.71$</td>
<td>$sd\pm9.17$</td>
<td>$sd\pm9.10$</td>
</tr>
<tr>
<td>Education # of years</td>
<td>$M=14.35$</td>
<td>$M=15.71$</td>
<td>$M=16.77$</td>
</tr>
<tr>
<td></td>
<td>$sd\pm2.37$</td>
<td>$sd\pm3.21$</td>
<td>$sd\pm9.04$</td>
</tr>
<tr>
<td>Mini Mental State</td>
<td>$M=29.21$</td>
<td>$M=26.82$</td>
<td>$M=23.30$</td>
</tr>
<tr>
<td>Examination</td>
<td>$sd\pm1.20$</td>
<td>$sd\pm3.79$</td>
<td>$sd\pm5.53$</td>
</tr>
</tbody>
</table>
### Table 2: Means and Standard Deviations of DAFS Subscales by Diagnosis

<table>
<thead>
<tr>
<th>DAFS Subtests</th>
<th>Normal Controls</th>
<th>Mild Cognitive Impairment</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DAFS Total</strong>&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>$M=86.92/\text{sd}\pm.3.45$&lt;sup&gt;a&lt;/sup&gt;</td>
<td>$M=79.39/\text{sd}\pm.13.92$</td>
<td>$M=70.62/\text{sd}\pm.14.31$</td>
</tr>
<tr>
<td><strong>Orientation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telling Time&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=7.86/\text{sd}\pm.66$</td>
<td>$M=8.16/\text{sd}\pm.1.34$</td>
<td>$M=6.75/\text{sd}\pm.2.42$</td>
</tr>
<tr>
<td>Orientation to Date&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=7.95/\text{sd}\pm.37$</td>
<td>$M=7.42/\text{sd}\pm.1.30$</td>
<td>$M=5.32/\text{sd}\pm.1.11$</td>
</tr>
<tr>
<td><strong>Communication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use a Telephone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>$M=7.66/\text{sd}\pm.57$</td>
<td>$M=7.39/\text{sd}\pm.1.36$</td>
<td>$M=6.64/\text{sd}\pm.1.90$</td>
</tr>
<tr>
<td>Mail a Letter&lt;sup&gt;a&lt;/sup&gt;</td>
<td>$M=5.75/\text{sd}\pm.617$</td>
<td>$M=5.47/\text{sd}\pm.1.00$</td>
<td>$M=4.60/\text{sd}\pm.1.64$</td>
</tr>
<tr>
<td><strong>Transportation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identify Road Signs&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=9.94/\text{sd}\pm.30$</td>
<td>$M=9.74/\text{sd}\pm.0.89$</td>
<td>$M=9.21/\text{sd}\pm.1.53$</td>
</tr>
<tr>
<td>Identify Driving Rules&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=2.91/\text{sd}\pm.29$</td>
<td>$M=2.68/\text{sd}\pm.0.70$</td>
<td>$M=2.34/\text{sd}\pm.0.91$</td>
</tr>
<tr>
<td><strong>Finance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identify Currency&lt;sup&gt;a&lt;/sup&gt;</td>
<td>$M=7.00/\text{sd}\pm.00$</td>
<td>$M=7.00/\text{sd}\pm.00$</td>
<td>$M=6.79/\text{sd}\pm.0.71$</td>
</tr>
<tr>
<td>Count Currency&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=3.97/\text{sd}\pm.175$</td>
<td>$M=3.74/\text{sd}\pm.0.72$</td>
<td>$M=3.11/\text{sd}\pm.1.39$</td>
</tr>
<tr>
<td>Write a Check&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=3.91/\text{sd}\pm.034$</td>
<td>$M=3.84/\text{sd}\pm.37$</td>
<td>$M=3.34/\text{sd}\pm.1.073$</td>
</tr>
<tr>
<td>Balance a Checkbook&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=3.11/\text{sd}\pm.1.12$</td>
<td>$M=2.68/\text{sd}\pm.1.37$</td>
<td>$M=1.64/\text{sd}\pm.1.54$</td>
</tr>
<tr>
<td><strong>Shopping</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free-Recall of Shopping&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>$M=3.98/\text{sd}\pm.1.30$</td>
<td>$M=2.34/\text{sd}\pm.2.00$</td>
<td>$M=1.04/\text{sd}\pm.1.20$</td>
</tr>
<tr>
<td>Recognition of Shopping&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>$M=4.98/\text{sd}\pm.088$</td>
<td>$M=3.66/\text{sd}\pm.1.80$</td>
<td>$M=2.15/\text{sd}\pm.2.03$</td>
</tr>
<tr>
<td>Shopping with a List</td>
<td>$M=4.00/\text{sd}\pm.00$</td>
<td>$M=3.79/\text{sd}\pm.0.81$</td>
<td>$M=3.85/\text{sd}\pm.0.49$</td>
</tr>
<tr>
<td><strong>Making Correct Change</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Making Correct Change&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>$M=95/\text{sd}\pm.021$</td>
<td>$M=.84/\text{sd}\pm.037$</td>
<td>$M=.55/\text{sd}\pm.50$</td>
</tr>
</tbody>
</table>

<sup>a</sup>Alzheimer’s disease < Normal Controls
<sup>b</sup>Mild Cognitive Impairment < Normal Controls <sup>c</sup>Mild Cognitive Impairment > Alzheimer’s disease