LANGUAGE IMPACT ON VERBAL MEMORY PROCESSING IN OLDER ADULTS: AN FMRI INVESTIGATION

by

COURTNEY LEE BROWN

(Under the Direction of L. Stephen Miller)

ABSTRACT

Verbal memory deficits have long been tied to both healthy and pathological aging. This dissertation experiment examined the interactions of contextual language components (syntactic and semantic), overall cognitive status, retention duration, and lateralization of cognitive resources on verbal memory encoding and recognition, within a community sample of older adults. Individuals completed neuropsychological measures of cognition and subsequently completed an fMRI task involving categorizing short phrases by language context. Immediate recall, delayed recall, and delayed recognition for target nouns of these phrases were used as measures of verbal memory retention. FMRI BOLD activation was measured in predicted regions of interest during verbal memory encoding and recognition then correlated with behavioral variables. Syntactic specific encoding included bilateral pars opercularis (PO) and middle temporal gyrus (MTG). Semantic specific encoding including left hemisphere PO, pars triangularis (PT), middle frontal gyrus (MFG), middle orbitofrontal gyrus (MOFG), and MTG. Semantic specific encoding also included right hemisphere MFG, MOFG, and MTG. Syntactic specific recognition activation was not significant. Semantic specific recognition activation was observed within left MFG and bilateral MTG. Semantic specific encoding activation was significantly related to cognitive status in left MOFG, left PO and left PT, as well as right MTG and PO at liberal thresholds. Semantic encoding demonstrated a recall benefit predominantly after a delayed duration. Number of total activated voxels did not vary across hemispheres, and scope of activation across left and right regions of interest are discussed. Results suggest benefit of bilateral resources on semantic processing with age, which in turn benefits verbal memory within older adults. They further suggest that semantic manipulation of phrases had a greater relationship with overall cognition in comparison to syntactic manipulation of phrases. The current findings are discussed framed by the processing model of verbal memory (Craik & Lockhart, 1972) and the HAROLD model of bilateral dedifferentiation (Cabeza, 2002).

Index Words: verbal memory, fMRI, language, syntax, semantic, older adults

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CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

Purpose of Study

Verbal memory deficits have been highlighted both in mild forms as a key component of the healthy aging process, as well as more clinically significant forms within pathological aging processes, most notably varying forms of dementia (APA, 2000). Traditionally, list learning tasks, such as the California Verbal Learning Test (CVLT) or the List Learning subtest within the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) have been used by neuropsychologists to conceptualize verbal memory deficits. Although invaluable as diagnostic tools and ecologically applicable to daily routines such as grocery or task lists, word lists deviate from one pervasive aspect of routine verbal memory: retention of information obtained through discourse interactions, involving words organized by semantic similarity and syntactic structure. Neuropsychologists have examined this form of verbal memory through discourse memory tools such as the Logical Memory (LM) subtest of the Wechsler Memory Scales (WMS) or Story Memory subtest of the RBANS. These types of tasks provide a context for information and have been shown to improve the differential diagnostic accuracy between memory deficits of normal aging and those seen with a sample experiencing Mild Cognitive Impairment (MCI; Rabin et al., 2009).

The potential benefit of context on verbal memory is intuitive in its organizational value for encoding information. However, the role specific features of this context play in driving language-memory interactions remain less clear. The implications for this line of investigation become especially pertinent when discussing verbal memory deficits experienced by older adults: In addition to the above described verbal memory deficits, deficits in structuring language material also appear with age. Specifically, semantic processing has been shown to be stronger within younger adults than older adults during a task of verbal memory (Jacobs, Rakitin, Zubin, Ventura, & Stern, 2001), while syntax processes have been suggested to maintain similar patterns in younger compared to older adults (Hoyte, Brownell, & Wingfield, 2009). Cortical BOLD activation patterns have been shown to be impacted by age, potentially impacting mechanisms for verbal memory and language processes: For example, the HAROLD and HERA models connect cortical reorganization to more preserved cognitive function (Cabeza, 2001). The current experiment seeks to explore these interactions between language manipulation, verbal memory performance, and related cortical BOLD reorganization within a community sample of older adults.

Literature Review

Verbal Memory

Verbal Memory Defined

Verbal memory encompasses components of both implicit and explicit memory. Explicit memory is defined as ‘top-down’ memory processes for specific facts (semantic memory), and memories for specific events (episodic memory; Kolb & Whishaw, 2009). Some have suggested that these systems may not be mutually exclusive, and that semantic features play a role in both forms of memory processes (McCloskey & Santee, 1981). In contrast, implicit memory has been described as a ‘bottom-up’ memory process that is not intentionally learned (i.e., procedural skills such as language; Kolb & Whishaw, 2009). Some have argued that syntax of one’s native language specifically is learned and retained in an implicit fashion, as opposed to second languages, learned in an explicit, semantic fashion (Fabbro, 1999).

