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Predictive Abilities of Neuropsychological Measures on Functional Outcomes in the Mild Cognitive Impairment (MCI) and Dementia Populations

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PREDICTIVE ABILITIES OF NEUROPSYCHOLOGICAL MEASURES ON FUNCTIONAL OUTCOMES IN THE MILD COGNITIVE IMPAIRMENT (MCI) AND DEMENTIA POPULATIONS

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DISSERTATION APPROVAL

This is to certify that the thesis presented to us by Morgan Bare on the 13th day of June, 2023, in partial fulfillment of the requirements for the degree of Doctor of Psychology, has been examined and is acceptable in both scholarship and literary quality.

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ABSTRACT

During the aging process, a decline in ability to perform everyday tasks is commonly observed. This is increasingly so for those with dementia and is a diagnostic requirement. These daily tasks require certain cognitive skills which can be measured by various neuropsychological measures. The purpose of this study is to examine which neuropsychological measures are able to detect various deficits in self-reported activities of daily living (ADL) and instrumental activities of daily living (IADL) in individuals with mild cognitive impairment (MCI) and dementia. It is hypothesized that Trail Making Test– B (TMT-B) would be the most sensitive predictor in functional abilities for IADLs and ADLs in both the dementia and MCI populations. This is a quasi-experimental study using archival data and regression statistical models. The only statistically significant finding was that the TMT-B and Mini Mental Status Exam (MMSE) were predictive of IADL functioning within the MCI group, thus incorporating these measures in neuropsychological batteries is warranted. By knowing this information, neuropsychologists may refine their understanding of the utility of neuropsychological assessment and its relationship to disability, implement early intervention techniques to further preserve cognition, as well as assess the most appropriate environmental supports such as residential placements.

CHAPTER 1: STATEMENT OF THE PROBLEM

Dementia is a broad term used to refer to the loss of cognitive abilities. As individuals age, their functional ability to perform every day activities are diminished and this is increasingly so for individuals with dementia. Moreover, functional decline is required for a diagnosis of dementia. For some of these activities, individuals may require more assistance than with others, or they may be fully dependent on others to help them. These daily tasks require a certain number of cognitive skills in order to be performed alone or with assistance. There are various studies examining the relationship between general cognitive domains and their impact on the performance of activities of daily living (ADL) and instrumental activities of daily living (IADL). ADLs typically include bathing, dressing, grooming, toileting, and eating (Marshall et al., 2012). IADLs typically include managing finances, household chores, and managing medications to name a few; More complex behaviors are needed to perform these activities (Farias et al., 2009). These are all common daily activities that allow an individual to function with ease throughout their life and therefore enhance autonomy.

Specifically, executive functioning (EF) has been one of the more highly researched cognitive domains in terms of its impact on ADLs and IADLs and is arguably one of strongest predictors of functional status (Farias et al., 2003). Executive dysfunction (ED) is thought to be highly related to ADLs and IADLs across the dementia disease process (Saari et al., 2018). EF has also been shown to be highly predictive of one's ability to write a check, balance a checkbook, and shop (Farias et al., 2003). Cahn-Weiner and colleagues (2000) found that ED is a crucial predictor of deficits of ADLs but not IADLs in community dwelling elderly individuals. Furthermore, EF was found to be the most significant factor in predicting functional ability, more so than the domains of language, visuospatial skills, memory, and psychomotor skills.

Since EF is such a broad term that encompasses many cognitive skills, this study will use more than one measure to try to capsulate the meaning of the term as much as possible. The difference in predictive abilities between ADLs and IADLs across literature may be due to the fact that the measures used do not sufficiently capture what EF is. This problem emphasizes the ambiguity of EF and outlines the difficulties of teasing apart what specific EF tasks are being measured. Specifically, Trail Making Test A (TMT-A) (Reitan, 1956), the clock drawing test (CDT), and animal fluency (or animal naming test [ANT]) are brief measures and have been shown to be tasks of EF that are highly predictive of IADLs and more advanced ADLs (Cornelis et al., 2018), but also are measures that have been classified under other cognitive domains. For example, ANT may fall under language and TMT-A, processing speed; Hence, adding to the complicated issue of what EF truly measures.

As mentioned, there are other cognitive domains that have been evaluated to determine their predictive power in various daily living skills, but the research is sparse and/or mixed. Specifically, immediate memory has been correlated with and found to be highly predictive of various daily living skills but across the research there are several different measures being used to assess this domain (Farias et al., 2003). There are further nuances to memory such as contextual versus non-contextual memory, with the contextual memory having more support in explaining the variance in functioning (McAllister et al., 2016). Additionally, verbal fluency has shown to have a relationship with ADLs, with some studies showing that it is highly predictive across the disease process and others showing that it is only predictive at later stages of the disease (Saari et al., 2018). One of the least researched neuropsychological tasks is the assessment of visuospatial skills and their relationship with daily functioning. Saari and colleagues (2018) showed that these skills are correlated with declines in IADLs, but only a modest degree. Lastly, there are arguably the most inconsistent and mixed results of research for brief cognitive measures such as a mental status exam (MSE). The MSE have been shown to explain up to one third of physical ADLs and IADLs (Reed et al., 1989) but had the smallest effect size out of eight other cognitive domains in another study (McAllister et al., 2016). TMT-A was a significant predictor of ADLs and IADLs for both the mild cognitive impairment (MCI) and dementia populations, but far more research has been done with Trail Making Test – B (TMT-B), arguing that this measure is consistently the highest predictor in functioning across studies. These measures are short, easy to administer, and serve a convenient purpose especially given the research defending the view that it is a predictor of functional status.

There are an enormous number of cognitive domains to be assessed within a neuropsychological evaluation. It is possible that these other domains actually do tap into various ADLs and IADLs, but have yet to be explored to the full extent in research. As briefly described, it is apparent that there are mixed results when it comes to the many neuropsychological measures and their relationship with one's ability to carry out daily tasks. Dementia is a complex disease and many neuropsychological measures are multi-faceted, therefore making it difficult to say that one specific cognitive skill versus the others are solely predictive of how an individual functions in their daily lives. Additionally, there are a number of ways to measure ADLs and IADLs. There are both standardized and unstandardized measures, self-report and informant measures, as well as subjective measures and performance-based measures. This, too, complicates the findings.

Quality of life (QOL) in individuals with dementia is most heavily impacted by their ability to perform daily activities. Individuals with more independence in terms of performing daily tasks had a great QOL in comparison to those with dementia who were more dependent upon others for these tasks (Anderson et al., 2004). Therefore, if we are able to better understand what deficits in skills are predictive of functional deficits, early prevention can be implemented in hopes of preserving one's QOL as long as possible. Knowing the predictive validity of functional decline with common neuropsychological measures takes treating these individuals to a higher level of care.

There is literature that backs up the claim that various cognitive domains assessed by neuropsychological testing have some degree of predictive ability in performance of ADLs and IADLs but there are some gaps in the research. These articles are lacking in terms of examining relationships between overall and specific cognitive domains with both IADLs and ADLs. A great deal of the empirical studies out there looks only at one cognitive domain or a brief cognitive measure such as a MSE and its effects on either ADLs or IADLs, not both (Razani et al., 2007). The literature is mixed in a way that the results are inconsistent perhaps due to samples utilizing a wide range of dementia severity, heterogeneity of cognitive domains (e.g., EF consists of many other cognitive domains) and IADL/ADL measures used, and different neuropsychological tests used (Ashendorf et al., 2018). Thorough examination of these variables can lead to a better understanding of which specific neuropsychological measures predict cognitive deficits that may lead to greater functional decline and therefore provide better utility of such neuropsychological measures (Cahn-Weiner et al., 2010). With a better understanding of these variables, improved treatment planning and possible risk prevention strategies can be implemented such as trialing pharmacological treatments, utilizing pill boxes, and other cognitive compensatory strategies (i.e., chunking information, writing important information down, using lists, etc. (Ashendorf et al., 2018).

Purpose of the Study

The aging population is tremendously growing and the number of individuals with dementia will be tripled by 2050 (Weiner & Lipton*,* 2009). As individuals age, cognitive functioning and ability to perform daily tasks may become compromised. This is what occurs in individuals diagnosed with dementia and is a crucial factor for diagnostic purposes. Therefore, the purpose of this study is to examine which common neuropsychological measures are able to detect various deficits in self-reported ADLs and IADLs in individuals with MCI and dementia. In accordance to the biopsychosocial model (Engel, 1977), this study is also looking at one other psychological factor (i.e., depression) to see if that also has predictive abilities to functionality. The biopsychosocial model states that biological factors such as genetics and biochemical variables along with psychological factors like personality, behavior, and mood, in conjunction with social factors like culture, socioeconomic variables and family all interact with one another to affect the development of an illness (Taukeni, 2020).

Furthermore, the purpose of this study is to examine the predictive ability of the independent contributions of neuropsychological measures and functioning to see if they are uniquely associated with ADLs/IADLs. Examination will be made looking at various neuropsychological measures and their relationship with functioning, specifically of the self-report type. Given that neuropsychologists rely on cognitive data to often times predict functioning and to come up with a diagnosis, a better understanding of the importance of such measures is warranted. Additionally, functional decline is required for a diagnosis of dementia, so knowing what neuropsychological tests are highly predictive of such decline can help assist in diagnostic purposes, treatment planning, and early intervention to preserve as much cognition as possible.

Research Questions and Hypotheses

Are various neuropsychological measures predictive of ADLs and IADLs in individuals with dementia and/or MCI?

Do predictive abilities of neuropsychological measures vary depending on diagnosis (MCI vs. dementia)?

Is depression a significant predictor of functioning only within the MCI population and not the dementia population?

It is hypothesized that:

H1: The regression model with the following predictor variables: Mini Mental Status Exam (MMSE), CDT, ANT, Controlled Oral Word Association Test (COWAT), Boston Naming Test – 15 item (BNT-15), TMT-A, TMT-B, Patient Health Questionnaire -9 (PHQ-9), and Total Trial 1-5, Short Delay Free Recall (SDFR), Long Delay Free Recall (LDFR), Recognition Discriminability, Repetitions, and Intrusions from the California Verbal Learning Test- 3rd Edition (CVLT-3) will significantly predict IADL function, with TMT-B being the strongest predictor in the MCI population.

H2: The regression model with the following predictor variables: MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, and Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 will significantly predict IADL function, with TMT-B being the strongest predictor in the dementia population.

H3: The regression model with the following predictor variables: MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, and Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 will significantly predict ADL function, with TMT-B being the strongest predictor in the MCI population.

H4: The regression model with the following predictor variables: MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, and Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 will significantly predict ADL function, with TMT-B being the strongest predict in the dementia population.

H5: Depression as measured by the PHQ-9 will be a significant predictor to functional impairment (total IADLs/ADLs) among individuals diagnosed with MCI but not those with dementia.

CHAPTER 2: REVIEW OF THE LITERATURE

Dementia is an umbrella term to describe a variety of neurological disorders that result in progressive decline. The Diagnostic and Statistical Manual of Mental Disorders - 5th edition (DSM-5; American Psychiatric Association, 2013) equivalent to a dementia diagnosis is major neurocognitive disorder (major NCD). Major NCD is categorized by substantial cognitive impairment that is a substantial decline from previous functioning, accompanied by a decline in their performance on neurocognitive assessments that is two or more standard deviations below the norm. Dementia can involve declines in memory, learning, visuospatial functioning, executive functioning, and language comprehension, or can involve a decline in more than one of these domains. Additionally, dementia can have an impact on behavior and decision making (Wahl et al., 2019).

There are many different types of dementia including vascular, Alzheimer's, frontotemporal, Lewy body, and much more, with the most common type of dementia being Alzheimer's disease (AD), occurring in about 65% of all dementias in individuals aged 65 or above (Arvanitakis et al., 2019; Kolb & Whishaw, 2021). AD was named after a German physician, Alois Alzheimer, who conducted a case study on a 51-year-old with cognitive impairment. Vascular dementia is the most frequent comorbid condition with Alzheimer's dementia and having a mixed dementia of these types is common (Arvanitakis et al., 2019). Dementia can be described as a clinical syndrome that encompasses a cluster of symptoms that must be met in order to receive the diagnosis; individual's must have enough cognitive deficit to impact their social or occupational functioning. The word dementia is derived from Latin, with *de* meaning *out of, mens* meaning *mind* and *ia* meaning *state of*. Other words that have been used throughout history to describe what we now call dementia include senility, idiotism, paranoia, and chronic organic brain syndrome (Weiner & Lipton, 2009).

Suspected causes and pathology vary depending upon type of dementia. Stanley Prusiner was acknowledged for his work in 1982, postulating the prion theory (Kolb & Whishaw, 2021). The prion theory states that neurogenerative conditions such as dementia all have similar causes which involve prions. Prion stands for *proteinaceous infectious particle*, and is an abnormally folded protein which causes a chain reaction in other similar proteins to also abnormally fold causing them to be less functional in their abilities (Kolb & Whishaw, 2021). Amyloids are formed when prions evoke other proteins to abnormally come together and as they accumulate in the brain tissue, the tissue is damaged resulting in cell death. These amyloids are commonly found in Alzheimer's disease.

The amyloid cascade hypothesis is being heavily researched to be utilized in potential therapeutic interventions for Alzheimer's dementia. This hypothesis describes that Alzheimer's is due to an accumulation of amyloid plaques and tau proteins resulting in neuronal death, ultimately leading to a diagnosis of Alzheimer's disease (Wahl et al., 2019). The age-based hypothesis proposes that Alzheimer's disease is a result of three events; the first being some type of injury that starts the pathology process resulting in an inflammatory process. This inflammatory process significantly negatively impacts the brain cells which are already declining from aging itself. Lastly, this chronic inflammation response then leads to a change in the physiology of the cells resulting in neuronal death and dysfunction of the synapses. Consequently, Alzheimer's dementia can occur (Herrup, 2010).

Various factors come into play when assessing risk factors of dementia. Dementia is more prevalent in women than men and an early onset of dementia is more likely to occur in individuals with a family history of dementia, especially with a history of this early onset (Weiner & Lipton, 2009). One of the biggest modifiable risk factors for development of dementia in early life is education, with continuing on to secondary education as a protective factor (Tisher & Salardini, 2019). Other modifiable factors include reducing fat in diet, being more socially and physically active, and abstaining from smoking and excessive alcohol intake (Wahl et al., 2019). In midlife, risk factors include obesity, hypertension, and hearing loss whereas later in life, smoking, depression, physical inactivity, social isolation, and diabetes are all factors that increase one's chance of developing a dementia (Tisher & Salardini, 2019). Other risk factors include cerebrovascular disease, moderate alcohol intake, being overweight, as well as history or current experiences of depression (Wahl et al., 2019; Weiner & Lipton, 2009). Protective factors such as a healthy diet, exercise, and level of education are shown to be somewhat resistant to various neurodegenerative disorders due to their ability to fight prions from forming together (Kolb & Whishaw, 2021; Wahl et al., 2019). Specific diets such as the Mediterranean diet or ketogenic diet has been associated with lower risk of developing dementia (Wahl et al., 2019). Nonetheless, aging is a significant risk factor in developing dementia but there are plenty of other factors that are modifiable throughout life as well that can modify these risks.

