Assessing Right Parietal Lobe Functions in Alzheimer's Disease Using the Mass Overlapping Figures Test

by

Charles Cullen Hicks

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Arts in Psychology

Middle Tennessee State University

Thesis Committee:

Dr. Paul Foster, Chair

Dr. Kim Ujcich Ward

Dr. James Loveless

ABSTRACT

The purpose of this study was to assess performance on the Mass Overlapping Figures Test (MOFT) between patients with Alzheimer's disease (AD) and controls. Thirty-nine control individuals were given this newly developed neuropsychological test, in addition other standardized tests. Thirty-nine AD patients were included as retrospective data from previous neuropsychological assessments. Controls were predicted to perform better on the MOFT than the AD group and that the AD group scores on the MOFT were predicted to significantly correlate to their mental status. The MOFT was predicted to demonstrate convergent validity with other tests of visuospatial and right parietal functioning. There was a significant difference in MOFT performance between controls and the AD group, and the MOFT scores had a positive significant correlation to the MMSE scores in the AD group. Convergent validity for the MOFT with the RBANS Line Orientation subtest and the Necker Cube Copy test was not significant.

Table of Contents

CHAPTER I: INTRODUCTION

Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia. The disease is known for gradual memory deficits and insidious onset, but also involves other cognitive processes, particularly visuospatial functioning (Braak & Braak, 1991; Jacobs et al., 2012). Alzheimer's Disease is theorized to develop from extracellular amyloid plaques and intracellular neurofibrillary tangles, which result in neuron damage, cortical atrophy, and cognitive deficits (Jacobs et al., 2012). The pathological process of AD progresses in a rather typical, orderly fashion. Pathologically, AD begins damaging the brain in the limbic areas of the cerebral cortex and sequentially spreads to the hippocampus, the neocortex, and the subcortical nuclei (Braak & Braak 1995). Amyloid deposits and neurofibrillary tangles accumulate before clinical symptoms occur (Braak & Braak, 1991). Amyloid deposits first begin in the basal regions of the brain and spread ventrally as AD progresses, while sparing the primary sensory and primary motor areas (Braak & Braak, 1991). The neurofibrillary tangles begin to appear before clinical symptoms and correspond to the transentorhinal stages, which represent a preclinical phase of AD (Braak & Braak, 1991). The limbic stages correspond to early or mild AD with the entorhinal region, including the hippocampus, being affected (Braak & Braak, 1991). Finally, the isocortical stages correspond to fully developed AD and affect most of the brain with the exception of the primary sensory areas (Braak & Braak, 1991).

There is some asymmetry in AD with the left hemisphere typically experiencing more atrophy and quicker atrophy than the right hemisphere (Thompson et al., 1998; Thomspon et al., 2003). It appears, however, that there are two forms of AD, in which

one variant exhibits greater left hemisphere grey matter atrophy and verbal deficits and the other variant exhibits greater right hemisphere grey matter atrophy and visuospatial deficits (Foster et al., 2013). The grey matter atrophy that occurs in AD also corresponds to the cognitive deficits seen in AD, with tests of left hemispheric functioning typically seeing more cognitive decline than tests of right cognitive functioning, while still not sparing the right hemisphere (Braak & Braak, 1995; Thompson et al., 1998). This grey matter atrophy also matches neurofibrillary tangle distribution observed postmortem in patients with severe dementia (Thompson et al., 2003).

Neuropsychologically, AD is primarily characterized by episodic memory impairment, but as the disease progresses there are also deficits in language, semantics, attention, executive functioning, and visuospatial functioning (Bondi et al., 2018; Weintraub et al., 2012). While AD cannot be definitively confirmed until post mortem, it can be detected through neuropsychological evaluations to provide a diagnosis while the patient is still alive (Thulborn et al., 2000). Visuospatial processing problems are an underreported symptom in early AD that is detectable through neuropsychological testing (Salimi et al., 2018). These visuospatial deficits may be present as early as five years before other AD symptoms arise (Salimi et al., 2018). When compared with a control group, AD patients need more visual information in order to identify an object and patients with moderate-AD perform worse on object identification than patients with mild-AD (Viggiano et al., 2007). Visuospatial skills involve recognition, location, construction and orientation in space, and rely on other cognitive skills such as attention, memory, and executive functioning (Salimi et al., 2018; Quental et al., 2013). Neuropsychological testing that includes extensive visuospatial tasks could be a helpful

assessment in better understanding parietal lobe functioning as well as gaining diagnostic information for Alzheimer's disease (Hänggi et al., 2011).

Parietal Lobes

The parietal lobes function as integration sites for the brain, making them important for a wide variety of cognitive abilities, such as attention, working memory, and visual selection (Bardi et al., 2013; Culham & Kanwisher, 2001). The parietal lobes are integral in spatial information processing, selective attention, spatial working memory, mental rotation, and mental imagery, and manipulation of visual images (Jacobs et al., 2012). Kravitz et al. suggests that the parietal lobe serves as connection of neural pathways that project to the prefrontal and premotor areas to support spatial perception, spatial working memory, and visually directed action (2011).

Multiple areas of the parietal lobes are affected by AD. The inferior parietal lobe is already affected in terms of reduced grey matter volume in preclinical AD patients (Jacobs et al., 2011). Jacobs et al. found that grey matter atrophy in the parietal lobe was worse in their participants that later went on to develop AD (2011). Atrophy of the precuneus, due to amyloid plaques, is also present in early stages of AD and spreads to the medial and lateral posterior areas of the parietal lobes as AD advances (Buckner et al., 2005). Retrieval is associated with decreased precuneus activation and this region appears to be one of the first neural areas to see atrophy in AD (Jacobs et al., 2012). The precuneus, posterior cingulate, and retrosplenial cortex are particularly vulnerable to atrophy due to amyloid plaques (Buckner et al., 2005). The posterior cingulate and precuneus area are likely the most influential areas of parietal lobe atrophy in early AD (Jacobs et al., 2012). Researchers found increased amyloid burden and decreased glucose

metabolism in the parietal lobes in relatively younger AD patients, which correlated with decreased visuospatial functioning, executive functions, and attention (Fukimori et al., 2000; Ossenkoppele et al., 2012). Visuospatial processing relies on the parietal structures that experience damage in early AD (Salimi et al., 2018). Visuospatial processing continues to decline as can be seen in poor performances of naming, object recognition, and object orientation in mild to moderate Alzheimer's patients (Caterini et al., 2002).

Patients with AD exhibit hypometabolism and an increased number of neurofibrillary tangles in the parietal lobes (Meguro et al., 2001). Hänggi et al. found that parietal lobe volume differed among a healthy control group, a group of patients with mild cognitive impairment, and a group of patients with AD (2011). The rate of atrophy progresses much more rapidly in the hippocampus than in the parietal lobes in AD patients (Firth et al., 2019). Individuals with posterior cortical atrophy performed worse on tasks of numeracy, visuoperception, and visuospatial processing, while AD patients performed worse in verbal episodic memory in a test of comparing a group of individual with posterior cortical atrophy and a group with typical AD (Firth et al., 2019).

Right Parietal Lobe

The right hemisphere is known for specializing in visuospatial attention, processing, and judgment (Hougaard et al., 2015; Jonas et al., 2014). The right parietal lobe is more dominant for more salient information and global processing, where the left is more dominant for less salient information and focal processing (Bardi et al., 2013). The right parietal lobe is also more involved in shifting attention spatially, where the left is dominant for non-spatial attention (Orlandi & Proverbio, 2019). The left hemisphere was more involved for recognizing and attending to single objects as opposed to an array

of objects in a task of object-based attention using three-dimensional figures (Orlandi & Proverbio, 2019).

Thompson et al. did a three-year longitudinal MRI study with AD subjects and healthy subjects and found that there was a significant grey matter deficit in the bilateral temporal and parietal cortices of AD subjects, with quicker and more severe atrophy occurring in the left hemisphere (2003). Thulborn et al. found that individuals with probable AD showed less right parietal activation than left parietal activation as well as increased prefrontal activation in comparison with a control group who showed strong right parietal activation and low prefrontal activation when performing visuospatial tasks (Thulborn et al., 2000). Activation increased in the prefrontal area in the probable AD group as the task became more difficult, demonstrating possible compensation for less right parietal activation (Thulborn et al., 2000). Asymmetry occurs in control groups for various reasons, but the asymmetry is more exaggerated in patients with AD (Thompson et al., 1998). The grey matter atrophy also occurs at a faster rate on the left than on the right in AD patients that is not seen in healthy control groups (Thompson et al., 2003). There is more pronounced grey matter atrophy in AD patients around the Sylvian fissure around the temporo-parietal cortex with more atrophy in the left hemisphere than the right (Thompson et al., 1998; Thomspon et al., 2003).

The Judgment of Line Orientation (JLO) assessment is a task of spatial perception and orientation items that utilizes the right parietal lobe (Della Sala, et al., 1995). Individuals with right parietal lesions experience difficulty in tasks involving visual perception tasks such as Benton's Judgment of Line Orientation (Tranel et al., 2010). Individuals with right parietal lesions perform worse on tasks of line orientation than

those with left parietal lesions, demonstrating specificity of line orientation tasks to right parietal functioning (Tranel et al., 2010). Line orientation tasks specifically target the posterior areas of the parietal lobe (Tranel et al., 2010). Tranel et al. found that low scores on the JLO were correlated with right parietal and right occipitoparietal lesions (2010). An abbreviated version of the JLO is available through the Line Orientation subtest of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

The Necker cube copy task is an assessment that utilizes the right parietal lobe, in which the participant copies an image of an ambiguous, bistable figure to the best of their ability (Britz et al., 2009; Salatine et al., 2019). Damage to the right inferior parietal cortex is known to lead to difficulties in copying of objects such as the Necker cube (Inui et al., 2000). The right posterior parietal cortex is important for orienting and spatial attention, particularly for estimating line lengths, necessary for the Necker cube copy task (Salatino et al., 2019). The right inferior and superior parietal areas are important for visual perception, including bistable shifts of spatial attention, which occurs in the Necker cube copy task (Britz et al., 2009; Sengpiel, 2000).

