THE SEMANTIC ASSOCIATION TEST FOR ALZHEIMER'S DISEASE: A PSYCHOMETRIC EVALUATION

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ABSTRACT

The purpose of this study was to determine whether there is an identifiable difference between patients with Alzheimer's disease (AD) and healthy controls on a semantic association task (SAT). The task was to investigate this newly developed assessment tool by comparing performance of healthy controls with patients diagnosed with AD. Thirty controls completed a short battery of standardized assessments and the SAT. Twenty-four AD participants were included as retrospective data from previous neuropsychological testing. Our predictions involved performance between groups on various aspects of the semantic categories within the SAT. Results indicated several significant differences supporting most of the original predictions. We measured convergent validity with two commonly used assessments, the Boston Naming Test and Semantic Fluency and found significant correlations. Further analyses conducted to analyzing group differences in spreading activation. Results indicated significant differences between the groups in the spread of activation associated with correct items on the SAT.

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CHAPTER I

INTRODUCTION

Over the last 30 plus years, Alzheimer's disease (AD) has been an increasing issue in both neurology and neuropsychology fields, including both the diagnosis and treatment of this disorder (Braak & Braak, 1997; Hodges & Patterson, 1995; Perri, Zannino, Caltagirone, & Carlesimo, 2012; Weintraub, Wicklund, & Salmon, 2012; Zannino, Perri, Pasqualetti, Caltagirone, & Carlesimo, 2005). A hallmark of Alzheimer's disease is memory loss (Braak & Braak, 1997; Vallet et al., 2016). Memory loss in general is something that occurs during normal aging, however, the extent observed in patients with AD is far greater than that of nonclinical memory decline (e.g., Weirngartner, Kawas, Rawlings, 1993; Wilson et al., 2012). Research conducted with patients experiencing cognitive decline found that initial deficits included an overall loss of memory, specifically episodic memory (Graham, Emery, Hodges, 2004; Hodges & Patterson, 1995; Nebes, 1989; for review see Weintraub et al., 2012). Tulving (1983) proposed that there were two types of memory storage: episodic and semantic memory. This distinction is helpful for assessment because it allows for greater precision regarding which areas of the brain and which memory systems are disrupted by AD. Episodic memory holds knowledge rooted in a person's life, including memories spanning a lifetime and personal experiences (i.e., autobiographical information; Hodges & Patterson, 1997; Nebes, 1989). The second area of memory storage, semantic memory, houses knowledge of worldly events, definitions of words, factual and meaningful knowledge among others (Daum, Riesch, Satori, & Birbaumer, 1996; Libon et al., 2013; Satori & Lombardi, 2004), which is often referred to as a semantic network.

Understanding the organization of this semantic network is important to understanding the deterioration brought on by AD (Zannino, Perri, Pasqualetti, Caltagirone, & Calesimo, 2006a). This semantic network organizes the word nodes activated during a semantic search. This search can be activated by both visual and verbal stimuli which result in the activation of representations within the network (Farah & McClelland, 1991). Damage to the semantic network is not as widespread when compared to the damage documented in the episodic networks in people with AD (Adlam, Bozeat, Arnold, Watson, & Hodges, 2006; Hodges & Patterson, 1997). However, some studies have shown patients with AD have deficits in the semantic network when compared to normal elderly controls (Chan, Butters, Salmon & McGuire, 1993; Hodges & Patterson, 1997; Libon et al., 2013; Nebes, 1989).

The deficits in semantic memory often seen when assessing patients with suspected AD include difficulty with recognition and identification of items (Hodges & Patterson, 1997; Weiner, Neubecker, Bret, & Hynan, 2008), word fluency and production (Diaz, Sailor, Cheung, & Kuslansky, 2003; Marczinski & Kertesz, 2006; Salmon, Butters, & Chan, 1999), word to picture matching tasks (Graham, Emery, & Hodges, 2004; Zannino, Perri, Pasqualetti, Caltagirone, & Calesimo, 2006b), and word associations (Garcea, Dombovy, & Mahon, 2013; Libon et al., 2013). These findings have been studied and documented for years (Hodges & Patterson, 1997; Martin & Fedio, 1983; Rosser & Hodges, 1994); however, within the last 30 years', specific features of semantic memory problems directly associated with AD have been scrutinized (Graham et al., 2004; Satori & Lombardi, 2004; Warrington & Shallice, 1984). Specifically, Fung et al. (2001) showed that, when compared to healthy controls, patients with AD

experience a naming deficit with biological elements over nonbiological. In this study, they also attempted to capture the deficit of the AD group with action verb naming versus object naming, unfortunately this hypothesis did not result in significance. Other research has also found that patients with AD experience greater difficulty identifying and naming living items (e.g., cat) versus nonliving items (e.g., hammer) (Zannino et al., 2006b). In addition, both Garcea et al. (2013) and Chan, Salmon, and Pena (2001) supported that patients with AD have lower accuracy when naming transitive (e.g., car) versus nontransitive items (e.g., nail). Transitive items are defined as items that convey movement or motion whereas nontransitive items are motionless (Handjaras et al., 2015). The overwhelming evidence supporting dysfunctional semantic memory networks in patients with AD is persuasive enough to warrant another useful test in this field.

Living versus Nonliving Stimuli and Alzheimer's Disease

Category specific memory deficits are found in a variety of different degenerative diseases; however, the presentation can differ within each disease. Some examples include patients who have experienced a temporal lobe lesion, herpes simplex encephalitis (HSE), primary progressive aphasia (PPA), and AD. These diseases present with some form of category specific deficit (for review see Capitani et al., 2003; Satori & Lombardi, 2004; Warrington & Shallice, 1984). There have been several hypotheses proposed to explain the type of category deficits seen with these patient groups (Sartori & Lombardi, 2004). The hypotheses we are concerned with, however, are specific to the AD patient group.

First, the neuroanatomical theory of semantic memory indicates that living items (e.g., animals, fruits) are prominently accessed through in the temporal lobe whereas

nonliving items (e.g., tools, modes of transportation) are accessible through the prefrontal cortex and other association areas (Capitani et al., 2003; Gonnerman, Anderson, Devlin, Kempler, & Seidenberg, 1997; Grossman et al., 2013; Warrington & Shallice, 1984). Regarding the progression of AD in the brain, it has a differential effect on each person affected, which might help explain why some researchers have found conflicting results on category impairments (Ralph, Patterson, & Hodges, 1997; Zannino, Perri, Carlesimo, Pasqualetti, & Caltagirone, 2002). Research conducted within the AD population has reported that the pattern of brain disruption is more of a widespread disturbance compared to other brain disorder populations, such as Semantic Dementia and Frontotemporal Dementia (Chan et al., 2001). Thus, research focused on the neuroanatomical aspect of categorical deficits have discovered a disparity by studying disorders that have more localized damage, such as HSE, Semantic Dementia (SD), or temporal lobe lesions **(**Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Gonnerman et al., 1997; Venneri et al., 2008). The impairment of categorical networks found through studying patients with AD has lead researchers to investigate the semantic network (Chan et al., 2001). Some researchers have hypothesized that this categorical semantic network has a larger span of connections than previously thought. Therefore, the widespread disruption reported in diseases such as AD may be explained better in that multiple features under a certain category have a higher chance of being damaged. For example, a patient may have once understood the features that make up a zebra, but now all those features (e.g., black and white, striped, lives in Africa, etc.) are scattered or missing, so much so the word itself is not readily available to access (Garrard et al., 1998;

Di Giacomo et al., 2012; Moss, Tyler, Durrant-Peatfield, & Bunn, 1998; Salmon et al., 1999).

