Lexical and Semantic Spreading Activation in Mild to Moderate Alzheimer's Disease

By

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ABSTRACT

The current study investigates potential significant differences in spreading activation within semantic networks in a sample of patients diagnosed with mild Alzheimer's Disease (AD), moderate AD, and normal, healthy controls. Prior research on spreading activation in semantic networks has used previously developed corpora that are either outdated and/or derived from various media materials (e.g., books, film, television). We developed a new corpus from participant responses to the Controlled Oral Word Association Test (COWAT) and the Animal Naming (AN) test to subsequently calculate the word frequencies of the responses from patients with mild AD, moderate AD, and controls to the same tests. Results indicated reduced spreading activation in the moderate AD group with relative lexical network preservation across all three groups. These results support known AD pathology with a degradation of semantic networks as the disease progresses through the entorhinal cortex. Implications and future directions are discussed.

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CHAPTER I

INTRODUCTION

Alzheimer's Disease (AD) is marked by the well-known phenomena of the degradation of semantic networks (Salmon et al., 1999; Nebes, 1989). Semantic networks are commonly investigated through naming to confrontation, verbal fluency, and semantic priming paradigms. All three of these methods have clinical and/or research utility outside of the scope of this study with typical utilization in language deficits and semantic fluency/access in the context of other mental disorders or cognitive processes (Basso et al., 1990; Marshall et al., 2018; Minzenberg et al., 2002). Each of these methods will be discussed in their respective contexts with Alzheimer's Disease and semantic networks and/or spreading activation.

Regarding naming to confrontation tasks, the degradation of semantic networks can be investigated through a bottom-up approach in which the patient is given the stimulus. On these tasks, patients with AD showed impaired performance when compared to normal, healthy controls and patients with amnestic mild cognitive impairment (aMCI; Balthazar et al., 2008; Lin et al., 2014). AD patients showed an increase in accuracy after a phonemic cue, but the same increase was not seen after a semantic cue (Lin et al., 2014), which further bolsters the breakdown of semantic networks as a cornerstone of Alzheimer's Disease.

Another method of investigation is measuring performance on verbal fluency tests through semantic and lexical lenses. Lexical fluency tests present the patient with a single letter and ask the patient to generate as many words as they can beginning with that letter.

Semantic fluency tests work in a similar fashion, but present the patient with a category (e.g., animals). Patients with early AD and amnestic mild cognitive impairment showed more impairment in semantic fluency tests than lexical fluency tests indicating a relative preservation of lexical networks (Lonie et al., 2009). The category used for the semantic test can have an effect on performance. One study used four noun (articles of clothing, vegetables, vehicles, animals) and four verb categories (preparing food, playing sports, construction, cleaning up) to compare mild and moderate AD with normal, healthy controls (Pekkala, 2004). They found variation in responses for the healthy controls and the mild AD group, with the animal category producing significantly more words, but no difference was found in moderate AD across categories. Comparisons of performance between groups revealed poorer performance of the mild AD group than the NC group, but better performance than the moderate AD group across semantic fluency tasks (Pekkala, 2004). A similar result was found in a study using 14 semantic categories, seven living and seven nonliving, and found the most profound impairment in the animal subcategory (Moreno-Martinez, 2008). Patients with AD consistently show impairment on semantic fluency tasks, with some regard for category used depending on the level of dementia severity.

Semantic priming paradigms are another common tool for studying semantic memory, specifically spreading activation. The theory of spreading activation labels semantic memories as nodes which are organized into a larger conceptual network. Nodes are organized within their conceptual network based on similarity. The more properties two nodes share, the more connected they are within their network (Collins & Loftus, 1975). When a node is activated, that activation can spread in a parallel fashion to

surrounding nodes within the same network. The more interlinked two nodes are, the more likely one will activate the other (Kumar et al., 2021). Spreading activation can then be measured by comparing reaction times in a semantic priming task (Lin et al., 2014).

Semantic priming paradigms differ from verbal fluency tasks in that it relies on bottom-up processing instead of top-down, in which words are provided to the patient rather than asking them to generate their own (Foster, 2013). Semantic priming paradigms differ from naming to confrontation tests in that it can assess spreading activation in semantic networks. The literature surrounding the efficacy of semantic priming paradigms when measuring performance in patients with AD is exceedingly conflicted. Results have found less-than-normal priming, equivalent priming, and hyperpriming (Hartmann, 1991; Nebes et al., 1984; Ober & Shenaut, 1988). Giffard et al. (2005) delineates the potential reasons for the discrepancies found in the literature to be inconsistent experimental designs, level of semantic structure, severity of dementia, degree of semantic impairment, and other cognitive disturbances. After considering these variables, the authors claim the previously contradictory results point to similar effects.

Given these three methods for investigating semantic network degradation, they each have respective strengths and weaknesses. Naming to confrontation is most appropriate when the study is focused on solely semantic network degradation in explicit memory implementing a bottom-up approach (Melrose et al., 2009). Verbal fluency tasks utilize a top-down approach to investigate the integrity of semantic networks which may more accurately assess the natural process of the patient and increase ecological validity of the study (Foster et al., 2013). This type of test alone, however, cannot assess spreading activation. Semantic priming paradigms look at the extent of spreading

activation in implicit memory in which the words are provided to the patient. The bottom-up approaches (naming to confrontation and semantic priming) are artificial in that they give the patient stimuli to then access semantic networks, whereas the top-down approach (verbal fluency) has access to the spontaneously generated semantic network of the patient after requiring the patient to come up with their own words (Foster, 2013). None of these approaches, however, can accurately assess the integrity of semantic networks and spreading activation implementing a top-down approach, hence the need for a new approach.

We propose implementing the Controlled Oral Word Association test (COWAT; Benton et al., 1983) and the Animal Naming test (AN; Goodglass & Kaplan, 1972) to investigate spreading activation in lexical and semantic networks. The patient will have 60 seconds to generate as many words as possible within the given semantic/lexical category. The word frequency is then averaged to measure the extent of spreading activation. Higher word frequency indicates reduced spreading activation and lower word frequency would indicate greater spreading activation. This method has been used to measure spreading activation in Parkinson's Disease (Foster et al., 2008), Alzheimer's disease (Foster et al., 2013), depression (Foster et al., 2011, patients with dementia on or off of acetylcholinesterase inhibitors (Foster et al., 2012), and as spreading activation relates to recall of word lists (Foster et al., 2013).

Review of Literature

Many of the memory and cognitive problems linked to Alzheimer's disease (AD) are caused by the well-known phenomena of the degradation of semantic networks. Currently, the most common methods of investigating this semantic disruption are

naming to confrontation, verbal fluency, and semantic priming paradigms. Outside of investigating semantic network degradation, naming to confrontation tests have been used to investigate aphasia, perceptual reasoning, and localization of language deficits in research and clinical settings (Basso et al., 1990; Hermann et al., 1999; Soble et al., 2016;). Verbal fluency tests have been used to investigate cognitive impairment, language deficits in deaf children, depression induced cognitive impairment, and aphasia in research and clinical settings (Bose et al., 2017; Crawford et al., 1992; Marshall et al., 2018; Ravdin et al., 2003;). Lastly, semantic priming paradigms, outside of semantic network degradation in AD, have been used to investigate schizophrenia, sleep stages, and attention and memory in depression (Brualla et al., 1998; Matthews & Southall, 1991; Minzenberg et al., 2002;). The majority of these clinical and research implementations involve language deficits and/or semantic fluency/access in the context of a mental disorder or cognitive process.