Dorsal and Ventral Pathways

The ventral and dorsal pathway support the brain's visuospatial processing (Jacobs et al., 2015). The ventral stream supports visuospatial processing by recognizing object shape and object identification, and is largely in the lateral temporal and occipitotemporal areas (Jacobs et al., 2015; Salimi et al., 2018). Alzheimer's patients see decreased activation in the dorsal visual stream (Thulborn et al., 2000). The dorsal stream helps visuospatial processing through spatial working memory, stimulus recognition, spatial orientation and spatial rotation (Jacobs et al., 2015; Salimi et al., 2018). The dorsal

stream consists of three main pathways, which span from the prefrontal region to the parietal lobe, the premotor region to the parietal lobe, and the medial temporal lobe to the parietal lobe (Jacobs et al., 2015). Early AD patients demonstrated increased activation in the dorsal and ventral pathways (Jacobs et al., 2015). This increased activation also occurs in the inferior parietal lobe and the precuneus as a compensation mechanism while engaging in object recognition tasks (Jacobs et al., 2015).

Poppelreuter-Ghent and Figures Tests

Poppelreuter-Ghent tests are visuoperceptual tasks that require the participant to distinguish objects or figures that are presented as overlapping ling drawings, and are sensitive to right parietal functioning (Ghent, 1956). The tests consist of two-dimensional line drawings, often recognizable objects, which are intertwined or stacked on top of each other to make visual recognition of each drawing more difficult (Della Sala et al., 1995). Poppelreuter-Ghent tests typically use a relatively small number of objects and have no time limit, which creates potential ceiling effects. The potential ceiling effects do not permit much variability in the data, making it not appropriate to use in a healthy population for assessing visuospatial functioning. These types of tests are often used to assess visual agnosia and visuospatial deficits (Alegret et al., 2009).

Poppelreuter-Ghent in Healthy Individuals

Della Sala et al. used a Poppelreuter-Ghent Test to assess 237 normal control participants to find if there were any patterns regarding age, sex, and education. The participants were asked to name the figures and then point to a multiple choice display with a correct object along with other semantically related distractor items (Della Sala, et al., 1995). Participants were given 19 different 11 by 38.5 centimeter charts with nine

charts of intermingled common objects, and nine charts of intermingled abstract shapes (Della Sala, et al., 1995). The participant was given 10 seconds per each line drawing on each chart, so if one chart had six figures the participant would have 60 seconds to identify all six figures (Della Sala et al., 1995). The researchers found that age and education influenced the participant's scores in healthy individuals (Della Sala, et al., 1995). Della Sala et al. also tested 12 participants with mild AD and found that the performance of these participants on the task was significantly impaired when compared to the control group (1995). The AD group also had more incorrect responses compared to omissions (Della Sala et al., 1995). Della Sala et al. also gave the AD group the JLO assessment and found a significant positive correlation between performance on the Poppelreuter-Ghent task and JLO (1995).

Poppelreuter-Ghent in Individuals with Alzheimer's Disease

There have been a variety of studies utilizing Poppelreuter-Ghent tasks to assess individuals with AD and other forms of dementia. Fujimori et al. tested 49 AD patients and 10 control participants on a visual counting task, overlapping figure identification, and a visual form discrimination task while doing a positron emission tomography (PET) measuring glucose metabolism (2000). Participants were given a sheet with shapes on it and the participants had to identify how many of the shapes were a particular color or specific shape for the visual counting task (Fujimori et al., 2000). Participants were given three trials of identifying overlapping line drawings for the overlapping figure identification (Fujimori et al., 2000). Participants had to discriminate three simple geometric figures from one another for the first trial of overlapping figure identification (Fujimori et al., 2000). Participants had to discriminate line drawings of four man-made

objects for the second trial of overlapping figure identification (Fujimori et al., 2000). Participants had to look at five overlapping fruits and then identify which fruit they had just seen from a multiple choice list for the third trial, with eight total non-overlapping fruits on each sheet, with one fruit from the overlapping fruit drawings and seven distractor fruit drawings (Fujimori et al., 2000). The maximum score for the task was 12 and the AD patient group had a mean score of 10.8 and a standard deviation of 1.7 (Fujimori et al., 2000). Participants were given 20 sheets with geometric figures for visual form discrimination and one of figures was distorted or rotated (Fujimori et al., 2000). The AD patients scored significantly lower than the controls in every task (Fujimori et al., 2000). The score on the overlapping figure identification was significantly correlated with metabolic rate in the right middle temporal gyrus, the right inferior parietal lobes, and the right lateral occipital lobe (Fujimori et al., 2000). This task further demonstrates the importance of the right hemisphere, and particularly the right parietal lobe on tasks of visuospatial functioning.

Ota et al. studied visuoperceptual skills in 35 dementia with Lewy bodies (DLB) patients, 35 Alzheimer's patients, and 30 control subjects (2015). The subjects were administered tests of pentagon copying, overlapping figures, clock drawing, cube copying, and line orientation (Ota et al., 2015). The overlapping figures task was from the Visual Perception Tests for Agnosia (VPTA), which is a standardized Japanese assessment for agnosia (Ota et al., 2015). The maximum score on the overlapping figures task was a 6 and the AD group scored a mean of 5.1 and a standard deviation of 0.9 (Ota et al., 2015). There was significant impairment on the overlapping figures task in the

DLB subjects compared to the AD and control groups, but the AD group also scored significantly lower than the control group (Ota et al., 2015).

Alegret et al. assessed 44 AD patients, 44 participants with mild cognitive impairment, and 44 control participants on visuospatial deficits using the 15-Objects Test (15-OT), which is based on the Poppelreuter Test (2009). The 15-OT contains one trial of 15 overlapping objects that are to be identified compared to the five of the Poppelreuter (Alegret et al., 2009). This more complicated task should be able to identify greater a wider range of deficit and have more sensitivity among the groups. The participants were shown the 15 overlapping figures and were asked to name all of the objects they could identify in the image (Algeret et al., 2009). The number of correctly identified objects was recorded and there was no time limit (Algeret et al., 2009). Algeret et al. found that individuals with mild cognitive impairment performed significantly better on the 15-OT than the AD group, and the MCI and AD groups both performed significantly worse than the elderly control group (2009). The results of this study show that there is the possibility that by using a more complicated task, one could distinguish the severity of an individual's visuospatial abilities and cognitive decline (Algeret et al., 2009). This more difficult task appears to have better sensitivity in detecting the severity of visuospatial and cognitive deficits compared to more simplified Poppelreuter-Ghent tasks (Algeret et al., 2009).

Summary and Purpose of Current Study

There is relatively little current neuropsychological research on right parietal lobe deficits in Alzheimer's disease, but there is evidence of visuospatial deficits in AD patients. Poppelreuter-Ghent tests assess right parietal functioning, but current versions of

this test have shortcomings due to a small amount of items to identify and no time limits to identify items. The shortcomings in these current versions of the Poppelreuter-Ghent task further demonstrate the need for a test of right parietal functioning that eliminates ceiling effects and increases sensitivity. It can be anticipated that a test of right parietal lobe functioning could be important for detecting AD due to the presence of parietal lobe atrophy in individuals that develop AD. Testing of the parietal lobes could also be helpful in staging the progression of AD due to atrophy progression corresponding to decline in cognitive functioning.

There is a problem with sensitivity in previous attempts of testing AD patients with a Poppelreuter-Ghent test. In the Della Sala et al. (1995) study, participants only had to identify four to six figures on an 11 by 38.5 centimeter chart with ceiling effect problems in the normative sample by using a multiple choice option and having 10 seconds per item to be identified. The Fujimori et al. (2000) study had ceiling effects and a sensitivity issue due to only having three to five figures to identify, in addition to the AD patient sample having a mean score of 10.8 out of a maximum 12. The Ota et al. study also has a ceiling effect with the mean AD patient score being 5.1 and a standard deviation of 0.9 out of a maximum score of 6. The Algeret et al. (2009) study with the 15-OT is better than the previous tests due to an increased number of overlapping items but there is a ceiling effect due to there being no time limit for the task and having a single trial.

The Mass Overlapping Figures Test (MOFT) was developed by Dr. Paul Foster to address these limitations, eliminate ceiling effects, and increase sensitivity. The MOFT, with its increased sensitivity and lack of ceiling effects, can be used with normal controls

and patients with dementia and Alzheimer's disease. The MOFT is more sensitive than these other Poppelreuter-Ghent tests due to it having three trials with each trial having more objects and an increased time limit. The first trial has 25 overlapping objects with a time limit of 15 seconds. The second trial has 50 overlapping figures with a time limit of 30 seconds. The third trial has 75 items to be identified with a time limit of 45 seconds. On the third trial, in addition to more objects and more time, the objects are also on a larger sheet of paper making the task more sensitive to visuospatial abilities. The MOFT also controls for a ceiling effect due to the short time limit on each task, but with a large number of objects to identify, allowing for good normative data. This normative data without ceiling effects will be helpful to demonstrate deterioration and cognitive changes in possible AD patients compared to a healthy population.

Visuospatial deficits are present and often underreported in AD patients. These visuospatial problems may also be present early in the progression of AD. The right hemisphere and the parietal lobes experience atrophy in AD, with the right hemisphere more responsible for visuospatial abilities and the parietal lobes responsible for visuospatial processing and integration of senses. Alzheimer's disease patients have also previously performed worse than control groups in Poppelreuter-Ghent assessments. As reported previously, it is anticipated that AD patients will also perform worse than control groups on the MOFT, which controls for ceiling effects and has greater sensitivity.

It is expected that the MOFT results will also correspond to the stages of Alzheimer's disease as based upon the Mini-Mental Status Examination (MMSE). The MMSE is sensitive to detecting dementia, especially in the moderate to severe stages with

92% sensitivity to detecting moderate AD (Benoit et al., 2020; Strauss et al., 2006). These scores are anticipated to have a positive correlation, which will enable the MOFT to assist in determining staging for AD. It is anticipated that AD patients will perform worse on the MOFT due to the way that AD progresses from basal regions to ventral regions as the disease progresses through stages. It is expected that there will be a positive correlation between MOFT and MMSE scores, due to the MMSE's role as a general cognitive screener and a staging tool for dementia.