There are many steps to take in order to diagnose and rule out differentials before diagnosing a dementia. Lab work should be updated and include a blood count to rule out anemia. Thyroid stimulating hormone should also be looked at to rule out hypothyroidism as well as looking at serum fasting glucose which can be used to rule out hyperglycemia (Feldman et al., 2008). Another important consideration is to look at B12 levels due to its effects on cognition. Neuroimaging whether that is a functional magnetic resonance imaging (fMRI), positive emission tomography (PET) scans, or computed tomography (CT) scans are highly recommended in order to take an in depth look at neuroanatomy, specifically functioning, structure, and any other abnormalities. Depending on the type of dementia, different neuroanatomical correlates have been associated with the disease. For AD specifically, the most common feature would be atrophy to the hippocampus. Atrophy to this region in individuals with MCI is a very strong predictor that they will progress from MCI to a dementia (Peng et al., 2015). Another common neuroimaging marker is ventricular enlargement due to the overall atrophy of the brain. Vascular dementia is diagnosed with the presence of white matter changes per imaging. All of these steps are taken in order to rule out other treatable causes to cognitive dysfunction such as inefficiencies as a result of a tumor, renal failure, psychiatric disorders, or normal pressure hydrocephalus (Feldman et al., 2008). It is recommended that there should be more effort in investigating other neurocognitive factors or biomarkers that are sensitive in detecting prodromal stage of dementia (Peng et al., 2015).

It is important to note that not everyone that grows into their older years will develop a type of dementia (Kolb & Whishaw, 2021). Many individuals age healthfully into their elder years, but by 2050, the prevalence of dementia will be tripled (Weiner & Lipton, 2009) and between 10 million and 20 million elderly adults will have some degree of cognitive impairment within the next two decades (Kolb & Whishaw, 2021).

This is important to discuss from an economical perspective because of the large financial impact dementia has from accompanied comorbidities, treatment costs, and costs of any in home-care needed. This impact is further highlighted through the cost that dementia will have, estimating 315 billion dollars in the United States with increased cost with degree of dementia severity (Weiner & Lipton, 2009). Those with dementia have a higher risk of any type of hospitalizations, longer length of stay in hospitals, and higher hospital expenses (Zhu et al., 2015). Cost of dementia increases by 9% per point on an ADL scale, therefore the more functional impairment someone is, the more they technically are costing the economy (Weiner & Lipton, 2009).

Treatment of Dementia

The purpose of this study is to investigate the predictive abilities of neuropsychological tests on functional outcome with implications to early detection and treatment of dementia. Since there is no cure for dementia, emphasis is given on finding ways to increase their quality of life to ensure their safety and independence as well as reduce risk factors to developing a dementia. It is important to note that many of the interventions available do not reverse the effects of dementia, but rather slow the progression or work on symptom management to reduce harm (Tisher & Salardini, 2019). These treatment options have moderate effect sizes and positively, when combining various treatments, they have a larger effect. For example, when combining a healthy diet and physical exercise, the chance of developing a dementia is lowered. Furthermore, interventions recommended that are low-cost, easy to do, and provide no harm include engaging in healthy diet and physical exercise, working with primary care doctors to decrease any other risk factors like hypertension, taking appropriate supplements (i.e., B12, Vitamin E, etc.), and many other cognitive rehabilitation interventions (Tisher & Salardini, 2019).

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) further supports these interventions. The FINGER study was a 24-month randomized controlled trial completed in 2014 with a population of older adults who were at risk for dementia (Rosenberg et al., 2018). The intervention group engaged in multidomain lifestyle interventions that focused on nutrition, exercise, cognitive training, and management of vascular risk factors. These are all interventions aimed to slow the treatment of dementia. Results of the study showed overall beneficial effects on cognitive outcomes measured by the total Neuropsychological Test Battery (NTB) as well as improvement in scores in the executive functioning (p = .039) and processing speed scores (p = .029). The effects of the intervention on total NTB as well as on executive functioning, processing speed, and memory scores did not vary on demographic factors (i.e., age, sex, and education), socioeconomic status, baseline performance on the MMSE, cardiovascular risk factors, or comorbidity of cardiovascular factors. These results suggests that multidomain lifestyle interventions are beneficial regardless of various existing factors (Rosenberg et al., 2018).

Unfortunately, efficacy for cognitive interventions is lacking, but there is some promise (Hogan et al., 2008). Individuals should surround themselves in intellectually stimulating environments to not only stimulate their minds, but also to improve overall mood and mental health (Tisher & Salardini, 2019). Cognitive neurorehabilitation involves various professionals such as speech therapists, occupational therapists, and neuropsychologists. The goal for these professionals is to increase functionality. An initial assessment is done in order to identify strengths and weaknesses to inform goals. During this type of therapy, the first aim it to assess current functioning and come up with a rehabilitation plan on how cognition can be improved. Once cognitive functioning relatively plateaus, the plan is shifted to create other manageable ways to complete and manage tasks. Individuals may learn different memory aids such as using mnemonics or associations to help them be able to do whatever they are trying to do (Tisher & Salardini, 2019).

Other interventions that are commonly used with this population is the use of pharmacological treatment. The U.S. Food and Drug Administration (FDA) has approved three pharmacological treatments, specifically cholinesterase inhibitors for the treatment of Alzheimer's disease: donepezil, rivastigmine, and galantamine (Hogan et al., 2008). These medications work to increase acetylcholine levels of the body which play a major role in attention and memory. Individuals with other types of dementia such as vascular or Lewy body disease also may respond well to these medications, but they do not help those with a frontotemporal dementia (FTD). Unfortunately, these medications do take a toll on the gastrointestinal tract with side effects possibly including vomiting, diarrhea, nausea and should be stopped immediately if these side effects occur. Other resolutions can be to decrease the dose. If a patient does start these medications, a follow up is recommended after three to six months to assess the effects. In cases of moderate to severe dementia, the use of Memantine, a N-methyl-D-aspartate (NMDA)-receptor antagonist is approved as well (Hogan et al., 2008). Memantine works by binding to receptors that glutamate would normally bind to therefore decreasing any of the potential harming effects that this neurotransmitter may have on the brain; it is thought to be neuroprotective (Tisher & Salardini, 2019). This medication has little to no effect in mild AD but there is some evidence for its efficacy with a Lewy body dementia and inconsistent results with FTD (Hogan et al., 2008).

Assessment of other psychological factors are important due to the increased comorbidity with dementia as well as and the fact that psychological factors hinder memory and cognition. Specifically, anxiety and depression are common occurrences in individuals among the dementia spectrum. Hallucinations and delusions also may occur, with an increased risk dependent upon which type of dementia (Tisher & Salardini, 2019). All of these psychological factors can be treated by either pharmacological treatment, psychotherapy, or a combination of the two. Other variables to be cognizant of and assess for due to the impacts on thinking and memory are sleep disorders, fatigue, agitation, and aggression (Hogan et al., 2008; Tisher & Salardini, 2019).

Dementia and Normal Aging

The question has been speculated whether or not dementia is part of the normal aging process. As we age, it is inevitable that we will experience slowing of cognitive functioning in all domains and this is observed in all species (Herrup, 2010). Aging is also a risk factor for various other diseases such as cardiovascular disease, diabetes, and osteoporosis, to name a few (Wahl et al., 2019). Changes to memory, executive function, attention, language, and reasoning skills all are affected as we age and are considered part of the normal aging process (Irwin et al., 2018). Some of the reasons for this decline is due to loss of neuronal dendrites, less efficient immune responses, and the reduction of the density of dendritic spines and synapses (Herrup, 2010). Although dementia generally affects the elderly, this process should not be thought of as a normal part of aging or even an exacerbation of aging (Herrup, 2010; Irwin et al., 2018).

Differences in neuroimaging also have been observed in normal aging versus pathological aging. For example, those who are at higher risk of developing Alzheimer's dementia have more reductions in grey matter and white matter in various areas of the brain. Reduction in brain volume particularly to the frontostriatal brain region network are commonly seen in normal aging versus those with a pathological process can be seen with medial temporo-parietal reductions which is thought of as the episodic memory network (Irwin et al., 2018). Significant atrophy is observed in the cortex of the frontal and temporal lobes, as well as in the hippocampi regardless of what subtype of dementia is being observed (Wahl et al., 2019).

The age-based hypothesis proposes that dementia is not a part of normal aging but rather begins when some type of precipitating injury triggers the cascade of events that then can lead to a dementia (Herrup, 2010). Thirty percent of elderly adults have plaque deposits but do not show any signs of dementia, and this are characterized as having no deficits to cognition. Rather, it is thought that these individuals are more at a risk for developing Alzheimer's but they should not be thought of as being in a preclinical stage of dementia because not all of them will develop a neurodegenerative disorder. On the other hand, it is not possible to have Alzheimer's disease without having these plaques. Although age is considered a risk factor of dementia, it certainly is not a definitive relationship.

In a study conducted in Denmark, 207 centenarians were evaluated for dementia. 51% of them were diagnosed with either mild, moderate, or severe dementia. On the contrary, 25% showed no signs of dementia (Andersen-Ranberg et al., 2001). In the group of 105 centenarians that were diagnosed with a dementia, they all also had various diseases that could be attributable to a dementia diagnosis including hypothyroidism, Parkinson's, and other cerebrovascular diseases that are known to increase risk of dementia. This study supported that the development of dementia does not exponentially increase as one ages. In conclusion, the degree of various pathological features such as plaques and tangles are what can differentiate someone with a dementia or those with normal aging (Wahl et al., 2019).

Mild Cognitive Impairment (MCI)

The DSM-5 equivalent to MCI is minor neurocognitive disorder (minor NCD) which is categorized by modest cognitive decline such as performance on a neuropsychological evaluation that is around one or two standard deviations below the norm but individuals are still able to function at an independent level (APA, 2013). A diagnosis of MCI has been viewed as a transitional phase between healthy aging and the development of dementia (McAlister et al., 2016). MCI is diagnosed when the rate of cognitive deficits is below age and education expectations but are not significantly impacting their everyday functioning (Gauthier et al., 2006; McAlister et al., 2016). This diagnosis can further be split up into amnesic and non-amnesic MCI with deficits in one or multiple cognitive domains (Kasper et al., 2020). Amnesic refers to a predominate memory dysfunction in the cognitive profile whereas non-amnesic has impairment to other cognitive domains (e.g., language, executive functioning; Petersen et al., 2018). A consensus among studies argues that there is no difference in the variance attributed to functioning from cognition with a diagnosis of amnesic versus non-amnesic MCI, although those with MCI who have deficits in multiple cognitive domains versus single domains had more functional difficulties (Aretouli & Brandt, 2010; McAlister et al., 2016). The prevalence of MCI varies depending on study, but it is generally thought to occur in 3-19% in older adults above the age of 65 (Gauthier et al., 2006).

Of important note, not all of those with MCI will transition to a diagnosis of dementia. Some will remain stable, but the diagnosis of amnesic MCI increases one's likelihood of the progression to dementia, specifically AD (Gauthier et al., 2006; Kasper et al., 2020; Petersen et al., 2018). Conversion rates vary but Ritchie and colleagues (2001) found that over a three-year time period, 18% converted from MCI to dementia. Those who are female, have less formal education, more dependent in functioning at baseline, and those who are of older age were more likely to progress from cognitively normal to either MCI or dementia (Nowrangi et al., 2016). Even if an individual reverts to normal cognition after a diagnosis of MCI, they still remain at higher risk to again revert back to MCI or even dementia in comparison to individuals who have never received a MCI diagnosis (Petersen et al., 2018). It is also important to assess whether the etiology of the MCI is reversible for treatment planning. Some examples of reversible etiology include complex medication use and untreated sleep apnea. Another factor that increases the likelihood of progression to MCI or dementia from healthy aging is functional impairment at baseline (Nowrangi et al., 2016). One-third of individuals with MCI diagnosis will have difficulties in some everyday tasks such as keeping appointments, finding personal items, and remembering current events (Aretouli & Brandt, 2010). Twenty percent from a sample taken from these same researchers reported difficulties with managing finances, organization, taking medications, and driving, thus highlighting the tremendous variability in clinical presentations of MCI.

There are several factors that work individually but more so in conjunction with each other that causes an individual to have cognitive deficits resulting in a diagnosis of MCI. Cerebrovascular risk factors are particularly important and increase one's likelihood of cognitive inefficiencies such as those with hypertension, type 2 diabetes, white matter lesions, or hypercholesterolemia, to name a few (Gauthier et al., 2006). Researchers also note that white matter lesions and cerebral infarcts can only be viewed with neuroimaging, which is why it is particularly important to recommend neuroimaging to help with diagnostic purposes and treatment planning. Other potential causes include cholinergic dysfunction, and buildup of amyloid and neurofibrillary tangles.

Treatment for MCI

Similar to the treatment of dementia, early interventions are crucial. These treatments are focused on symptom improvement and disease modification or delaying any further decline (Kasper et al., 2020). The diagnosis of MCI is often accompanied with depression, anxiety, and lower QOL (Gauthier et al., 2006). Therefore, one of the main goals in these treatments are to reduce cognitive, psychiatric, and behavioral symptoms as well as improve their overall QOL.

There are pharmacological and non-pharmacological treatments for the diagnosis of MCI. Pertaining to non-pharmacological treatments, interventions that target lifestyle changes such as motivations to modify diet and increase exercise are first-line treatments (Kasper et al., 2020). Exercising regularly as little as six months has been shown to increase cognitive processes. Additionally, the same author postulates that cognitive training has shown to be somewhat effective in enhancing cognition although the literature is mixed and may only improve cognition to a small extent (Petersen et al., 2018). Although these are all promising treatments, none have shown prevention of the progression from MCI to dementia.

Interventions that are aimed at slowing the progression of MCI to a dementia have little evidence and are even less clear than interventions for dementia (Tisher & Salardini, 2019). Again, combination of various treatment modalities is the best approach in limiting decline such as reducing cerebrovascular risk factors, engaging in a healthy diet and exercise, as well as social stimulation (Gauthier et al., 2006; Tisher & Salardini, 2019). Other suggestions include treatment of other comorbidities such as depression and hypothyroidism as well as decreasing use of anticholinergic medications (Gauthier et al., 2006). There is evidence to suggest that the use of cholinesterase inhibitors, a common treatment for dementia previously discussed, is of minimal benefit for treating those with MCI and if any benefit does occur, it is not sustained. This is possibly due to the heterogeneity of the presentations of individuals with MCI. Cognitive training can work to a degree depending on severity of deficits.