Confrontation to Naming

Regarding confrontation naming tests, their utility in assessing language deficits is widely agreed upon as they are incorporated into the majority of standard language batteries (e.g., Boston Diagnostic Aphasia Examination, Multilingual Aphasia Examination; Hermann, 2006). The Boston Naming Test is the most commonly used confrontation to naming test (Raymer, 2017). It is a naming vocabulary test ranging from easier items to subsequently more difficult items. The patient is presented with a line drawing and asked to name the picture. A phonemic cue is provided when the patient cannot name the line drawing, though these instances are not scored. A stimulus cue is provided when the patient misperceives the item and these instances are counted toward

the final score. Finally, if the patient still does generate the correct response, the patient is provided with a choice of four options to then pick the correct response (Kaplan et al., 1983). The semantic network degradation seen in Alzheimer's Disease is expected to manifest as impaired performance on confrontation naming tests.

According to Lin et al, patients with mild to moderate AD performed worse on the Boston Naming Test (BNT) when compared to normal, healthy controls (NC). Alzheimer's disease patients in this study also showed lower accuracy rate after a semantic cue than the NC groups, but both groups showed increased accuracy following a phonemic cue (2014). A similar trend was found when comparing patients with mild AD, patients with aMCI, and a NC group. The mild AD group showed impaired performance on spontaneous naming and after semantic cues than the aMCI group and NC group, but there was no significant difference between the groups after phonemic cues. This result led the authors to conclude that the degradation of semantic networks must not be the only contributor to the impaired performance on the BNT shown by AD patients (Balthazar et al., 2008).

Additionally, a longitudinal investigation into performance on a confrontation naming task (BNT), a letter verbal fluency task (FAS), and a written discourse task (Cookie Theft Picture) compared patients with neuropathologically determined AD and patients without criteria for AD. They found a significant decrease in performance of the AD group with the written discourse task 7-9 years before death, but impaired performance in the other two tasks was only seen 2-4 years before death, leading the authors to conclude lexical-retrieval deficits in written discourse could be contributing to the language impairments seen in the progression of AD and be detected earlier than the

other deficits shown (Pekkala et al., 2013). Combining the conclusions of the two aforementioned studies points to a weakened ability of AD patients' semantic networks in accessing or activating the phonological lexicon.

Another potential contributing factor was a visual perceptual deficit, but this hypothesis was disproven by Smith and colleagues (1989). They investigated the types of errors committed by patients with AD during a confrontation naming task and found that the patients could recognize objects and identify their semantic class but could not provide the name of the object (Smith et al., 1989). This further supports a semantic network disruption and lexical-retrieval deficits as contributors for the shown impaired performance of AD.

The stages in lexical retrieval outlined by Freidman et al. (2013) indicate the first stage as the formation of a conceptual system which involves the representation of the concept without words. This non-lexical concept continues on and activates the semantic lexicon which stores words and the information necessary to attribute accurate meaning to the word, such as categorical identifiers and semantic properties. Once the semantic representation is selected, the phonological output lexicon is activated in which the information about the verbal formation of the word is stored, such as the metrical information (e.g., syllable structure and stress pattern) and segmental information (e.g., discrete phonemes; Roelofs & Meyer, 1998). Once the information is gathered, it is stored in the phonological output buffer where it remains active until the buffer fully composes the word by inserting the phonemes into the metrical frame and the word is fully produced (Friedman et al., 2013). The breakdown of communication between these three stages of word production explains the contribution of both semantic network

degradation and lexical retrieval deficits for impaired performance of AD patients on naming confrontation tests.

Verbal Fluency

The breakdown of semantic networks in the AD population has also been investigated through performance on verbal fluency tests. Verbal fluency tasks assess language abilities and executive functioning by requiring the patient to generate orally or physically produced words, usually in a specified time (Alegret et al., 2018). One can expect impaired performance on the semantic tests as a result of impaired semantic networks, with relatively preserved lexical performance (Foster, 2013). When comparing lexical and semantic fluency in patients with early AD and aMCI with NC and depressive groups, AD and aMCI patients show a greater impairment in semantic fluency than lexical fluency (Lonie et al., 2009). The semantic impairment shown by AD patients in verbal fluency tests is not consistent across all contexts and variables, however.

Performance on semantic fluency tests can vary based on the type of dementia and the type of category being used in the task. According to Davis et al. (2010), when comparing patients with cortical dementia (e.g., AD), subcortical dementia (e.g., normal pressure hydrocephalus), and dementias mainly affecting the frontal cortex (e.g., behavioral variant frontotemporal dementia and progressive nonfluent aphasia), the AD patients showed impaired performance on the noun fluency test and on the action fluency test. The patients with normal pressure hydrocephalus, behavioral variant frontotemporal dementia, and progressive nonfluent aphasia performed better than the AD group on noun fluency but performed worse than AD on action fluency. The authors concluded that action fluency must rely more on frontal-subcortical connections and noun fluency must

rely more on the temporoparietal cortex (Davis et al., 2010). The poor performance of AD patients on both tasks in this study points to the overall issue of lexical-retrieval deficits and semantic network breakdown, regardless of the semantic category.

Other investigations have employed different types of semantic categories to investigate fluency, including both living and nonliving categories. One study used four living categories (animals, fruits, birds, dog breeds) and four nonliving categories (household items, tools, vehicles, types of boat) in a semantic memory battery to compare performance between vascular dementia patients and patients with AD (Graham et al., 2004). The category fluency task was combined with two other tasks (naming task and word-picture matching task) to comprise the semantic memory battery. The AD patients showed significantly worse performance on the category fluency task than they did on the other two tasks in the battery but did not show significantly more impairment than the patients with vascular dementia. The patients with vascular dementia showed significantly worse performance on all of the tasks in the semantic battery. No further analysis was reported on the differences of impairment between the different categories (Graham et al., 2004). Even though the authors did not report any specific analysis between categories, it is important to note the isolated impaired performance of the AD patients on the category fluency task as a whole compared to the rest of the battery.

Semantic fluency in mild and moderate AD was investigated using four noun categories (articles of clothing, vegetables, vehicles, animals) and four verb categories (preparing food, playing sports, construction, cleaning up; Pekkala, 2004). There was no difference found in the number of words produced across categories for moderate AD, but the mild AD patients and the NC groups showed variation in the number of words

produced across categories, with animals being the most productive. Furthermore, performance was broadly analyzed and compared between the groups. The mild AD patients performed poorer than the NC group, but better than the moderate AD group across semantic fluency tasks (Pekkala, 2004). Moreno-Martinez et al. (2008) used 14 semantic subcategories of which seven were living (animals, body parts, insects, flowers, fruits, trees, vegetables) and seven were nonliving (buildings, clothing, furniture, kitchen utensils, musical instruments, tools, vehicles) to investigate age and sex differences in performance on a semantic fluency task. AD patients were impaired across all subcategories, with the most profound impairment being shown in the animal subcategory (Moreno-Martinez et al., 2008). A longitudinal study focusing on verbal fluency in NC, preclinical AD, and prevalent AD, found steeper impairment in animal fluency in preclinical AD and prevalent AD than letter fluency as time progressed (Clark et al., 2009). Across all of the previously discussed studies, the most appropriate semantic category to implement appears to be animals. If there is a difference between categories found, the animal category is the most sensitive and productive (Clark et al., 2009; Moreno-Martinez et al., 2008; Pekkala, 2004). As concluded by several of the previous studies, patients with AD perform significantly worse on semantic fluency tests (e.g., animals) than lexical or phonemic fluency tests as a result of impaired semantic networks.