We believe that the MOFT will positively correlate with other tests of right parietal lobe functions. This positive correlation will provide convergent validity to further establish the MOFT as a valid assessment of right parietal functioning. Della Sala et al. has already found significant positive correlation between their Poppelreuter-Ghent task and the JLO assessment, thus demonstrating that the MOFT would also be expected to positively correlate with the RBANS Line Orientation task. The Necker cube copy task incorporates use of the right parietal lobe and is expected to positively correlate with scores on the MOFT. The positive correlations also provide evidence of the MOFT being a right parietal and visuospatial task.

CHAPTER II: METHOD

Participants

A total of 78 individuals participated in this study with 39 (26 female and 13 male) normal control participants and 39 (29 female and 10 male) AD patients. The demographic information is summarized in Table 1. The information collected was partly retrospective data and partly prospective data. The 39 patients with AD represent the retrospective data, given that they had undergone previous neuropsychological testing at Murfreesboro Medical Clinic (MMC). Patients met the criteria for AD based on the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann, 1984). The 39 control participants were the prospective portion of our participant group. The control group included patients' family members, caregivers, and patients seen at the clinic without any degenerative diseases or cognitive deficits. Exclusionary criteria for the control group included history of significant head trauma, depression, stroke, neurological illness, or dementia. Exclusionary criteria for the Alzheimer's disease group included history of significant head trauma, stroke, and other neurological illnesses.

Materials

Demographic and Medical History Questionnaire

The control participants completed a form to indicate their age, education, gender, handedness, height, and weight. This questionnaire also assessed for the presence of any head injury or neurological illness (See Appendix A).

Mini-Mental Status Exam (MMSE)

The MMSE (Folstein et al., 1975) is a commonly used screening test to evaluate general cognitive functioning based upon testing an individual's orientation to place and time, attention, working memory, language, immediate and delayed recall, and construction. Participants were asked various questions to assess these cognitive areas. The MMSE is often used to track cognitive decline over time and assess effectiveness of interventions to aid cognitive functioning. The scores for this test range from 0 to 30, with higher scores indicating more intact cognitive and memory functioning. The MMSE has test-retest reliability estimates between 0.80 and 0.95 with two months between initial test and the subsequent retest (Strauss et al., 2006). The MMSE has good predictive validity for individuals who are likely to develop probable AD (Folstein et al., 2001).

The MMSE has moderate to high correlations with assessments such as the Dementia Rating Scale, Wechsler Memory Scale, and other tests of memory, intelligence, and attention (Folstein et al., 2001; Strauss et al., 2006). The MMSE is sensitive to detecting moderate to severe dementia, including AD (Folstein et al., 2001; Strauss et al., 2006). The dependent variable for the current study is the total score achieved.

Mass Overlapping Figures Test (MOFT)

The Mass Overlapping Figures Test, developed by Dr. Paul Foster, is a visuospatial task in which participants identify two-dimensional line figures that represent common items, which have been intermixed with other two-dimensional line figures. The MOFT is based upon the Poppelreuter-Ghent tasks, but includes many more two-dimensional line figures to be a more sensitive task of right parietal functioning and

also to test limits of a normative sample. The MOFT was developed for use with both healthy populations and with patients diagnosed with dementia.

Each line drawing image of the MOFT was presented one image at a time, in a pseudorandom order, on a PowerPoint presentation to a group of 36 undergraduate students. The students wrote down what each image was to ensure that the images could be seen and identified, as well as to form agreement on what each image represented. There was 100% agreement on the images but there were different names used for the same item. The exact responses varied but still communicated what the object was, such as in the second trial 19 students identified the image as a bird and 17 students labeled the image specifically as a dove. Eighty-six percent of responses in trial one used the same identifying label and 14 percent of responses were similar responses but not exact For example, 23 students used the same identifying label of spray can, 7 students labeled it as an aerosol can, 3 students labeled the image as spray paint, 2 students labeled it as hair spray, and 1 student labeled it as a spray bottle. Two responses in trial one were left blank. Ninety-four percent of responses in trial two used the same identifying label and 6 percent of responses were similar responses but not exact. For example, 32 students used the same identifying label of hat and 2 students labeled the drawing as a fedora. Eighty-five percent of responses in trial three used the same identifying label and 15 percent of responses were not the same but communicated the same image shown. For example, 28 students used the same identifying label of axe and 8 students labeled the image as a hatchet. Eight responses in trial three were left blank.

The MOFT consists of a training trial and three subsequent trials. The participant is instructed to name as many of the figures as they can in each trial as quickly as they

can, and if they cannot think of the name for an object they should describe the figure or object in few words. The training trial consists of showing the participant three independent two-dimensional figures: a cat, a leaf, and a sock. The participants are then presented the same three figures, but the figures are intermixed (See Appendix B). The first trial of the MOFT has 25 overlapping line figures on an 8.5 by 11 inch page and the participant has 15 seconds to identify as many figures as possible. The second trial is also on an 8.5 by 11 inch page but has 50 overlapping figures and the participant has 30 seconds to identify as many figures as possible. The third trial of the MOFT has 75 overlapping figures on an 11 by 17 inch page and the participant has 45 seconds to name as many figures as possible. None line drawing is presented more than once. Each trial is scored separately and the score is the total number of correct items identified within the time restraints. The total score for the MOFT is the total number of items correctly identified across all three trials. The dependent variable is the total number of correct figures identified from the intermingled displays.

Line Orientation

The Line Orientation subtest from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is a visuospatial task (Randolph, 1998). The participant is presented a pattern with 13 lines radiating from a central point along with two lines below that correspond to the directions of two of the 13 lines. The individual must identify which two lines of the thirteen that the two lower lines match directionally. There are 10 items of this task with a maximum score of 20. The RBANS has split-half reliability coefficients above 0.80 but the manual does not include reliability coefficients for individual subtests (Strauss et al., 2006). The RBANS total score correlates strongly

with the Full Scale Intelligence Quotient of the WAIS-R short form (Strauss et al., 2006). The Line Orientation subtest is a part of the Visuospatial/Constructional Index of the RBANS, which has an average reliability coefficient of 0.80 (Randolph, 1998). The dependent variable in the current study is the total number of correct lines that match the display lines.

Necker Cube Copy

The Necker Cube Copy task is a visuospatial paper and pencil test where an individual is instructed to copy a Necker Cube. The Necker Cube is a two-dimensional wireframe line drawing of a three-dimensional cube with ambiguity as to which side is the front and which side is the back. There is no time limit or time recording. The normative data and scoring system that will be used for this study was developed for a healthy elderly population (Mathew et al., 2018). The test has a moderate specificity of 53.9% and a good sensitivity of 81.9% for diagnosing dementia, as well as good interrater reliability (Mathew et al., 2018). The task also has a good correlation with cognitive screening tasks like the MMSE (Mathew et al., 2018). The dependent variable in this current study is total score achieved on the assessment.

Procedure

Following approval from the MTSU Institutional Review (See Appendix C), the participants were provided with an informed consent form detailing the purpose of the study and the implications of the results (See Appendix D). The data for the patients with AD was archival, existing from a previous larger neuropsychological evaluation. These participants had come to Murfreesboro Medical Clinic with complaints of memory problems, received a full neuropsychological evaluation, and have received a diagnosis of

AD from a licensed neuropsychologist. The MOFT, Line Orientation, Necker Cube, and MMSE were all administered as a part of the full neuropsychological battery. The control participants were family members or caregivers of patients or family members of individuals complaining of memory problems. The control participants provided consent and then were escorted to a quiet exam room within the clinic. The tests were presented in a pseudorandom order and all participants were tested individually. The participants were verbally debriefed after testing on the purpose of the testing.

CHAPTER III: RESULTS

Initial Analyses

An initial analysis was conducted to determine if any differences occurred between groups in age, education, or depression. By utilizing three separate one way between-subjects ANOVAs ($\alpha = 0.05$), we found that age $F(1, 76) = 2.89$, MSE = 60.66, $p = .09$, education $F(1, 76) = 1.15$, MSE = 5.41, $p = .29$, and depression $F(1, 76)$, MSE = 28.90, $p = .20$ were not significantly different for the AD group and the control group (See Table 1).

Primary Analyses

Analyses using a one-way between subjects ANOVA were conducted to confirm the AD group performed worse than the controls on the MMSE, Necker Cube Copy, and Line Orientation task as expected due to cognitive degenerative disease. The results indicated that the AD group performed worse on the MMSE than the control group, $F(1,76) = 119.44$, MSE = 11.76, $p < .001$. The AD group also performed worse on the Line Orientation task than the control group, $F(1,76) = 10.17$, MSE = 8.60, $p = .002$. The AD group performed worse on the Necker Cube copy task than the control group, $F(1,76) = 17.28$, MSE = 58.52, $p < .001$.

First, we hypothesized that individuals with Alzheimer's disease would perform worse on the MOFT than the control group. This hypothesis was analyzed by a one-way between groups ANOVA. The results indicated a significant difference between the groups with the AD group performing worse than the control group, $F(1,76) = 71.83$, MSE = 135.11, $p < .001$ (See Table 2). There was a large effect size for the two groups,

d = -1.92. Subsequent analyses for each trial of the MOFT were conducted and indicated that the AD group performed worse than the control group on all three trials of the MOFT. A one-way ANOVA indicated that the AD group performed worse than the control group on the first trial, $F(1,76) = 58.11$, MSE = 6.99, $p < .001$, d = -1.72, on the second trial, $F(1,76) = 48.25$, MSE = 25.21, $p < .001$, d = -1.58, and on the third trial, $F(1,76) = 62.49$, MSE = 30.25, $p < .001$, d = -1.79.

Second, we hypothesized that the MOFT results would correspond to the stages of Alzheimer's disease in our AD group based upon the MMSE scores. These scores were anticipated to have a positive correlation, which would enable the MOFT to be used to assist in determining the staging of AD. This hypothesis was analyzed by a Pearson product moment correlation in the AD group. The results indicated that the MMSE and the MOFT have a significant positive correlation ($r = 0.60$, $r^2 = 0.36$, $p < .001$) in the AD group (See Table 3). This significant positive correlation was not seen in the control group, likely due to a ceiling effect on performance on the MMSE.