Instrumental Activities of Daily Living (IADLs)/ Activities of Daily Living (ADLs)

To assess one's functional abilities, although multidimensional, measures are usually broken down into ADLs and IADLs. ADLs are activities involving self-maintenance and commonly consist of dressing, grooming, and toileting, all of which encompass the basic needs to stay autonomous and independent (Cornelis et al., 2018). It is suggested that ADLs are more preserved in the light of cognitive deficits and are activities that are learned earlier on in life. Additionally, they are also more affected in moderate to severe stages of dementia (Ashendorf et al., 2018). IADLs are more complex activities involving multiple cognitive domains (Burton et al., 2018) and maintaining independence more so within the community setting such as grocery shopping, cooking, managing finances, etc. These are thought to be more sensitive to any type of cognitive deficits that may occur due to disease progression of a neurodegenerative disorder (Cornelis et al., 2018). Specifically, the IADL of managing finances are one of the earliest changes seen in those diagnosed with MCI and dementia (Farias et al., 2003; Nowrangi et al., 2016). McCue and colleagues (1990) drew the conclusions that neuropsychological tests can be predictive of ADLs that rely more heavily on cognitive and reasoning skills but not much when it comes to ADLs that are dependent upon physical mobility. Both IADLs and ADLs are activities that rely on various complex cognitive skills. The relationship between neuropsychological testing and functional abilities is a complicated one due to this reason. For example, being able to operate a telephone would likely require someone to tap into their working memory, language, and motor skills at the very least. For various functional domains, there has been found to be significant correlations across multiple neuropsychological measures further providing evidence for many cognitive abilities playing a role in functional performance (Farias et al., 2003).

When utilizing proxy-rated QOL scores, functional impairment was the most commonly found factor to negatively impact overall quality of life for individuals with dementia (Burks et al., 2021). Performance on IADLs and ADLs may be impacted by other factors such as mood, physical limitations, motor skills, or other changes in their environment (Cornelis et al., 2018). Nonetheless, it is very likely that all of these variables intertwine and interact with one another in impacting functional impairment. When assessing someone's IADLs and ADLs, it is important to consider other physical limitations that may be hindering the individual's performance of activities rather than automatically attributing the decline to cognitive deficits. Asking appropriate questions to parse out these two contributing factors (i.e., physical versus cognitive limitations) are important in the diagnosis of dementia. As mentioned earlier when discussing the definition and symptoms of dementia, in order to receive a diagnosis of dementia, some decline in functional abilities must be observed (APA, 2013). In general, individuals with dementia will score poorer on measures of ADL and IADL abilities in comparison to heathy individuals as well as someone with a diagnosis of MCI (Cornelis et al., 2018). Those who have more difficulties performing such ADLs are more likely to progress from a diagnosis of MCI to dementia (Cornelis et al., 2018; Thomas et al., 2018). In a study of 525 healthy individuals, poorer functional ability per the informant-rated Functional Activities Questionnaire (Pfeffer et al., 1982) was predictive of these individuals progressing to a diagnosis MCI (Thomas et al., 2018). Individuals with MCI still can have subtle difficulties in performing ADLs (Cornelis et al., 2018).

The neuropsychology field has commonly used both self/informant and performance-based measures to assess how individuals' function in the real world on a daily basis, such as how well they are performing ADLs and IADLs (Cahn-Weiner et al., 2007). Some studies have used both a self-report questionnaire and a performance-based measure for ADL's (Razani et al., 2007). Advantages to informant reporting is that perhaps you get information from an individual who is familiar with how that person is truly functioning and is an efficient way in collecting information (Cahn-Weiner et al., 2007). On the other hand, there is more room for biases and inadequate reporting due to either the person not knowing the individual being asked about or this individual has a lack of insight into how they are doing in their day to day lives. Informant reports had a better relationship with test scores of cognitive functioning than self-report ratings in a population of head-injured adults (Goldstein & McCue, 1995).

Measures that are performance-based consist of raters observing patients and providing them with scores directly, however disadvantages to this method are that they are observing patients in a controlled environment and may not truly reflect one's functional abilities information (Cahn-Weiner et al., 2007). These also are more time consuming and therefore less practical in clinical settings. Performance based measures for functional abilities was not feasible for this study as archival data was used. When an informant is not available, neuropsychological tests can provide adequate information on how the patient is functioning, thus providing more importance for the conduction of this study (Ashendorf et al., 2018). In a meta-analysis, strength of relationship between cognitive predictors and functional outcome did not change whether a questionnaire was used or if functional outcomes were assessed based on performance within an MCI population (McAlister et al., 2016). Regardless of what kind of measure is used, the relationship between the two is only moderately correlated (r =-0.66), suggesting that there is still much variance to be explained (Farias et al., 2003). When a questionnaire was used, there was a significant difference in variance found among informant report (28%) and self-report (21%; McAlister et al., 2016). Strength of relationship among these variables were the same when assessing for only ADLs and when assessing for both IADLs and ADLs. However, Farias and colleagues (2003) study revealed 50% of the variance was contributed by a performance-based measure of functioning versus 25% in a self-report measure.

The Lawton- Brody Instrumental Activities of Daily Living Scale (1969) is a highly popularized measure that is used to assess one's functional abilities, specifically advanced IADLs like shopping and managing finances. The questions are based on a 2-point scale across eight domains with higher scores yielding more functional impairment. The Lawton- Brody (1969) measure was used to base this current studies measurement of ADLs and IADLs, thus it is an unstandardized measure, but was adapted in hopes to make scores more informative. Thus, this study used a 3-point scale for functioning (e.g., 0 = *independent*, 1 = *needs assistance/reminders*, 2 = *dependent*). Similar studies have also adapted this scoring system in order to provide more information regarding patient's current functioning (Warren et al., 1989). Lee and colleagues (2019) have shown that scores on this measure were significantly higher for those diagnosed with a mild severity of dementia versus moderate and severe groups. Additionally, there are other psychometric measures out there that already use this same 3-point scoring system when assessing functional abilities such as the Occupational Therapy Assessment of Performance and Support (OTAPS). On the contrary, Monaci and Morris (2011) suggest that the Lawton and Brody (1969) measure may not be sensitive enough to detect changes in a dementia sample although it is commonly used.

Much of the literature is varied in terms of the relationship between cognition and functional abilities. For example, various neuropsychological tests can do fairly well in predicting ADL activities, but not when the ADLs involves physical mobility. McCue and colleagues (1990) suggest that neuropsychological testing can provide good insight as to whether someone can use a telephone or manage medications, but not when it comes to feeding or dressing oneself. These researchers came to the conclusion that there is some utility in employing neuropsychological tests for predicting impairment in functioning but only to specific domains involving memory, problem solving, and other more higher levels of cognitive skills. To further complicate the relationship, IADL scores are more significantly correlated with neuropsychological measures but the association is weakened as the disease progresses (Monaci & Morris, 2011). Individuals diagnosed with dementia scored an additional point on the Blessed Roth Dementia Rating Scale per year across a 5-year span, which is roughly equivalent to becoming functionally unable to perform one additional IADL per year (Farias et al., 2009). Additionally, a meta-analysis of 68 articles encompassing a wide range of populations revealed that the total variance between the two ranged from 0-80%, with an average of 21% (Royall et al., 2007). Since neuropsychologists are often asked to make complex decisions about the patient's ability to care for themselves, the accumulation of more research on this topic is warranted. It would be of high clinical significance to conduct more of this type of research in order to show the empirical support or lack thereof for the relationship between neuropsychological testing and predictive abilities of functioning (McCue et al., 1990). As particular judgments are made regarding someone's living arrangement, ability to manage their finances, and more, such empirical work would provide more ease in making such judgements. Assessing such functional abilities also is a time and cost-efficient approach in order to provide early treatment options to slow the progression (Ashendorf et al., 2018). Lastly, education has been found to be correlated with functional measurement scales and thus premorbid educational attainment should be a variable to keep in mind when assessing individuals' functional capacity (Farias et al., 2003).

Depression

Depression is fairly common at all stages of dementia, affecting up to 40% of those with Alzheimer's disease and is particularly more prevalent at the beginning and middle stages of the disease (Alzheimer's Association, 2022). Depression is also common in those just diagnosed with MCI (Gauthier et al., 2006). Not only will the cognitive deficits as a result of dementia brain pathology impact every day functional outcomes, behavior changes such as depression and disinhibition can also impact them (Cahn-Weiner et al., 2002; Payne et al., 1998). Importantly, attention, concentration, memory, processing speed, motivation, and organization are all affected by the presence of a mood disorder (Tisher & Salardini, 2019). Those with both depression and dementia are high utilizers of the healthcare system and unfortunately, depression can increase the disease progression and lead to a higher likelihood of requiring nursing home care (Kales et al., 2005). The rate of nursing home admissions at a follow up post one year for those with diagnosed depression and dementia were almost doubled in comparison to those with pure dementia or pure depression. Additionally, those with comorbid depression and dementia had more functional impairment at baseline in comparison to those with just dementia (Kales et al., 2005).

Self-reported QOL for individuals with dementia are most negatively impacted by levels of depression and functional impairment (Burks et al., 2021; Weiner & Lipton, 2009). Depression as an independent factor appears to affect one's QOL, with depression resulting in the inability to perform daily activities (Burks et al., 2021; Kales et al., 2005).

Other factors that contribute to depression include history of falls or frequent hospitalizations associated with one's inability to physically perform daily activities, all of which contribute to lower QOL (Burks et al., 2021).

Several studies have found a relationship between depression and dementia, but the direction of the relationship is complicated to parse out. This relationship may be bidirectional; dementia may put one at higher risk for developing depression or having depression may be a risk factor for developing dementia (Kessing, 2012). Thomas and colleagues (2018) revealed that higher depression scores revealed on the Geriatric Depression Scale (GDS; Sheikh & Yesavage, 1986) were predictive of a healthy individual progressing to a diagnosis of MCI. This relationship is still poorly understood, especially due to the fact that several symptoms of depression and dementia overlap. It is not surprising that if someone has insight into their memory decline, they may develop depression years before a diagnosis of dementia is even made. The consensus is that with each depressive episode, the risk of developing dementia increases. It is also hypothesized that long term antidepressant use is a protective factor for developing dementia in those who have recurrent depressive episodes (Kessing, 2012).

It is unclear whether or not depression is more associated with one type of dementia versus another (Kessing, 2012). In a study conducted by Payne and colleagues (1989), they did not find a difference among AD, vascular dementia, or other undifferentiated dementia (UD) for scores of depression as measured by the Cornell Scale for Depression in Dementia (Alexopoulos et al., 1988; Payne et al., 1989). They did find that 34% of those with AD had mild ADL impairment and low MMSE scores (0-9 points), suggesting those with more cognitive and functional impairment were more likely to be depressed. Therefore, having disproportionate levels of cognitive and functional impairment puts one at risk for developing depression. For those diagnosed with UD, more functional impairment yielded higher levels of depression. In vascular dementia, neither cognitive or functional impairment resulted in an association with increased risk for depression. On the contrary, Warren and colleagues (1989) exhibited that depression as assessed by the GDS was not found to be correlated with scores on MMSE, indicating that there is no correlation between feelings of depression and cognitive status per this study. Additionally, Farias and colleagues (2003) found that depression as measured by the GDS was not significantly related to any of the neuropsychological variables (i.e., CVLT, Wechsler Memory Scale, Rey-Osterrieth Complex Figure Test, BNT, COWAT, Similarities from the Wechsler Adult intelligence Test, or the Western Aphasia Battery) or an informant based functional measures (i.e., Lawton-Brody IADL scale) in a population diagnosed with possible or probable AD, despite mild degrees of depression reported.

In a study viewing the continuum of normal aging, to MCI, to dementia, Rog and colleagues (2014) found that one of the variables that uniquely contributed to everyday function was depression. Memory and executive functioning were unique predictors, but the addition of depression further contributed in predicting greater impairment. Additional analyses revealed that this varied by diagnosis on the aging spectrum. For example, depression was independently contributing to everyday function in individuals diagnosed with MCI and those in the healthy aging group, but not nearly as much as in the dementia group. Additionally, Lam and colleagues (2007) found in their study that depression did not have an impact on IADLs but rather apathy alone did in regard to initiating tasks. This suggests that depression and other neuropsychiatric variables play a role in the beginning stages of disease pathology, with cognition more so affecting functioning later on. When the severity of the dementia progresses, it appears that other behavioral disturbances such as apathy can impact functioning but the impact of depression decreases. This makes sense given that the criteria for MCI is largely described as having minimal functional impairment. More functional impairment was related to worse cognitive impairment along with more reports of depression and apathy across all groups. On the contrary, Burton and colleagues (2018) did not find depression to be associated with IADLs in groups diagnosed with MCI, AD. or non-AD (i.e., vascular dementia, Lewy Body Dementia, etc.). Rather, apathy was significantly correlated with IADLs. Those with initial functional impairment along with depression can be used as a warning sign of worsening cognitive and functional decline (Rog et al., 2014). By continuing to investigate the relationship among depression and dementia, more information can be gained about adequate treatment resulting in the potential for gaining cognitive efficiency with this population (Kales et al., 2005).

Memory

Neuropsychological evaluations can be seen as an extension of a typical neurology evaluation, but with more emphasis on detailed information on various cognitive and psychological domains. A typical neuropsychological battery will generally consist of tests that measure one's overall memory. When assessing memory, they are many different distinct sub domains within this category to look at, similar to executive functioning, and can be seen as a limitation of this research. Another important note from a meta-analysis is that age is found to be moderately correlated with memory performance (r = -0.35, $p < 0.1$), whereas education had minimal relation with memory (r = 0.13, p <0.1; Rog et al., 2014)

In a different meta-analysis, overall memory explained 23% of the variance in IADLs in individuals with MCI (McAlister et al., 2016). Short and long delays on a memory measure accounted for more variance in functional outcomes (35% and 31% respectfully) in comparison to episodic memory (18%). On the other hand, Nguyen and colleagues (2019) did not find immediate and delayed memory as measured by the Repeatable Battery for the Assessment of Neuropsychological Status Update (RBANS; (Randolph et al, 1998) to be significantly able to predict IADL functioning. There was not a statistically significant difference among variance between visual and verbal memory tests (33% and 24% respectfully), indicating that the type of memory test used may be insignificant (McAlister et al., 2016). Additionally, Hall and colleagues (2011) found that visual memory was a significant predictor of both IADL and ADL functioning in individuals with AD. Measures of list learning such as those on the CVLT-3 are assessing episodic memory specifically. Episodic memory falls under declarative memory and refers to the actively being able to recall information that is learned (Schoenberg & Scott, 2011). Those with lower scores on episodic memory measures were more likely to convert from normal cognition to MCI or dementia as well as having lower baseline functional status (Nowrangi et al., 2016). This type of memory plays a role in remembering to turn the stove off, pay bills, and take medications; all of which are crucial IADLs for individuals to adequately be able to do (Ashendorf et al., 2018). Longitudinally, poorer scores on measures of a list learning and memory task (i.e., Memory Assessment Scales Word List Learning Test, Williams, 1991) resulted in more functional decline across a span of five years (Farias et al., 2009). The correlation between scores on this memory task with IADLs were strongly correlated with one another (r=-.69, p <.001). Measures of list learning were recommended by Ritchie and colleagues (2001) to be used in neuropsychological batteries because of their ability to be sensitive to early dementia one to two years before diagnosis. Further providing evidence for the use of list learning neuropsychological measures, Farias and colleagues (2003) found that trial five on the CVLT contributed 25% of the variance to IADLs.