Verbal memory occurs within stages. Encoding information entails storing newly presented information for future use. Retrieval entails bringing information out of memory stores to conscious thought for current use. Verbal retrieval of encoded information may be further broken down to controlled recollection (akin to verbal recall), and familiarity (akin to verbal recognition; Lou, & Craik, 2008). Although overlap between these domains exists, distinctions may be found through patterns of deficits within recall and recognition tasks: those experiencing difficulties with encoding typically show difficulty on both free recall and recognition, while difficulties with retrieval will yield greater struggle with free recall than recognition (Butters & Delis, 1995).

Learned information moves between short term and long term stores of information. Short term stores of information are those that may be imminently manipulated. Several tools exist within the short term store to facilitate the ‘top down’ encoding of information facilitating movement to long term store: Rehearsal entails repetition of pertinent information. Coding involves placing the information within a context to facilitate memory, one such context involving creating a sentence. Imaging entails creating a visual representation of material. Some have equated the short term store with a working memory system, as information is manipulated and easily retrieved for current use. In contrast, long term stores facilitate more permanent memory for verbal information. However, this information requires active retrieval back into short term stores before it can be manipulated. One form of retrieval strategy may include using currently available information as a “probe” to identify information related to this probe within the long term store. Associative information therefore works either during the encoding phase, to act as organizational context for the target verbal information, or during the retrieval phase, as a cue to isolate related information in the long term store (Atkinson & Shiffrin, 1971). Some have suggested that this relationship need not be considered mutually exclusive: Event-related potentials (ERP) and reaction times in one such study suggested that encoding verbal information involve both activation of semantic representations in the short term and maintenance of these representations at a high level of activation during a delay interval (Cameron, Haarmann, Grafman, & Ruchkin, 2005).

Verbal Memory Organization

In this sense, organizational tools hold particular relevance in the domain of verbal memory. Verbal information typically is not presented within an isolated word list fashion in the realm of everyday interactions. Individuals frequently must remember information in the midst of contextual cues of phrases and sentences. Semantic representations may be one such contextual cue but are often not the only cues embedded within everyday language. A question then arises as to what aspects of narrative speech, including but not limited to semantic information, may impact memory.

Verbal Memory Encoding

Several models exist regarding the organization of verbal memory, and a lack of consensus remains regarding the most parsimonious and effective way to conceptualize the core of verbal memory, encoding of information. Currently, various models implicate forms of declarative memory, procedural memory, and working memory as active to varying degrees within the process of verbal encoding.

Declarative memory has been consistently linked with verbal memory, particularly as a vehicle for semantic verbal memory. The process model relates patterns of activation to the methods with which verbal memory is processed during encoding, not the content of the material being processed (i.e., forced choice categorization versus inhibition of distracter). Support for this model comes from research showing differing stimuli eliciting similar patterns of activation based on task: Manipulation of information elicited greater dorsolateral and parietal information than pure maintenance regardless of whether stimuli being manipulated (i.e., organized by size or alphabetized) and retained contained semantic information (words) or no semantic information (non-words; Barde and Thompson-Schill, 2002).

The material model arises out of the dorsal and ventral stream of visual information processing, where the former processes visual-spatial information and the latter processes visual-object information (Goldman-Rakic, 1987). It suggests that cortical activation for verbal memory will be based on the differences in stimuli being presented, rather than how these stimuli are processed (e.g., words versus non-words; Barde and Thompson-Schill, 2002). Support comes from research that shows similar activation patterns for verbal materials despite encoding task (Baker, Sanders, Maccotta, & Buckner, 2001).

Due to the strongly integrated nature of syntax and semantic information, it is difficult to conceptualize language components of verbal memory within mutually exclusive categorical process or material frameworks. The ‘level-of-processing’ model of Craik & Lockhart (1972) takes a different approach. This theory states that an individual may view similar material but engage in varying intensities of encoding. In this manner, processes for encoding are not necessarily mutually exclusive in cortical regions activated, but vary in terms of the cortical and temporal resources required for adequate processing. Lower level encoding (e.g., structural encoding of letter case) requires fewer resources than a higher level of encoding (e.g., lexical decision making), which in turn, requires fewer resources than even higher levels of encoding (e.g., semantic categorization tasks; Craik & Lockhart, 1972; Bonner-Jackson, Csernansky & Barch, 2007).