Semantic Priming

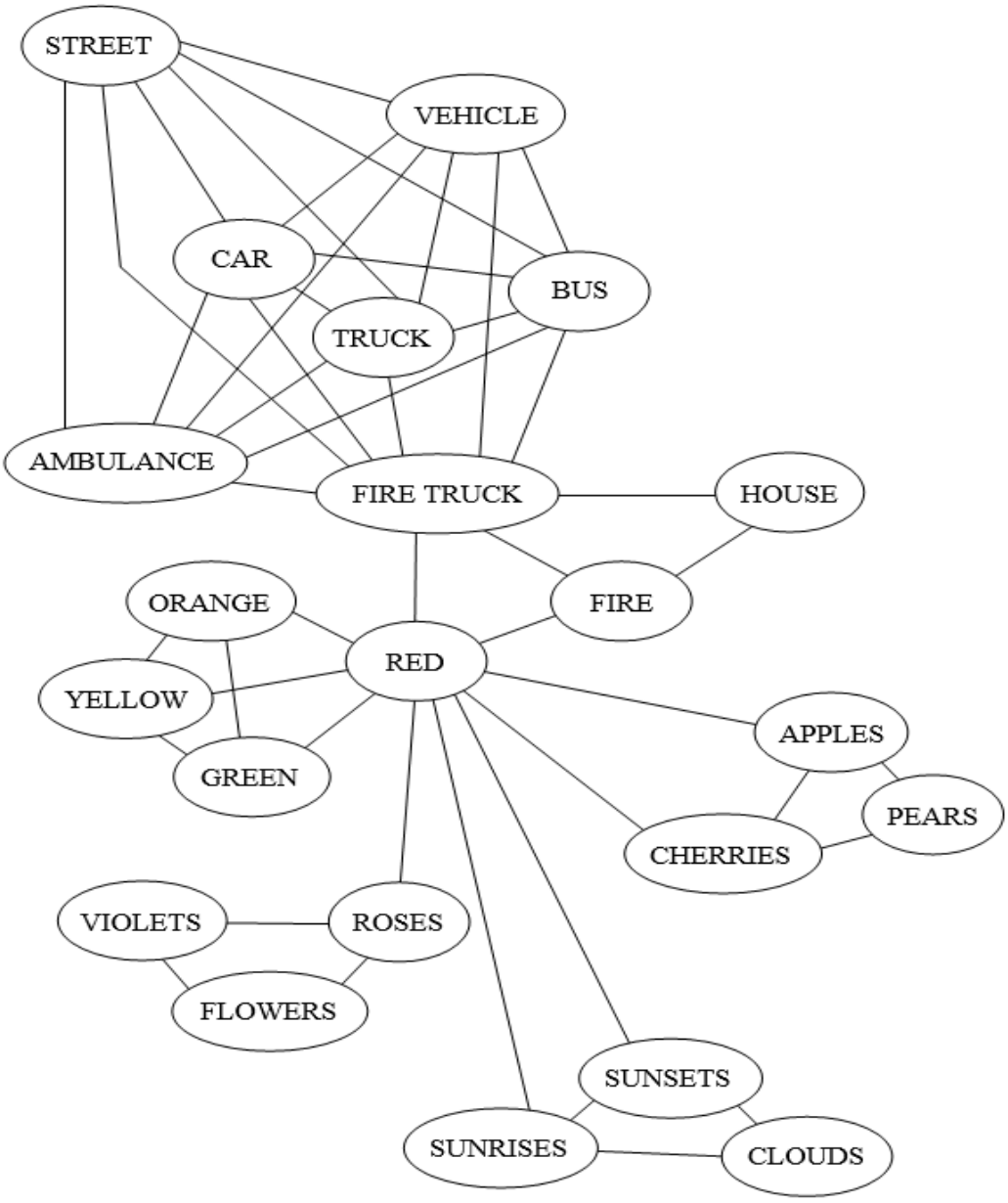
Semantic priming paradigms are another commonly used tool for investigating semantic memory. Specifically, these paradigms are especially useful in studying spreading activation within the semantic memory networks. The initial theory of spreading activation was developed to introduce human semantic structure and

processing into a computer. This early theory, as noted by the author, had psychologically unrealistic constraints as it primarily focused on the theory in computer terms, rather than psychological terms (Quillian, 1967). Collins and Loftus (1975) expand on Quillian's theory implementing psychological terminology while preserving the assumptions and basic theory previously laid out.

Specific semantic memories, such as fire engine, are organized into a larger semantic network symbolizing the concept, such as vehicles. These memories are represented as nodes within the larger conceptual network of vehicles and organized based on similarity and interconnectedness between nodes and concepts. As properties in common increase between two nodes or concepts, their interconnectedness increases as well, interlinking the two nodes or concepts within their semantic network. Nodes or concepts could have properties in common, but not be interlinked as they are not closely associated outside the shared property (e.g., fire engine and cherry). Therefore, one must take into account the aggregate interconnectedness and similarity between two concepts (Collins & Loftus, 1975). Strength of the links between nodes within a network can range from relatively weak (e.g., fire engine and bicycle) to relatively strong (e.g., fire engine and ambulance). Activating a node in a semantic network is then proposed to spread in a parallel fashion to other nodes comprising the same network. The more interconnected two nodes are, the more likely the activation will spread from one to the other (Kumar et al., 2021). See Figure 1, which was developed specifically for this study, for a partial

illustration of the semantic network for fire truck.

Figure 1. *Semantic network of the word "fire truck".*



The strength of the association is partly determined by the frequency of use of the link between the two nodes or concepts. The authors referred to this as production

frequency norms (Collins & Loftus, 1975). This relationship can be seen in an experiment by Loftus in which the participant was primed with a letter and category or with an adjective or a category and the subsequent reaction time was recorded. Some trials gave the category before the letter or adjective and in other trials the letter or adjective was given first. They found that participants reacted quicker when the category was introduced first in the task. This result can be explained by the spreading activation theory laid out previously. When primed with a category (e.g., fruit), highly interconnected nodes are activated (e.g., apple, orange, peach) within a relatively small, interlinked conceptual network. When primed with a letter or adjective (e.g., "A" or sour), however, the activation spreads to a much wider set of concepts that do not necessarily have strong associations with each other. Therefore, with such a large number of concepts that could be activated by the letter or adjective prompt, the priming advantage dissipates and results in a slower reaction time (Collins & Loftus, 1975).

Semantic priming paradigms differ from the other two previously mentioned investigative methods by relying on implicit memory instead of explicit memory, as well as being able to ascertain spreading activation (Foster et al., 2013). While this method can measure spreading activation, the effect semantic priming has on performance in AD patients has not been concretely established.