According to McCue and colleagues (1990) the memory scale on the Luria-Nebraska Battery (LNNB) was the most powerful predictor for performance on ADLs in a population of individuals diagnosed with dementia among other common neuropsychological domains. Intrusions can be defined as any word that is generated that was not on the list being recalled. The intrusions score on the Rey Auditory Verbal Learning Test is specifically important due to the evidence of this score being able to uniquely predict progression to MCI from an otherwise health sample as well as the progression to a mild dementia (Thomas et al., 2018). It has been suggested that under the cued recall conditions such as those in the CVLT-3, individuals are likely to have the highest intrusions within that category, but these researchers showed that this was not specific to that condition but that it also occurs in the free recall phase. Results from this study suggest that intrusion scores are able to detect the subtle cognitive changes that are arising in healthy individuals at risk of progressing to MCI or a mild dementia. The predicted etiology to this relationship is generally unknown, but it is suspected that due to impaired semantic memory networks that result in impaired associated pathways. Searching through a wide variety of one's vocabulary can be confusing to parse out irrelevant words. Other mechanisms may be due to impaired frontal networks and self-monitoring strategies. Additional future suggestions from these researchers include that variables from word list tasks be investigated in combination with the intrusions scores to see if these scores can create an appropriate method of predicting cognitive decline. In the current study, multiple sub scores from a word list will be used to assess predictive abilities of function.

Overall memory scores or composite scores can also be an important variable when it comes to prediction of disease progression. In a study comprised of 124 people (52 cognitively normal, 35 MCI, and 37 with dementia), lower scores on a memory composite score at baseline was predictive of poorer baseline functional status along with a faster rate of decline (Cahn-Weiner et al., 2007). This score had somewhat more of a stronger relationship than the executive functioning composite score upon observation of *p*-values, although both were significant. The memory composite score was made up of the MAS Word List Learning Test (Williams, 1991), specifically, sum of free recall after a short delay, cued recall after a short delay, and trial 1 and 3 total recall. Rog and colleagues (2014) showed that memory as measured similarly from a word list was an independent predictor for global functioning as well as within specific functional domains (i.e., everyday memory, everyday language, everyday visuospatial functions, everyday planning, everyday organization, and everyday divided attention). Similarly, Ashendorf and colleagues (2018) also showed that scores on a list learning test from the Neuropsychology Assessment Battery (NAB; Stern & White, 2003) was the most predictive of functional impairment in those with dementia. Additionally, immediate memory such as a task of list learning and story memory as measured by the RBANS

(Randolph et al, 1998) accounted for changes in IADLs as a whole beyond that of age, education, and general cognitive functioning. The sample included those with healthy aging, diagnosis of MCI, non-AD, and AD. Interestingly, immediate memory was not significantly correlated with functioning in either the non-AD or AD group. Given that for the AD group, poor memory is a core diagnostic feature, these findings were surprising (Burton et al., 2018).

Visuospatial Functioning

There is an abundance of research out there on cognitive domains such as memory and executive functioning, but very little when it comes to visuospatial abilities such as assessed by the clock drawing test (CDT), the measure used in this current study. Of important note, the CDT also encompasses more abilities than just the visuospatial domain. The CDT also encompasses executive functioning (e.g., motor functioning and execution, abstract thinking, and planning), as well as visual memory and knowledge of numbers (Shulman, 2000). This relates back to the idea that many neuropsychological tasks involve several cognitive domains which makes it difficult to classify tests into singular domains (Razani et al., 2007). For this study, the CDT is included under the visuospatial domain. There is great utility to using the CDT. Specifically, there is a uniform consensus that the CDT is good at detecting cognitive change and is an important asset to neuropsychological evaluations (Shulman, 2000). It is appealing to those clinicians who are busy and work in fast paced environments.

The CDT has shown to be useful in detecting early-stage dementia, with those with more impairment on the CDT after a 1 year and 2 years follow up were more likely to be placed in 24/7 dementia care units (Shulman, 2000). Therefore, it seems as though the CDT has some predictive ability but the extent to which for functional impairment specifically needs further researched. McCue and colleagues (1990) found that measures that assess visuospatial or tactile skills were predictive of ADLs specifically reliant upon physical demands related to self-care such as cleaning and making the bed. In a meta-analysis of 68 articles across the aging continuum, the visuospatial cognitive domain accounted for 26% of the variance of functional outcomes within the MCI population (McAlister et al., 2016). Similarly, the CDT contributed 26% of the variance in IADLs in those with AD (Hall et al., 2011). There was a significant moderate correlation for individuals with dementia between the CDT with more advanced ADLs (Cornelis et al., 2018). Additionally, the CDT only contributed 4% of the variance in functional outcomes in a population of 124 individuals diagnosed with MCI (Aretouli & Brandt, 2010).

Executive Functioning (EF)

EF is a broad term that can be described as higher order cognitive processes that involve emotions and/or motor activities during the performance novel tasks (Cornelis et al., 2018). It plays a role in organizing, inhibition, working memory, and adaptability (Cornelis et al., 2018; Aretouli & Brandt, 2010). Age is correlated to EF to an extent (r = 0.27, $p < .01$) whereas education is moderately correlated to EF (r = 0.32, $p < 0.1$; Rog et al., 2014). In regard to the normal aging process, EF is likely more sensitive to every day functional changes (Farias et al., 2009). Measures of EF are arguably the most researched domain in terms of their relationship and predictive ability with ADLs/IADLs and are found to be the most correlated with such activities (Cornelis et al., 2018; Monaci & Morris, 2011, Cahn-Weiner et al., 2007, Cahn-Weiner et al., 2002; Farias et al., 2003; Nguyen et al., 2019; Royall et al., 2007).

To understand if EF plays a role in functional impairment, many cognitive domains must be assessed to see if EF is truly uniquely contributing to functioning (Cahn-Weiner et al., 2007). Given this fact, this current study will be utilizing multiple neuropsychological measurements that assess EF to see what each of their unique contributions are. Similarly, Nguyen and colleagues (2019) conducted a study utilizing four different measures of EF; TMT-B, COWAT, WASI-II Similarities and Matrix Reasoning. Results showed that only TMT-B and Similarities significantly contributed to a performance based IADL measure. Thus, some of the various measures that fall within the EF domain are more predictive of functional impairment than others. Using only one measure of EF is not recommended as being the primary measure to assess functional impairment due to such measures also tapping a broad range of other cognitive abilities such as processing speed, memory, and psychomotor skills (Razani et al., 2007). Importantly, using more than one measure of EF is important to get a better sense of how the individual is functioning.

To measure pure EF is very complex and arguably impossible. There are many different definitions and therefore a lack of consensus on what EF truly is measuring. There is an understanding the EF predominately occurs in the prefrontal cortex, but it is important to keep in mind there is a vast number of other connections that this area of the brain has to other cortical and subcortical structures (Rubiales et al., 2018). Alan Parkin (1998) states that there is unequivocally no evidence to suggest that there is one brain area that is associated with EF measures. The three main components to EF can arguably be broken down into working memory, cognitive flexibility, and inhibition (Miyake, et al., 2000). These researchers suggest that EF has unity and diversity, stating that there are some underlying abilities that are shared within this domain but can also be separated into different contributions to an individual's performance. It is crucial that the reader keep this information in mind when interpreting results and viewing this study. Thus, the vagueness and disagreement of a definition for the EF domain will remain a limitation in this study.

In this current study, the interest is in looking at the relationship between functional outcomes and cognitive abilities specifically within the MCI and dementia populations. A meta-analysis was conducted consisting of 68 articles that investigated the variance of cognitive tasks among functional outcomes; variance from EF attributed 37% in a population of individuals diagnosed with MCI (McAlister et al., 2016). Age nor education moderated this relationship. In a study conducted by Aretouli & Brandt (2010), working memory, a subdomain of EF, was the only cognitive measure to significantly contribute variance to functional outcomes in a population consisting of 124 patients with MCI, although the relationship was modest (3.8%). Working memory domain consisted of several tests such as the Delis-Kaplan Executive Functioning System (D-KEFS; Delis et al), Stroop Test and the TMT. After controlling for demographic, health-related, and cognitive variables, working memory no longer uniquely contributed for functional outcomes. Therefore, lower scores on working memory tests were indicative of poorer functional outcomes only when not taking into consideration other important variables such as age and education.

As previously mentioned, much of the literature support the notion that EF is a very important, if not most important contributor to IADLs and ADLs. To further support that claim, McAlister and colleagues (2016) revealed that EF attributed the most variance of functional outcome (37%) and was statistically significantly different in comparison to other cognitive domains (i.e., memory, executive functioning, global cognitive status, attention, visuospatial abilities, working memory, processing speed, and language) in a meta-analysis of 68 articles looking at the MCI (i.e., amnesic and non-amnesic) diagnosis specifically. TMT-B and the COWAT made significant contributions to the prediction of self-reported IADL functioning as reported by one's caregiver. Twenty percent of the variance was explained by TMT-B as well as an additional 14% explained by the COWAT (Cahn-Weiner et al., 2002). In another study, fluency measures such as the COWAT attributed 22% of the variance to functional outcomes in an MCI population whereas naming measures like the Animal Naming Test (ANT) attributed 21% (McAlister et al., 2016). However, these were not statistically significant. Fluency measures were specifically recommended in neuropsychological evaluations when cognitive decline is noted due to their sensitivity to prediction of conversion of healthy aging to dementia one to two years before diagnosis (Ritchie et al., 2001). Both these scores (i.e., COWAT and TMT-B) were also significant in showing the progression of healthy individuals or in progressing to someone with MCI or preclinical AD, meaning that more intrusions were predictive of individuals progressing to an MCI diagnosis (Thomas et al., 2018). The set-shifting and alternating of attention that is assessed through TMT-B therefore is deemed useful in various IADLs. Measures that require switching abilities such as the TMT-B attributed the largest variance among the EF domain (63%), followed by inhibition (32%), planning (25%), reasoning (11%), and initiation (11%) but with no statistically significant differences between the latter. Additionally, response generation and cognitive flexibility as measured by the COWAT is also essential in IADLs commonly performed (Cahn-Weiner et al., 2002). Other studies showed EF explaining up to 52% of the variance in IADLs (Farias et al., 2009).

Measures of EF in a study of community dwelling older adults explained more variance in ADLs than other variables such as age, level of education, and overall health status (Cahn-Weiner et al., 2002). In other studies, ANT, TMT-A, and the Frontal Assessment Battery (FAB) had moderate correlations with basic ADLs such as bathing and dressing in individuals diagnosed with dementia (all $p < 0.01$; Cornelis et al., 2018). The COWAT showed predictive ability of baseline functional status and changes in IADLs across approximately 5.5 years (Cahn-Weiner et al., 2007). None of the measures of EF were related to any of the physical ADLs, suggesting that perhaps different ADLs yield different cognitive and motor abilities and therefore may correlate with different measures more so than others (Cahn-Weiner et al., 2002).

On the contrary, Burton and colleagues (2018) found that measures such as TMT-B, COWAT, and the Stroop Test were not significantly correlated with IADLs in groups of both AD and non-AD. Measures of abstract thinking such as in the task of similarities had weak but significant correlations (Cornelis et al., 2018). Additionally, there was a significant moderate correlation for individuals with dementia between the CDT, TMT-A, TMT-B, and the FAB with more advanced IADLs such as engaging in crafts and computer technology. This indicates that EF may be more closely implicated in IADLs versus ADLs (Cornelis et al., 2018). The EF domain was the single most important domain due to its strong relationship with both performance based and informant reports of functioning in individuals with possible or probable AD (Farias et al., 2003).

Measures such as Wisconsin Card Sorting Test (WCST) perseverative responses, D-KEFS Tower Achievement Score, and D-KEFS Trail Making Test (letter – number) were classified as some of the EF measures that were found to not have a relationship with self-reported IADLs in individuals with varied degrees of dementia (Razani et al., 2007). Other measures such as verbal fluency (e.g., COWAT) and WCST Total errors were correlated with self-reported measures of IADLs (r =.48, r = -.35, respectfully, Razani et al., 2007). Specifically, verbal fluency (COWAT) was the best predictor of a direct observation of basic ADLs within the financial outcome domain, as well as second best predictor for the shopping subscale (Razani et al., 2007). It is important to note that this measure also has a language component to it, but is thought to predominantly measure EF. The skills that underly verbal fluency tasks are suggestive of being useful in tasks such as shopping or managing finances and planning tasks. EF measured by a composite score of category and letter fluency, and a digit span subtest was a significant independent predictor of global functioning as well as within specific domains of functioning except everyday memory (i.e., other domains include everyday language, everyday visuospatial functions, everyday planning, everyday organization, and everyday divided attention (Rog et al., 2014).

As previously discussed, another cognitive domain heavily research in terms of its relationship with functional outcome is memory. Both individuals diagnosed with MCI and dementia (i.e., vascular, AD, and mixed) showed a substantial decline in EF (R^2= 52%) compared to memory (R^2= 48%) across a 5-year time span, although memory also was also a unique contributor to decline (Farias et al., 2009). Scores on measures such as digit span backward, spatial span forward, initial/perseveration scales on Mattis Dementia

Rating Scale (Mattis, 1973), as well as letter fluency made up a composite EF scale and showed longitudinally a steeper decline signifying more impairment on IADLs. Therefore, more changes in EF resulted in more functional decline and were strongly correlated with IADLs (r=-.72, p <.001). The previously stated results indicate that EF has uniquely affected one's ability to perform IADLs, meaning those who exhibit declines in EF also will likely have decline in functioning across time. Those with decline in both memory and EF, will have an even substantial degree of decline in every day functioning. Those who converted from healthy aging to either MCI or dementia had lower scores on executive functioning measures, specifically with the TMT-B as well as lower baseline functional status (Nowrangi et al., 2016). Importantly, the visuospatial/executive functioning domain on the Montreal Cognitive Assessment (MoCA) was the most predictive of functional outcomes which entails a smaller version of the TMT-B (Durant et al., 2016).

Processing Speed

The domain of processing speed or speed of mentation is one that is under researched in comparison to the many other neuropsychological measures in regard to its relationship with functional abilities. TMT-A is one of the measures that fall in this domain. Processing speed composite scores were significant predictors of IADLs in individuals with MCI, contributing 20% of the total variance (McAlister et al., 2016). Additionally, better processing speed scores were predictive of better driving ratings (Wadley et al., 2021). Given that a composite score of processing speed measures was significantly correlated with both IADLs and driving ratings, it can be inferred that this cognitive ability is strongly implicated in everyday activities and functioning in individuals with MCI or early AD. With the results suggesting such as significant relationship of processing speed and ability to drive, as well as some studies suggesting that processing speed accounted for 49% of the variance of IADLs, further highlights the importance of knowing such information when neuropsychologist make decisions about an individual's every day abilities (Wadley et al., 2021). This is especially true given that neuropsychologists can suggest that patients stop driving when they have significant concerns.