Another hypothesis, the feature hypothesis, states that living and nonliving categories rely on specific types of features to properly be organized within the brain (Warrington & Shallice, 1984). More specifically, living items (e.g., animals) rely more on sensory features and less functional features whereas nonliving items (e.g., tools) show the reverse results (Moss et al., 1998; Satori & Lombardi, 2004). The sensory versus functional hypothesis states that the associations that are accessed when thinking of a living item (e.g., cat) are more sensory features that have several shared features instead of functional features. Additionally, these sensory features seem to have a more widespread association network throughout the semantic network. Therefore, these nodes are more susceptible to deteriorate than the functional features, which are less shared within the network (Moss et al., 1998; Warrington & Shallice, 1984; Zannino et al., 2006a). Nonliving items are less shared within the network because of their unique functionality often being paired with a specific task (e.g., hammer and nail) or a distinct motion (e.g., back and forth motion used with a saw). The superordinate category hypothesis presents with the idea that specific feature knowledge is more vulnerable within the semantic network than the overall category (Chan et al., 1993). Therefore, when patients attempt to access specific knowledge about animals to distinguish one from another (e.g., lion from a tiger), patients will run into an information blockage (Hodges & Patterson, 1997). These appear to be the more widely used theories and thus are the ones focused on in this study.

Each of these hypotheses contributes knowledge toward the category specific deficit with the patients with AD. To examine this deficit, semantic and lexical neuropsychological tests are given to patients with AD and the results are analyzed. One of the most popular measures used to research semantic deficits in patients with AD is the semantic decision task, which has been described by Nebes as follows:

> Here, the time a subject takes to process a stimulus is measured under two conditions: In one, the preceding item (prime) is semantically related to the item being processed, whereas in the other the prime is unrelated. Any decrease in the time needed to process a stimulus when it is preceded by a related prime in comparison with an unrelated prime is assumed to be due to a spread of activation from the related prime to the stimulus, facilitating its processing. Thus, the word *doctor* will be processed faster if it is preceded by a related prime (e.g., *nurse)* than if it is preceded by an unrelated prime (e.g., *shoe).* (Nebes, 1989, pp. 384)

The idea is that patients with deteriorated semantic networks will have a slower reaction time than nonpatient controls. For example, Giffard et al. (2001) found that when patients with AD are presented with a target word that is a living item, they have longer reaction times to the prime target task versus when a nonliving item is presented. Other methods of investigating deterioration of the semantic networks in AD include semantic fluency tasks (e.g., animal category fluency), naming to confrontation (e.g., name a specific pictured item), word associations (e.g., item most similar to another word or picture), and matching tasks (e.g., target item matched closer with one other stimuli).

Crutch and Warrington (2003) researched the performance of patients with AD on semantic fluency assessments and found that they generated more nonliving man-made items and fewer items in living categories. In addition, Marczinski et al. (2006) found that patients with AD, when compared to SD and PPA patients' performance on grocery naming fluency, produced words with higher frequency of use whereas the reverse effect was shown for the other semantic task of animal naming. Moss et al. (1998) utilized the naming to confrontation task to determine any deficits in living versus nonliving items and found that patients with temporal lobe dysfunction had greater difficulty finding specific names of living items. Alternatively, some patients with AD could access the overall superordinate category that the item pertained to (e.g., animal versus elephant) (Martin & Fedio, 1983; Rogers & Friedman, 2008).

As for matching tasks, word to word matching, picture to word matching, and picture to picture matching have been used to measure semantic memory of patients with AD (Chan et al., 1993; Libon et al., 2013). For example, Adlam et al. (2006) sought to determine if there was a difference in semantic memory between Mild Cognitive Impairment (MCI) and mild AD. They administered a variety of different modality specific matching tasks and found that the mild AD group performed worse than the MCI group on most of the matching tasks. Zannino et al. (2006b) reported that when patients are introduced to living items and asked to make a matching decision between one or more items, patients with AD are more impaired with living than with nonliving items. Yet another method, that has yet to be sufficiently explored patients with AD, is the assessment of their ability to accurately choose words that are semantically more similar than other words. Respectively, this task represents the category assessment known as

word association tasks. In these tasks, the patient is introduced to three or more words, pictures, or a mixed method and are then asked to decide amongst all the words which two of the three (or more) is the most similar (Di Giacomo et al., 2012). Research using this semantic association task indicates that patients with AD have more difficulty finding similarities in the living items when compared to healthy controls; this is potentially due to the number of features living items have opposed to nonliving items (Passafiume, Federicis, Carbone, & Giacomo, 2012). Further results indicate that nonliving items are more associated with functional features than living items (Ralph et al. 1997).

Research supports that patients with AD have a greater difficulty identifying living verses nonliving objects regardless of stimuli presentation (i.e., picture or written format) (Adlam et al., 2006). Specifically, Chan et al. (2001) examined AD and nonclinical participants by presenting pictorial stimuli in a triangular array and asking participants to identify the two out of the three that were the most alike. They found that when patients with AD were compared to nonclinical participant performance, the living (animals) stimuli performance was disrupted in the AD group, whereas the performance on the nonliving (tool) stimuli was intact (Chan et al. 2001). Passafiume et al., (2012) also investigated this phenomenon by developing a test that incorporated different levels of semantic association. They included both living versus nonliving stimuli within the context of a semantic association task and presented this task with a target picture and associated word pairings. The task is similar to that of the PPT mentioned earlier in that it is more of a matching task; however, this test incorporated different levels of association between the words and pictures that led to a more specific analysis of the data. When mild to moderate patients with AD were compared to a nonclinical sample

the results showed that there were two levels of semantic knowledge that were far more deteriorated than others: the broad categorical level and specific attributes of the items. Additionally, they could conclude that this specific deterioration was more linked within the associative links between concepts. They found that on a semantic association task the AD group was significantly more deteriorated for living stimuli than on the semantic naming task and semantic concept knowledge portion. The results of this study supported that of Chan et al. (2001).

Transitive versus Nontransitive Stimuli and Alzheimer's Disease

Performance on tests that have transitive and nontransitive items have not been studied as extensively as the categorical disparity between living and nonliving items in patients with AD. As previously stated, transitive items are stimuli that can move (e.g., car) whereas nontransitive stimuli cannot (e.g., cucumber). Research that has been conducted on this category discrepancy shows AD performance on items that are transitive is poor relative to their performance on items that are nontransitive (Chan et al., 2001). Graham et al. (2004) sought to find neuropsychological assessments most appropriate to distinguish AD profiles from other dementias and healthy control participants. Amongst all the areas tested, the semantic memory assessments resulted in tests similar to the Pyramids and Palm Trees Test (PPT) and categorical fluency both of which indicated AD impairment. The PPT is a measure that can utilize different methods of administration of the stimuli (i.e., pictorially, written, or a mixture of pictures and words) to evaluate semantic association similarities between items. The categorical fluency assessment is similar to using animal naming; however, in this study they used categories from both living and nonliving items, as well as transitive and nontransitive

items. They did not examine whether the differences in the items could have contributed to performance, but the researchers mentioned that the naming task and the semantic association task were impaired similar to the performance of the other dementia group.