Semantic processing is frequently viewed as a higher level of processing within the realm of language comprehension. However, its relationship to syntax and specific patterns of cortical activation elicited by isolating interrelated processes has yet to be determined (Craik & Lockhart, 1972; Bonner-Jackson, Csernansky & Barch, 2007). Researchers have noted positive behavioral effects for higher levels of encoding and subsequent retention tasks (Bonner-Jackson, Csernansky & Barch, 2007; Baker et al, 2001), and greater cortical activation in response to higher level (i.e., semantic) over lower level (i.e., structural) encoding (Baker et al., 2001). Regions named as differentially impacted by higher levels of verbal encoding (e.g., semantic encoding) include left inferior frontal and prefrontal regions, left inferior parietal (BA 39, 40) and middle temporal regions (BA 19, 21), and right supramarginal regions (Bonner-Jackson, Csernansky & Barch, 2007; Henson, Hornberger, & Rugg, 2005). In populations where higher forms of verbal encoding are strained (i.e. semantic dementia), lower levels of processing have exhibited relative preservation within short-term memory (Majerus, Norris, & Patterson, 2007).

In addition to these forms of declarative memory, procedural memory has been cited by some as playing a role within verbal encoding of syntactic information. Some have placed one’s native syntax among the skills encoded on an implicit procedural level (Fabbro, 1999). Memory for these syntax skills have been shown to benefit verbal processing in the form of listening comprehension (Call, 1985). Evidence for the idea of syntax being encoded and manipulated using procedural memory includes research demonstrating that syntax is regenerated within short-term memory rather than actively retained as declarative facts from verbally presented materials. Syntactic cues were suggested to be implicitly rather than explicitly driven in influencing processing of subsequent sentences (Lombardi & Potter, 1992). Further support comes from work with amnestic patients given sentences with varying syntactic structures, describing pictures that lent themselves to the primed structures, and making recognition judgments for primed sentences. Amnestic patients showed poor recognition for syntactic primes but maintained equivalent degrees of syntax in their discourse, implicating syntax as maintained implicitly within procedural memory rather than though declarative mechanisms (Ferreira, Bock, Wilson, & Cohen, 2008). In contrast to the ‘levels-of-processing’ model, proposing that semantic material requires a higher level of cortical activation (Bonner-Jackson, Csernansky & Barch, 2007; Henson, Hornberger, & Rugg, 2005; Craik & Lockhart, 1972), some have suggested that syntax performance requires efficient use of resources more so than additional resources, and this need increases with increasing syntactic complexity (Vos et. al., 2001).

In contrast to declarative or procedural memory systems, some have linked verbal memory processes to the working memory system. Baddeley and Hitch (1974) described a phonological loop model of working memory including a sub-vocal rehearsal component and “visual-spatial sketchpad” component. The sub-vocal rehearsal component suggests that similarity may interfere with transferring information into long-term memory. Length of words negatively impacts encoding and supports the existence of a sub-vocal rehearsal system as part of working memory. In addition to the above system, a visual sketchpad facilitates manipulation and storage of visually presented information. Both systems are managed through an executive control mechanism (Baddeley, 2003).

The role of semantic and syntactic information within working memory is an area of continued debate within the literature. Within the phonological loop framework, semantic category interference does not hinder word list encoding to the extent that phonological interference does (Baddeley, 2003; Chasse & Belleville, 2009), and comprehension of syntax appears to be benefited by the sub-vocal rehearsal mechanism, supporting syntax as a short-term process (Papagno, Cecchetto, Reati, & Bello, 2007). In linking semantic and syntactic processes in working memory, some integrate them and others separate their roles. Just & Carpenter (1992) put forth a single processing resources theory that suggests semantic, phonological, and syntactic processes converge onto one system of working memory, suggesting that each individual holds a finite amount of activation available for the entirety of their language processing needs. These available resources impact speed and accuracy within processing language. Walters & Caplan (2004), propose an alternative, the separate language interpretation resource theory, suggesting a first pass of implicitly driven discourse meaning processing, and a second pass that takes into account semantic memory and is consciously controlled by the working memory system. Support for the latter theory comes from researchers relating on-line and off-line language comprehension: Individuals suffering from Alzheimer's disease have been shown to have a greater correlation between off-line grammar judgment difficulties and working memory than online language comprehension difficulties and working memory. These findings implicate working memory as part of the post-interpretive aspects of language processing rather than implicated with online semantic or syntactic processing (Kempler, Almor, Tyler, Andersen, & MacDonald, 1998).

Verbal Recall/ Recognition

Inextricably tied to encoding is the ability to accurately retrieve this information at a later point. A distinction made within neuropsychology involves retrieval or recollection of words (free recall) and identifying words upon hearing them as familiar or novel (recognition). Recognition has been identified as involving both recollection and familiarity processes, and impaired function on both processes have been related to deficits with initial encoding of information (Lou & Craik, 2008; Anderson et al, 2011). In contrast, deficits have been seen within recollection but not familiarity, both clinically and empirically. In a task extrapolating familiarity estimates from retrieval, right inferior regions were identified as integral in manipulating retrieval cues, although familiarity processes remained equally effective following damage to these regions (Anderson et al, 2011).