Third, we hypothesized that the results of the MOFT, Line Orientation, and the Necker Cube Copy task in the control sample would correlate and provide convergent validity. This hypothesis was analyzed by a Pearson product moment correlation. The results indicated that neither Line Orientation ($r = -0.04$, $r^2 = 0.001$, $p = .42$) nor Necker Cube Copy ($r = 0.26$, $r^2 = 0.06$, $p = .054$) had a significant positive correlation with the MOFT total score in the control sample (See Table 4). The control group was used to establish convergent validity due to the absence of degenerative disease and a larger generalizability; however, there were significant correlations when Pearson product

moment correlations were analyzed on the control and AD groups together. Line Orientation ($r = 0.25$, $r^2 = 0.06$, p=0.02) and Necker Cube Copy ($r = 0.51$, $r^2 = 0.26$, $p < .001$) both had a significant positive correlation with the MOFT total score when analyzed among all participants (See Table 5).

CHAPTER IV: DISCUSSION

Visuospatial skills are an underreported deficit in Alzheimer's disease, despite right parietal lobe functioning being affected early on in the disease (e.g., Bondi et al., 2018; Buckner et al., 2005; Salimi et al., 2018; Thulborn et al., 2000; Weintraub et al., 2012). Current Poppelreuter-Ghent tasks assess visuospatial and right parietal functioning, but have low sensitivity and ceiling effects due to long or non-existent time limits and only a few two-dimensional images to name (Alegret et al., 2009; Della Sala et al., 1995; Fujimori et al., 2000; Ota et al., 2015). There is a lack of research on right parietal functioning in AD partially due to this low sensitivity and ceiling effects of current Poppelreuter-Ghent tasks. The Mass Overlapping Figures Test (MOFT), with its lack of ceiling effects and high sensitivity, therefore could help detect and stage AD.

The current study sought to establish the MOFT as a viable neuropsychological assessment by comparing MOFT performance between a control group and a group of AD patients. The control group performed significantly better than the AD group on all three trials and the total score of the MOFT, demonstrating that the MOFT is an effective tool for discriminating between those with and without AD. The MOFT total scores had a significant positive correlation with the MMSE in the AD group. The MMSE's usage as a staging tool for AD demonstrates that MOFT performance in AD patients corresponds to the stages and severity of the disease. This indicates that the MOFT will be able to assist in determining the stage of AD progression.

The correlation between MMSE scores and MOFT total scores in the AD group ($r = .60$, $r^2 = 0.36$, $p<.001$) was a higher significant relationship than between the Line Orientation task and the MMSE in the AD group ($r = 0.35$, $r^2 = 0.12$, $p = .03$). This

demonstrates that the MOFT is a better predictive tool of AD severity than the RBANS Line Orientation task. There was not a significant relationship in the AD group for the MMSE and the Necker Cube Copy, demonstrating that the Necker Cube Copy is not a good predictor of disease severity in AD patients. These findings establish the MOFT as helpful for clinical use as a staging tool. The MMSE is used to staging tool for AD with scores less than 13 being indicative of severe AD, 13-19 being indicative of moderate AD, and 20-30 being indicative of mild AD. Staging tools are particularly important for neuropsychological evaluations as patients may have a diagnosis of AD but also score well on the MMSE due to being early in AD progression as well as the MMSE not having an episodic memory component, demonstrating a need for other additional staging tools that may be more sensitive to other areas of cognitive functioning to be used alongside the MMSE. MOFT scores were calculated into z scores and compared with the mentioned MMSE scale for AD, with MOFT scores at or below 2nd percentile being impaired, 3rd to 8th percentile being moderate and 9th to 100th percentile being mild. There was approximately a 50% agreement between the categorization of AD in the MOFT and MMSE, with 19 AD patients scoring in the same classification on both tests and 20 AD patients not scoring in the same classification for both tests.

Convergent validity for the MOFT as a visuospatial task was investigated by looking for correlations between MOFT scores and scores of two other visuospatial tasks: the Line Orientation subtest and the Necker Cube Copy. The correlations between the MOFT and the other two visuospatial tasks were not significant. This would argue that there is a lack of convergent validity for the MOFT, however, convergent validity for the MOFT was likely not established due to lack of variability of scores on the Line

Orientation task and the Necker Cube Copy in the control group. Thirty-six percent of the control group scored a perfect score on the Necker Cube Copy and 13% of the control group scored a perfect score on the Line Orientation task. Nearly the entire control group's performance on these two visuospatial tasks was cognitively intact. This lack of variability in the control group scores is likely due to ceiling effects in these cognitive measures and therefore supports the need for tasks like the MOFT that increase variability and eliminate ceiling effects. Convergent validity may have been established if we had chosen the more comprehensive Benton's Judgment of Line Orientation task, instead of the abbreviated RBANS Line Orientation subtest. There was a positive significant relationship between the Necker Cube Copy and the MOFT Trial 1 in the control group ($r = 0.27$, $r^2 = 0.07$, $p = .049$), and the Necker Cube Copy had positive significant correlations with MOFT Trial 1 ($r = 0.50$, $r^2 = 0.25$, $p = .003$), MOFT Trial 3 ($r = 0.37$ $r^2 = 0.14$, $p = .03$), and MOFT Total scores ($r = 0.38$, $r^2 = 0.14$, $p = .02$) in the AD group. The increased number of significant correlations between the Necker Cube Copy and the MOFT in the AD group was likely due to a greater variability of Necker Cube Copy scores in AD patients. The Necker Cube is primarily a visuoconstructual task, which could explain the lack of convergent validity as well. The RBANS Line Orientation task did not have any significant relationships with the MOFT in either the control or AD group. The ceiling effects in the control group on the Necker Cube and Line Orientation resulted in a restricted range and a lack of variability to establish convergent validity with the MOFT. Correlations were analyzed with the MOFT and the other visuospatial tasks using the entire sample to examine a wider range of scores in

these assessments in comparison to only the control group. The MOFT total score did have significant positive correlations with the Necker Cube Copy ($r = 0.51$ $r^2 = 0.26$, $p < .001$) and the Line Orientation ($r = 0.25$, $r^2 = 0.06$, $p = .023$) when the AD group and the control group were combined. This further demonstrates that the difficulty establishing convergent validity was likely due to ceiling effects and lack of variability in the control group. The lack of significant correlation between the MOFT and the RBANS Line Orientation task could be due to testing different right parietal and visuospatial abilities, in addition to the lack of variability in the control group scores. The Line Orientation task primarily tests the posterior areas of the parietal lobe, but also requires the frontal lobes as well (Tranel et al., 2010). This usage of the frontal lobes requires information to be passed along through the superior longitudinal fasciculus, where the MOFT likely utilizes the left hemisphere to some degree because of the verbal response aspect of the test and thus relies on the corpus callosum. Further research is needed to establish the convergent validity of the MOFT as a task of right parietal functioning.

Future research may seek to establish divergent validity with the MOFT and tasks of left parietal and left posterior functioning such as Gerstmann's Exam, the Semantic Fluency, or the Boston Naming Test. The Semantic Fluency test, often given as Animal Naming, assesses semantic fluency and the temporal lobes (Henry & Crawford, 2005; Strauss et al., 2006). Tests of semantic memory, such as Semantic Fluency, are associated with decreased grey matter volume in the left temporal and left parietal lobes (Bejanin et al., 2017). Double dissociation research has also demonstrated that tasks of semantic memory utilize the left temporal and left parietal lobes (Schmidt et al., 2019). The Boston Naming Test is a naming to confrontation task that is sensitive to left temporal lobe

dysfunction and AD patients often exhibit impaired performance on the task (Strauss et al., 2006). The MOFT is not a visual naming to confrontation task, as participants can briefly describe the items they visually identify, and thus should provide some divergent validity for the MOFT. The Boston Naming Test is also a semantic memory task that incorporates object naming, incorporating the temporal lobes as well (Henry & Crawford, 2005; Strauss et al., 2006). Utilizing these tasks for discriminate validity should further establish the MOFT as a right parietal task.

In conclusion, the current study supports previous research on AD performance on Poppelreuter-Ghent tasks and differences in right parietal functioning between control and AD groups. The MOFT may be helpful in assessing a healthy and normal population due to its lack of ceiling effects. Limitations of the study include using an abbreviated Line Orientation task instead of the full Benton's Judgment of Line Orientation, which may have prevented us from establishing convergent validity. There is a strong need for more scoring criteria of the Necker Cube to make the scores more representative of the task, as the three-dimensional concept of the task accounts for only 2 of the 28 points of the assessment but is a large component of the visuoconstructional task. We also did not test for divergent validity to see if the MOFT could be used to distinguish individuals with AD from those with other forms of dementia. The majority of the sample used identified as Caucasian and thus may not be generalizable to a broader, more diverse population. This initial study of the MOFT may be important in establishing the MOFT as a staging and diagnostic tool in the neuropsychological evaluation of AD patients, with the possibility of its usefulness for a wider range of dementia patients.

References

Alegret, M., Boada-Rovira, M., Vinyes-Junqué, G., Valero, S., Espinosa, A., Hernández, I., Modinos, G., Rosende-Roca, M., Mauleón, A., Becker, J. T., & Tárraga, L. (2009). Detection of visuoperceptual deficits in preclinical and mild Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology, 31*(7), 860-867. https://doi.org/ 10.1080/13803390802595568

Bardi, L., Kanai, R., Mapelli, D., & Walsh, V. (2013). Direct current stimulation (tDCS) reveals parietal asymmetry in local/global and salience-based selection. *Cortex, 49*(3), 850-860. https://doi.org/10.1016/j.cortex.2012.04.016

Bejanin, A., Schonhaut, D. R., La Joie, R., Kramer, J. H., Baker, S. L., Sosa, N., Ayakta, N., Cantwell, A., Janabi, M., Lauriola, M., O'Neil, J. P., Gorno-Tempini, M. L., Miller, Z. A., Rosen, H. J., Miller, B. L., Jagust, W. J., & Rabinovici, G. D. (2017). Tau pathology and neurodegeneration contribute to cognitive impairment in Alzheimer's disease. *Brain, 140*(12). https://doi.org/10.1093/brain/awx243

Benoit, J. S., Chan, W., Piller, L., & Doody, R. (2020). Longitudinal sensitivity of Alzheimer's disease severity staging. *American Journal of Alzheimer's Disease & Other Dementias, 35.* https://doi.org/10.1177/1533317520918719

Bondi, M. W., Edmonds, E. C., & Salmon, D. P. (2017). Alzheimer's disease: Past, present, and future. *Journal of the International Neuropsychological Society, 23*(9-10), 818-831. https://doi.org/10.1017/S135561771700100X