Libon et al. (2013) sought further investigation into the relationship between transitive and nontransitive items. They investigated patients with AD and SD performance on a test of similarity judgments with stimuli only representative of inanimate items (e.g., tools and vegetables). They discovered that patients with SD experienced impaired performance with the natural items (e.g., vegetables) compared to the manufactured items (e.g., tools); however, the AD group did not show a distinctive difference. In this study, the researchers did not investigate the difference between transitive and nontransitive objects. Ultimately, Libon et al. (2013) noted that their findings were different from previous category specific research because they limited the stimuli to only include inanimate objects. Other studies that have included animate items (e.g., animals) have found a categorical deficit amongst living versus nonliving items, but they have not examined the difference in performance with transitive versus nontransitive items (Chan et al., 2001; Ralph et al., 1997; Zannino et al., 2002). Chan et al. (1993) chose stimuli that incorporated living (e.g., animals) and nonliving (e.g., tools) items, these stimuli were incorporated into tasks to access semantic association areas. One of their tasks, the triadic comparison task structured similar to the triangular format of the PPT, instructed the participant to indicate which two pictures out of three were the most similar. The results from this triadic comparison task revealed that the participants with AD placed the nontransitive (e.g., tool) stimuli in their correct categorical groups, whereas the transitive (animal) stimuli were far less categorically structured when

compared to the control group. Therefore, we can postulate that their findings of poorer AD performance when compared to healthy elderly on a triadic comparison task for animals (living/transitive) is indicative that there is something worth investigating.

Davis et al. (2010), sought to determine the difference of action verb fluency (transitive stimuli) compared to noun fluency (animal naming) in a population of frontal and subcortical dementias and AD. The results of this study yielded no significant difference between the two stimuli for the participants with AD. This result could be due to the use of two categories considered to be transitive in terms of movement. Other researchers' attempt to capture the effect of transitive item impairment with a patient diagnosed with a CVA, the area that causes a CVA is similar to the areas that are affected in patients with AD. In this study, they used three action verbs and asked the patient to indicate the most similar two of the three (Garcea et al., 2013). The researchers found that their patient performed worse on transitive actions but exhibited a ceiling effect with nontransitive actions. Ochipa, Gonzalez, and Heilman (1992) examined this deficit with a closer consideration of the semantic association aspect. Patients with AD were required to access tool knowledge, tool-object association, and tool mechanical use concept knowledge. The results of these three tasks showed the AD group was impaired on all three tasks when compared to a healthy control group. Ochipa et al. (1992) noted in their discussion that there is limited research to explain the reason behind the impairment within the AD group across these three-conceptual knowledge and association tasks. Additionally, they found that these tasks were impaired even when semantic language was not impaired. This finding is significant considering semantic impairment is one of

the cornerstones of AD. Further, their results strengthen the argument for investigating the deficit between transitive and nontransitive items.

Given all the studies on transitive and intransitive stimuli previously reviewed (e.g., Garrard et al., 1998; Hodges & Patterson, 1997; Marczinski et al., 2006; Zannino et al., 2002), there has not been one study that incorporates the aspects of living and nonliving stimuli in conjunction with transitive and nontransitive stimuli. Although, Fung et al. (2001) incorporated these categories in their study, they structured their test similar to the PPT, kept categorically related items in the same question, and asked participants to name the closest matched item. However, they were unable to determine actual scored results due to their measurement of only reaction time. Therefore, they reported accuracy scores, which indicated that patients with AD performed worse on the living items, but performed remarkably well on both the static and animated stimuli. They did note that this result is different from previous studies potentially due to the type of stimuli that were used.

Methods of Assessing Semantic Disturbance with Alzheimer's Disease Patients

A variety of methods have been used to assess semantic memory and each test has a different modality including naming pictured items, fluency of words, matching items, and association of words or pictures. These most commonly used neuropsychological tests include Boston Naming Test (BNT), Semantic fluency (AN), Pyramids and Palm Trees (PPT), and the Animal and Tools Triplets Test (AT; Breedin, Martin, and Saffran, 1994; Power, Code, Croot, Sheard, & Gonzalez Rothi, 2009). The BNT has been widely used, along with other assessment measures, to identify the patient's ability to accurately name line drawn items when it is presented (Strauss, Sherman, & Spreen, 2006).

Semantic Fluency (AN), often paired with the Controlled Oral Word Association Test (COWAT), measures a person's ability to name as many different exemplars within a given category under a time constraint within rule specific guidelines. Both previously mentioned tests are commonly used during neuropsychological assessments, specifically for results on semantic memory functioning (Rabin, Barr, & Burton, 2005).

Also, included in Rabin et al. (2005) was an overall compilation of most commonly used neuropsychological assessments in the United States and Canada; the use of Pyramids and Palm Trees test and Animal and Tool Triplets test were not reported. The PPT test presents patients with three items in a triangular format then asks the patient to match one of the items on the bottom row that is most closely associated with the top item. However, the normative data for the PPT originated from the United Kingdom; thus, many items are more suited for British culture (Rabin et al., 2005). Finally, the Animal Triplets test (AT) requires participants to indicate which two out of three animal pictures "went together the best". In Breedin et al. (1994) this test was altered to incorporate more Australian content for more accurate assessment of the Australian culture (Power et al., 2009). This test, in comparison to other tests reviewed, is the closest representation of what the current study is going to investigate, however, it is lacking in further research backing its reliability or validity. These tests, while useful in identification of semantic disturbance, are not comprehensive enough to adequately address all the semantic categorical issues involved in AD.

Theory of Spreading Activation and Understanding Semantic Memory

Another method of investigating semantic memory networks is by examining spreading activation. The theory of spreading activation, first proposed by Collins and

Loftus in 1975 will be useful for understanding the changes that occur in the semantic networks of patients with AD. The theory posits that semantic information is organized within a large network (e.g., food). This network is important for finding specific memories (e.g., apple) which are called nodes. These nodes are classified under specific categories within the larger network. Initial activation of a node (through either pictorial, written, or spoken stimuli) is then followed by a "spreading" of information, which activates other nodes that are semantically associated to the activated node (McNamara, 2005). The more frequently these nodes are accessed the stronger the association connection will be between nodes within the same network. Some nodes have stronger connections than others which results in a higher frequency of activation of these words together. In fact, this theory of spreading activation has often been paired with the Hebbian principle of "neurons that fire together wire together" (Foster, Drago, et al., 2013). The stronger the initial activation results in a wider net cast out to other nodes both strongly associated with the initial node and those that are less frequent but still associated directly or indirectly. Every person has a different network setup due to personal experiences and education, therefore the nodes activated for one person may not be similarly activated in another (Foster, Roosa, et al., 2013).