In many ways, organization during the encoding phase facilitates organization and resources required for recognition phases. Researchers found that individuals with TBI tended to require additional encoding resources, processed in a less effective manner, to perform similarly to controls on neuropsychological verbal memory tasks. In contrast, controls employed strategies during encoding such as semantic clustering to condense memory load, and as a result, required relatively fewer cortical encoding resources than future recognition resources (Arenth, Russell, Scanlon, Kessler, & Ricker, 2008). In considering location of cortical involvement, some have suggested that recognition activity correlates with the encoding task, with middle frontal regions active during a match between encoding and retrieval domains, despite behavioral success rate (Ranganath, Johnson, & D’Esposito, 2000). Recognition of old items has been suggested to potentially activate similar temporal regions as encoding new items (Henson, 2005). Other regions, namely the DLPFC have been identified as being related more to encoding of verbal information than to either recollection or familiarity (Turriziani, Smirni, Oliveri, Semenza, & Cipolotti, 2010).

While some relate encoding activation to future retrieval activation, others isolate retrieval activation, and at times spatially isolate activation related to recognition versus recall. Though the left hemisphere has been identified as active within verbal encoding and is well supported as being the dominant cortical region for language, some suggest the right hemisphere may play a more active role within verbal recognition of familiar words (Johnson, Saykin, Flashman, McAllister, & Sparling, 2001). Some have related location of activation to shared and distinct recall/ recognition regions: Activation within the left inferior frontal gyrus and hippocampus were associated with success in future associative recognition, and activation magnitude in these regions showed a positive relationship with future recall. This pattern indicates shared regions, but additional resources required for recall of information over recognition of information. Recall specific regions were also noted and included left mid/dorsolateral PFC and bilateral posterior parietal regions (PPC; Staresina & Davichi, 2006). Cortical areas implicated in verbal recognition include bilateral inferior frontal gyrus, inferior temporal gyrus, and occipital lobe. Words identified as familiar upon recognition (whether correct or not) implicated left medial and lateral parieto-occipital cortices as well (Heun et al, 2004).

Diversity in cortical regions implicated in recognition has been attributed to varying mechanisms. Some have linked level of confidence in responding to location of activation, distinguishing high confidence, bottom-up judgments from the use of higher complex, lower confidence, top down decisions. The MTG was associated with higher confidence judgments (i.e., recollection), while the prefrontal cortex was related to lower confidence judgments (i.e., familiarity), necessitating higher use of executive processes within these judgments. Regions of the posterior parietal cortex were likewise noted to have dorsal familiarity and ventral recollection processes (Kim & Cabeza, 2009). Others have found that this pattern extends to clinical samples, with amnestic MCI individuals engaging more frontal and fewer medial temporal resources during successful recognition, and less engagement of both regions when encoding novel information (Trivedi et al, 2008). Still others relate syntax and semantic processing to such retrieval processes, engaging individuals in a recognition task for sentences with varying language-based changes from initial presentation. MTL activation was related to semantic novelties. Inferior frontal regions (Broca's region) demonstrated a bias for syntactic novelties (Poppenk et al, 2008). Research has shown that even in the face of a traumatic brain injury, semantic relatedness and directed semantic associations benefit verbal recognition over unrelated verbal stimuli (Strangman et al, 2009). Similar effects occurred when the connection was actively contrived by the individual rather than passively provided (i.e., pairing real words related to target non-words; Marshall & Smith, 1977), illustrating the potential power of verbal manipulation of memory stimuli on behavioral performance.

Short versus Long Term Verbal Recall

Researchers suggest that the cortical regions activated may change as a function of short term versus long term memory. Some have suggested that short term memory implicates posterior superior temporal and inferior parietal regions (related to phonological working memory), while long term memory uses more inferior frontal regions. In particular, the pars triangularis has demonstrated increasing activation with increasing lag of repetition and a negative relationship between activation and behavioral performance with increasing recognition delay. Researchers suggest that increased delays relate to a greater shift to semantic functions for facilitated retrieval (Buchsbaum, Padmanabhan, & Berman, 2010). In contrast, some have shown that within the short term (15 second delay), correct syntactic order facilitates short term memory (Perham, Marsh, & Jones, 2009). Others have isolated frontal cortical long-term memory to the DLPFC in processing relationships during verbal encoding and general long term memory faciliatation to VLPFC. They suggest that the VLPFC showed a greater predictive value for behavioral long term memory success (Murray & Ranganath, 2007). Others have further specified long term memory cortical regions to include both left mid/dorsolateral PFC and bilateral posterior parietal cortices. The role of the PPC was suggested to involve its role in mnemonic representations and the benefit of strong representations on future recall of verbal information (Staresina & Davichi, 2006).