Semantic priming paradigms also have varied results in the literature and are conflicting in the effect priming has on patients with AD (Giffard et al., 2005). Some studies have found less-than-normal priming in AD, some have found equivalent priming, and some have found hyperpriming in AD when compared to NC groups. Less-than-normal priming was found when patients with probable AD were equally slow at

making lexical decisions whether the target word was related or not. The control group, however, showed a facilitatory effect of semantic primes (Ober & Shenaut, 1988). Silveri et al., found a similar effect with AD patients showing a weaker priming effect on a lexical decision task than the NC groups (1996). Equivalent priming effects in AD have also been found between a demented group and NC group. Both groups showed an equally facilitatory semantic priming effect on naming latency during a semantic memory test (Nebes et al., 1984). Another study compared semantic priming facilitation between mild AD patients, NC, and semantic dementia patients (SD. Priming effects were shown in the AD group and NC group, but not in the SD group (Nakamura et al., 2000). Lastly, paradoxical priming (hyperpriming) has also been seen in patients with AD. Nebes et al. found significantly greater semantic priming facilitation in the AD group than a young NC group or an old NC group conflicting with the previously delineated studies (1989a). AD patients also showed a larger facilitation effect compared to NC groups in a study by Hartmann, with the effect most observable in AD patients with longer naming latencies (1991). With such a wide discrepancy found regarding the effect semantic priming has on AD patients, other variables must also be influencing performance on these tests.

According to Giffard et al. (2005), these contradictory results could be a product of inconsistent experimental designs and several confounding variables including the level of semantic structure, the severity of dementia, the degree of semantic impairment, and other cognitive disturbances (e.g., attentional deficits). Semantic priming effects are especially sensitive to experimental variations and can cause the participant to develop attentional strategies, such as the expectancy mechanism. Once the participant understands the task at hand and they have successfully responded correctly to their

priming target, they can attempt to guess at what the next priming target might be and start to activate potentially associated nodes. The expectancy mechanism facilitates the patient's processing of expected or guessed targets but inhibits processing if the target is unexpected or incorrectly guessed. Levels of semantic organization is another important variable to consider when reviewing the conflicting literature surrounding semantic priming paradigms (Giffard et al., 2005). As mentioned previously by Smith et al., patients with AD have the ability to recognize the semantic class of a presented object during a naming confrontation task but have impaired ability when it comes to naming the object (Smith et al., 1989). A similar result was found by Glosser et al, in which different semantic relationships were used to measure semantic priming effects. They used pairs of coordinate words (e.g., table-desk) and pairs of superordinate/subordinate words (e.g., furniture-table). There was a hyperpriming effect found with the superordinate/subordinate pairs and a suggested impairment for the coordinate pairs, suggesting the level of semantic organization could significantly affect priming results (Glosser et al., 1998). Lastly, the severity of dementia is a critical factor to consider. A longitudinal investigation by Chertkow and Bub (1990) found hyperpriming effects at the initiation of the study, but as it progressed over 18 months, the priming scores continued to fall as the AD worsened. Given the small sample size, four patients with AD, these results are far from conclusive, but are informative for the heterogeneity of the literature. According to Giffard et al. (2005), once these delineated confounding variables are considered, the previously contradictory results point to similar effects.

Strengths and Weaknesses

Each of the aforementioned methods of investigating semantic network degradation is associated with various strengths and weaknesses. Naming to confrontation tests are widely used in research and clinical settings. This is an appropriate method of investigating semantic networks if the objective is to assess the degradation of semantic networks in explicit memory using a bottom-up approach (Melrose et al., 2009). However, naming to confrontation relies on cues given to the participant and their subsequent performance and precludes any potential spreading activation measure (Lin et al., 2014). Without requiring the patient to spontaneously generate responses, spreading activation is difficult or even impossible to ascertain. Verbal fluency tests are another commonly used approach to investigate semantic memory networks in both clinical and research settings (Foster et al., 2013). The advantage of this approach is that it uses a top-down approach in requiring the patient to generate responses. The use of a top-down approach has more ecological validity since the patient generates their own stimuli as opposed to the stimuli being provided to them (Foster et al., 2013). However, verbal fluency tasks are not capable of assessing the extent of spreading activation. Finally, semantic priming paradigms have the advantage of being able to measure the extent of spreading activation within semantic memory networks and therefore provide an assessment of the integrity of these networks (Giffard et al., 2005). However, as with naming to confrontation, this method also uses a bottom-up approach and thus limits the ecological validity of the test. Additionally, semantic priming paradigms are used within research settings as these approaches are not readily

amenable to clinical use (Foster, 2013). Given the research question of this study, none of these three approaches are appropriate, hence the need for a new method.

A New Approach

A newer approach to investigate the integrity of semantic networks is to calculate word frequencies from the words generated on verbal fluency tasks. This method has the advantage of being a top-down approach for assessing semantic memory networks and is also capable of assessing the extent of spreading activation. The Controlled Oral Word Association Test (COWAT; Benton et al., 1983) is a measure of lexical fluency that requires the patient to generate as many words as they can beginning with a given letter within 60 seconds. The Animal Naming (AN; Goodglass & Kaplan, 1972) test is a measure for semantic fluency by requiring the patient to come up with as many names of animals as they can within 60 seconds. To measure the extent of spreading activation the word frequency for each response is then averaged, with the word frequencies being determined by corpora such as the Francis and Kucera (1982) and the Brysbaert and New (2009) corpora or by a newly developed corpus.

Averaging the word frequencies of patients and subsequently comparing them to a word frequency corpus measures spreading activation (Foster et al., 2013). As previously stated by Collins and Loftus, associated nodes within a conceptual network should have increased interconnectedness with increased frequency of use (1975). Therefore, higher frequency words should in turn have higher connectivity with other words in the network through stronger associations and more associations. Lower frequency words, however, should have weaker associations and fewer associations with other nodes in the network. To activate a lower frequency word a greater spreading activation is necessary due to the

lack of interconnectedness. Furthermore, if spreading activation is increased, one would expect a higher occurrence of lower frequency words on the COWAT and AN test and decreasing spreading activation would cause a higher occurrence of higher frequency words (Foster, 2013).

Using the COWAT as a measure of spreading activation is supported by the results of research implementing lexical decision tasks. These studies indicated a significantly quicker reaction time for higher frequency words than for lower frequency words bolstering the use of a timed semantic fluency test to assess spreading activation. A longer reaction time indicates a lower frequency word, which in turn indicates greater spreading activation to access the word (Allen et al., 1992). This method has been used to measure spreading activation in numerous different patient populations. A version of this method was used in a German study focusing on spreading activation in Parkinson's Disease patients on and off of dopaminergic medication (Tiedt et al., 2022). This has also been used to measure spreading activation in depression by combining performance on the COWAT and AN with results from the Beck Depression Inventory (BDI-II) in a college student population (Foster, 2011). Lastly, this method has been used to measure spreading activation in patients with dementia on or off acetylcholinesterase inhibitors (Foster, 2012). The COWAT is an appropriate tool to assess spreading activation based on the previously mentioned research.

Approaching semantic memory from a top-down strategy can be achieved by measuring spreading activation using word frequencies from verbal fluency tasks, such as the COWAT and AN test. Implementing a top-down approach by having the patient generate their own words allows for a more "natural" flow of spreading activation. Using

this method avoids some of the issues from semantic priming paradigms like the inconsistent experimental variations that semantic priming effects are particularly sensitive to. Due to the inconsistency seen in priming paradigms, the approach is not clinically amenable. Without the constraint from experimental methodologies, ecological validity may increase as well (Foster, 2013).