To provide tangible evidence in support for spreading activation most studies have used a bottom up approach. This approach is used in lexical priming research where the participants are given stimuli followed by a delay then presentation of another word, then are asked if these words are similar or different (McNamara, 2005). We seek to use a different method, one that will allow more of a free flow access of the lexical-semantic network, called the top down approach (Foster, Roosa, et al., 2013). In this study, we

will examine performance on an episodic memory task requiring participants to name words when given a specific category (e.g., animals) within a set time limit. This method of investigating spreading activation is assessed using a measure of sematic fluency (Animal Naming). With the lack of restriction for the participants we seek to identify the variability amongst their answers in direct correlation with word frequencies and how often similar words are grouped within this free flow access task (Foster, Roosa, et al., 2013). To measure the frequencies of the words produced, we will use the Kucera Francis (KF) database (Francis & Kucera, 1982). Utilization of this method allows researchers to determine how frequently a specific word is accessed when compared with other words. In addition, words with small frequencies indicate a metaphorical wide spread net of activation required to access that specific word. In contrast, words with large frequencies indicate they are accessed more frequently require less of a spread of activation. Therefore, within the context of the current research we will seek to prove that when you have two words of similar high frequency the semantic network will find this similarity easier to identify compared to words with a low or greater difference in frequencies (Collins & Loftus, 1975).

The utilization of word frequencies to determine semantic distance and the spreading activation theory aids in our hypothesis that patients with AD will not be able to conduct a mental search wide enough to access the correct information to answer the association questions. The reverse will stand true for the healthy elderly; they should be able to access their semantic network in its entirety allowing them to produce correct answers to the association questions. Power et al. (2009) provides research support relevant to the current study in that they tested healthy participant's performance on a test

of semantic association. They sought to provide a new battery of tests for assessing patients who have experienced a left CVA. This area affected by a CVA is around the same area initially affected in patients with AD, therefore this research sparked some interest in development of a similar association task for patients with AD (Etiene et al., 1998).

Research on the performance of patients with AD on semantic association tasks is similar to that of patients that have experienced left medial temporal lesion or other impairment such as a CVA (Power et al. 2009). In Power et al. (2009) they utilized the AT with normal elderly participants in order to research on a test specific for examining this temporal area of the brain. They found that the normal controls all demonstrated a ceiling effect. This specific semantic association research has not been widely studied amongst AD population, therefore given their results with healthy elderly participants we sought explore the data for further experimentation. The reason this study sparked such an interest is because of the intricacies of the semantic association network and how a healthy brain can navigate this network to provide the correct response. In patients with AD, their semantic network is already disrupted; therefore, the question remains if their semantic network is not working properly, then how is their association network functioning? As previously mentioned the area affected by CVA's is similar to that affected by AD, however this research did not do comparative data on the performance of CVA patients (Power et al., 2009). Additionally, due to previous research indicating that patients with AD have greater difficulty with animals and transitive items, this AT test would not be ethically sound to use with this group of patients.

Semantic Association Test

Given all the previous research and results, there is a clear need for a new freely available and effective test in semantic association performance with AD. There are no other tests currently available that incorporate all the categories that this new semantic test is going to incorporate. Additionally, some tests that do incorporate similar stimuli do not have normative data in the United States (U.S.). Therefore, this test will include areas that have been lower performance for patients with AD and will be able to be compared to others in the U.S. population. The Semantic Association Test (SAT) combines both living and nonliving aspects to confirm previous results of patients with AD performing better with nonliving than living stimuli (Zannino et al., 2006b). Additionally, the SAT will incorporate both moving and nonmoving items under the categories of living and nonliving, this concept is one that has not been widely researched. The word frequencies for all the words included in the SAT were obtained using the KF word frequency database. Using word frequency will provide an additional measure of the integrity of semantic networks and permit an analysis of the extent of spreading activation in semantic memory networks.

The presentation of the stimuli for the SAT will be similar to that of the previously mentioned AT test (Breedin et al., 1994) in that it will be presented in written form, three words per stimuli, and the participant will be asked which 2 out of the 3 is the most similar. Another similar test, the PPT, is also available in this written format; however, as previously mentioned this test is more of semantic pair matching than semantic associations. Several researchers have shown that association networks tend to break down later in life; therefore, it is our hypothesis that healthy elderly adults will

perform better on this SAT compared to patients with AD (Chan, Butters, & Salmon, 1997; Passafiume et al., 2012).

As far as scoring of the SAT, there are 5 total scores that are derived from this assessment. There is a total score that encompasses living and nonliving stimuli and transitive and nontransitive stimuli. There are 40 trigrams total worth 1 point each. There are 4 primary subscale score within this total score each of them is worth 10 points. There is a living scale which includes plants (nontransitive) and animals (transitive). There also is a nonliving scale which includes nontransitive items (e.g., man-made items and stones) and transitive items (e.g., transportation and tools). Correct and incorrect items are separated by varying degrees of semantic distance. The theory is that the closer the distance between the correct choices the easier it should be for control participants to identify, but for the larger distanced items the decision will become more difficult but not unachievable by the control group.

Summary and Purpose of Current Study

The previous research leading up to the current study has shown that there have been a variety of methods used to attempt to determine this specific categorical deficit seen in patients with AD. Several studies have assessed both clinical and nonclinical samples compared to AD sample groups and have come up with similar results, but all have used different methods of assessment and some even experienced ceiling effects within their sample (Chan et al., 2001; Davis et al., 2010; Passafiume et al., 2012; Power et al., 2009 and many others). If one thing was clear it is that there are categorical differences within AD groups. Patients with AD tend to show greater difficulty when presented with living versus nonliving stimuli, regardless of how the stimuli is presented.

Additionally, this group experiences greater difficulty with moving (transitive) versus nonmoving (nontransitive) items, although this research has not been investigated as extensively as the previous category (living vs. nonliving).

The purpose of the current research was to determine if healthy individuals could accurately indicate correct similarities between living and nonliving categories some with transitive and some with nontransitive features. To compare these groups, we measured the semantic distance between the correct pair of words, the larger the distance between these words indicated a larger search throughout the semantic network to find the correct similarity between the two out of the three choices. Based on previous research it was predicted that the healthy group would perform better on these items when compared to the AD group. Conversely, items with a shorter semantic distance between the two most similar words would be relatively easy for both groups because they would not have to search their semantic network as extensively. Previous research indicated that there would be a difference in performance between the categories of living and transitive for the AD group.

First, we hypothesized that the control participants would perform better than the patients with AD on the SAT. We analyzed this by comparing the total SAT scores between the AD and healthy control groups. Second, we predicted that the patients with AD would perform worse than the healthy controls on the items requiring them to indicate which two of three living items are more similar. Third, we predicted that the patients with AD would perform worse than the healthy control group on items that have transitive features.

We predicted that patients with AD would perform worse on the living items versus the nonliving items when a within group comparison was conducted. Additional analyses were conducted on the transitive and intransitive subcategories within the living and nonliving categories. We predicted that when a within group comparison was analyzed the patients with AD would perform worse on the items that are transitive versus intransitive.