Notably, processing speed was an even bigger predictor of functional abilities than neuroimaging correlates that are generally consistent with an AD profile. That being said, it is important that in neuropsychological testing the domain of processing speed is assessed because it is more cost effective and accessible than neuroimaging. This is not to say that neuroimaging is not a crucial and excellent variable in assisting the diagnoses of dementia or other cognitive impairments. Diagnostically, processing speed can be a good indicator of deficits in those who are vulnerable in developing dementia (Wadley et al., 2021). To further provide evidence for this conversion, Nowrangi and colleagues (2016) showed that those who converted from healthy aging to either MCI or dementia had poorer scores on the TMT-A, as well as having lower baseline functional status.

Language

The language cognitive domain is broad but still nonetheless can overall give important information regarding one's cognitive functioning. This is especially true for the diagnostic purposes of primary progressive aphasia (PPA) and even AD. The BNT is a commonly used language measure to assess language impairment, specifically anomia. Reduction in both the left and right hippocampal regions was also correlated with lower

BNT scores (Peng et al., 2015). Additionally, in a meta-analysis consisting of 68 articles, the language domain accounted for 22% of the variance in functional outcomes in individuals with MCI, but were of the lowest explained variance in comparison to other cognitive domains like memory and executive functioning (McAlister et al., 2016).

The BNT has also been shown to be useful in longitudinal studies. Poorer scores on the BNT were predictive of a sample of otherwise healthy individuals in progressing to a diagnosis of MCI over a 5-year time span (Thomas et al., 2018). Additionally, 27 individuals with dementia who performed more poorly on the BNT were more likely to progress to a more severe degree of AD than the other participants in the study. Duration of how long they have been living with AD was not a contributing factor in this finding. These findings suggest that those who have some type of aphasia or word finding difficulties (WFDs) may be more at risk for progressing into a more severe range of dementia, outlying the important predictive abilities of this neuropsychological measure. Those classified as a mild severity of dementia still had difficulties on the BNT in comparison to controls, but not as severe as the moderate and severe dementia groups. The BNT explained 39% of the variance in a clinical dementia rating at 30 months after the study was conducted (Knesevich et al., 1986). In a study conducted by Ritchie and colleagues (2001) investigating conversion of healthy aging to MCI and dementia recommended that naming measures such as the BNT is to be used in such assessments because it was sensitive enough to detect conversion to dementia one to two years before diagnosis. These same individuals had a lower baseline functional status, too. When looking at an informant based IADLs measure specifically, the BNT along with immediate memory, EF, and apraxia were most consistently correlated with such measure

(Farias et al., 2003). This was not true when directly assessing functional status. Lastly, in a study of 80 participants (22 amnesic MCI and 38 AD), those with AD had significant reductions in BNT scores and ADL scores in comparison to healthy controls after a two year follow up. Those just with a diagnosis of MCI did not show these relationships at either a one or two year follow up (Peng et al., 2015).

Orientation/Global Cognitive Status

Measures such as the MoCA and the MMSE are all standardized, brief, cognitive measures that are able to adequately assess the presence and severity of a dementia or cognitive changes (Reed et al., 1989). The abilities of such brief measures to give adequate enough information about one's functional status is suspect and much of the literature is mixed regarding this question. Although there are mixed results and arguments are made that these brief measures of orientation such as the MMSE are not specific or informative enough to predictive functional impairment, several studies have shown that the MMSE does correlate to an extent with IADLs. For example, Razani and colleagues (2007) found a strong relationship between MMSE scores and functional outcomes (r =.75). Furthermore, global cognitive functioning accounted for 20% of the variance in functional outcomes in a meta-analysis consisting of 68 articles within the MCI population (McAlister et al., 2016). Similarly, in a population of 124 patients diagnosed with MCI, the MMSE contributed 8.2% of the variance of functional outcomes (Aretouli & Brandt, 2010). MMSE scores but not immediate memory scores on the RBANS were significantly correlated with functioning in both a non-AD group and those with AD (Burton et al., 2018). Importantly, lower scores on the MMSE were predictive of converting from healthy aging to either MCI or dementia (Nowrangi et al., 2016). These same individuals had a lower baseline functional status, too.

On the contrary, Reed and colleagues (1989) study showed that MMSE scores explained only approximately one-third of the variance in both ADL and IADL scores in individuals diagnosed with a wide range of dementia severity. Therefore, though MMSE scores can provide some insight of functional abilities, it only explained a fraction of the variance for ADLs/IADLs and are even worse at predicting these abilities in individuals with milder severity of dementia (Reed et al., 1989). This is troublesome because at the earlier stages of dementia, clinicians are trying to figure out their patient's true functional capacity in their everyday lives and to assist in treatment planning. Monaci and Morris (2011) found no significant correlations between ADL performance on MMSE scores or measures of EF at baseline or at an 18 to 24 month follow up within a population of individuals with dementia. At initial assessment, IADL scores were significantly correlated with MMSE scores, indicating that IADLs are more strongly predictive of cognitive abilities at least at the beginning stages of dementia. One issue with the MMSE that can add to these mixed findings is that cutoff scores of 24 and below have been labeled as being in the "*demented*" range. The majority of individuals who scored in this range scored high on measures of ADLs, despite correlation of MMSE and ADL questionnaires. Speculations for this finding is due to specificity of age; it is speculated that MMSE measures have low specificity for the elderly population and suggestions of lowering this cut off are made (Warren et al., 1989).

Other brief measures mentioned such as the MoCA have been studied to investigate its link to functional status (Nasreddine et al., 2005). The MoCA is a measure that looks at domains of orientation, attention, language, memory, executive function, and visuospatial function. As age increases, scores on both the MoCA and the Lawton- Brody (1969) IADL scale decreased as well. Lee and colleagues (2019) suggested a cutoff of 81.2 years or older being the age at which functional decline is clinically observed. This age may be suggested as a cutoff when considering deterioration of functional status but also provides the implication that the MoCA may not be as accurate in prediction of functional decline in those who are below this age. On the other hand, the MoCA has been shown to have a weak to moderate correlation with the Activities of Daily living Questionnaire (ADL-Q; $r = -0.34$), meaning that lower scores on the MoCA had a relationship with more functional impairment (Durant et al., 2016). The MoCA added above and beyond the variance of the demographic variables alone.

Overall, there are mixed results on predictive abilities of various neuropsychological measures but there is ample evidence to back up the fact that most, if not all of these measures provide some type of predictive ability in functioning with individuals with dementia or MCI, with some more than others. For example, the EF domain had the most abundance of literature on this topic and consistently showed to have the highest predictive power in functioning with other domains such as visuospatial and language has far less more research. The continuation of future research on this topic is much needed.

CHAPTER 3: METHOD

The purpose of the present study was to examine which neuropsychological measures are sensitive enough to detect various deficits in self-reported ADLs and IADLs in individuals with dementia and/or MCI. The functional status of individuals with memory and thinking deficits is a core criterion that must be assessed when making the diagnosis of dementia. Therefore, knowing specific neuropsychological tests that are highly predictive of functional impairment would be beneficial for treatment planning and assessing differential diagnoses. Additionally, those diagnosed with MCI that have more functional impairment are more likely to transition to a dementia process, thus, emphasizing the importance for treatment planning and considering future implications.

Design

This study used archival data and is a quasi-experimental study using regression models to determine the predictive abilities of various neuropsychological tests in relation to functional impairment in individuals with dementia and MCI.

Participants

The subjects included 207 individuals referred to a memory care clinic in the mid-Atlantic region for a neuropsychological evaluation for suspected diagnosis of dementia or memory decline. Data was collected on the individuals first visit as part of the routine initial evaluation of the clinic. Since archival data was used, for those participants whose education was noted as less than eigth grade with no further specifics, they were assigned an education level of eigth grade.

Inclusion and Exclusion Criteria

Individuals were excluded from the study if they did not have a diagnosis of dementia or MCI, if data did not exist for the measures that are being investigated in this study, or if English was not their first language.

Inclusion criteria included anyone who is referred by their appropriate provider to the memory care clinic and is subsequently diagnosed with any type of dementia or MCI.

Measures

Global Cognitive Status/MMSE

Questions to assess the patient's global cognitive status were derived from and are quite similar to those of other brief measures such as the MMSE (Folstein et al., 1975) The MMSE can separate healthy individuals with those that have cognitive impairment and can be used repeatedly to track disease progression. Importantly, although the MMSE can monitor disease progression, it should not be used diagnostically in terms of diagnosing dementia. The MMSE consists of questions related to five areas of functioning: orientation, registration, attention, calculation, and recall. The questions for assessment of global cognitive status for this current study focused on orientation. Questions asked included: What is your full name? What is your age? What is your date of birth? What is the current month, date, year, day of the week? Where are you right now? What city are you in? Who is the current president of the United States? Who is the current vice president of the United States? Tell me about a current event. The answers were scored off of a binary scale, with 1 point for correct answers and 0 points for incorrect answers. Some of these questions included cues (e.g., "the last name starts with a 'b'"), but responses that needed cueing were scored as 0 points or incorrect. Only the answers that did not require cueing counted as 1 point.

In a study with 29 individuals with dementia, 63 healthy controls, 10 with depression and cognitive dysfunction, and 30 with depression without cognitive dysfunction, the MMSE accurately predicted the severity of cognitive impairment with the dementia group having the lowest scores (i.e., more cognitive deficits), followed by the depression and cognitive dysfunction group, then depression without cognitive complaints (Folstein et al., 1975). The results were the same when completed with an age-matched sample. Additionally, the scores for the MMSE in the dementia group had little significant change across time whereas the depression group scores had a large substantial increase over time. This is to be expected given that dementia is uncorrectable whereas changes in cognition fluctuate with depression and are more successfully treated, exhibiting the validity of the MMSE. Reliability has also been established with the MMSE. When patients with dementia took the MMSE approximately 28 days from initial test, scores were not statistically significantly different ($p = 0.887$).

California Verbal Learning Test, 3rd Edition (CVLT-3)

The CVLT-3 is a measure that assesses verbal auditory learning and memory (Delis et al., 2017). The CVLT-3 has two lists (i.e., List A and List B) of 16 words from four different semantic categories. The standard and alternate versions of the test were both used for this study's purposes. Encoding took place over five trials where the 16 words from List A were read to the patient in the same order. After each trial, the patient is asked to recall as many words as they can remember, including ones that they already said. After the recall of trial five, they are then verbally given a distractor list that also has 16 words consisting of four semantic categories and asked to recall as many words from this list as they can (i.e., List B). Then, the patient is asked to recall as many words as they can from List A. Following this, they are cued given the semantic categories and asked to recall as many words from List A that fall into those categories. After a 20-minute delay, the patient is then asked again to freely recall as many words from List A that they can remember, followed by a cued recall within each semantic category. Finally, recognition is assessed by asking the patient to respond with "yes" or "no" to a list of 44 words that may or may not have been on List A. There are several scores that can be derived for the CVLT-3; All of which are scaled scores with the Total Trial 1-5 being a standard score. Primary measures used for this current study included the sum of words recalled across five trials (Total Trial 1-5), numbers of words freely recalled after a short delay following a distractor list (Short Delay Free Recall), number of words freely recalled after a longer delay of approximately 20 minutes (Long Delay Free Recall), the ability to discriminate between target words and non-target words (Recognition Discriminability), number of words repeated across the task (Repetitions), and words that were recalled that were not on the first list (Intrusions). Age adjusted scores were used.

Clock Drawing Test (CDT)

The CDT is a test that measures spatial dysfunction, planning, visuospatial skills and constructional praxis. Specific points were given for ability to draw clock contour, spatial arrangement of numbers, and ability to place hands at designated time (i.e., 10 minutes after 11). Contour for the clock was given 1 point if they were able to accurately draw the circle of the clock and 0 points for all other contours or inability to draw the circle of the clock. One point was given if spatial arrangement of numbers was correct, with all appropriate numbers in the correct positions and 0 points if there was a spatial planning deficit or numbers missing. Lastly, 1 point was given if the hands were placed at the correct time with the shorter hand being the hour hand and the longer one being the minute hand. Zero points were given for all other hand placements.

Animal Naming Test (ANT)

The ANT or animal fluency is a measure of semantic fluency. The patient was given 60 seconds to come up with as many animals as they can think of. One point is given for each unique animal given. Points were given for different breeds or subspecies (e.g., golden retriever and bulldog or bird and parrot) but if the patient gave an animal at different developmental stages, only one was counted (e.g., puppy and dog). Scoring is based off of number of animals given in a period of time and is calculated taking into consideration their age and education level (Tombaugh et al., 1999). *Z*-scores were used.

Controlled Oral Word Association Test (COWAT)

The COWAT measure's phonemic fluency. The patient was given a different letter (i.e., F, A, S) across three trials and asked to come up with as many words as they can think of that begin with that appropriate letter. They were given 60 seconds per trial. Instructions included for them to exclude words that are proper nouns, numbers, and words with different endings (e.g., big, bigger, biggest). The number of words across the three trials were totaled and accounted for the total COWAT score with consideration of age and education (Tombaugh et al., 1999). *Z*-scores were used.

Boston Naming Test - 15 Item (BNT-15)

The BNT-15 measures object naming to confrontation. The BNT-15 is adapted from the BNT - 2nd edition which has 60 black and white line drawings in which the patient was asked to name (Kaplan et al., 2001). The current use of BNT-15 in this study was abbreviated and only consisted of 15 items. The use of semantic and phonemic cues was able to be given if the patient was unable to recall the object, as well as multiple choice options as the last resort. Four multiple choice options were given in order to name the item being displayed. When the use of a semantic cue was given and the patient then reported the correct answer, this was counted as correct and they were given one point. When the use of a phonemic cue was given and the patient then reported the correct answer, this was not counted as correct and was scored as 0 points. If they did not get the correct answer after a phonemic cue was given, they then were given the option of four multiple choice options. When given the multiple-choice options, regardless if they answered correctly or incorrectly, it was scored as 0 points. Age and education were taken into consideration for scoring (Lansing et al., 1999). *Z*-scores were used.

Trail Making Test A (TMT-A)

The TMT-A is a measure of speed of mentation (Armitage, 1946). The patient is given the paper and told to draw a line connecting the numbers (i.e., 1 to 25) from lowest to highest and to work as fast as they can without making mistakes. First, a sample is completed to ensure they comprehend the task demands and then the actual test is given with numbers ranging from 1 to 25. Scoring is based off of the number of seconds it took them to perform the task with higher numbers indicating more impairment. If the task was unable to be completed within three minutes, the highest amount of time in seconds was given to them as a score (i.e., 180 seconds) and a *z*-score was then calculated based off of their age and education per Reitan (1956) test instructions. Other studies also used this method of cutoff scores (Marshall et al., 2011; Rasmusson et al., 1998). Tombaugh norms were used based off of age and education (Tombaugh, 2004). *Z*-scores were used.