This study is an extension of a previous study done by Foster et al. (2013), additionally examining the difference in performance between mild and moderate AD on lexical and semantic fluency tests. We developed a new corpus in order to update from previously used options such as the Francis-Kucera and American Heritage corpora, which are between 40 and 50 years old (Carroll et al., 1971; Francis et al., 1989;). Certain trends were found in the older corpus that were not reflected in the new corpus and vice versa. The wide gap of time between the collection of words for each corpus could point to the higher frequency of some words in the newer corpus (e.g., fudge, airplane, suck) than in the Francis-Kucera corpus. Language tends to change and develop in response to the changing world around it leading to different trends in word frequency across time (Jatowt & Duh, 2014). This phenomenon gives rise to the need for updated word frequency corpora. While a newer corpus is available (e.g., $SUBTLEX_{US}$), our corpus is derived from responses on the COWAT and AN tests, unlike the more recent corpus, which is derived from television shows and film subtitles (Brysbaert & New, 2009). Using the responses on the test itself to comprise the corpus, may allow for a more specific and sensitive comparison between the patient populations and NC groups in this study.

Hypotheses

H1a: Based on the previous research supporting degradation of semantic networks in Alzheimer's Disease, a higher average word frequency, as measured by the AN test, was predicted for patients with mild AD when compared to normal, healthy controls due to the decrease in spreading activation.

H1b: A related hypothesis was that a higher average word frequency, as measured by the AN test, would exist for patients with moderate AD when compared to normal, healthy controls.

H2: It was also predicted that patients with moderate AD would exhibit a higher average word frequency, as measured by the AN test, than patients with mild AD.

H3: Finally, word frequencies based on the COWAT were expected to be equal across groups as lexical networks are relatively preserved in mild and moderate AD as evidenced by the literature.

CHAPTER II

METHOD

Participants

The sample included 60 patients (13 men and 47 women) diagnosed with mild and moderate AD who were evaluated at Murfreesboro Medical Clinic and diagnosed with AD based on neuropsychological evaluation. Patients meet 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; McKhann et al., 1984). Mild versus moderate AD was determined by scores on the Mini Mental Status Exam, with scores 20 and above being considered mild disease and scores between 13 and 19 being considered moderate disease. Patients with AD did not have any history of stroke or other neurodegenerative diseases or neurological illnesses.

A sample of 60 normal, healthy control participants (17 men and 43 women) was also used. The controls consisted of individuals who were evaluated at Murfreesboro Medical Clinic for suspected memory deficits but were not found to have any memory or cognitive impairment from extensive neuropsychological testing. The normal, healthy control participants did not have any history of neurodegenerative disease, stroke, or other neurological illnesses or diseases. The controls were matched to the patient sample by age and education, as will be described.

Apparatus

Mini-Mental State Examination (MMSE). The Mini-Mental State Examination (MMSE; Folstein et al., 1975) is a 30-point screening test to measure general cognitive functioning and impairment. It assesses areas of functioning including orientation,

registration, attention, recall, working memory, language, and construction or drawing ability. The range of scores possible is from 0 to 30 and the variable used in the present study was the total score.

The MMSE demonstrates adequate test-retest reliability (r = .80 to .95; Tombaugh & McIntyre, 1992). The test demonstrated adequate internal consistency (α = .78) and high concurrent validity (r = .77) with the Montreal Cognitive Assessment, another commonly used assessment tool to detect cognitive impairment (Kabátová et al., 2016). The MMSE also was shown to have adequate sensitivity and specificity to detect mild to moderate dementia (Baek et al., 2016; Tombaugh & McIntrye, 1992;). Regarding construct validity, scores from the MMSE correlate highly with scores from other types of cognitive screening tests, intelligence assessments, and memory tests. MMSE scores are also able to adequately illustrate cognitive change in dementia patients, as found through longitudinal research (Tombaugh & McIntrye, 1992).

Geriatric Depression Scale (GDS). The Geriatric Depression Scale (Yesavage et al., 1982) is a 30-item self-report questionnaire designed for use with older populations. Participants are asked to respond either "yes" or "no" to each item, with a range of possible scores from 0 to 30 indicating the number of items positively endorsed. The dependent variable was the patient's raw score.

The GDS shows high internal consistency (α = .94) and adequate test-retest reliability (r = .85). The GDS demonstrates construct validity through high correlations with other scales measuring depression, such as the Zung Self-Rating Depression Scale and the Hamilton Rating Scale for Depression (Yesavage et al., 1982). With a cutoff

score of 11, a sensitivity rate of 84% and a specificity rate of 95% for depression indication were shown (Brink et al., 1981).

Controlled Oral Word Association Test (COWAT). The COWAT instructs the patient to generate as many words as they can that begin with a specific letter (e.g., F, A, S) within 60 seconds. They cannot use proper nouns (Florida, Fred), numbers, or the same root word with different endings (e.g., eat, eats). The dependent variable of interest in this study was the average word frequency for the words generated on the test.

The COWAT has been shown to have adequate test-retest reliability (r = .74) and acceptably high internal consistency (α = .83; Ruff, 1996). It has demonstrated moderate to strong construct validity regarding phonemic fluency (r = .44 to .87) and semantic fluency (r = .57 to .68; Henry & Crawford, 2004). The test also has demonstrated adequate concurrent validity in a meta-analysis comparing phonemic and semantic fluency across patients with a traumatic brain injury (TBI) and healthy controls. The patients with TBI showed greater impairment on the COWAT than would be predicted on their premorbid intelligence quotient (IQ), their current verbal IQ, or psychomotor speed. The meta-analysis also demonstrated the COWAT was sensitive across groups with a clear relationship based on severity (Henry & Crawford, 2004).

Animal Naming (AN). The AN test instructs the patient to generate as many different names of animals as they can within 60 seconds. There are no restrictions outside of the category. The dependent variable of interest in this study was the average word frequency for the words produced on the test.

This test of semantic fluency has shown adequate test-retest reliability (r = .71) and adequate sensitivity for assessing degradation of semantic networks (St. Hilaire et al., 2016).

Verbal Fluency Word Frequency Corpus (WFC). We developed this corpus for this study by administering the COWAT and the AN test to a sample of 342 individuals. These administrations were part of previously completed studies conducted at Middle Tennessee State University. This corpus was developed using previous administrations in an effort to update from the outdated Francis-Kucera corpus (Francis & Kucera, 1982). Additionally, this corpus was developed to be more sensitive to word frequencies in response to the COWAT and AN than a corpus developed from subtitles from fil and television shows (Brysbaert & New, 2009). The ages of the individuals ranged from 18 to 93 (M = 51.77, SD = 24.21) and the education level ranged from 8 years to 20 years. The corpus was created by first cataloguing each word generated on the COWAT and the AN tests. Regarding the words generated on the COWAT, plural forms for the words were counted as separate words, as were different tenses of the same word. However, no distinction was made between nouns and verbs, i.e. "saw" as a noun versus "saw" as a verb. Regarding the words generated on the AN test, plural forms were included with singular forms of words. For instance, "dog" and "dogs" were counted as the same base word. No distinction was made between plural and singular forms on the AN test since the objective is to measure semantic memory networks. Based on this process a total of 591 words beginning with F were identified, a total of 729 words beginning with A were identified, and a total of 1,032 words beginning with S were identified. The frequencies ranged from 1 to 183. A total of 362 different animals were

generated, with a range of frequencies from 1 to 301. The word frequencies from this corpus were then used to determine the average word frequency for the response generated on the COWAT and the AN test in the current sample. Instances for which the patient generated a word that was not included the WFC were assigned a frequency of 0.