We planned to investigate differences in spreading activation in semantic memory networks between patients with Alzheimer's disease and normal controls. The word frequency for each pair on the SAT were determined and a difference score was calculated. This difference score is a measure of the extent of spreading activation, with larger difference scores representing a greater extent of spreading activation. The average difference scores for all items correctly answered were then calculated for each participant and used for statistical analyses. We predicted that patients with Alzheimer's disease would exhibit lower average word frequency differences than the normal controls.

Finally, the relationship between performance on the SAT and other indices of semantic memory networks was examined. Convergent validity was verified by using two standardized assessments of semantic memory, Boston Naming Test (BNT) and Semantic fluency (Animal Naming, AN). Also, we predicted there would be a significant positive correlation between the BNT and AN with the SAT.

CHAPTER II

METHOD

Participants

A total of 53 males and females participated in this study, 29 (25 female and 5 male) healthy control participants and 24 (16 female and 8 male) AD patients were included. Table 1 summarizes the demographic information. The information collected was partly retrospective data and partly prospective data. The 24 patients with Alzheimer's disease (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). An additional 30 healthy control participants were the prospective portion of our participant group. These healthy control participants included patients' family members, staff from Middle Tennessee State University, and volunteers from churches around the Murfreesboro area contacted via flyer (See Appendix A). Ages in the control group ranged from 54 to 79 (M = 64.13, SD = 7.70). Ages in the AD group ranged from 67 to 88 (M = 78.38, SD = 5.75). Exclusionary criteria included history of significant head trauma, neurological illness, or dementia. To rule out dementia in the control group, measures of general cognitive functioning and memory were administered. Specifically, the Mini Mental Status Exam (MMSE) was used as a memory screener, any participant that scored 24 or below on this assessment was not included. The Hopkins Verbal Learning Test- Revised (HVLT-R) was used to assessed memory function, any participant that was impaired on either the

total immediate recall or the delayed portion were not included. Ultimately, there were no participants that were included in the study that met any of the exclusionary criteria.

Materials

Demographic and Medical History Questionnaire. The participants were given a form to indicate their age, education, gender, height, weight and handedness. This questionnaire also assessed for the presence of any head injury or neurological illness (See Appendix B).

Boston Naming Test – Short Form 4 (BNT-SF4; Mack, Freed, Williams, & Henderson, 1992). The BNT-SF4 is an abbreviated version of the full Boston Naming Test (BNT). Participants were shown 15 lined drawings of objects presented in an order of increased difficulty. The participants were tasked with identifying the correct name for the object in the lined drawing. Reliability of this test in healthy elderly population is .49 to .54, also on several short forms the correlations are in the moderate to high range (Strauss et al., 2006). The dependent variable was the total number of correctly identified items.

Geriatric Depression Scale (GDS; Brink et al., 1982; Yesavage et al., 1983). The GDS utilizes 30 short statements that evaluate the participant's depressive symptoms at the time of testing. This is a forced choice questionnaire requiring participants to evaluate the most descriptive choice in the given time frame. The GDS score ranges from 0 – 30, with 1 to 9 indicating no depression, 10 to 19 indicating mild depression, and score from 20 to 30 indicating severe depression. The test-retest reliabilities for this tool are .80 to .98 for elderly adults, and the validity of the GDS with other self-

assessment measures of mood is .73 - .90 (Strauss et al., 2006). The dependent variable was the total number of endorsed yes or no responses.

Hopkins Verbal Learning Test – Revised (HVLT-R; Brant & Benedict, 2001). This supra-span list learning task contains 12 words from 3 different semantic categories. This list is read to participants over three consecutive learning trials resulting in a summation score of all words recalled equaling to the total immediate recall score. Following a 20 to 25 minute delay period, participants then are asked to recall the words previously learned. The number of correct words recalled is calculated as the delayed recall score. Following the delay, the participants are read another list of words, some of which were on the list previously read, and asked to determine if the word was contained within the list or not. This assessment yields scores for learning and memory. For older adults, the reliability of the total recall is .74, delayed recall is .66, percentage of retained words is .39, and recognition discrimination is .40 (Strauss et al., 2006). The dependent variables for the HVLT-R were total immediate recall score, the delayed recall score, and the recognition score.

Mini Mental Status Exam (MMSE). The MMSE (Folstein et al., 1975) is a screening test to evaluate general cognitive functioning. The areas assessed in this screener include: orientation to place and time, attention, working memory, language, immediate and delayed recall, and construction. Participants were asked different questions within each of these areas and their scores were assessed. The scores for this test range from 0 to 30, with higher scores meaning more intact memory functioning. This tool has a test-retest reliability of .55 amongst a group of middle age to elderly adults. Also, moderate to high construct validity between the MMSE and other tests of

memory and cognitive functioning have been reported (Strauss et al., 2006). The dependent variable on this test was the total score achieved by the participant.

Semantic Fluency (SF; Strauss et al., 2006). The SF is a measure that examines participant's ability to name either as many different animals as possible or as many different fruits and vegetables as possible within a 60 second time frame. Tombaugh et al. (1999) found a reliability of .52 within an elderly population on the task of animal naming fluency. The validity of correlations between other categories (i.e., grocery store items and animals) is moderately high. The dependent variable was the total number of correct words produced during the time limit.

Semantic Association Test (SAT). The SAT is a newly developed tool created for this thesis by the thesis chair. The stimuli are presented on standard 8 x 11-inch printer paper with the words bolded, lowercase, and a 22-point font size. The individual assessment items are structured in a horizontal format with the 3 words equally spaced from each other. There are two items per page parallel to each other, centered on the page, and separated by 5 inches. Participants were instructed to look at each of the three words in front of them and point to two words out of the three that have the most in common. There was no time limit, and the instructions were repeated if the participant appeared to struggle. The SAT consists of 40 items, with 20 items in two primary categories, living and nonliving. Each of these two categories is further subdivided into two categories each. The living category consisted of plants and animals, with each subcategory consisting of 10 items. The nonliving category consisted of transitive and non-transitive items, again with 10 items each. The items are presented in a predetermined randomized order during administration. Additionally, the items were

chosen by their varying semantic distance from the other items to utilize the Kucera Francis (1982) word frequencies. The test results in a total of 5 scores: the overall score reflecting performance, the animal and plant scores that make up the living category, and the transitive and nontransitive scores that make up the nonliving category. Each item was scored either 1 point per correct response or 0 points for an incorrect score, resulting in a maximum score of 40 and minimum of 0. The living and nonliving categories separately can equal up to 20 points. To determine the spread of activation with each of the items, a difference score was calculated using the word frequencies for the 2 correct words. The difference score represents the semantic distance between the two correct items, which was an indication of the difficulty of the item.

Procedure

Following approval from the MTSU Institutional Review Board (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 were archival, existing from a previous larger neuropsychological evaluation. The control participants provided consent then were escorted to a quiet exam room within the clinic. All the assessments for the control participants were randomized by standardized procedures to minimize the effects of sequencing or carry over effects, with the SAT being given last to keep consistent with the AD group and the HVLT-R being given first to manage the delay time portion. The data for the patients with AD were existing data, and the administration order was not randomized, however in all cases the SAT for the patients was given last. Both groups provided data to analyze the SAT.