Trail Making Test B (TMT-B)

The TMT-B is a measure of executive functioning, specifically with set-shifting and alternating attention or mental flexibility (Armitage, 1946). The patient is told to draw a line in order alternating between letters and numbers and to work as fast as they can without making mistakes. First, a sample is conducted to ensure that they comprehend task demands and then the full test is attempted. Scoring is based off of the number of seconds it took them to perform the task with higher numbers indicating more impairment. If the task was unable to be completed within five minutes, the highest amount of time in seconds was given to them (i.e., 300 seconds) and a *z*-score was then calculated based off of their age and education per Reitan (1956) test instructions. Other studies also used this method of cutoff scores (Marshall et al., 2011; Rasmusson et al., 1998). Tombaugh norms were used based off of age and education (Tombaugh, 2004). *Z*-scores were used.

Patient Health Questionnaire – 9 (PHQ-9)

The PHQ-9 is a self-report measure that is based on the DSM-5 (American Psychiatric Association, 2013) criteria for major depressive disorder (Kroenke et al., 1999). The PHQ-9 is scored on a 4-point scale with 0 = *not at all*, 1 = *several days*, 2 = *more than half the days*, and 3 = *nearly every day*. Scores can range from 0-27, with higher scores signaling more depression severity. The internal reliability for this measure is very high, with a Cronbach's alpha of 0.89 and test-retest validity was also excellent (*r* = 0.84; Kroenke et al., 2001). In a study of 580 individuals who completed an interview with a mental health professional, 93% of the sample with no depressive disorder scored a 10 or less on the PHQ-9, whereas 88% of those with a major depressive disorder diagnosis had scores of 10 or greater (Kroenke et al., 2001). When a patient scored less than 5, 73.4% of those were not diagnosed with a depressive disorder (Kroenke et al., 2001). Cutoff scores of 0-4 were considered minimal severity, 5 to 9 mild, 10 to 14 moderate, 15 to 19 moderately severe, and 20 to 27 severe.

Activities of daily living (ADL) and Instrumental Activities of Daily Living (IADL)

Functional status was assessed through self-report (i.e., filled out by self or informant) regarding the patient's ability to perform various ADLs/IADLs. All of the ADLs/IADLs must be answered with either "no help needed", "needs assistance/reminders", or "unable to do". Answers were quantified with 0 points for "no help needed", 1 point for "needs assistance/reminders", and 2 points for "unable to do". Points were then calculated as a total. The higher the score, the more functional impairment the individual has. ADLs that were investigated include grooming, walking, toileting, and bathing. IADLs that were investigated include managing medications, managing finances, cooking, household chores, shopping, and using the telephone (see Appendix).

Procedures

Relevant data was extracted from an archival database that consists of regularly collected data per patient at a memory care clinic and inputted into an excel document. This data then was uploaded into one SPSS data file and used for this present study. Scoring was previously completed by third or fourth year extern students as well as fifth year clinical psychology interns that are all supervised under clinical neuropsychologists. All procedures were approved by the Philadelphia College of Osteopathic Medicine's Institutional Review Board (IRB) as well as the IRB from the hospital in which the data was extracted.

CHAPTER 4: RESULTS

Initially, a multiple linear regression was intended for all 14 predictor variables predicting total ADL scores for the MCI population and another for total IADLs. The same analyses were intended for ADL and IADL scores for the dementia group. However, in order to use a linear multiple regression, the following assumptions must be met: linearity, independence, homoscedasticity, and normality (Field, 2018). To ensure linearity between the predictor variables and dependent variable, the normal probability plot was viewed for outliers, as well as looking at the line of best fit to ensure that the points fall approximately in a linear pattern. Independence was met, as residual terms were uncorrelated upon any two observations. Homoscedasticity is the assumption that the residuals at each level of the predictors should have equal variance. Homoscedasticity was met following review of the standardized residual to standardized predicted value regression plot. To remove outliers, a casewise diagnostic was computed to ensure that the standard residual was within three standard deviations. Any residual outside of 3 standard deviations was removed. Additionally, an absence of multicollinearity was guaranteed by looking at correlation coefficients among the predictor variables and ensuring these numbers do not exceed 0.80. Tolerance and variance inflation factor were computed for all variables, and no multicollinearity was identified.

Lastly, normality refers to the assumption that the residuals being used in the model are random and normally distributed with a mean of zero. To check normality among the dependent variables (ADLs/IADLs), a Shapiro-Wilk test was conducted to look for a non-statistically significant result. In all cases, significance was reached ($p < .001$) and thus, normality was not assumed because of the extremely non-normally distributed data. Therefore, the use of a nonparametric test was used, specifically a Poisson regression along with a zero-inflated negative binomial (ZINB) regression. This type of analysis is typically used for data involving counts, and it was discovered that the

ADL and IADL data resembled frequencies, as the total number of individuals for each one-unit increase in disability could be counted. A Zero-inflated Poisson (ZIP) model is used when there are too many zeros such that a Poisson regression cannot adequately predict an outcome. Concerning the negative binomial regression, this is used when overdispersion is detected (Grace-Martin, n.d.).

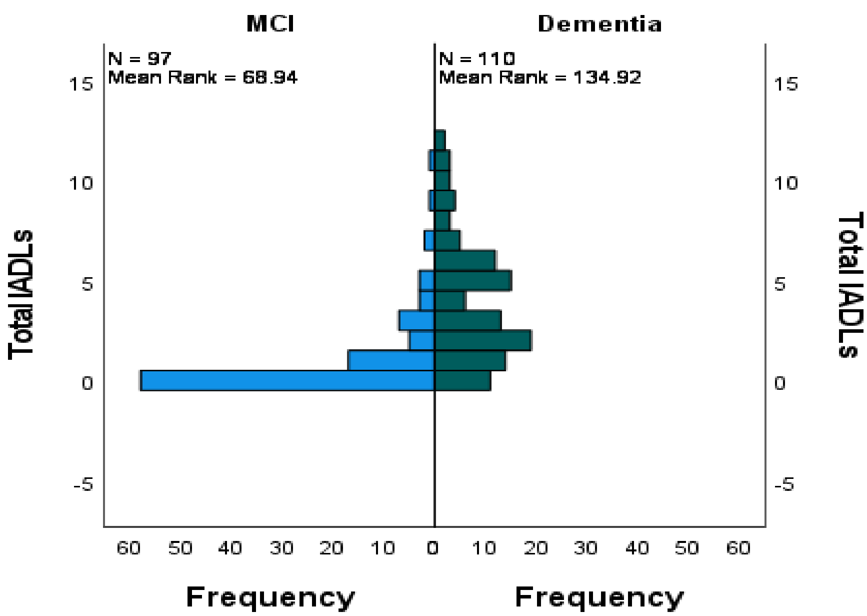
A Poisson regression, a nonparametric test, was used because the data was not normally distributed. In order to use a Poisson regression, the following assumptions must be met: the dependent variable must be count data, independent variable(s) must be continuous, ordinal, or nominal, independent observations, distribution of counts must follow a Poisson distribution, and the mean and variance of the model have to be identical (Laerd Statistics, 2023). If the variance and mean are not identical, overdispersion is a concern, so a negative binomial regression is then utilized. Overdispersion is the presence of greater variability in a data set than would be expected based on a given statistical model.

Hypothesis 1

It is hypothesized that the regression model with the following predictor variables: MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, and Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 will significantly predict IADL function, with TMT-B being the strongest predictor in the MCI population. A Poisson regression revealed overdispersion as exhibited by the deviance value equaling 2.32. A deviance value should be below 1.10 or else the data is considered to have overdispersion. Overdispersion refers to the concept of more variation in the data than expected (APA, 2023). In addition, it was detected that a large number of participants indicated zero for IADL impairment (59.8%). Because of this overdispersion, and majority of sample indicating zero current need for assistance, a zero-inflated Negative Binomial (ZINB) regression was performed. In other terms, as expected, the overwhelming majority of individuals diagnosed with MCI in this sample did not report having much, if any, difficulties performing IADLs (See Figure 1).

Figure 1

Dispersion of Total IADL impairment across the MCI and Dementia Populations



Note. A zero score indicates “no help needed”, 1 meaning “needs some assistance”, and 2 meaning “unable to do”. A total score was calculated across 6 different IADLs and are displayed here. There is more variability in IADL performance across the dementia sample versus MCI group.

First, the Count Model Coefficients were analyzed and revealed several significant findings. This model predicts when an individual will indicate one or more IADL difficulties using the measures total score. When variables are significant, these measures are indicative of the individual having zero IADL impairment or one or more IADL impairments. This model revealed that the ANT (*p* = .001), TMT-A (*p* =.000), PHQ-9 (*p* = .002), and CVLT Recognition Discriminability (*p* = .010) all can predict whether an individual has zero IADL impairment or one or more impairments.

A ZINB model was conducted to differentiate between the MCI participants who did not have any impairments with IADLs versus those who may have some difficulty with IADLs but perhaps not at the time of the evaluation. The ZINB model revealed that the MMSE (*p* = .038) and TMT-B (*p* = .045) were both significant predictors for IADL functioning. In other words, the MMSE and TMT-B were able to differentiate between those who did not have any issues with IADLs (i.e., certain zero) versus those who do have difficulty but reported zero on the current evaluation. Thus, hypothesis one has been accepted with the addition of MMSE also being a significant contributor to IADL functioning.

Hypothesis 2

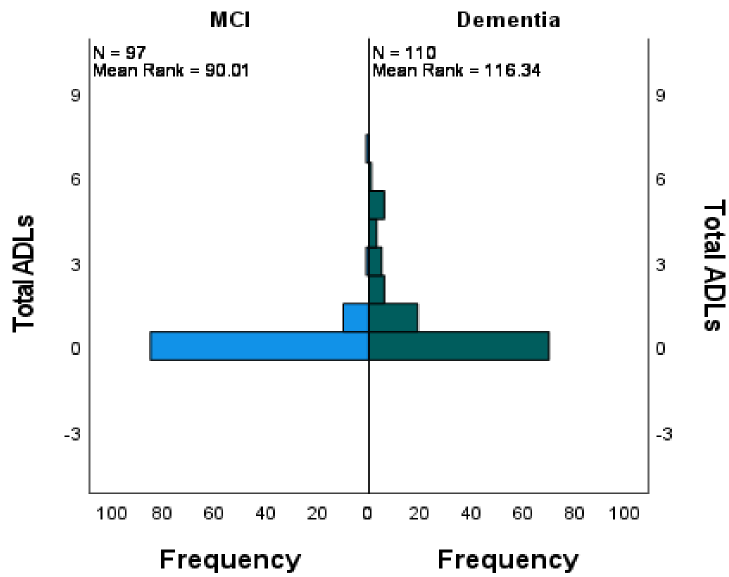
It is hypothesized that the regression model with the following predictor variables: MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, and Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 will significantly predict IADL function, with TMT-B being the strongest predictor in the dementia population. A Poisson regression was conducted and revealed overdispersion of the reports of IADLs in this group (Deviance value = 2.33), so a negative binomial regression was completed. The overall model was not significant, X^2 (14) = 13.21, *p* = .510. Hypothesis 2 was rejected, meaning that for this sample no neuropsychological measures were statistically significant enough to predict IADL functioning in the dementia population.

Hypothesis 3

It is hypothesized that the TMT-B will be the strongest predictor among a number of other variables (i.e., MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 in the prediction of daily functioning in terms of total ADL functioning in the MCI population. To test this hypothesis, a Poisson regression was attempted, but due to the majority of ADL data being homogenously zero (87.6%), the analysis could not be performed. Approximately 88% of the MCI sample endorsed "no help needed" across ADL activities with only 12% reporting any level of issues with ADLs (See Figure 2).

Figure 2

Dispersion of Total ADL impairment across the MCI and Dementia Population



Note. A zero score indicates "no help needed", 1 meaning "needs some assistance", and 2 meaning "unable to do". A total score was calculated across 5 different ADLs and are displayed here. The overwhelming majority of individuals diagnosed with MCI did not report needing help with ADLs whereas more individuals with dementia endorsed an increase need of ADLs with more dispersion across the continuum.

Hypothesis 4

It is hypothesized that the regression model with the following predictor variables: MMSE, CDT, ANT, COWAT, BNT-15, TMT-A, TMT-B, PHQ-9, and Total Trial 1-5, SDFR, LDFR, Recognition Discriminability, Repetitions, and Intrusions from the CVLT-3 will significantly predict ADL function, with TMT-B being the strongest predict in the dementia population. A Poisson regression was conducted and revealed overdispersion (Deviance value = 2.08), so a negative binomial regression was performed. The overall model was not significant, X^2 (14) = 19.45, p = .148. Hypothesis 4 was rejected, meaning that for this sample no neuropsychological measures were statistically significant enough to predict ADL functioning in the dementia population.

Hypothesis 5

It is hypothesized that depression as measured by the PHQ-9 will be a significant predictor to functional impairment (total ADLs/IADLs) among individuals diagnosed with MCI, but not those with dementia. Specifically, this hypothesis examined the PHQ-9 scores across both total ADL and IADL scores among the MCI and dementia groups to see whether the predictive value of the PHQ-9 varies across populations. To test this hypothesis, the same analyses were used as above to examine the PHQ-9 specifically. For the MCI population, the overall model was not significant and upon evaluation of the PHQ-9 specifically it too was not significant in predicting IADL functioning ($p = .190$). An analysis could not be completed for ADL functioning with this population as previously stated. For the dementia population, both models for IADL and ADL functioning were not significant. An examination of the predictive ability of only the PHQ-9 was performed and it alone was not predictive of IADL ($p = 0.162$) or ADL ($p = 0.414$) impairment. Hypothesis 5 was rejected.

Additional Analyses

Related to hypothesis 5, additional analyses were performed to compare the means of the PHQ-9 between the MCI and dementia populations. A Mann-Whitney U test was found to be not significant for reporting of the PHQ-9 when looking at the MCI and dementia groups ($U = 4963$, $p = 0.385$). The average ratings on the PHQ-9 were similar between the MCI population ($M = 5.85$, $SD = 5.061$) and the dementia population

(*M* = 5.59, *SD* = 5.395). This indicates little variation in depression reporting between the two populations in this sample.

Further investigation revealed a relationship between some of the various neuropsychological measures with IADL functioning in the dementia population. A Pearson correlation revealed that five out of the 14 predictor variables were significantly correlated with IADL functioning in the dementia population. These variables included the MMSE ($r = -0.25$, $p = 0.005$), CDT ($r = -0.20$, $p = 0.021$), TMT-A ($r = -0.19$, $p = 0.025$), TMT-B ($r = -0.17$, $p = 0.037$), and CVLT Recognition Discriminability ($r = -0.18$, $p = 0.030$). Though a relationship was detected at the .05 level, all are considered weak relationships. Additionally, there was a difference in both ADL and IADL functioning across the MCI and dementia populations. As expected, the dementia population had significantly more issues with both IADLs ($p < .001$) and ADLs ($p < .001$).