Procedure

Approval from Middle Tennessee State University's Institutional Review Board was obtained prior to conducting this study (see Appendix A). All participants were treated in accordance with the ethical principles of the American Psychological Association. There were no financial or other conflicts of interest associated with this study. The MMSE, COWAT, and AN tests were administered to the patients with AD and controls using standard procedures. As stated previously, the patients with AD were matched with the normal, healthy participants to control for known potential confounds. Specifically, patients with AD were matched to the normal, health control participants on age and education. To match on age a difference of no more than ±5 years was used as the matching standard. This matching standard is consistent with normative studies and data that often use 10 years as an age range. The criteria for matching on education included 0 to 8 years of education, 9 to 12 years of education, and 13 or more years of education. This matching standard is also consistent with many normative studies on neuropsychological functioning and in particular those of Tombaugh et al. (1999). Following the matching process, the word frequency for each word generated on the COWAT and the AN test then were obtained using the WFC. The average word frequency for each participant then was calculated by averaging the word frequencies

across all three letters used on the COWAT. The average word frequency for the AN test was measured by averaging the word frequencies for each animal listed.

CHAPTER III

RESULTS

Preliminary Analyses

The statistical software SPSS (version 28) was used to perform all statistical analyses. Preliminary analyses were conducted to examine the relationship between the newly developed WFC and existing corpuses, the Francis-Kucera (1982) and the $SUBTLEX_{US}$ corpus (Brysbaert & New, 2009). A series of correlations were conducted between the WFC, the Francis-Kucera corpus, and the Brysbaert corpus using the average word frequencies from the COWAT and the AN test (see Table 1). Given the number of correlations and the concern for experiment-wise error rate, a Bonferroni correction was used and the new alpha was .0125. The results indicated no significant correlations for the average word frequencies based on the COWAT between the WFC and either the Francis-Kucera, r (120) = -.084, p = .36, or the Brysbaert, r (120) = -.05, p = .59. However, significant correlations were found for the average word frequencies based on the AN test between the WFC and both the Francis-Kucera, r (120) = .55, $p < .001$, and the Brysbaert, r (120) = .70, $p < .001$.

Additional preliminary analyses were conducted to determine if any relationship existed between age, education, and depression and the average word frequencies from the COWAT and the AN test in the present sample using the WFC. Hence, a series of correlations were conducted between these variables. As before, given the number of correlations and the concern for experiment-wise error rate, a Bonferroni correction was used with the new alpha being .008. The results (see Table 1) demonstrated no significant correlation between age and the COWAT average frequency, r (120) = -.09, p = .33.

However, a significant correlation was found between age and the AN average word frequency, r (120) = .243, p = .007. Education was significantly correlated with the COWAT average word frequency, r (120) = -.29, p = .002, but not with the AN average word frequency, r (120) = -.188, p = .04. These results support matching the AD patients on age and education to the controls. There were no significant correlations found between scores from the Geriatric Depression Scale (GDS) and either the COWAT average word frequency, r (120) = -.014, p = .88, or the AN average word frequency, r (120) = -.011, p = .91.

Table 1

Correlations Between Age, Education, GDS, and Each Corpus

	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. Age	-								
2. Education	-.01	-							
3. GDS	-.15	-.05	-						
4. WFC-FAS	-.09	-.29**	-.01	-					
5. FK-FAS	.06	-.01	-.09	-.08	-				
6. BRYS-FAS	.10	.01	-.09	-.05	.94**	-			
7.WFC-AN	.24**	-.19*	-.01	.19*	-.15	-.12	-		
8.FK-AN	.29**	-.06	-.18	.06	-.16	-.14	.55**	-	
9.BRYS-AN	.26**	-.17	-.17	.10	-.22*	-.20*	.70**	.59**	-

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

Finally, a series of one-way between groups ANOVAs was conducted to determine if any group differences existed in age, education, and depression. The purpose of these analyses was to ensure the success of the matching process as well as to determine if depression would need to be entered as a covariate in subsequent analyses due to significant group differences between the AD and normal, healthy control participants. These analyses were conducted between the overall AD sample and the overall sample of normal, healthy control participants. Additionally, these analyses were conducted between the mild and moderate AD groups and the groups of respective matched normal, healthy control participants. Given the number of comparisons conducted a Bonferroni correction was used to control for experiment-wise error rate, with the new alpha being .004. The results of these analyses indicated no significant differences between the overall AD group and the overall group of normal, health controls on age, $F(1, 118) = .028$, $p = .87$, education, $F(1, 118) = .14$, $p = .71$, or GDS score, $F(1, 118) = 2.16$, $p = .15$. There also were no significant differences found when comparing the mild AD group with the normal, healthy controls for age, $F(1, 58) = .011$, $p = .92$, education, $F(1, 58) = .065$, $p = .80$, or GDS score, $F(1, 57) = .098$, $p = .76$. No significant differences between the moderate AD group and the normal, healthy controls was found for age, $F(1, 58) = .018$, $p = .90$, education, $F(1, 58) = .073$, $p = .79$, or GDS score, $F(1, 56) = 3.871$, $p = .054$. Finally, there were no significant differences found when comparing the mild and moderate AD group for age, $F(1, 58) = .915$, $p = .34$, education, $F(1, 58) = .033$, $p = .86$, or GDS score, $F(1, 56) = 6.716$, $p = .01$. The results of the one-way ANOVA for age and education were expected given the controls are matched to the patients based on age and education, whereas the lack of significance for

GDS further supports its exclusion as a covariate. See Table 2 for means and standard deviations of basic demographic variables.

Table 2

Basic Demographic Information from the AD sample and Healthy Controls

Overall Sample			
Group	Age	Education	GDS
AD	75.48 (7.69)	13.13 (2.83)	7.00 (5.74)
Control	75.25 (7.62)	13.32 (2.53)	8.66 (6.46)
AD Subgroups and Respective Matched Healthy Controls			
Mild AD	74.53 (7.61)	13.07 (2.73)	8.86 (6.37)
Control	74.33 (7.46)	13.23 (2.31)	9.40 (6.79)
Moderate AD	76.43 (7.78)	13.20 (2.98)	5.14 (4.40)
Control	76.17 (7.79)	13.40 (2.77)	7.90 (6.14)

Note. Means are reported with standard deviations in parentheses.

Primary Analyses

Although the hypotheses were a-priori, a Bonferroni correction was used to ensure protection against experiment-wise error rate. This correction resulted in a new alpha of .008. Hence, all primary analyses were conducted using this corrected alpha.