Braak, H. & Braak, E. (1991). Neuropathological stageing of Alzheimer-related changes. *Acta Neuropathologica, 82*(4), 239-259. https://doi.org/10.1007/BF00308809

Braak, H. & Braak, E. (1995). Staging of Alzheimer's disease-related neurofibrillary changes. *Neurobiology of Aging, 16*(3), 271-284. https://doi.org/ 10.1016/0197-4580(95)00021-6

Britz, J., Landis, T., & Michel, C. M. (2009). Right parietal brain activity precedes perceptual alternation of bistable stimuli. *Cerebral Cortex, 19*(1), 55-65. https://doi.org/10.1093/cercor/bhn056

Buckner, R. L., Snyder, A. Z., Shannon, B. J., LaRossa, G., Sachs, R., Fotenos, A. F., Sheline, Y. L., Klunk, W. E., Mathis, C. A., Morris, J. C., & Mintun, M. A. (2005). Molecular, structural, and functional characterization of Alzheimer's disease: Evidence for a relationship between default activity, amyloid, and memory. *The Journal of Neuroscience, 25*(34), 7709-7717. https://doi.org/ 10.1523/JNEUROSCI.2177-05.2005

Caterini, F., Della Sala, S., Spinnler, H., Stangalino, C., & Turnbull, O. H. (2002). Object recognition and object orientation in Alzheimer's disease. *Neuropsychology, 16*(2), 146-155. https://doi.org/10.1037//0894-4105.16.2.146

Culham, J. C. & Kanwisher, N. G. (2001). Neuroimaging of cognitive functions in human parietal cortex. *Current Opinion in Neurobiology, 11*(2), 157-163. https://doi.org/10.1016/s0959-4388(00)00191-4

Della Sala, S., Laiacona, M., Trivelli, C., & Spinnler, H. (1995). Poppelreuter-Ghent's overlapping figures test: Its sensitivity to age, and its clinical use. *Archives of Clinical Neuropsychology, 10*(6), 511-534. https://doi.org10.1016/0887-6177(94)00049-V

Firth, N. C., Primativo, S., Marinescu, R.-V. Shakespeare, T. J., Suarez-Gonzalez, A., Lehmann, M., Carton, A., Ocal, D., Pavisic, I., Paterson, R. W., Slattery, C. F., Foulkes, A. J. M., Ridha, B. H., Gil-Néciga, E., Oxtoby, N. P., Young, A. L., Modat, M., Cardoso, M. J., Ourselin, S., . . . Crutch, S. J. (2019). Longitudinal neuroanatomical and cognitive progression of posterior cortical atrophy. *Brain, 142*(7), 2082-2095. https://doi.org/10.1093/brain/awz136

Folstein, M. F., Folstein, S. E., Fanjian, G. (2001). *Mini-Mental State Examination: Clinical Guide.* Psychological Assessment Resources, Inc.

Folstein, M. F., Folstein, S. E., McHugh, P. R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, *12*, 189-198. https://doi.org/10.1016/0022-3956(75)90026-6

Foster, P. S., Roosa, K. M., Williams, M. R., Witt, J. C., Heilman, K. M., & Drago, V. (2013). Immunological functioning in Alzheimer's disease: Differential effects of relative left versus right temporoparietal dysfunction. *Journal of Neuroimmunology, 263,* 128-132. https://doi.org/10.1016/j.jneuroim.2013.07.011

Fujimori, M., Imamura, T., Hirono, N., Ishii, K., Sasaki, M., & Mori, E. (2000). Disturbances of spatial vision and object vision correlate differently with regional cerebral glucose metabolism in Alzheimer's disease. *Neuropsychologia, 38*(10), 1356-1361. https://doi.org/10.1016/S0028-3932(00)00060-9

Ghent, L. (1956). Perception of overlapping and embedded figures by children of different ages. *American Journal of Psychology*, *69*(4), 575-587.

Hänggi, J., Streffer, J., Jäncke, L., & Hock, C. (2011). Volumes of lateral temporal and parietal structures distinguish between healthy aging, mild cognitive impairment,

and Alzheimer's disease. *Journal of Alzheimer's Disease, 26*, 719-734. https://doi.org/10.3233/JAD-2011-101260

Henry, J. D. & Crawford, J. R. (2005). A meta-analytic review of verbal fluency deficits in depression. *Journal of Clinical & Experimental Neuropsychology, 27*(1), 78-101. https://doi.org/10.1080/138033990513654

Hougaard, A., Jenson, B. H., Amin, F. M., Rostrup, E., Hoffmann, M. B., & Ashina, M. (2015). Cerebral asymmetry of fMRI-BOLD responses to visual stimulation. *PLoS ONE, 10*(5). https://doi.org/10.1371/journal.pone.0126477

Inui, T., Tanaka, S., Okada, T., Nishizawa, S., Katayama, M., & Konishi, J. (2000). Neural substrates for depth perception of the Necker cube; a functional magnetic resonance imaging study in human subjects. *Neuroscience Letters, 282*(3), 145-148, https://doi.org/ 10.1016/s0304-3940(00)00899-5

Jacobs, H. I. L., Gronenschild, E. H. B. M., Evers, E. A. T., Ramakers, I. H. G. B., Hofman, P. A. M., Backes, W. H., Jolles, J., Verhey, F. R. J., & Van Boxtel, M. P. J. (2015). Visuospatial processing in early Alzheimer's disease: A multimodal neuroimaging study. *Cortex, 64,* 394-406. https://doi.org/10.1016/j.cortex.2012.01.005

Jacobs, H. I. L., Van Boxtel, M. P. J., Jolles, J., Verhey, F. R. J., & Uylings, H. B. M. (2012). Parietal cortex matters in Alzheimer's disease: An overview of structural, functional and metabolic findings. *Neuroscience and Biobehavioral Reviews, 36*(1), 297-309. https:// 10.1016/j.neubiorev.2011.06.009

Jacobs, H. I. L., Van Boxtel, M. P. J., Uylings, H. B. M., Gronenschild, E. H. B. M., Verhey, F. R., & Jolles, J. (2011). Atrophy of the parietal lobe in preclinical

dementia. *Brain and Cognition*, *75*(2), 154-163. https://doi.org/ 10.1016/j.bandc.2010.11.003

Jonas, J., Frismand, S., Vignal, J.-P., Colnat-Coulbois, S., Koessler, L., Vespignani, H., Rossion, B., & Maillard, L. (2014). Right hemispheric dominance of visual phenomena evoked by intracerebral stimulation of the human visual cortex. *Human Brain Mapping, 35*(7), 3360-3371. https://doi.org/10.1002/hbm.22407

Kravitz, D. J., Saleem, K. S., Baker, C. I., & Mishkin, M. (2011). A new neural framework for visuospatial processing. *Nature Reviews Neuroscience*, *12*(4), 217-230. https://doi.org/10.1038/nm3008

Mathew, R., Renjith, N., & Mathuranath, P. S. (2018). A new scoring system and norms for, and the performance of cognitively-unimpaired older adults on the cube copying test. *Neurology India, 66*(6), https://doi.org/ 10.4103/0028-3886.246242

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology, *34*, 939-944. https://doi.org/10.1212/01.wnl.0000400650.92875.cf

Meguro, K., Shimada, M., Someya, K., Horikawa, A., & Yamadori, A. (2001). Hemispatial visual-searching impairment correlated with decreased contralateral parietal blood flow in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 14*(4), 213-218.

Orlandi, A. & Proverbio, A. M. (2019). Left-hemispheric asymmetry for object-based attention: An ERP study. *Brain Sciences, 9*(11), 315. https://doi.org/10.3390/brainsci9110315

Ossenkoppele, R., Zwan, M. D., Tolboom, N., van Assema, D. M. E., Adriaanse, S. F., Kloet, R. W., Boellaard, R., Windhorse, A. D., Barkhot, F., Lammertsma, A. A., Scheltens, P., van der Flier, W. M., & van Berckel, B. N. M. (2012). Amyloid burden and metabolic function in early-onset Alzheimer's disease: parietal lobe involvement. *Brain, 135,* 2115-2125. https://doi.org/10.1093/brain/aws113

Ota, K., Murayama, N., Kasanuki, K., Kondo, D., Fujishiro, H., Arai, H., Sato, K., Iseki, E. (2015). Visuoperceptual assessments for differentiating dementia with Lewy bodies and Alzheimer's disease: Illusory contours and other neuropsychological examinations. *Achivers of Clinical Neuropsychology, 30*(3), 256-263. https://doi.org/10.1093/arclin/acv016

Quental, N. B. M., Brucki, S. M. D., & Bueno, O. F. A. (2013). Visuospatial function in early Alzheimer's disease - The use of the visual object and space perception (VOSP) battery. *PLOS One, 8*(7), 1-7. https://doi.org/10.1371/journal.pone.0068398

Randolph, C. (1998). *Repeatable Battery for the Assessment of Neuropsychological Status: Manual.* The Psychological Corporation.

Salatino, A., Chillemi, G., Gontero, F., Poncini, M., Pyasik, M., Berti, A., & Ricci, R. (2019). Transcranial magnetic stimulation of posterior parietal cortex modulates

line-length estimation but not illusory depth perception. *Frontiers in Psychology, 10*. https://doi.org/ 10.3389/fpsyg.2019.01169

Salimi, S., Irish, M., Foxe, D., Hodges, J. R., Piguet, O., & Burrell, J. R. (2018). Can visuospatial measures improve the diagnosis of Alzheimer's disease? *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 10,* 66-74. https://doi.org/10.1016/j.dadm.2017.10.004

Sengpiel, F. (2000). Visual perception: An alternative view of perceptual rivalry. *Current Biology, 10*(13), R482-R485. https://doi.org/10.1016/S0960-9822(00)00553-4

Schmidt, C. S. M., Nitschke, K., Bormann, T., Römer, P., Kümmerer, D., Martin, M., Umarova, R. M., Leonhart, R., Egger, K., Dressing, A., Musso, M., Willmes, K., Weiller, C., & Kaller, C. P. (2019). Dissociating frontal and temporal correlates of phonological and semantic fluency in a large sample of left hemisphere stroke patients. *NeuroImage: Clinical, 23*. https://doi.org/10.1016/j.nicl.2019.101840

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). A compendium of neuropsychological tests (3rd ed.). Oxford University Press.