We administered the following assessments in a pseudorandomized order mentioned above. Randomized tests include: the MMSE to determine the mental status of the participant, the GDS questionnaire to evaluate their mood at time of testing administration, the BNT and the semantic fluency test, both of which are measures of semantic memory. Finally, the SAT was administered. In conclusion, the participants were verbally debriefed on the purpose of the testing.

CHAPTER III

RESULTS

Initial Analyses

To determine if any differences occurred between the groups, an initial analysis was conducted to determine if there were group differences in age, education, or depression. By utilizing three separate one way between-subjects ANOVAs ($\alpha_{FW} = .05$), we found that age $F(1,53) = 56.770$, $p = .000$, education $F(1, 53) = 12.887$, $p = .001$, and depression $F(1, 53) = 8.141$, $p = .006$ were significantly different for the AD group and the healthy control groups. Therefore, all three of these variables were used as covariates for the subsequent analyses (see Table 1).

Primary Analyses

First, we hypothesized that the control participants would perform better than the patients with AD on the SAT. To analyze this hypothesis, a one-way between groups ANCOVA ($\alpha_{FW} = .05$) was conducted. The results indicated a significant difference between the groups, $F(1, 53) = 18.477$, $p = .000$ (See Table 2). Specifically, we found that the control group answered significantly more of the SAT items correctly, which supports our hypothesis.

Second, we hypothesized that patients with AD would perform worse on the SAT's living items when compared to the control group. To analyze this hypothesis a one-way between groups ANCOVA ($\alpha_{FW} = .05$) was conducted. The results indicated a significant difference between the groups, $F(1, 53) = 16.626$, $p = .000$ (See Table 2). Specifically, we found that the control group performed better on the living items when compared to the AD group.

Third, we hypothesized that the AD group would perform worse on items that were transitive when compared to the control group. To analyze this hypothesis, a one-way between groups ANCOVA ($\alpha_{FW} = .05$) was conducted. The results indicated a significant difference between the groups, $F(1, 53) = 16.491$, $p = .000$ (See Table 2). Specifically, we found that the control group performed better on the transitive items when compared to the AD group.

Fourth, we hypothesized that the AD group would show differences in performance when the living and nonliving items were compared. Initially, we conducted correlations to determine if there were any significant correlations within the group when considering age, education, and depression. Results indicated that there was a significant correlation between education and the overall SAT score ($r = .476$, $p = .019$). Therefore, education was entered as a covariate for the subsequent analysis. To analyze our hypothesis a repeated measures ANCOVA ($\alpha_{FW} = .05$) was conducted and results showed there to be no significant difference within the AD group for the living versus nonliving variables $F(1, 22) = .117$, $p = .736$.

Fifth, we hypothesized that the overall word frequency (WF) difference scores on the SAT spreading activation would be significantly different between the AD and healthy control groups. The prediction was that the patients with AD would not have as much of a spread of activation in the semantic networks, therefore the average distance of their responses would be lower. Since we were conducting a between groups analysis and had previously reported there were significant differences of age, education, and depression between the groups, we made sure to include those as covariates. A one way between groups ANCOVA ($\alpha_{FW} = .05$) was conducted and the results indicated

significant differences between the groups, $F(1, 53) = 5.094$, $p = .028$ (See Table 2). Specifically, we found that the control group had a greater average word frequency distance, meaning a greater spread of activation than the AD group.

Lastly, we predicted a significant positive correlation between the SAT and other measures of semantic memory. To analyze this hypothesis, correlations were conducted using the entire set of participants. Results indicated that the BNT ($r = .609$, $p = .000$) and SF ($r = .374$, $p = .003$) correlate significantly, positively with the SAT (See Table 3). This statistic gives us convergent validity for this new assessment.

Secondary Analyses

As mentioned previously, there are separate subcategories within the living and nonliving categories. For our secondary analyses, we sought to determine if there were differences between the groups on the animal and plants subcategories. Therefore, we gathered the individual scores for both subcategories and conducted a between groups analysis. As with the primary analyses, using a between groups analysis we continued to control for age, education, and depression. Here, a one way between group ANCOVA ($\alpha_{FW} = .05$) was conducted and results showed that the variable SAT-A $F(1, 53) = 9.229$, $p = .004$ was significantly different between the groups. However, the variable SAT-P $F(1, 53) = 2.867$, $p = .097$, did not significantly differ between groups. Specifically, we discovered that performance on the animal variable was significantly better in the control group than the AD group.

Also, the primary analyses were conducted to determine group difference in the transitive category. We also wanted to determine if there were group differences in the

non-transitive category. The results of a one way between group ANCOVA indicated a significant difference between the groups, $F(1, 53) = 8.523$, $p = .005$.

It became apparent that there may have been a significant gender difference between the two groups. Therefore, analyses were conducted to ensure there were no significant differences with gender between the two groups. A Chi-Square (1) = 2.026, $p = .206$, was conducted and results indicated there was not a significant difference of gender between the groups.

CHAPTER IV

DISCUSSION

Semantic deterioration has been one of the main conclusions drawn from many different researchers regarding categorical deficits in patients with AD (Diaz et al., 2003; Garcea et al., 2013; Graham et al., 2004; Hodges & Patterson, 1997; Libon et al., 2013; Marczinski & Kertesz, 2006; Salmon et al., 1999; Weiner et al., 2008; Zannino et al., 2006b). Studies have been conducted using many different modalities and assessments to attempt to find the right method to assess the categorical deficits that are seen in patients with AD (Chan et al., 2001; Libon et al., 2013; Ralph et al., 1997; Zannino et al., 2002). These studies have included a mixture of stimuli from living items to nonliving and transitive to nontransitive items. Although, there has been a wealth of information regarding better performance by patients with AD on living items over nonliving items (e.g., Ralph et al., 1997; Warrington & Shallice, 1984; Zannino et al., 2002), other categories, such as transitive and nontransitive, have yet to be properly investigated.

The current study sought to further evaluate the patterns from previous studies, while providing additional data assessing new patterns of semantic deterioration. Specifically, our research supported that healthy control groups out performed AD groups on the overall SAT, which included living, nonliving, transitive, and nontransitive stimuli. Additionally, our research found that the healthy control group showed better performance with living stimuli compared to the AD group. We also found that the healthy control group showed better performance with the transitive items compared to the AD group. However, when an analysis of the within groups performance was conducted, we discovered that the AD group had no significant difference in performance

on items that were living versus nonliving. Most of research cited in this study reported findings of between group analysis and thus our findings of a nonsignificant difference within groups could be because of the stimuli that we chose to use.

Other assessments that analyzed individual differences within these categories used mainly picture naming, picture categorization, and picture matching (Gonnerman et al., 1997; Libon et al., 2013; Ralph et al., 1997). Research that utilizes pictures introduces another aspect to the stimuli with which the participant must deduce categorical similarity. The current study sought to reduce the amount of visually competing stimuli by including only written words for the items. By limiting the addition of pictorial stimuli, we hoped to accurately access the semantic association network via the semantic pathway instead of the visual association pathway. Therefore, the differences in our results could very well be attributed to the limitation of complicated stimuli.