Hypothesis 1a. To investigate the hypothesis that patients diagnosed with mild AD would exhibit a significantly higher average word frequency for the AN test a one way between groups ANOVA was conducted between these groups. Only the healthy controls who were matched to the patients with mild AD were included in this analysis. The result indicated no significant difference in average AN word frequency between the mild AD group and the normal, healthy control group, $F(1, 58) = 3.46$, $p = .068$. Consult Table 3 for means and standard deviations. This hypothesis was not supported by the data.

Hypothesis 1b. A one way between groups ANOVA was also conducted between the moderate AD group and the normal, healthy control group to examine the hypothesis that a higher average word frequency on the AN test would exist for those with moderate AD when compared to normal, healthy controls. As before, only those normal, healthy control participants who were matched with the moderate AD patients were included in this analysis. The result of this analysis indicated a significant difference in average AN word frequency between the moderate AD and the normal, healthy control group, $F(1, 58) = 11.33$, $p = .001$, $\eta^2 = .16$. As predicted, the moderate AD average AN word frequency was significantly higher than that of the normal, healthy control group (see Table 3). The hypothesis is supported by the data.

Hypothesis 2. To investigate the hypothesis that patients with moderate AD would exhibit a higher average word frequency on the AN test as compared to those with mild AD a one way between groups ANOVA was conducted. The result of this analysis indicated no significant difference in average AN word frequency between the mild and

the moderate AD groups, $F(1, 58) = 1.56$, $p = .22$ (see Table 3). This hypothesis was not supported by the data.

Hypothesis 3. Finally, relative preservation of lexical networks across groups was predicted to exist, as indicated by average COWAT word frequency. To investigate this hypothesis a series of one-way between groups ANOVAs was conducted between the mild AD, moderate AD, and normal, healthy control groups. As before, for comparisons involving the normal, healthy control participants only those participants who were matched to the respective AD group were included in the analysis. The results indicated no significant difference in average COWAT word frequency between mild AD group and the normal, healthy control group, $F(1 , 58) = 4.56$, $p = .04$. There was also no significant difference in average COWAT word frequency found between the moderate AD group and the normal, healthy control group, $F(1 , 58) = 2.74$, $p = .10$. Finally, the difference in average COWAT word frequency between the mild AD and the moderate AD groups was also not significant, $F(1 , 58) = 4.57$, $p = .81$ (see Table 3). This hypothesis was supported by the data.

Table 3

Descriptive Statistics of the Sample

Group	WFC	
	COWAT	AN
Total AD	25.89 (8.55)	146.57 (43.65)
Mild AD	25.62 (7.81)	139.58 (35.15)
Mod AD	26.17 (9.35)	153.55 (50.41)
Control	22.32 (5.89)	121.69 (25.87)

Note. Means are reported with standard deviations in parentheses.

CHAPTER IV

DISCUSSION

The purpose of this study was to determine if there were significant differences in spreading activation within semantic networks between mild AD, moderate AD, and controls. The results of this study supported the hypothesis that patients with moderate AD would demonstrate reduced spreading activation within their semantic networks as shown by significantly higher word frequency on the AN test than normal, healthy controls. This difference was found across the newly developed WFC, the Francis-Kucera, and the Brysbaert corpora (Brysbaert & New, 2009; Franic & Kucera, 1982). Even though each corpus had different restrictions and limitations, the result could be found in each one. This finding was in agreement with the literature demonstrating the degradation of semantic memory networks in AD through various methods of investigation such as confrontation to naming (Lin et al., 2014), verbal fluency (Davis et al., 2010), and semantic priming (Ober & Shenaut, 1988). Higher word frequency is indicative of reduced spreading activation as more commonly used words have stronger associations and interconnectedness within their network. Less spreading activation is needed to access and activate commonly used words as they are more central to their semantic networks and associated nodes. Semantic networks of moderate AD patients have been previously described as smaller and more dense networks than their normal, healthy counterparts. The normal, healthy semantic networks of these counterparts were described to be larger and less dense allowing for greater spreading activation and lower frequency words (Zemla & Austerweil, 2019).

This same trend, however, was not seen with mild AD group. No significant difference was found between mild AD average word frequency when compared to controls or to moderate AD. One explanation for this discrepancy could be due to the smaller size of our corpus (WFC) compared to the Francis-Kucera corpus and the Brysbaert corpus. Significance was not found in any of the corpora, but the Francis-Kucera and the Brysbaert could have found significance with a less conservative alpha, such as .05 (Brysbaert & New, 2009; Francis & Kucera, 1982). This discrepancy could also be explained by analyzing the progression of AD neurologically.

The characteristic progression of neuropathology associated with AD is described as travelling along a precise pathway (Delacourte, 2006). It begins with subtle neurofibrillary changes in the transentorhinal cortex (stages I and II) that are not associated with any clinical impairment. Then lesions in the medial temporal lobe begin to develop (limbic stages III and IV) as indicated through atrophy of the hippocampus and amygdala in addition to the thinning of the entorhinal cortex (Braak & Braak, 1996; Peña-Casanova et al., 2012). The deficits in episodic memory characteristic of AD can be attributed to the deterioration of these structures as they are critical in the mediation of episodic memory (Zola-Morgan & Squire, 1993). AD then progresses to isocortical destruction (stages V and VI), which heavily reduces the brain's weight (Braak & Braak, 1996). The end stages of AD progression are also associated with deficits in primary sensory and motor areas in the idiotypic cortex (Peña-Casanova et al., 2012).

When comparing mild to moderate AD, the early transition from the subtle neurofibrillary changes in the transentorhinal cortex to the lesions in the entorhinal cortex could explain why there was not a significant difference between WFC-AN scores. The

progression of AD may be defined by discrete stages as laid out by Braak & Braak (1996), but the beginning of the deterioration described in stages III and IV could encompass both mild and moderate AD with the last stages (V and VI) encompassing moderately severe to severe AD. Patients with moderate AD could be closer to the end of stage III and IV where entorhinal lesions are expected and the patients with mild AD could be in the beginnings of those stages. This conceptualization accounts for no significant difference between the mild and moderate AD groups as the mild AD patients are in the first half of the stage the moderate AD patients are in the latter half of experiencing more impairment in their semantic networks. This conceptualization also potentially explains the lack of significant difference between mild AD and the controls due to being in the stage where subtle neurofibrillary changes in the transentorhinal cortex are beginning to progress to the entorhinal lesions causing the common symptoms of episodic memory loss (Braak & Braak, 1996). With these stages of progression in mind, the phonological lexicon, hypothesized to be modulated in Wernicke's area in the dominant superior and middle temporal gyri, degrades relatively late in the disease (Ardila et al., 2016; Berron et al., 2020).