Verbal Memory Conclusion

The debate regarding specific mechanisms of verbal memory continues within the literature. Several theories implicate declarative memory in verbal encoding (process theory, materials theory, 'level-of-processing' theory), while others point to the procedural memory systems as implicated in at least a portion of verbal encoding (i.e., that of over-learned syntactic information), and still others struggle with the role of working memory within verbal processing and verbal encoding. Semantic and syntactic information could be processed using one combined pool of resources, managed by working memory (single-process resource theory; Just & Carpenter, 1992). In contrast, processing of verbal information could occur first for lower level information and then be integrated with semantic information by working memory (separate language interpretation theory; Waters & Caplan, 2004). Semantic and syntactic processes may be implicated within both encoding and future retrieval of information. A debate remains regarding the location of recall and recognition activation and its connection to encoding processes. The duration of delays may further interact with memory mechanisms to influence location and intensity of activation. The idea that aspects of language may be processed in slightly different ways, be it by varying mechanisms, spread of cortical resources, or timing of processing, appears to be well agreed upon within the literature. The fact that these processes interact with memory to some extent appear similarly well agreed upon. What appears less clear is the relative role that syntax and semantic information play within accuracy for verbal memory, particularly within a population of individuals who are beginning to experience varying levels of cognitive decline. Furthermore, moderating variables related to the impact of semantic and syntactic context remain largely unexamined.

Cognitive Difficulties of Aging

The Centers for Disease Control estimates that within the next 20 years (by the year 2030), the population of older adults in the United States (i.e., >= 65 years old) will more than double to an estimated 71 million individuals (CDC, 2011). Cognitive decline within the aging population may be best viewed along a continuum of deficits. In addition to those experiencing healthy aging, mild cognitive impairment (MCI) occurs when cognitive deficits are found to a greater extent than what would be expected for healthy aging, but functional status is comparable to those experiencing healthy aging (Petersen, 2004). Some have proposed an intermediary step between healthy aging and MCI (age-associated cognitive decline), involving cognitive deficits at least 1 standard deviation (SD) away from age-related norms on neuropsychological assessments (Levy, 1994). In contrast, dementia involves both impairment of memory (encoding and/or recall), as well as impairment in at least one additional cognitive domain: language deficits (aphasia), motor deficits (apraxia), object identification difficulties (agnosia), and/or difficulties with executive functioning. In addition, significant impairment in daily functioning must be documented within this category. Dementia of the Alzheimer’s Type is a large focus of the literature, however dementia may occur secondary to vascular difficulties, substance use, or other medical conditions (APA, 2000). In addition to differences between diagnostic groups, variety in cognitive impairments occurs within non-clinical samples as well, which emphasizes their gradual nature and also that cognitive deficits may be preclinical MCI or deficits that reach the level of cognitive impairment without sufficient evidence for a formal diagnosis (Cargin, Maruff, Collie, Shafiq-Antonacci, & Masters, 2007).

The predominant difficulties of aging have been suggested to include maintaining relevant, ignoring irrelevant and quickly processing information as we age (Li, Lindenberger, & Sikstrom, 2001). Cognitive slowing and reduced attentional resources could impact greater difficulties with higher levels of cognitively complex tasks such as recall over recognition (Lou & Craik, 2008). This could feasibly extend to higher levels of processing such as semantic context being less effectively utilized than lower level syntactic context. Language deficits have also been discussed in the context of aging. In a study examining Dementia of the Alzheimer's Type and normal aging, it was determined that semantic reading comprehension and level of syntactic complexity best differentiated healthy and pathological aging (Emery & Breslau, 1988). In a review of language research within AD, Emery (2000) suggested that semantic processing was widely accepted as deteriorated within DAT, but more debate surrounded syntactic processing. Although relatively preserved in comparison to semantics, syntax appeared to exist on a continuum and show deterioration at more complex levels.

Verbal Memory and Aging

Memory, although not sufficient for a diagnosis of pathological aging, is a common component of deficits (APA, 2000). It has been suggested that the deficits associated with aging impact explicit memory but not implicit memory (Cabeza, 2001). Verbal memory exhibits a significant change between younger and older adulthood, more so than its non-verbal counterpart. Part of this differential effect has been linked to the asymmetric pattern of neural degeneration during the aging process, with left frontal regions that assist with active organization of verbal material by semantic relationships tending to be impacted significantly.

Variables of verbal memory have been suggested as predictive of pathological aging, specifically total words learned, and long delayed free recall on the CVLT-II (Greenaway et al, 2006). While the APOE genotype has been cited as carrying 12 times the risk for future conversion to AD, each 1 SD on Short Delay Free Recall and Long Delay Free Recall carries a risk of the individual being 8 times and 3 times as likely to convert to possible or probable AD, respectively (Lange et. al, 2002). Age related recognition changes include speed of process, recognition accuracy, and reduced specificity in cortical resources recruited for a given task (Madden et al, 1999). Some researchers suggest that the increased difficulties with inhibition may relate to challenges in older adults with difficulties in recognition sensitivity, but note that recall and recognition both show detriments within older adults, negating inhibition as the full isolating factor between the processes (Lou & Craik, 2008).