A Mann-Whitney U test was performed to evaluate whether performance on neuropsychological measures differed between the MCI and dementia populations. It was concluded that MMSE scores in the MCI group (*M* = 10.75, *SD* = 1.53) were significantly higher than the dementia group (*M* = 8.78, *SD* = 2.28; $U = 2419$, $p < .001$), indicating that the MCI group had better overall orientation/global cognitive status, as expected. The CDT scores for the MCI group (*M* = 2.64, *SD* = 0.68) were significantly higher when compared to the dementia group (*M* = 1.95, *SD* = 0.86; $U = 2890.5$, $p < .001$), indicating more impairment in spatial dysfunction, planning, visuospatial skills and constructional praxis for the dementia group. ANT *z*-scores were significantly higher in the MCI group (*M* = -0.25, *SD* = 1.06) in comparison to the dementia group (*M* = -1.44, *SD* = 1.03; $U = 2144$, $p < .001$), representing better semantic fluency in the MCI group. Participants in the MCI group (*M* = -0.82, *SD* = 0.90) performed significantly better on the COWAT than the dementia group (*M* = -1.29, *SD* = 1.01; $U = 3775.5$, $p < .001$), meaning that the MCI group had better phonemic fluency skills. Scores on the BNT-15 were significantly higher for the participants in the MCI group (*M* = -0.90, *SD* = 1.80) than the dementia group (*M* = -1.84, *SD* = 2.19; $U = 3807.5$, $p < .001$), signifying better object naming in the MCI group. When comparing the MCI group (*M* = -0.92, *SD* = 2.34) to the dementia group (*M* = -2.64, *SD* = 4.89) on TMT-A scores, as well as TMT- B scores (*M* = -3.89, *SD* = 5.72; *M* = -4.56, *SD* = 4.49, respectively), findings indicated a significant difference ($U = 3684$, $p < .001$; $U = 4004$, $p = .002$ respectively). The MCI group demonstrated better speed of mentation along with set-shifting and alternating attention skills in this sample.

Concerning the CVLT-3, the total score for trials 1 to 5 was significantly higher in the MCI population (*M* = 81.45, *SD* = 13.05) than the dementia population (*M* = 71.91, *SD* = 11.68; $U = 3157.5$, $p < .001$), indicating better overall learning across five trials. When comparing the MCI group to dementia, the SDFR (*M* = 6.32, *SD* = 2.47; *M* = 4.38, *SD* = 2.09, respectively) and LDFR (*M* = 6.20, *SD* = 2.32; *M* = 4.30, *SD* = 1.96, respectively) were consistently better for the MCI group ($U = 2944.5$, $p < .001$; $U = 2837.5$, $p < .001$, respectively), indicating better overall retention of words after a short and long delay. The Recognition Discriminability score was significantly higher in the MCI group (*M* = 6.97, *SD* = 2.58) compared to the dementia group (*M* = 5.82, *SD* = 4.89; $U = 3548$, $p < .001$), signifying that the MCI group is better able to differentiate between words that were on the list versus those that were not. Interestingly, the Repetitions score for the CVLT-3 was statistically significant for differentiating the MCI group (*M* = 12.06, *SD* = 2.16) versus the dementia group (*M* = 12.93, *SD* = 2.11; *U* = 4050, *p* = .002), with the MCI group having more repetitions. Lastly, there was no statistically significant difference for the Intrusions score between the MCI (*M* = 8.71, *SD* = 3.00) and dementia groups (*M* = 8.28, *SD* = 3.60; *U* = 5041.5, *p* = .493). Globally, the dementia group performed worse on all measures except for CVLT Repetitions.

To further investigate whether cognitive reserve (CR) played a role in results obtained, further analyses was conducted. Cognitive reserve was operationally defined as level of education. In the MCI group, approximately 60% of the individuals reported that they need no help at all in performing IADLs. A *t*-test was conducted to analyze the differences in CR between the individuals who need no help and those who reported any kind of help for managing IADLs. When accounting for heterogeneity of variances, there is a difference between groups with no issues with IADLs and those with any issues. The group with no issues had slightly more years of education than the group who indicated any issues with IADLs, *t*(94.49) = 2.03, *p* = .045. Though, effect size, as measured by Cohen's *d*, was small to moderate (*d* = .41).

Statistical analysis was conducted using the International Business Machines (IBM) Statistical Package for the Social Sciences version 28 (SPSS; IBM Corp, 2020). A significance level (*p*-value) of .05 or smaller was used to signify statistically significant findings and is derived from the conventional standards of social sciences (Cohen, 1988, 1992). However, this study used multiple significance tests and therefore a Bonferroni correction was implemented to reduce the likelihood of Type I error, making the alpha level .0125 across analyses. A post hoc power analysis was performed using the following criteria, moderate effect size of .15, alpha set at .0125, a sample size of 207, and 14 predictors. The power analysis revealed power to be 0.896 for the current study, which is considered sufficient.

Demographic Data

Demographic data reported by frequencies, means, and standard deviations in Table 1. Of the 207 participants in the study, 46.9% ($n = 97$) had an MCI diagnosis whereas 53.1% ($n = 110$) had a dementia diagnosis. Education and biological sex were nearly identical between the two groups. There were no differences in reporting ADLs between males and females in the MCI group, $t(95) = -0.771$, $p = 0.443$ in addition to no differences in reporting IADLs between males and females in this group, $t(95) = 0.688$, $p = 0.493$. Lastly, there were no differences in reporting ADLs between males and females in the dementia group, $t(108) = -0.934$, $p = 0.352$ as well as no difference in reporting IADLs between males and females in the dementia group $t(108) = -1.240$, $p = 0.218$.

Table 1

Demographics of Participants

Variables	Total Subjects *n* = 207	MCI *n* = 97	Dementia *n* = 110
Biological Sex [*n* (%)]			
Female	105 (50.7)	48 (49.4)	57 (51.9)
Male	102 (49.3)	49 (50.5)	53 (48.2)
Race [*n* (%)]			
White	195 (94.2)	91 (93.8)	104 (94.5)
Black/African American	7 (3.4)	4 (4.1)	3 (2.7)
Asian	1 (0.5)	0 (0)	1 (0.9)
Other	4 (1.9)	2 (2.1)	2 (1.8)
Ethnicity [*n* (%)]			
Non-Hispanic/Latino	200 (96.6)	94 (96.9)	106 (96.4)
Hispanic/Latino	7 (3.4)	3 (3.1)	4 (3.6)
Education in years [*n* (%)]			
8 or below	5 (2.4)	3 (3.1)	2 (1.8)
9	3 (1.4)	1 (1.0)	2 (1.8)
10	7 (3.4)	3 (3.1)	4 (3.6)
11	4 (1.9)	1 (1.0)	3 (2.7)
12	90 (43.5)	39 (40.2)	51 (46.4)
13	4 (1.9)	4 (4.1)	0 (0)
14	17 (8.2)	9 (9.3)	8 (7.3)
15	2 (1.0)	1 (1.0)	1 (0.9)

Variables	Total Subjects *n* = 207	MCI *n* = 97	Dementia *n* = 110
16	42 (20.3)	21 (21.6)	21 (19.1)
18	23 (11.1)	9 (9.3)	14 (12.7)
20	4 (1.9)	4 (4.1)	0 (0)
21	6 (2.9)	2 (2.1)	4 (3.6)
Age [years (SD)]	75.60 (7.60)	74.21 (7.51)	76.84 (7.50)
Education [years (SD)]	13.88 (2.91)	13.97 (2.92)	13.80 (2.90)

CHAPTER 5: INTERPRETATION AND IMPLICATIONS

There has been a wide range of previous research studying various cognitive domains and their relationship with functional outcomes, with more support of some cognitive domains over others and less research specifically on their predictive abilities. The current study further added to that research regarding the implications of specific and commonly used neuropsychological measures in predicting functional abilities across the dementia and MCI populations as well as what might not be so useful in terms of ADL/IADL measures. Referral questions are moving from diagnostic questions to questions regarding the patients cognitive functioning implicated in everyday activities (Chaytor & Schmitter-Edgecombe, 2003). By knowing this information, neuropsychologists can then make appropriate recommendations about the patient in hopes to increase their overall quality of life and prolong cognition. These recommendations may have significant consequences (e.g., recommending to cease driving), which highlight the importance of showing ecological validity of such measures.

As the number of aging adults continue to rise in the United States, the prevalence of dementia will also continue to rise and will be tripled by 2050 (Weiner & Lipton, 2009). Furthermore, individuals diagnosed with dementia over a 10-year time period were found to be at significantly higher risk for any type of hospitalizations, had a longer length of stay at the hospital, and had higher Medicare expenses in comparison to propensity-matched controls (Zhu et al., 2014). Those with more cognitive decline and functional dependence regardless of diagnosis per neuropsychological evaluation had a higher risk of these outcomes. Identifying the relationship between neuropsychological measures of various cognitive domains and functioning can provide information for preventative strategies and how to best support those with such disabilities. Knowing this information will also help implement ways to lower hospitalization rates and other substantial healthcare costs.

Literature has provided evidence for the claim that ADLs are more preserved during the presence of any decline in cognition and are seen as more effected in the moderate to severe stages of dementia (Ashendorf et al., 2018; Cornelis et al., 2018). Interestingly, the current study did not reveal any neuropsychological measures to be sensitive enough to predict functional outcomes in the dementia population. Given the previously stated research, it would have been expected that at least some of the neuropsychological measures would predict a degree of IADL functioning in the dementia population, but no association was found for either ADLs or IADLs in this group. Limitations of the sample such as the lack of the degree of help needed in a dementia population may be the cause of these findings and are further highlighted in the subsequent sections. Nonetheless, one of the interpretations of this finding is that in a relatively mildly impaired population, the constructs of neurocognitive functioning and activities of daily living are sufficiently different from each other to warrant a thorough examination of both with valid and reliable measures.

Additionally, analyses could not be performed for participants with a MCI diagnosis to look at their ADL functioning. This was due to 88% of the sample endorsing that they required “no help needed” for such activities. This would be expected given the MCI diagnosis requiring that the cognitive deficits do not interfere with daily functioning whereas the dementia diagnosis does require deficits to functioning. Intriguingly, the only model that showed neuropsychological measures to be predictive of functioning was within the MCI sample for IADL functioning. The TMT-B and MMSE were the two neuropsychological measures that were sensitive enough to predict functioning in this population. IADLs are thought of to be more sensitive to any type of cognitive decline and this likely can explain this current result which aligns with hypothesis one (Cornelis et al., 2018).

Although the MMSE was found to be predictive of IADLs in the MCI population, Lee and colleagues (2019) suggested that a similar measure of orientation or global cognitive status, the MoCA, might not be as accurate in prediction of functional decline in those who are below the age of 81.2. They suggested this is the age at which functional decline is clinically observed and can be suggested as a cutoff when considering deterioration of functional status. Conversely, the average age of the MCI sample in this study was 74.21, thus below that cutoff score but still was able to show predictive abilities in functioning.

EF such as that measured with TMT-B plays an important role in terms of progression of functional instability (Cahn-Weiner et al., 2007). EF is used in everyday tasks and has a role in regulating and controlling many other important cognitive functions. If EF begins to fail, it makes sense that even when other cognitive functions are intact, functional disability is still seen. Concerning the normal aging process, EF is likely more sensitive to every day functional changes (Farias et al., 2009). Another explanation could be that ED results in more cortical involvement. It is somewhat like a domino effect in that when EF fails, other cortical controlled functions fail and ultimately, because of much failure to cognitive domains, functional impairment is seen.

Longitudinally, baseline EF was associated with a more rapid decline of functional status (Cahn-Weiner et al., 2007), so the group of participants in this MCI category may be more susceptible to decline in their functioning. EF, specifically TMT-B was a substantial frontrunner in its ability to predict functional decline in the majority of the literature on this topic.

Lastly, hypothesis 5 stated that depression, as measured by the PHQ-9, would be a predictor in functional impairment in those with MCI but not dementia**.** This hypothesis was rejected. This hypothesis was based off a study conducted by Rog and colleagues (2014) where they found that one of the variables that uniquely contributed to everyday function was depression in a sample consisting of a continuum of normal aging to MCI and then dementia. Depression was found to be independently contributing to everyday function in the MCI population as well as those in the healthy aging group, but depression was much less of a contributor in the dementia group. The theory behind this was that neuropsychiatric symptoms such as depression were more strongly associated with everyday functioning in healthy aging and MCI groups whereas cognitive impairment is more strongly associated with everyday functioning in dementia (Rog et al., 2014).

Research has been mixed with some others finding depression to be unassociated with IADLs in groups diagnosed with MCI, AD, or non-AD (Burton and colleagues, 2018); with others finding that up to 40% of those with AD had depression. This was particularly more prevalent at the beginning and middle stages of the disease (Alzheimer's Association, 2022). Potential reasonings behind our findings that depression was not predictive of IADLs or ADLs in the MCI or dementia population could be due to the sample potentially being in the early stages of the dementia process. To further backup this hypothesis, the majority of the dementia sample did not require a substantial amount of help needed in self-reported IADLs/ADLs, promoting the assumption that this sample was early on in the neurodegenerative process because at this time not as much help is needed in comparison to later stages. Additionally, this study did not find statistically significant differences in PHQ-9 reports across the two samples.

Limitations

It is important to note that clinically, the evaluation of a person's ability to perform various daily activities should not be considered solely through the assessment of a single cognitive domain. The purpose of this study was to see if one neuropsychological measure over the others weighs more heavily on functional outcome and consequently can provide more information on the individual's functional capacity and reduce the amount of time and measures in the neuropsychological battery. One limitation includes the inability to add additional measures due to using archival data. The role of compensatory strategies, motivation, family dynamics, the role of the testing environment, demographic variables, and behavioral observations, to name a few, are also other extraneous variables that may affect current results. Furthermore, the use of acetylcholinesterase inhibitors as medications was not considered an exclusionary criterion in this study and could have an influence on the findings.

Sample

Several limitations need to be addressed for this study pertaining to the sample. The sample primarily consists of white, older adults (94.2%) and non-Latino/Hispanic (96.6%), thus, likely may not generalize to other races or ethnicities. This study did not control for demographic factors such as socioeconomic status due to not having that information upon data extraction. The dementia population in the study was not separated into specific types of dementia, but rather consisted of many different types (e.g., Alzheimer's, vascular, mixed, etc.). Parsing out the group further into specific types of dementia may have shown more relationships for one group versus the others. The same is true for the MCI group, as it was not separated into amnesic versus non-amnesic type of MCI. Additionally, other comorbid disorders, such as cancer, chronic obstructive pulmonary disease or chronic kidney disease, were not excluded in this sample, and the findings could have been influenced.