The lexical networks of the mild AD, moderate AD, and control groups were all relatively preserved, as expected based on the outline of the progression of AD (Braak & Braak, 1996). This conclusion was supported by a previous study finding impaired semantic fluency but preserved lexical fluency in patients with early AD and patients with amnestic mild cognitive impairment (Lonie et al., 2009). Lexical preservation was also determined when AD patients performed significantly better on a repetition task using real words versus pseudowords. Better performance on this task points to the use

and preservation of the phonological lexicon network in AD (Glosser et al., 1997). Lexical preservation can be used to discuss potential causes of the impaired semantic networks in AD. There are two proposed underlying mechanisms responsible for the breakdown common in AD patients. The first theory links the impairment to deficits in the organization and the structure of the semantic network itself (Martínez-Nicolás et al., 2019). This theory is supported by the earlier conceptualization of the difference in size and density between AD semantic networks and healthy networks (Zemla & Austerweil, 2019). The impaired performance and higher word frequency found in AD, according to this theory, would be due to the degradation of neocortical association areas which is thought to store conceptual information (Rogers & Friedman, 2008). There is a loss of knowledge causing impairment at the core of this theory. The other theory focuses on deficits in the retrieval of semantic network information, due to executive control impairments. The relative preservation of lexical networks in AD, however, bolsters the initial theory of organization and storage breakdown causing the degradation. Lexical and semantic fluency tasks involve similar executive control demands and would both show impairment if their retrieval deficits were the main underlying cause (Martínez-Nicolás et al., 2019). There is also an argument for combining the two theories and relating the interplay of the breakdown of organization and structure with the retrieval deficits as contributing to the impaired performance of semantic networks in patients with AD.

Our preliminary analyses indicated no relationship between our newly developed corpus (WFC) and the Francis-Kucera or Brysbaert on the COWAT, but there was a relationship found on the AN test between the corpuses (Brysbaert & New, 2009; Francis & Kucera, 1982). One potential explanation for this could be the size of the networks

being activated in each task. On the COWAT, the cue is lexical and subsequently activated a much larger set of concepts that were not closely associated. Therefore, the set of potential responses was much more vast than the semantic cue leading to weaker associations and interconnectedness between responses. The responses to the lexical cue, depending on the specific response could also be assigned immensely different frequencies depending on the corpus. If a more modern word was used (i.e., "fax" or "fridge"), the Francis-Kucera corpus would have a low frequency or no frequency (Francis & Kucera, 1982). If a word commonly said in speech was used (i.e., "a" or "and"), the Brysbaert corpus would have extremely high frequencies since it was derived from scripted films and television shows (Brysbaert & New, 2009). Considering the sheer size and nature of the Brysbaert corpus and the obsoleteness of the Francis-Kucera corpus, the finding of no correlation between the three corpuses is not necessarily surprising (Brysbaert & New, 2009; Francis & Kucera, 1982). If there had been correlation between the corpuses, the findings for the COWAT might have been different, but given the size and expanse of the lexical networks activated by the COWAT cues, correlation might not be likely.

Limitations

The limitations of this study should be considered when conceptualizing the results. The development of our own corpus needs to be continued. Compared to the other two corpora used in analysis (i.e., Francis-Kucera and Brsybaert), ours was much smaller with only 2,820 words from 343 participants. The Francis-Kucera corpus was based on about one million words and the Brysbaert corpus was based on 51 million words (Francis et al., 1982; Brysbaert & New, 2009). The sheer size of the Brysbaert

corpus is probably to blame for the excessively high frequencies assigned to some patient responses. If a patient responded with articles, prepositions, or conjunctions to the FAS prompts, such as “for” or “an”, the frequencies were extremely high compared to other responses. This is a result from developing the corpus from film and television subtitles. The frequency of those words could be much higher in a scripted context than during a lexical fluency task. The Francis-Kucera corpus was clearly larger than the newly developed corpus, but it was outdated enough that this corpus typically had consistently lower word frequencies. The corpus was developed in 1961 from printed media either classified as informative prose or imaginative prose. They only included adult reading materials in this development (Francis et al., 1989). The size of this corpus was substantial, but obsolete given the method and chronological gap between development and current utilization. While our corpus’s smaller size could make it more sensitive to detecting differences in word frequencies in the COWAT and AN tests specifically, it needed to be further developed and expanded. After increasing the size of the corpus, it may be better at distinguishing between mild and moderate AD scores and mild AD and control scores.

Another potential limitation of this study was the sample size. Increasing the sample size will in turn increase the statistical power. Furthermore, a larger sample size could potentially detect differences between groups that were not found within this sample size. It was also important to note that all of the data from the AD patients and matched controls were obtained from the Murfreesboro Medical clinic in Tennessee. Results from this study may lack generalizability due to the restricted context and region that patients and controls were from.

The current study is an extension of previous research and encourages further research on this topic. Future research could include a larger and contextually more diverse sample potentially from other clinics in different areas. While there is currently no data supporting a difference in semantic networks based on geographic location, including a more diverse population in the patient population would increase the generalizability of any significant findings.

Our corpus should also be further developed to increase sensitivity and accuracy in detecting word frequency differences on the COWAT and AN tests. For future development, more COWAT and AN responses should be included in the WFC corpus. These responses could be from other previously conducted research, clinic patients who did not receive a diagnosis of AD and were administered these tests during their neuropsychological evaluation, or from new participants being administered these tests solely for the development of the corpus.

Conclusions

In this study, lexical and semantic spreading activation in mild and moderate AD was investigated by averaging patient's response on the COWAT and AN tests and comparing them to a newly developed corpus (WFC) specifically for this research. This corpus was developed in response to two widely used corpuses. Firstly, it was developed in an effort to update from an outdated option (Francis & Kucera, 1982). Secondly, our corpus was developed from participant responses to the COWAT and AN tests to compare patient responses within the context of the tests themselves rather than subtitles from film and television shows (Brysbaert & New, 2009). Results indicated reduced spreading activation in the moderate AD group with relative lexical network preservation

across all three groups. These results support known AD pathology with a degradation of semantic networks as the disease progresses through the entorhinal cortex. This result is in agreement with the literature identifying semantic network degradation as a cornerstone of the progression of AD (Salmon et al., 1999; Nebes, 1989). While significance was not found for all of our hypotheses, significance may be found in future research with an expanded WFC corpus showing the importance of considering situational context within this realm of research.

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APPENDIX

MTSU IRB APPROVAL LETTER

11.14.22

Investigator: Paul S. Foster
Investigator Email: paul.foster@mtsu.edu

Protocol Title: Logical and Semantic Spreading Activation in Mild to Moderate Alzheimer's Disease
Protocol Number: 23-2045

Dear Dr. Foster,

The MTSU Institutional Review Board or its representative has reviewed the research proposal identified above and has determined that the study poses minimal risk to participants or that you have satisfactorily worked to minimize risks, and you have satisfactorily addressed all of the points brought up during the review.

Approval is granted for one (1) year from the date of this letter for 1000 participants.

Please note that any unanticipated harms to participants or adverse events must be reported to the Office of Compliance. Any change to the protocol must be submitted to the IRB before implementing this change.

You will need to submit an end-of-project form to the Office of Compliance upon completion of your research. Complete research means that you have finished collecting data. **Should you not finish your research within the one (1) year period, you must submit a Progress Report and request a continuation prior to the expiration date.** Please allow time for review and requested revisions. Failure to submit a Progress Report and request for continuation will automatically result in cancellation of your research study. Therefore, you will not be able to use any data and/or collect any data. Your study expires **11.30.23**.

According to MTSU Policy, a researcher is defined as anyone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to complete the required training. **If you add researchers to an approved project, please forward an updated list of researchers to the Office of Compliance before they begin to work on the project.**

All research materials must be retained by the PI or faculty advisor (if the PI is a student) for at least three (3) years after study completion and then destroyed in a manner that maintains confidentiality and anonymity.

Sincerely,

Aleka Blackwell and William Langston
Chairs, Institutional Review Board
Middle Tennessee State University