On the analysis of spreading activation, we utilized the difference of the word frequency of the correct item pairs. We hypothesized that the items that had a greater word frequency difference would be harder for the AD group to answer correctly, and conversely, the items that had a shorter word frequency difference would be easier for both groups to answer correctly. Our results showed a significant difference between the controls and the AD group, indicating that the controls had a greater spread of activation. This was supported by other research that has indicated AD groups have difficulty searching within their semantic networks for either low frequency words or words that have a great disparity in similarity (Collins & Loftus, 1975; Foster et al., 2013; Milberg, McGlinchey-Berroth, Duncan, & Higgins, 1999). When it comes to understanding the

limitations and strengths of a certain assessment, maybe the missing key is the analysis of the spreading activation. For instance, if an individual with AD was unable to access the totality of their semantic network and the stimuli presented was outside of that mental search area, they would be set up for failure from the start. Identifying these limitations and creating assessments that help to identify specific semantic deficits known and unknown to the AD population was the ultimate goal here.

Another major purpose we sought to achieve was to develop a measure that would solve some of the limitations of other measures used for AD groups. Some of these limitations include the variations of presentation of stimuli, the use of items known to be a deficit in AD population samples, and the lack of specific semantic association tasks. Many of the assessments used in previous studies are naming, matching, or priming tasks. Our findings support that we could find differences between the two groups regarding the overall SAT. Additionally, we found differences in the specific categories of animals, transitive and nontransitive (nonliving) items. The overall implication of these findings is that we have found an assessment that will show differences in specific semantic categories between normal control groups and AD groups. Many other studies have also found differences in the performance of the two groups as we have in the current study; however, the investigation into performance between the two groups specifically breaking down of the categories into subcategories has not been conducted. Therefore, because this new assessment has been shown to support convergent validity it could be a worthy semantic assessment to utilize in diagnosing and treatment of AD. However, other studies would need to be conducted on other groups to provide other types of validity.

Further analyses were conducted that were not part of the original predictions. We sought to find the difference in the variables that were contained within the living and nonliving categories on the SAT. When a between group analysis was conducted, we found significant differences between the variables of animals, transitive and nontransitive. The findings of the transitive and nontransitive variables have been discussed previously. However, our original findings between the groups for the living items lead us to conduct additional analyses for the variables within the living category (e.g., animals and plants) between the groups. Here we found significant differences between the groups for the variable of animals but not plants; specifically, the control group outperformed the AD group on animal variable. Other researchers have utilized assessments with animals as a variable and have found significant differences in the AD group. However, this research did not conduct analyses on the different variables within their overall living category, therefore a distinction cannot be determined regarding the present research as to what overall affect the plants variable may have had (Satori & Lombardi, 2004; Zannino et al., 2002; Zannino et al., 2006).

Given all the uncertainty when a diagnosis such as AD is concerned, it is important to have all the tools to assess this disorder accessible to use. What we sought to achieve with this semantic associations test is to relate it to other semantic assessments thus contributing to the integrity of this new assessment. Additionally, we sought to have something that was simple enough to administer, yet still contributed to the current research on semantic deterioration in patients with AD. Considering all of the different findings that have been reported here, further research may seek to investigate if there is a difference in performance amongst other forms of dementia or other neurologically

affected groups (e.g., Traumatic Brain Injuries, Left Hemisphere Strokes, etc.) that also experience a semantic deficit. It would be interesting to know if this assessment was able to further differentiate not only from healthy elderly, but from other forms of dementia that may take on similar symptoms of AD.

In conclusion, the current study supported most of what previous research has reported regarding the categorical difficulties experienced by AD groups when compared to healthy controls. Some limitations of the current study were that we had to statistically control for the differences in age, education, and depression for the groups. Our entire sample, healthy controls and AD group, identified their ethnicity as Caucasian; therefore, these findings may not be applicable to another ethnic group. Additionally, we did not investigate divergent validity to assess whether performance on the SAT would distinguish between individuals with AD and other types of dementia, such as vascular dementia or Lewy body dementia. Also, while there was no suspected lack of effort seen in the healthy participants, I feel a limitation could have been the emotionally taxing environment that they were in. A depression scale was utilized, however, maybe an additional indication of situational anxiety may have been useful. Several of the patient's family members expressed great stress or sadness during the research session.

This initial study of the SAT may be important in that this measure may be used to assess semantic association deficits in patients with a wide range of neurological disorders and diseases. There is a possibility that this measure may be useful in distinguishing between different types of dementia. The SAT may also be a useful tool in investigating semantic networks in healthy, normal populations. Additionally, the results of this research provide further evidence for the breakdown of semantic associations in

patients with AD. The results indicate a general breakdown of semantic networks in patients with AD. However, an unexpected finding was the lack of any difference between the controls and the patients with AD in regard to plants subcategory. Additional research will need to be conducted to determine why networks associated with plants remain intact but networks associated with animals are impaired.

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APPENDICES

APPENDIX A

Recruitment Materials

RESEARCH PARTICIPANTS NEEDED

Psychology department at Middle Tennessee State University

Tuesday, August 01, 2017

Investigator(s): **Katelyn M. Roosa**

Study Title: ***The Semantic Association Test for Alzheimer's disease: A psychometric evaluation***

Protocol ID: **17-2249**

Expiration: **8/31/20**

Study Description

I will be conducting a study on a newly developed test that is going to aid in diagnosis and research toward patients with Alzheimer's disease (AD). Research with patients with Alzheimer's disease have documented the difficulty these people have finding words, indicating similarities between words, and even matching words to pictures. The current research is going to investigate these differences amongst 4 different categories, 2 of which have been shown to be a deficit for patients with AD. Therefore, I will present participants with paper and pencil tests that assess memory and cognitive functioning. These tests have been used for years amongst neuropsychologists to aid in diagnosis of a variety of degenerative diseases. Following this administration of approximately 13 assessments, we will present the new assessment.

Target Participant Pool

We will be seeking English speaking male and female individuals aged 55 and older. Individuals interested in participating in this research will be asked if they have experienced any traumatic brain injuries, other neurological illnesses, or diagnosis of dementia. If any of the previous medical information is present the individual will not be able to provide data we are searching for within the context of this research study.

Additional Information

This research study is being conducted for a thesis in order to fulfill requirements for a Master's degree in Clinical Neuropsychology. In addition, anyone interested in participating will be contributing to future research that can aid in diagnosis and treatment of Alzheimer's diseas. Thank you for your consideration.

Contact Information

Katelyn M. Roosa; kmr3z@mtmail.mtsu.edu

Paul S. Foster (615) 898-2007; paul.foster@mtsu.edu

INSTITUTIONAL REVIEW BOARD

Middle Tennessee State University, 2269 Middle Tennessee Blvd, Murfreesboro, TN 37129

URL: www.mtsu.edu/irb – Tel: 615 898 2400 – Email: irb_information@mtsu.edu

APPENDIX B

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 meds for depression or anxiety?

If yes then explain. What meds?