Education

Archival data was used for this study and some participants were noted to have less than an eighth-grade education. No specifics could be obtained as to what was the last grade they finished. These participants were input into the data collection as having an 8^{th} grade education and might not be truly reflective of their educational status since some likely had less than that. Furthermore, the average years of education of the sample was 13.88. This indicates that on average, the sample had higher than a 12^{th} grade education and therefore may not be generalizable to the general population. When looking at the MCI and dementia samples individually, they also had higher than 12 years of education on average. Specifically, 47.3% of the total sample had a 12^{th} grade or higher level of education. Importantly, Farias and colleagues (2003) found education to be correlated with functional measurement scales and thus premorbid educational levels should be considered when assessing functional capacity in any population. Because this was a better-educated group, it may not generalize to the general population and the concept of cognitive reserve may have played a role in the results. Additionally, Farias and colleagues (2003) found education to have a moderate correlation with EF (r = .44). Because this sample was found to have higher levels of education, the results from hypothesis one may have been affected by this relationship and the findings influenced.

Statistical Analysis

Another limitation to this study involves the use of non-parametric statistics or *distribution free tests*. The use of non-parametric statistics had to be used due to the non-normally distributed data. Non-parametric tests are considered less powerful in comparison to parametric tests in that parametric tests are more likely to detect a statistically significant difference if one truly exists (Rana et al., 2016). In other words, non-parametric tests have a lower probability of showing that two variables are related when they indeed are (Abdulazeez, 2014). Additionally, non-parametric tests are often thought of as being less easy to interpret because they often use rankings of the values in the data instead of the actual data.

Executive Functioning (EF)

A major issue of using the term EF is the ambiguity and breadth of the definition as well as the differences in definitions across users. The measures that were used in this study do not encompass the full nature of the EF domain, no neuropsychological measures do; specifically, this study will only assess a piece of EF being set-shifting/alternating attention and verbal fluency. Therefore, this study will not measure EF in a comprehensive sense, although that is very difficult due to the many cognitive domains and tasks that fall under EF and the infiltration of EF into many other tasks. For example, EF can entail working memory, inhibition, organization, and adaptability

(Aretouli & Brandt, 2010; Cornelis et al., 2018). Someone with poor working memory may not be able to follow a multi-step task demand and therefore perform poorly. This may artificially be viewed as difficulty with whatever the task is supposed to be measuring but rather it is reflective of the individual's poor working memory.

Additionally, there is a lack of consensus for theoretical and empirical support on what exactly EF measures. For example, the Wisconsin Card Sorting test is described differently by many neuropsychologists, some noting it to be a task of inhibition, mental set shifting, or categorization. Miyake and colleagues (2000) discovered that executive functions can be distinct from one another but they also share a significant amount of overlap and commonality. This highlighted the importance of administering more than one EF measure in order to understand an individual's true abilities.

Furthermore, many of the EF tasks are based on the loosely defined definition of being somewhat sensitive to any damage to the frontal lobe, though other brain region damage such as those to the thalamus or limbic system can also yield ED (Miyake et al., 2000). Notably, TMT-B has been found to be a significant predictor, if not the most significant of functional dependence in several studies (Cahn-Weiner et al., 2002; Cahn-Weiner et al., 2007; Cornelis et al., 2018; McAlister et al., 2016; Monaci & Morris, 2011; Royall et al., 2007). The use of other measures of EF may produce different results than the current study.

ADL/IADL Measures

Measures of ADL/IADL performance in the current study included self-report measures filled out either by the patient or an informant. When the patient fills out the measure himself or herself, there is a risk of under or over reporting due to the possibility of being poor historians for various reasons (i.e., poor insight, unable to recall, etc.; Chong et al., 1995; Law, 1993). Additionally, when measures are filled out by an informant who is not living with the participant and therefore is unsure of their true daily functioning, this also can result in poor or inconsistent results. According to Goldstein & McCue (1995), informant reports had a stronger relationship with test scores of cognitive functioning in comparison to self-report ratings in a population of head-injured adults. Another limitation is the influence of biases on self-report measures, affecting both when a patient or an informant completes the measure. The current results of this study may have been impacted by self-report measures in that the researcher was unable to identify who filled out each participants ADL/IADL questionnaire.

Furthermore, these findings may be impacted by an unstandardized measure of ADL/IADL functioning. Firstly, there are many more ADL instruments but far less measures to assess IADLs (Law, 1993). The measure itself used in this study likely was not sensitive enough to predict differences in the neuropsychological measures that were used in this study. The majority of the dementia population (63.6%) reported to having “no help needed” across ADLs, which is relatively uncommon for this population. While there was more of a variety of functional abilities for IADLs in this population, the majority was still on the minimal side of needing assistance. It is suggested that the Lawton and Brody (1969) measure may not be sensitive enough to detect changes in a dementia sample although it is commonly used. Monaci and Morris (2011) postulated that in their study, the Lawton & Brody IADL measure (1969), which was the measure this study was based off of, was not sensitive enough to identify changes in functioning at an 18 and 24 month follow up. To complicate the relationship further, IADL scores are more significantly correlated with neuropsychological measures in comparison to ADLs, but the association is weakened as the disease progresses (Monaci & Morris, 2011). Thus, operationalizing ADLs/IADLs differently may have yielded altered results. Another possible explanation is that those who are more severely impaired in terms of their abilities to perform IADLs/ADLs will not present for evaluation or those with cognitive changes to a milder extent are more in support of being assessed and thus will show to be assessed for a neuropsychological evaluation.

Assessing one's functional capacity may best be measured by performance-based measures alone or with the addition of a self-report measure. Farias and colleagues (2003) revealed that 50% of the variance in cognitive measures were contributed by use of a performance-based measure of functioning versus 25% in a self-report measure, arguing for the use of performance-based measures. On the contrary, the use of performance-based ADL/IADL questionnaires such as the Texas Functional Living Scale (TFLS; Cullum et al., 2009) are often more time consuming, can be less generalizable due to observations being in a controlled setting, and are overall less practical in clinical settings (Cahn-Weiner et al., 2007). To support the use of solely using either a performance-based measure or a self-report measure, McAlister and colleagues (2016) investigated through a meta-analysis that the relationship of cognitive predictors and functional outcome did not differ when using a performance based or self-report measure of functional outcome in a population consisting of individuals diagnosed with MCI. These results may differ for a dementia population. It is important to make the distinction that a self-report or subjective measure of functioning is not ideal for the use of research and to obtain a diagnosis of dementia which is highlighted through the results and limitations of this study. Utilizing objective neuropsychological measures to predict subjective, self-reported functional abilities did not yield expected results and it further complicates the relationship. Although these measures are flawed, they are still commonly used and are what neuropsychologists have to work with in the meantime until a more psychometrically sound instrument is created.

The Role of Cognitive Reserve (CR)

CR is a term that explains why individuals with a higher level of education, higher IQ, and/or higher occupational attainment have less of a risk of developing a neurodegenerative disorder (Meng & D'Arcy, 2012). Specifically, higher educational attainment has shown to reduce both the prevalence and incidence of AD, vascular dementia, and unspecified dementia. CR can be seen as a moderator between pathology and clinical manifestations. It can describe how differently the clinical manifestations of a neurodegenerative disorder can present depending on these variables (Meng & D'Arcy, 2012; Stern, 2012). The same amount of brain damage will differ in its presentation for different people because of this concept (Stern, 2012). Both mental and physical stimulation is important early on as they both are thought to increase CR, which plays a role as a protective factor against dementia but also delays the onset (Dekhtyar et al., 2015; Meng & D'Arcy, 2012. According to Meng and D'Arcy (2012), the hypothesis of CR indicates that higher education:

1. Reduces the prevalence of dementia
2. Reduces the incidence of dementia
3. Has no effect on the age of onset of dementia
4. Results in an accelerated cognitive decline – as a result of a threshold effect

5. Has no effect on the age of death

6. Leads to a higher level of clinical performance on initial assessment

7. Shows greater brain pathology in postmortem and imaging studies among those with dementia (p. 2)

The concept of CR can be a complex concept to grasp especially when thinking about the various variables that affect it. Dekhtyar and colleagues (2015) conducted a study consisting of 7,574 individuals across a 21-year period and found that those who went on to higher education had reduction in their dementia risk. Similarly, Stern (2012) found that individuals with less than eight years of education were 2.2 times more vulnerable to developing a dementia in comparison to those with higher education. Interestingly, when controlled for the participants occupational complexity, this relationship no longer existed, suggesting that higher levels of education are only a protective factor if it is then utilized in complex jobs, similar to the “use it or lose it” hypothesis. Again, in Stern’s (2012) study, he found that those with lower occupational attainment had 2.25 times more of a risk of developing dementia. Another finding from this study revealed that elementary school grades but not high school was found to be a protective factor for developing dementia. Perhaps those with lower elementary school grades likely have neuronal networks that are less efficient and flexible, which in return makes them more vulnerable in developing a neurodegenerative disorder.

As previously stated, the majority of this sample had higher than a 12th grade education and thus can be seen as having CR. CR, as defined in this study as level of education, likely played some sort of role in the findings of this study. Approximately 60% of those in the MCI group self-reported that they need no help at all in performed

IADLs. When looking at the group needing no help and comparing it to the rest of the sample that did require some type of assistance in performing IADLs, the group with no issues had slightly more years of education than the other group. Thus, higher level of education can be viewed as a protective factor in this study.

Strengths

Some strengths of this study include the incorporation of measures that are outside the typical neuropsychological evaluation, such as the PHQ-9 to screen for depression. It is important to consider other non-neurological variables when an individual is having difficulty performing everyday activities like ADLs and IADLs. The addition of the PHQ-9 makes it possible to assess for the effect of a common disorder, such as depression, as well as how it might affect an individual's functional ability, in addition to cognitive difficulties. Additionally, this study examined both ADLs and IADLs where most other studies in the literature only investigate one or the other, not in conjunction with one another. By looking at both ADLs and IADLs, a more holistic picture of how the individual is truly performing in their daily lives, regardless of difficulty, is portrayed. Another strength includes the integration of multiple commonly used neuropsychological measures that address several cognitive domains (i.e., processing speed, executive functioning, memory, etc.) rather than just one or two. Looking at a diverse range of cognitive domains allowed for more investigation into the many variables that can tap into functional decline.

Future Directions

The use of neuropsychological measures can only provide so much insight into an individual's functional abilities. Hence, the importance to keep into consideration the use of other psychological measures (e.g., personality measures, achievement tests, etc.) and clinical judgement that should be incorporated into neuropsychological evaluations and noting their impact on daily skills (Chaytor & Schmitter-Edgecombe, 2003). Because there are multitudes of factors that can affect an individual's functional abilities from a social, psychiatric, and environmental perspective, such variables should also be incorporated into case conceptualization and future research to better understand the role that noncognitive factors play in functioning (McAlister et al., 2016). For example, behavioral disturbance such as changes in apathy and disinhibition can commonly be seen in people who have dementia or MCI. Future research should also incorporate measures of behavior changes due to the possibility of these variable also impacting one's ability to perform their IADLs. The use of such behavior disturbance variables in conjunction with EF or other cognitive variables may add more to the predictive functional ability of such measures (Cahn-Weiner et al., 2002).

There are several other suggestions for future research that surfaced from this study. First, controlling for intelligence as measured by an intelligence quotient (IQ) may be worthwhile due to premorbid abilities having the capability to affect various test scores. Future research should control for these factors to minimize their effect on the assessment of functional abilities. Concerning functional abilities, the use of more standardized assessments such as the Lawton & Brody (1969) is recommended. To add more specificity to the functional abilities research, it is suggested that researchers also look at individual ADLs/IADLs (e.g., managing finances, bathing, etc.) to see if there are any type of relationships with specific task and cognitive measures. As previously mentioned, some demographic variables and severity of dementia were not controlled for in the current study and should be incorporated into future research. Separating the specific types of dementia and MCI diagnoses would also be interesting to research to see if the neuropsychological tests affect these populations differently in terms of predictive abilities. The use of longitudinal studies would be also beneficial when investigating these variables to control for various extraneous variables and give more confidence in the findings over time. Lastly, instead of using a predictive model of ADL/IADL functioning like this study used, future research should look at the differences of test performance between MCI and dementia and their impact on functioning, questioning if the variables are strong enough to differentiate between the two populations. Additionally, further research into methodologies to obtain more accurate and objective estimates of activities of daily living (e.g., benefit of getting input from multiple sources versus just one) is warranted.

Conclusion

The role of neuropsychologist may be to help in the assessment of an individual's ability to function in their everyday lives such as performing various ADLs (e.g., dressing and grooming) and IADLs (e.g., managing finances and medications). This can have important ramifications for those with suspected dementia or other various neurological issues such as assessment for driving, ability to manage finances, suitability for in-home assistance, or qualification for disability. The data from neuropsychological tests can assist neuropsychologists' in making recommendations for such tasks and evaluate an individual's ability to perform everyday activities. Because these recommendations can have immense effects on an individual's life, it is important to assess what neuropsychological measures have ecological validity. Ecological validity can be defined as the extent to which neuropsychological tests relate to real world performance (Chaytor & Schmitter-Edgecombe, 2003). The literature is replete with a heterogeneity of results when it comes to ascertaining whether neuropsychological tests are ecologically valid, highlighting the need for further research to better understand the real-world value of neuropsychological tests and what particular cognitive domains are related to specific functional tasks. The vast assortment of neuropsychological measures in general, but also just within one cognitive domain, makes it hard to draw conclusions on their predictive abilities. IADL/ADL measures itself are flawed and come with their own complications mostly surrounding standardization and subjective reports. Likewise, the complexity of addressing the ecological validity of neuropsychological testing is further exacerbated by considering the different types of populations and their varying degrees of severity of cognitive difficulties.

Additionally, this study further highlighted the value or lack thereof of such neuropsychological measures when used in thorough neuropsychological evaluations and correlating with daily functioning in a relatively unimpaired or mildly impaired population. The question is whether or not cognitive abilities are as strongly associated with functioning as we think or the measures being used are insufficient in showing their relationship with such populations. This does not impede on the valuable use of neuropsychological services because of their diverse purposes aside from predicting functioning. Understanding the differences in predictive abilities of such measures may refine our understanding of the utility of neuropsychological assessment and its relationship to disability, particularly for a population that already has limited patience for such long, in-depth evaluations. Though they have many different various clinical uses, this study’s findings highlight the limitations of various neuropsychological and their ecological validity with functional abilities measures. Nonetheless, the results would argue that having the TMT-B and some type of mental status exam incorporated into your battery is essential because of their independent ability to predict IADLs. Most importantly, when highly predictive measures of functional disability are observed below baseline expectations, neuropsychologists will be better able to implement early intervention techniques to further preserve cognition, as well as assess for the most appropriate environmental supports such as residential placements.

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Appendix

Functional Status Table

ADLs	
Bathing:	
Dressing:	
Toileting/bathroom:	
Grooming:	
Walking:	
IADLs	
Using the phone:	
Shopping:	
Cooking:	
Housekeeping:	
Managing medications:	
Managing Finances:	

Table A1. Table of ADLs/IADLs that the individual must report on. Participants either responded with “No help needed,” “Needs assistance,” or “Unable to do” for all ADLs and IADLs.