One line of reasoning states that verbal memory impairments within older adults vary by the deficits in specific processes impacting verbal encoding (Lou & Craik, 2008). Part of the difficulty could relate to a reduction of dopamine in frontal regions, which may modulate attention towards relevant stimuli within a given task. Dopamine could be related to facilitating the signal to noise ratio within cortical information processes (Li, Lindenberger, & Sikstorm, 2001). Some researchers have examined executive dysfunction as a possible variable within verbal memory of older adults. It has been shown to have a role within total list learning and short delay free recall on the CVLT-II among older adults with MCI, mild dementia, and no dementia. No differences were found within the immediate and delayed story memory (Logical Memory, WMS-R) or upon long delayed free recall on the CVLT-II. It is possible that narrative structure reduces the organizational load on the executive functioning system through contextual cues, and reduces the corresponding processing load on the frontal-striatal network in comparison to the CVLT-II (Brooks, Weaver, & Scialfa. 2006).

Imaging studies have shown a relationship between neural activation and verbal memory. Shifts in activation for memory occur: Healthy controls have been shown to have greater temporal activity and less prefrontal activity than MCI participants during an encoding and retrieval task (Clement & Belleville, 2009). Others implicate the role of the PFC within verbal memory, correlating reduced memory accuracy in an AD sample with reduced activation within this region (Lim el al, 2008). The role of verbal memory may not lie in one specific region, but could instead relate to deficits between regions, namely the PFC and the anterior cingulate cortex. (Otsuka & Osaka¸ 2005). Other researchers have reported a frontal hyperactive pattern of activation as a means of compensating for temporal lobe deficits within the aging brain (Rajaha & MacIntosh, 2008). Some have noted increased right parahippocampal, parietal, prefrontal, and left precuneus activation within older adults during recognition tasks. Left prefrontal and precuneus activity were correlated with recognition accuracy scores, linking them to potential compensatory memory mechanisms within the aging brain (Rajah & McIntosh, 2008). Due to the nature of verbal memory deficits within regions also identified as language processing regions (temporal, frontal, prefrontal regions), it is important to view verbal memory as the culmination of processing components of verbal information, semantic and syntactic information.

The HAROLD model proposed by Cabeza (2002) (hemispheric asymmetry reduction in older adults) suggests that neural deficits lead to greater spread of cortical activation during a given task within older adults, implicating more bilateral resources. Cabeza (2002) suggests that maximizing cortical resources may relate to general or specific tasks, and may or may not hold a facilitative effect on behavioral performance. Stroke victims have been shown to exhibit greater levels of language recovery with greater bilateral cortical resources (Cao, Vikingstad, George, Johnson, & Welch, 1999). Cabeza, McIntosh, Tulving, Nyberg, & Grady (1997) found some support for this within encoding and recall tasks in the inferior frontal region. Older adults have shown further support for this theory when activating greater bilateral resources in response to deeper levels of verbal memory encoding (Stebbins et al, 2002). Part of the dedifferentiation of resources includes those specialized for implicit and explicit learning. In an fMRI examination of these systems across younger and older adults, researchers found that older adults tended to recruit resources from both systems (striatum for implicit, MTL for explicit) and reduced competition between the systems. These systems in this manner become less specialized within older adulthood (Dennis & Cabeza, 2011).

Further mechanisms implicated in cognitive difficulties of older adults have been shown to possess compensatory mechanisms. Research suggests that despite objective impairments within the domain of memory, older adults who perceive more difficulties with memory will utilize more tools for memory, including internal and external aids, as well as increased time and effort (Garrett, Grady, & Hasher, 2010). Frontal under-recruitment of resources and non-selective recruitment of resources have been found in older adults during memory encoding when compared with younger adults. This occurred particularly within anterior ventral cortical regions associated with semantic processing. Under-recruitment was ameliorated by adding a semantic elaboration component to the task, demonstrating the benefit of focusing attention on language resources and engaging older adults in active manipulation of verbal material, though non-selectivity continued despite manipulation (Logan, Sanders, Snyder, Morris, & Buckner, 2002). Older adults have been suggested to have higher difficulties in self-initiating processes but benefit greatly from contextual support. Two types of memory that tend to be better preserved with age include implicit/ procedural memory and memory for semantic information. Ways to improve memory of older adults outside of direct memory training would be to place higher reliance on processes with lower required resources and reduced age-related deficits such as these. Reduced specificity and higher context are two mechanisms to consider in this regard (Lou & Craik, 2008).