Thompson, P. M., Hayashi, K. M., de Zubicaray, G., Janke, A. L., Rose, S. E., Semple, J., Herman, D., Hong, M. S., Dittmer, S. S., Doddrell, D. M., & Toga, A. W. (2003). Dynamics of gray matter loss in Alzheimer's disease. *The Journal of Neuroscience, 23*(3), 994-1005. https://doi.org/10.1523/JNEUROSCI.23-03-00994.2003

Thompson, P. M., Moussai, J., Zohoori, S., Goldkorn, A., Khan, A. A., Mega, M. S., Small, G. W., Cummings, J. L., & Toga, A. W. (1998). Cortical variability and

asymmetry in normal aging and Alzheimer's disease. *Cerebral Cortex,* 8(6), 492-509.

Thulborn, K. R., Martin, C., & Voyvodic, J. T. (2000). Functional MR imaging using a visually guided saccade paradigm for comparing activation patterns in patients with probable Alzheimer's disease and in cognitively able elderly volunteers. *American Journal of Neuroradiology, 21*(3), 524-531.

Tranel, D., Vianna, E., Manzel, K., Damasio, H., & Grabowski, T. (2009). Neuroanatomical correlates of the Benton facial recognition test and judgment of line orientation test. *Journal of Clinical and Experimental Neuropsychology, 31*(2), 219-233. https://doi.org/10.1080/13803390802317542

Viggiano, M. P., Gori, G., Zaccara, G., Righi, S. Vannucci, M., & Giovannelli, F. (2007) Category-specific visual identification of filtered objects in Alzherimer's disease. *Archives of Gerontology and Geriatrics, 44*(2), 125-139. https://doi.org/10.1016/j.archger.2006.04.003

Weintraub, S., Wicklund, A. H., & Salmon, D. P. (2012). The neuropsychological profile of Alzheimer's disease. *Cold Spring Harbor Perspectives in Medicine, 2*(4), 1-18. https://doi.org/10.1101/cshperspect.a006171

APPENDICES

APPENDIX A: DEMOGRAPHIC FORM

Demographic Form

Subject History and Demographics

Subject Number:

Date of Birth:

Date of Study:

Sex:

Age:

Height:

Weight:

Handedness:

Education:

History of significant head injury (meaning loss of consciousness)? Y/N

If yes then explain. How long was the loss of consciousness?

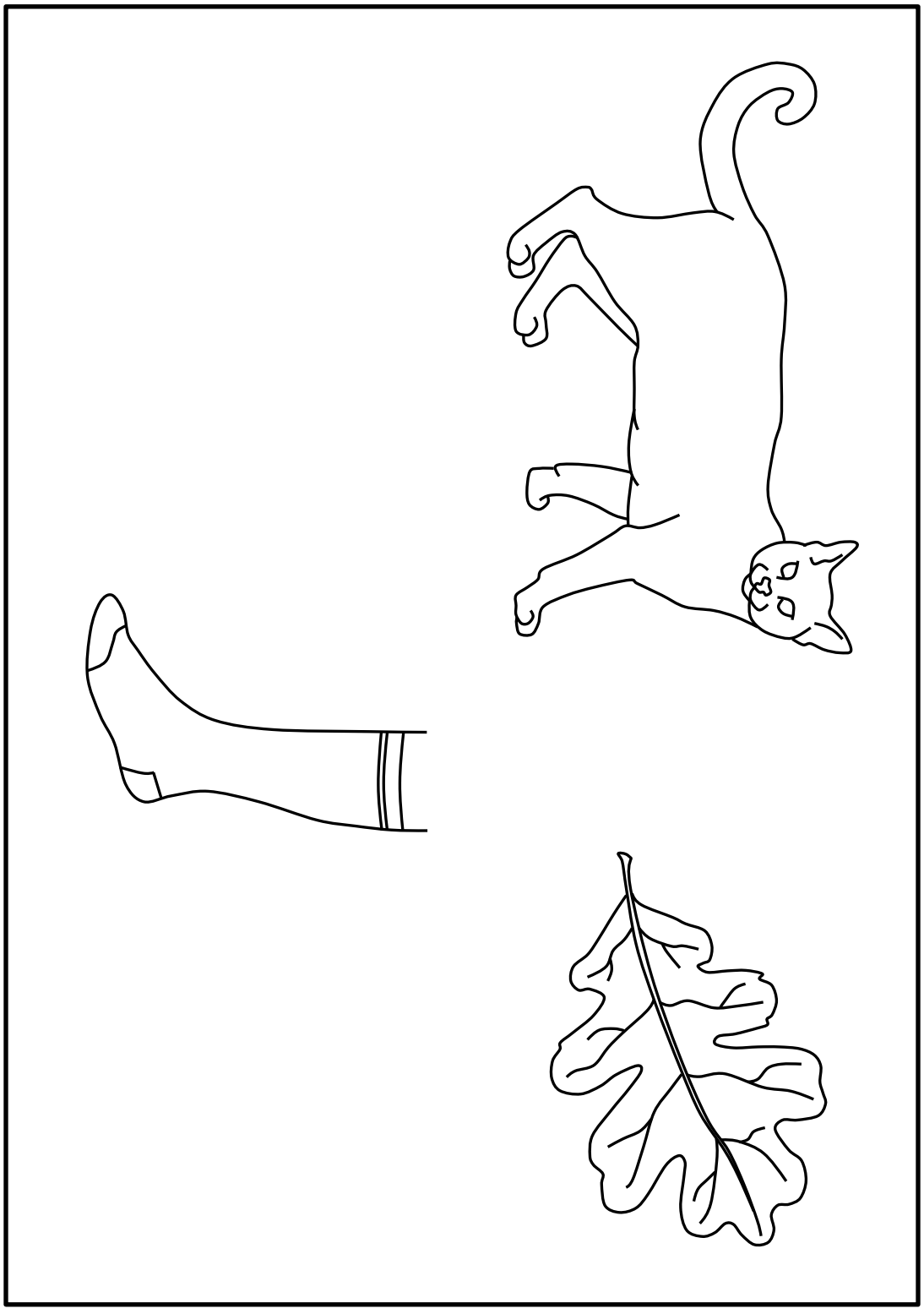
History of neurological or psychological/psychiatric illness? Y/N

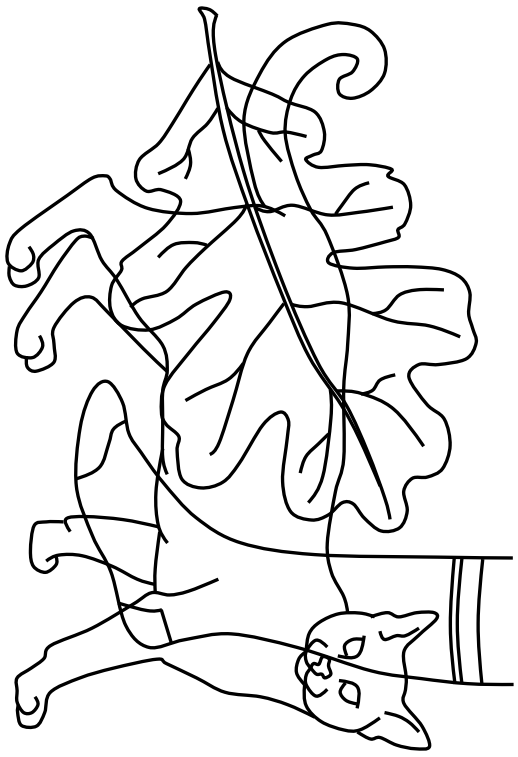
If yes then explain.

Currently taking psychotropic medications? Such as medications for depression or anxiety? Y/N

If yes then explain. What medications?

APPENDIX B: SAMPLE ITEM





APPENDIX C: MTSU IRB APPOVAL LETTER

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129
FWA: 00005331/IRB Regn. 0003571

MIDDLE TENNESSEE STATE UNIVERSITY

IRBN001 - EXPEDITED PROTOCOL APPROVAL NOTICE

Wednesday, March 31, 2021

Protocol Title	***Assessing Right Parietal Lobe Functions in Alzheimer's Disease Using the Mass Overlapping Figures Test***
Protocol ID	**21-2136 7i**
Principal Investigator	**Charles Cullen Hicks** (Student)
Faculty Advisor	Paul Foster
Co-Investigators	NONE
Investigator Email(s)	*cch4x@mtmail.mtsu.edu; paul.foster@mtsu.edu*
Department	Psychology
Funding	**NONE**

Dear Investigator(s),

The above identified research proposal has been reviewed by the MTSU IRB through the **EXPEDITED** mechanism under 45 CFR 46.110 and 21 CFR 56.110 within the category *(7) Research on individual or group characteristics or behavior*. A summary of the IRB action is tabulated below:

IRB Action	**APPROVED for ONE YEAR**		
Date of Expiration	**3/31/2022**	*Date of Approval*: 3/31/21	*Recent Amendment*: NONE
Sample Size	ONE HUNDRED (100)		
Participant Pool	*Target Population:* Primary Classification: **Adults (18 or older)** Specific Classification: **Individuals with history of head injury, neurological illnesses or degenerative disease**		
Type of Interaction	☐ Non-interventional or Data Analysis ☐ Virtual/Remote/Online interaction ☒ **In person or physical interaction – Mandatory COVID-19 Management**		
Exceptions	1. Participant information for potential contact tracing is allowed. 2. Obtaining participant age and date of birth for analysis is permitted.		
Restrictions	**1. Mandatory SIGNED Informed Consent.** **2. Other than the exceptions above, identifiable data/artifacts, such as, audio/video data, photographs, handwriting samples, personal address, driving records, social security number, and etc., MUST NOT be collected. Recorded identifiable information must be deidentified as described in the protocol.** **3. Mandatory Final report (refer last page).** **4. The protocol details must not be included in the compensation receipt.** **5. CDC guidelines and MTSU safe practice must be followed**		
Approved Templates	*IRB Templates:* Signature Inforemd Consent *Non-MTSU Templates:* Recruitment script		
Research Inducement	NONE		
Comments	NONE		

Post-approval Requirements

The PI and FA must read and abide by the post-approval conditions (Refer "*Quick Links*" in the bottom):

- ***Reporting Adverse Events:*** The PI must report research-related adversities suffered by the participants, deviations from the protocol, misconduct, and etc., within 48 hours from when they were discovered.
- ***Final Report:*** The FA is responsible for submitting a final report to close-out this protocol before **3/31/2022 (Refer to the Continuing Review section below)**; REMINDERS WILLNOT BE SENT. **Failure to close-out or request for a continuing review may result in penalties** including cancellation of the data collected using this protocol and/or withholding student diploma.
- ***Protocol Amendments***: An IRB approval must be obtained for all types of amendments, such as: addition/removal of subject population or investigating team; sample size increases; changes to the research sites (appropriate permission letter(s) may be needed); alternation to funding; and etc. The proposed amendments must be requested by the FA in an addendum request form. The proposed changes must be consistent with the approval category and they must comply with expedited review requirements
- ***Research Participant Compensation:*** Compensation for research participation must be awarded as proposed in Chapter 6 of the Expedited protocol. The documentation of the monetary compensation must Appendix J and MUST NOT include protocol details when reporting to the MTSU Business Office.
- ***COVID-19:*** Regardless whether this study poses a threat to the participants or not, refer to the COVID-19 Management section for important information for the FA.