APPENDIX C

MTSU IRB Approval Letter

Tuesday, August 01, 2017

Principal Investigator Katelyn M. Roosa (Student)

Faculty Advisor Paul Foster

Investigator Email(s) kmr3z@mtmail.mtsu.edu; paul.foster@mtsu.edu

Department Clinical Psychology

Protocol Title: The semantic association test for Alzheimer's disease: A psychometric evaluation

Protocol ID 17-2249

Dear Investigator(s),

The above identified research proposal has been reviewed by the MTSU Institutional Review Board (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 and other particulars in regard to this protocol application is tabulated as shown below:

IRB Action APPROVED for one year from the date of this notification Date of expiration 8/31/2018 Participant Size 100 (ONE HUNDRED) Participant Pool Normal healthy adult individuals (18+ in age) Exceptions Allowed to use existing medical data collected as part of the FA's routine evaluation (Expedited Category 5: Research with materials).

Restrictions 1. Mandatory signed informed consent. 2. NO Identifiable information must be collected or recorded.

Comments The protocol involves two procedures: 1. Use and analysis of existing medical data collected for non-research purposes; and, 2. Recruit and collect comparative data from healthy individuals for data analysis.

This protocol can be continued for up to THREE years (8/31/2020) by obtaining a continuation approval prior to 8/31/2018. Refer to the following schedule to plan your annual project reports and be aware that you may not receive a separate reminder to complete your continuing reviews.

Failure in obtaining an approval for continuation will automatically result in cancellation of this protocol. Moreover, the completion of this study MUST be notified to the Office of Compliance by filing a final report in order to close-out the protocol.

Continuing Review Schedule: Reporting Period Requisition Deadline IRB Comments First year report 7/31/2018 TO BE COMPLETED Second year report 7/31/2019 TO BE COMPLETED Final report 7/31/2020 TO BE COMPLETED

Post-approval Protocol Amendments: Date Amendment(s) IRB Comments NONE NONE NONE

The investigator(s) indicated in this notification should read and abide by all of the post-approval conditions imposed with this approval. Refer to the post-approval guidelines posted in the MTSU IRB's website. Any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918 within 48 hours of the incident. Amendments to this protocol must be approved by the IRB. Inclusion of new researchers must also be approved by the Office of Compliance before they begin to work on the project.

All of the research-related records, which include signed consent forms, investigator information and other documents related to the study, 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 storage must be maintained for at least three (3) years after study completion. Subsequently, the researcher may destroy the data in a manner that maintains confidentiality and anonymity. IRB reserves the right to modify, change or cancel the terms of 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

APPENDIX D

Informed Consent

Principal Investigator: Katelyn M. Roosa

Study Title: The Semantic Association Test for Alzheimer's disease: A psychometric evaluation

Institution: Middle Tennessee State University

Name of participant: _____ Age: _____

The following information is provided to inform you about the research project and your participation in it. Please read this form carefully and feel free to ask any questions you may have about this study and the information given below. You will be given an opportunity to ask questions, and your questions will be answered. Also, you will be given a copy of this consent form.

Your participation in this research study is voluntary. You are also free to withdraw from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to participate in it, you will be notified so that you can make an informed decision whether or not to continue your participation in this study.

For additional information about giving consent or your rights as a participant in this study, please feel free to contact the MTSU Office of Compliance at (615) 494-8918.

1. **Purpose of the 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.

2. **Description of procedures to be followed and approximate duration of the study:**

   If you agree to participate, a battery of standardized neuropsychological tests assessing memory and cognitive functioning, mood characteristics, and a demographic questionnaire will be administered. Following this battery, we will conclude the assessment with the administration of the newly developed test. There will be no time limit for this assessment. However, the duration of the study will be between 45 minutes to 1 hour.

3. **Expected costs:**

   There are no costs for participation.

4. **Description of the discomforts, inconveniences, and/or 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.

5. Compensation in case of study-related injury:

MTSU will not provide compensation in the case of study related injury.

6. Anticipated benefits from this study:

a) The potential benefits to science and humankind that may result from this study are that we gain further understanding to help assess and diagnose the unique deficits seen in degenerative diseases such as Alzheimer's disease. The subtle differences that separate Alzheimer's disease from other dementias are well documented, but few encompass all the factors we seek to investigate with this new assessment.

b) The potential benefits to you from this study are gaining a better understanding of how research is conducted. As well as, contributing to research that is new to this field.

7. Alternative treatments available:

N/A

8. Compensation for participation:

N/A

9. Circumstances under which the Principal Investigator may withdraw you from study participation:

Non-compliance with the study procedures, or failure to follow instructions. Also, you may be withdrawn if you have any history of traumatic head injury, neurological illness, or are taking psychotropic medication.

10. **What happens if you choose to withdraw from study 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. The participants may choose to withdraw from the study at any point.

11. **Contact Information.** If you should have any questions about this research study or possible injury, please feel free to contact Katelyn M. Roosa at (931) 409-9347 or my Faculty Advisor**,** Paul S. Foster at (615) 898-2007.

12. **Confidentiality.** All efforts, within reason, will be made to keep the personal information in your research record 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.

13. **STATEMENT BY PERSON AGREEING TO PARTICIPATE IN THIS STUDY**

I have read this informed consent document and the material contained in it has been explained to me verbally. I understand each part of the document, all my questions have been answered, and I freely and voluntarily choose to participate in this study.

_____ _____

Date Signature of patient/volunteer

Consent obtained by:

_____ _____

Date Signature

_____

Printed Name and Title

APPENDIX E

TABLES

Table 1

Descriptive Statistics for Groups

Variable	Control Group (n = 30)		AD Group (n = 24)	
	M	*SD*	*M*	*SD*
Age	64.13	7.70	78.38	5.75
Years of Education	15.37	2.83	12.58	2.83
MMSE	29.27	0.78	20.46	4.72
GDS	4.2	5.33	9.88	3.93
AN	21.03	4.94	9.17	2.70
BNT	14.37	0.96	8.50	5.72

Table 2

Descriptive Statistics and ANCOVA Results for Between Group Analysis when Controlling for Age, Education, and Depression

Variable	Control group (n = 30)		AD group (n = 24)		Results
	M	*SD*	*M*	*SD*	
SAT	36.03	1.83	29.71	4.66	F (1, 53) = 18.477, p = .000
SAT-L	17.67	1.54	14.63	2.90	F (1, 53) = 16.626, p = .000
SAT-NL	18.37	1.00	15.13	2.36	F (1, 53) = 10.128, p = .003
SAT-T	9.5	0.68	7.79	1.28	F (1, 53) = 16.491, p = .000
SAT-NT	8.87	0.86	7.33	1.37	F (1, 53) = 8.523, p = .005
SAT-A	9.43	0.86	7.83	1.49	F (1, 53) = 9.229, p = .004
SAT-P	8.23	1.25	6.75	2.17	F (1, 53) = 2.867, p = .097
SAT-Corr	19.88[1]	1.05	19.67[2]	1.89	F (1, 53) = 5.094, p = .028

Note. Possible range of scores for each category: SAT 0 – 40; SAT-L, SAT-NL, SAT-T, SAT-NT 0 – 20; SAT-A and SAT-P 0 – 10.

[1]SAT-Corr scores range 18.1 – 22.1

[2]SAT-Corr scores range 17 – 23