Language

Semantic- Behavioral Research

Semantic processing has been well researched within the language literature, and conceptualized by the Collins & Loftus (1975) spread of activation model, which states that semantically related concepts form a network of information, whereby those more closely related exhibited a stronger connection than weaker relationships. In this manner, activation of one concept through presentation of a specific word will be highly likely to activate similar concepts (e.g., dog, pet, 'Fido') within the network. A related theory, the conceptual structural account, suggests that similar objects would activate similar networks (or nodes) of information, and could therefore share cortical space. Two such categories include nature related objects (possessing shared characteristics) and man-made objects (possessing shared functions; Devlin et al., 2002). In addition to specific regions for specific semantic categories, researchers have examined the potential for an amodal system of semantic processing. Some suggest initial modality specific processing followed by amodal processing of semantic information (Kuperberg et al, 2000). The amodal system of semantic processing has been corroborated by ERP research of verbal and pictorial materials (West & Holcomb, 2002).

Memory for semantic information entails retaining information regarding general concepts and world knowledge (Bartha et al, 2003). Although frequently related to overt verbal processing, semantic processing takes place within non-vocalized thoughts and assessment of object relationship (Covington et al, 2005), such as during viewing of pictures (McPherson & Holcomb, 1999) and during videos of real world activity (Sitnikova, Kuperberg, & Holcomb, 2003). Differences in organization of materials within verbal memory may relate to the organization of semantic cortical networks: Warrington & Shallice (1984) proposed the "perceptual-functional" model, implicating organization as being driven by salient semantic characteristics: information regarding living things is organized by their perceptual characteristics, while information about tools will be grouped more so by their functional properties (Canessa et al, 2008). Support for this theory comes from findings of category-specific deficits between man-made and nature related information (Forde & Humphreys, 1999). Others propose specific categories for only 'animal' and 'tool' and further describe a conceptual structure involving broader networks connecting specific networks of semantic information. These broad networks facilitate initial integrity of abilities to work with generalized conceptual information despite deterioration within semantic networks, until neural damage spreads to a greater degree within the broad conceptual network (Devlin et al, 2002). Two such broader categories could potentially include man-made items and nature-related items, as opposed to specifically 'animals' or 'tools.'

Semantic Processing- Neurocognitive Findings

The debate regarding semantic category specific processing versus generalized processing exists within behavioral and neurocognitive related semantic research. Support has been found for a category specific model of semantic cortical organization (Sitnikova, West, Kuperberg, & Holcomb, 2005). Support has been shown for the non-specific model through evidence that the dorsolateral prefrontal cortex processes verbal relationships independent of specific category (Murray & Ranganath, 2007). Further support has been found regarding bilateral medial and inferior temporal regions processing of semantic tasks, regardless of handedness (Bartha et. al., 2003), and has implicated left medial temporal regions in semantic processing, regardless of stimulus modality (Muller, Kleinhans, & Courchesne, 2003). Some have implicated the spread of cortical semantic activation to be related to the levels-of-processing memory model, illustrating performance on memory tasks was positively correlated with activation in left prefrontal, temporal parietal, and bilateral medial temporal regions, while poor performance related to activation isolated within the right temporal-parietal regions (Cassanto et. al, 2002).

In addition to the preponderance of temporal regions named as active above, the left frontal regions, particularly Broca's region, have been implicated within semantic processing research. The pars opercularis (PO) has been implicated in comprehension of semantic information (Newman, Ikuta & Burns, 2010), while the PO and pars triangularis (PT) have been named by others as sharing the semantic processing load (Muller, Kleinhans & Courchesne, 2003). Some have named more inferior frontal regions as integral in semantic relatedness of nouns (Newman, Ikuta, & Burns 2010), or involved in ambiguities related to imaginability of nouns (Bedny & Thompson-Schill, 2006).

Syntax- Behavioral Research

Syntax is less frequently linked directly to measures of verbal memory, but remains a component of language that plays a large role in facilitated verbal comprehension and in so, verbal memory. Syntax involves the grammatical structure of words to form meaningful language units (i.e., phrases or sentences; Kircher, Oh, Brammer, & McGuire, 2005). It involves taking smaller units of information and combining them into more complex units through a process of ‘syntactic unification’ (Hagoort, 2005). Some have argued that this process occurs early in language processing, and if syntactic ambiguities hinder the first pass of sentence processing, than semantic information within would not be subsequently evaluated (Kuperberg et al, 2000). Others have demonstrated the preference for simpler syntactic units in facilitating assigning the appropriate noun to related verb information for improved verbal comprehension (Bahlmann, Roddrigues-Fornells, Rotte, & Munte, 2007).

As discussed earlier, preliminary work with syntax and its connection to verbal memory has focused within the procedural domains of grammar skills and within the debate regarding syntax and verbal memory. Waters & Caplan (2004) suggested the separate language interpretation resource theory, indicating that syntax did not load onto the traditional working memory system utilized by traditional verbal working memory tasks, but rather noted the potential existence of a distinct syntactic working memory system. Support for this theory comes from clinical research indicating intact syntax processing in the midst of low working memory spans within individuals experiencing a history of strong or current diagnosis of Parkinson’s disease (Waters & Caplan, 2004). Preliminary work with syntax and verbal memory appear to demonstrate a potential protective interaction: Verbal memory in a group of Alzheimer’s patients was shown to increase at a rate comparable to a healthy aging sample as grammatical structure increased and word lists more closely approximated discourse text. Full sentences were best remembered when they lacked either semantic or syntactic errors, implying a benefit towards retention for verbal material couched in appropriate syntax. The implicit “over-learned” nature of syntactic skills of reading could impact this effect (Nebes, Brady, & Jackson, 1989). It has been suggested that the short term memory system in particular benefits from syntactic structure (Perham, Marsh, Jones, & 2009).