Continuing Review (The PI has requested early termination)

Although this protocol can be continued for up to THREE years, The PI has opted to end the study by **3/31/2022** **The PI must close-out this protocol by submitting a final report before 3/31/2022 Failure to close-out may result in penalties that include cancellation of the data collected using this protocol and delays in graduation of the student PI.**

Post-approval Protocol Amendments:

The current MTSU IRB policies allow the investigators to implement minor and significant amendments that would fit within this approval category. ***Only TWO procedural amendments will be entertained per year*** *(changes like addition/removal of research personnel are not restricted by this rule).*

Date	Amendment(s)	IRB Comments
NONE	NONE.	NONE

Other Post-approval Actions:

The following actions are done subsequent to the approval of this protocol on request by the PI/FA or on recommendation by the IRB or by both.

Date	IRB Action(s)	IRB Comments
NONE	NONE	NONE

COVID-19 Management:

The PI must follow social distancing guidelines and other practices to avoid viral exposure to the participants and other workers when physical contact with the subjects is made during the study.

- The study must be stopped if a participant or an investigator should test positive for COVID-19 within 14 days of the research interaction. This must be reported to the IRB as an "adverse event."
- The MTSU's "Return-to-work" questionnaire found in Pipeline must be filled by the investigators on the day of the research interaction prior to physical contact.
- PPE must be worn if the participant would be within 6 feet from the each other or with an investigator.
- Physical surfaces that will come in contact with the participants must be sanitized between use
- **FA's Responsibility:** The FA is given the administrative authority to make emergency changes to protect the wellbeing of the participants and student researchers during the COVID-19 pandemic. However, the FA must notify the IRB after such changes have been made. The IRB will audit the changes at a later date and the FA will be instructed to carryout remedial measures if needed.

Data Management & Storage:

All research-related records (signed consent forms, investigator training and etc.) must be retained by the PI or the faculty advisor (if the PI is a student) at the secure location mentioned in the protocol application. The data must be stored for at least three (3) years after the study is closed. Additional Tennessee State

data retention requirement may apply (*refer "Quick Links" for MTSU policy 129 below*). The data may be destroyed in a manner that maintains confidentiality and anonymity of the research subjects.

The MTSU IRB reserves the right to modify/update the approval criteria or change/cancel the terms listed in this letter without prior notice. Be advised that IRB also reserves the right to inspect or audit your records if needed.

Sincerely,

Institutional Review Board
Middle Tennessee State University

Quick Links:

- Post-approval Responsibilities: http://www.mtsu.edu/irb/FAQ/PostApprovalResponsibilities.php
- Expedited Procedures: https://mtsu.edu/irb/ExpeditedProcedures.php
- MTSU Policy 129: Records retention & Disposal: https://www.mtsu.edu/policies/general/129.php

APPENDIX D: INFORMED CONSENT

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129

IRBF016: INFORMED CONSENT

(Use this consent template for in person or virtual interactions)

General Information

1. Use this consent form for requesting a participant for
    a. In person interviews or other interactions
    b. Virtual interviews or other interactions using Zoom
    c. Online consent via Qualtrics
2. This template is suitable for studies that qualify for Expedited as well as a full review.
3. Alterations and waiver of this template are strongly discouraged. The elements not applicable to the study can be indicated by the provided check boxes with a suitable justification.
4. Web-based Studies – this form is not currently available for web-based administration through Qualtrics.
5. The Faculty Advisor information will be removed at the review/approval stage if the PI is NOT a student.
6. COVID-19: for in person protocols, there is a COVID-19 avoidance plan

Instructions

1. This form contains TWO sections:
    A. General Information section – signed by the researcher and given to the participant
    B. The signature section has to be signed by the participant
    Please note that there are multiple options: first one for traditional pen signature, a second option is for virtual administration via Zoom, and a third option for Qualtrics
2. If signature waiver is approved or required by the IRB, then the signature section will be filled by the PI with a random identifier and saved with rest of the research records
3. Other than the actual signatures, the text boxes in two sections must be properly completed before submitting for IRB approval.
4. The investigators have the option for requesting the removal of certain elements in this form by entering their justification in the boxes highlighted in yellow. All of the pre-approval request boxes will be removed at the approval stage.

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129

MIDDLE TENNESSEE STATE UNIVERSITY

IRBF016 – Participant Informed Consent

A. INFORMATION AND DISCLOSURE SEGMENT
(Participant Copy)

Primary Investigator(s)	Charles Cullen Hicks		**Student ☒**
Contact information	706-573-6047		
Department & Institution	Clinical Psychology		
Faculty Advisor	Dr. Paul Foster	***MTSU Department***	Clinical Psychology
Study Title	Assessing Parietal Lobe Functions in Alzheimer's Disease Using the Mass Overlapping Figures Test		
IRB ID	**21-2136 7i** **Approval: 03/31/2021**		**Expiration: 03/31/2022**

The following information is provided to inform you about the research project in which you have been invited to participate. Please read this disclosure and feel free to ask any questions. The investigators must answer all of your questions and you must be given a signed copy of this disclosure.

- Your participation in this research study is voluntary.
- You are also free to withdraw from this study at any time without loss of any benefits.
- In the event new information becomes available that may affect the risks or benefits associated with this research study, you will be notified so that you can make an informed decision at that time.

For additional information on your rights as a participant in this study, please contact the Middle Tennessee State University (MTSU) Office of Compliance (Tel 615-494-8918 or send your emails to irb_information@mtsu.edu. (URL: http://www.mtsu.edu/irb).

Please read this section and sign Section B if you wish to enroll in this study. The researcher will provide you with a copy of this disclosure form for you to keep for your future reference.

1. **What are the prime types of physical contact the participant will have?**
   The participant will have the following type(s) of contact(s) with the investigators or/and other participants at least sometimes during this research:
   - ☐ 1.1 ***Virtual Interactions*** **NONE**
   - ☒ 1.2 ***In person interactions***
     - ☒ With PPE ☐ Without PPE ☒ With Social Distancing ☐ Without Social Distancing
     - The participants will be asked to provide their contact details to be used by MTSU COVID-19 task force for contact tracing if needed
2. **What is the main category of this research?**
   - ☐ 2.1 ***Educational Tests***
   - ☐ 2.2 Social/***Behavioral Evaluation***
   - ☐ 2.3 ***Psychological intervention or procedures***
   - ☐ 2.4 ***Physical Evaluation or Procedures***
   - ☐ 2.5 ***Medical Evaluation***
   - ☒ *2.6 Clinical Researc*
3. **What is the purpose of this study?**
   You are being asked to participate in a research study because we are interested in collecting normative data on a newly developed neuropsychological assessment to aid in diagnosis of Alzheimer's disease, as well as assess left and right parietal lobe functioning.

4. **What type of data will be collected from you?**
   You will be asked to fill out a demographic form and history questionnaire. You will then be given a neuropsychological battery of paper-and-pencil types of tests. The entire study may take up to an hour and a half.

5. **What are procedures we intend on doing to collect the above described data?**
   We intend to use the Mini Mental Status Exam (MMSE), Geriatric Depression Scale (GDS), Hopkins Verbal Learning Test - Revised (HVLT-R), Trail Making Test (TMT), Line Orientation subtest from the Repeatable Battery of Neuropsychological Status (RBANS), Necker Cube Copy, and the Mass Overlapping Figures Test (MOFT).

☐ 5.1 ***Audio recording*** ☐ 5.2 ***Video Recording*** ☐ 5.3 ***Photography*** ☒ **5.4** ***NO audio/video recording***

6. **What will you be asked to do in this study?**
   You will be asked to participate in neuropsychological testing

7. **What are we planning to do with the data collected using your participation?**
   We are planning to use the data to find convergent validity between tests and compare results from a control group and an Alzheimer's disease group.

8. **What are the expected results of this study and how will they be disseminated?**
   We expect that the control group will perform better on the MOFT than the Alzheimer's disease group and that results of the MOFT, Line Orientation, and Necker Cube Copy will be comparable.

9. **What is the approximate time commitment not including your preparation time for participating in this study?**
   The testing will take approximately one hour.

10. **What are your expected costs to you, your effort, and etc.?**
    There are no expected costs to you or your effort.

11. **What are the potential discomforts, inconveniences, and/or possible risks that can be reasonably expected as a result of participation in this study?**
    It is possible that some of the neuropsychological tests will cause some mental fatigue.

12. **What are the risks and bodily harm due to COVID-19 exposure?**
    Although the MTSU IRB considers this research as "no more than minimal risk." the participants will be in physical contact with the PI and other participants during this study. Therefore, the participants will be exposed to the risk of contracting COVID-19.
    - The participants must adhere by the following to reduce the risk for infection. The participants must wear proper PPE as designated by Murfreesboro Medical Clinic and socially distance when possible.
    - The investigator will follow these precautions: The investigator will wear PPE as designated by Murfreesboro Medical Clinic and socially distance when possible.
    - ***COVID-19 Contact Tracing:*** The participants will be asked to provide their contact details will be given to the MTSU COVID-19 task force if someone you came in contact with tested positive for COVID-19. Your contact details provided in this form will be destroyed after a few days if no positivity of COVID-19 is detected.

13. **What are the anticipated benefits from this study?**
    a. The benefits to science and humankind that may result from this research:

Anticipated benefits from this study include development of a new neuropsychological assessment of right parietal functioning.

b. ***The direct benefits to you which you:*** There are no direct benefits to the partipants

14. How will you be compensated for your participation?
You will not be compensated for your participation.

15. Will you be compensated for any study-related injuries?
MTSU will not provide compensation in the case of study related injury.

16. Circumstances under which the researcher may withdraw you from this study:
You will be withdrawn from this study if you have a history of significant head trauma, depression, stroke, neurological illness, or dementia.

What happens if you choose to withdraw your participation?
Participation in this study is voluntary and there are no penalties for refusing to participate and there are no consequences from withdrawing from the study.

17. Can you stop the participation any time after initially agreeing to give consent/assent?
The participants may choose to withdraw from the study at any point.

18. Contact Information. If you should have any questions about this research study or possibly injury, please feel free to contact Charles Cullen Hicks by telephone 706-573-6047 or by email cch4x@mtmail.mtsu.edu OR my faculty advisor, Dr. Paul Foster, at paul.foster@mtsu.edu. For additional information about giving consent of your rights as a participant in this study, to discuss problems, concerns and questions, or to offer input, please feel free to contact the MTSU IRB by email: compliance@mtsu.edu or by telephone (615) 494 8918.

19. Confidentiality. All efforts, within reason, will be made to keep your personal information private but total privacy cannot be promised. Your information may be shared with MTSU or the government, such as the Middle Tennessee State University Institutional Review Board, Federal Government Office for Human Research Protections, *if* you or someone else is in danger or if we are required to do so by law.

20. Confidentiality and COVID-19: Your information will be provided to the University COVID-19 task force or other public health officials in the event you or one of the research participants or investigators should test positive for COVID-19. Complete the COVID-19 Contract Tracking Page after you agree to consent.

You do not have to do anything if you decide not to participate. If you wish to enroll however, please f enter your name and age in the attached Segment B document and sign in the space provided. Please complete the contact tracing page (last page).

Consent obtained by:

_____ _____

Researcher's Signature Name and Title Date

This study involves in person interactions. Therefore, the participant is required to complete the details in the next page to allow COVID-19 contact tracing if needed

IRBF016 – Participant Informed Consent

B. Consent Segment 1 - IN PERSON INTERACTION
(Researchers' Copy)

Primary Investigator(s)	Charles Cullen Hicks		**Student ☒**
Contact information	706-573-6047		
Department & Institution	Clinical Psychology		
Faculty Advisor	Dr. Paul Foster	***MTSU Department***	Clinical Psychology
Study Title	Assessing Parietal Lobe Functions in Alzheimer's Disease Using the Mass Overlapping Figures Test		
IRB ID	**21-2136 7i** **Approval: 03/31/2021**		**Expiration: 03/31/2022**

PARTICIPANT SECTION

To be filled by the participant and returned to the researcher	**Participants give consent**
I have read this informed consent document	☐No ☐Yes
The research procedures to be conducted have been explained to me verbally	☐No ☐Yes
I understand all of the interventions and all my questions have been answered	☐No ☐Yes
I am aware of the potential risks of the study	☐No ☐Yes
I understand that my information will be shared with health professionals in the event an investigator or a participant should test positive for COVID-19	☐No ☐Yes

By entering my name and signing below, I affirm that I freely and voluntarily choose to participate in this study. I understand I can withdraw from this study at any time without facing any consequences.

Name and Signature of the Participant Date Participant's Age

RESEARCHER SECTION
(To be filled by an investigator and the FA if applicable)

Informed Consent obtained by:

Name Signature Date

Faculty Verification (if administered by a student)

Name Signature Date

This study involves in person interactions. Therefore, the participant is required to complete the details in the next page to allow COVID-19 contact tracing if needed

IRBF016 – Participant Informed Consent **COVID-19 Contact Tracing**

PARTICIPANT SECTION
(To be filled by the consenting participant and returned to the researcher)

Confidentiality and COVID-19:
Your information will be provided to the University COVID-19 task force or other public health officials in the event you or one of the research participants or investigators should test positive for COVID-19.

Name: ***Contact Address:*** ***Telephone:*** ***Email Address:***

Office Use:
Information Date: (Today's Date)
Expiration Date: (Date on which this sheet will be destroyed if no COVID-19 is detected)

Instruction to PI:
- Destroy this page if no COVID-19 is detected by the expiration date above
- If positivity for COVID-19 is known, then provide the participant contact information to MTSU's COVID-19 task force

Ensure to cut the box out when providing the participant's contact details and hide any protocol details from being transmitted.

APPENDIX E: TABLES

Table 1

Descriptive Statistics for Groups

Variable	Control Group (n = 39)		AD Group (n = 39)	
	M	*SD*	*M*	*SD*
Age	74.05	8.85	77.05	6.56
Years of Education	13.38	2.13	12.82	2.50
GDS	6.59	5.03	8.15	5.70

Note. GDS = Geriatric Depression Inventory Scores. Possible range of scores for GDS are 0 - 30

Table 2

Descriptive Statistics and ANOVA Results for Between Groups Analysis

Variable	Control Group (n = 39)		AD Group (n = 39)		Results
	M	*SD*	*M*	*SD*	
MMSE	27.15	2.10	18.67	4.37	F (1,76) = 119.44, $p < 0.001$
LO	16.58	2.68	14.25	3.25	F (1,76) =10.17, $p = 0.002$
Necker Cube	21.77	7.01	13.89	8.46	F (1,76) = 17.28, $p < 0.001$
MOFT Trial 1	8.79	2.89	4.23	2.37	F (1,76) = 58.11, $p < 0.001$
MOFT Trial 2	19.31	4.79	11.41	5.24	F (1,76) = 48.25, $p < 0.001$
MOFT Trial 3	18.10	6.03	8.26	4.91	F (1,76) = 62.49, $p < 0.001$
MOFT Total	46.21	11.87	23.90	11.37	F (1,76) = 71.83, $p < 0.001$

Note. MMSE = Mini Mental Status Exam; LO = Line Orientation subtest from the RBANS. MMSE scores range from 0-30, LO scores range from 0-20, Necker Cube scores range from 0-28.

Table 3

Pearson Product-Moment Correlations in the Alzheimer's Disease Group

Variable	MMSE	LO	Necker	MOFT Trial 1	MOFT Trial 2	MOFT Trial 3	MOFT Total
MMSE	-	.35* (.034)	.28 (.073)	.50** (.001)	.53** (<.001)	.58** (<.001)	.60** (<.001)
LO	.35* (.034)	-	.67** (<.001)	.25 (.102)	-.01 (.474)	.04 (.415)	.06 (.375)
Necker	.28 (.073)	.67** (<.001)	-	.50** (.003)	.22 (.127)	.37* (.027)	.38* (.024)
MOFT Trial 1	.50** (.001)	.25 (.102)	.50** (.003)	-	.76** (<.001)	.67** (<.001)	.85** (<.001)
MOFT Trial 2	.53** (<.001)	-.01 (.474)	.22 (.127)	.76** (<.001)	-	.73** (<.001)	.94** (<.001)
MOFT Trial 3	.58** (<.001)	.04 (.415)	.37* (.027)	.67** (<.001)	.73** (<.001)	-	.91** (<.001)
MOFT Total	.60** (<.001)	.06 (.375)	.38* (.024)	.85** (<.001)	.94** (<.001)	.91** (<.001)	-

Note. MMSE = Mini Mental Status Exam; LO = Line Orientation subtest from the RBANS.

*p<.05, **p<.01

Table 4

Pearson Product-Moment Correlations in the Control Group

Variable	MMSE	LO	Necker	MOFT Trial 1	MOFT Trial 2	MOFT Trial 3	MOFT Total
MMSE	-	-.08 (.317)	.10 (.283)	-.01 (.471)	.06 (.364)	.06 (.357)	.05 (.378)
LO	-.08 (.317)	-	-.13 (.211)	.06 (.371)	.03 (.424)	-.12 (.233)	-.04 (.416)
Necker	.10 (.283)	-.13 (.211)	-	.27* (.049)	.20 (.106)	.22 (.085)	.26 (.054)
MOFT Trial 1	-.01 (.417)	.06 (.371)	.27* (.049)	-	.58** (<.001)	.54** (<.001)	.75** (<.001)
MOFT Trial 2	.06 (.364)	.03 (.424)	.20 (.106)	.58** (<.001)	-	.67** (<.001)	.88** (<.001)
MOFT Trial 3	.06 (.357)	-.12 (.233)	.22 (.085)	.54** (<.001)	.67** (<.001)	-	.91** (<.001)
MOFT Total	.05 (.378)	-.04 (.416)	.26 (.054)	.75** (<.001)	.88** (<.001)	.91** (<.001)	-

Note. MMSE = Mini Mental Status Exam; LO = Line Orientation subtest from the RBANS.

*p<0.05, **p<0.01

Table 5

Pearson Product-Moment Correlations in All Participants

Variable	MMSE	LO	Necker	MOFT Trial 1	MOFT Trial 2	MOFT Trial 3	MOFT Total
MMSE	-	.39** (.001)	.48** (<.001)	.65** (<.001)	.67** (<.001)	.69** (<.001)	.72** (<.001)
LO	.39** (.001)	-	.34** (.004)	.32** (.005)	.22* (.040)	.19 (.066)	.25* (.023)
Necker	.48** (<.001)	.34** (.004)	-	.54** (<.001)	.43** (<.001)	.49** (<.001)	.51** (<.001)
MOFT Trial 1	.65** (<.001)	.32** (.005)	.54** (<.001)	-	.80** (<.001)	.77** (<.001)	.89** (<.001)
MOFT Trial 2	.67** (<.001)	.22* (.040)	.43** (<.001)	.80** (<.001)	-	.82** (<.001)	.94** (<.001)
MOFT Trial 3	.69** (<.001)	.19 (.066)	.49** (<.001)	.77** (<.001)	.82** (<.001)	-	.95** (<.001)
MOFT Total	.72** (<.001)	.25* (.023)	.51** (<.001)	.89** (<.001)	.94** (<.001)	.95** (<.001)	-

Note. MMSE = Mini Mental Status Exam; LO = Line Orientation subtest from the RBANS.

*p<0.05, **p<0.01