Syntax- Neurocognitive Findings

Similar to semantic processing findings, cortical activity has been shown to be impacted by complexity of processing. The left supramarginal gyrus is one area implicated in processing ambiguities related to subject-first versus object-first sentence comprehension, whereas non-ambiguities were processed within the left inferior frontal gyrus (Bahlmann et al, 2007). Researchers have linked higher cortical activation within left anterior temporal regions to infrequent syntactic structures as further support for this model (Noppeney & Price, 2004), though others caution against the potential for BOLD artifact within this region, obscuring results (Visser, Jeffries, & Lambon Ralph, 2009). Others have isolated syntactic processing to the middle temporal gyrus (Visser et al., 2009; Shetreet, Friedmann, & Hadar, 2009; Christensen, 2010) or the left perisylvian fissure proximal to other cognitive sequencing processes (Lelekov, Franck, Dominey, & Georgieff, 2000). Researchers have also contrasted the findings of specific regions for verb processing (dorsolateral frontal and medial temporal activation), with the lack of such a specific region for nouns. It has been suggested that verbs require access to specific syntactic information needed for comprehension, while semantic information within nouns would be dispersed across semantic regions (Perani et. al, 1999).

As with semantic information, Broca's region (PO and PT) remains a region debated as important for syntactic processing, beyond the expressive language needs of the sub-rehearsal component of the phonological loop (Caplan, Alpert, Waters, & Olivieri, 2000; Papagno, Cecchetto, Reati, & Bello, 2007). Syntactic processing has been isolated to PO (Caplan, Alpert, & Waters, 1998; Lee & Newman, 2009; Newman, Ikuta, & Burns, 2010), with others isolating a subset of syntax, verb-argument processing, to this area (Raettig, Frisch, Friederici, & Kotz, 2010). Some believe that while these general syntax processes such as inflection occur in PO, more abstract processes occur within more ventral and dorsal regions (inferior frontal gyrus, IFG; Sahin et al, 2006), or more complex processing is occurring within neighboring PT and middle frontal gyrus (MFG) (PT: Shetreet, Friedmann, & Hadar, 2009; PT, MFG: Perani et al, 1999). Others have identified posterior and superior regions as related to subject/ object manipulations and anterior/ inferior Broca's regions being reserved for processing phrases with reflexive pronouns (Santi & Grodzinsky, 2007). Syntactic complexity, working memory, and action perception have been implicated as occurring within Broca's region (Grodzinsky & Santi, 2008).

Semantic and Syntax- Clinical Findings

Several groups have sought to directly compare semantic and syntactic processing of information within clinical samples. Those experiencing thought disorder have been shown to exhibit difficulties on tasks of semantic fluency but no significant impairment on syntactic processes both on neuropsychological batteries, (Stirling, Hellewell, Blakely, & Deakin, 2006), and when speech was examined by linguists (Covington et al, 2005). When previous speech deficits in those experiencing schizophrenia were examined, childhood difficulties with speech complexity but not accuracy were noted (Kircher et al, 2005). In contrast, within a sample of individuals experiencing Alzheimer's disease, syntactic complexity was preserved by quantity and semantic accuracy of information was significantly impaired (Lai, Pai, & Lin, 2009). Syntactic processing within this population appear to degrade only within more severe stages of dementia (Bickel, Pantel, Eysenbach, & Schroder, 2000), while degradation of declarative memory and semantic networks is well documented in this population (Rogers & Friedman, 2008). Some suggest that difficulties in differentiating old and new words stem from a breakdown in left cortical structures (IFG, MTG, parahippocampal, cingulate, fusiform, perirhinal) with DAT individual that activate for novel stimuli, in contrast to those experiencing healthy aging (Olichney et al, 2010).

Semantic and Syntax- Neurocognitive Findings

Due to their tightly integrated nature, much attention has been paid to the feasibility of separating syntax from semantic processes. Commonalities do still occur between these integrated language components. Several such regions relate to verbal fluency, verbal integration, and concrete visual imagery (Kuperberg et al., 2000). Some have argued against their mutual exclusivity, stating that organizing syntactic material occurs within posterior medial temporal regions for the semantic categories for tools/ imitation (Davis, Meunier, & Marslen-Wilson, 2004). Support comes from evidence for distinct lateral frontal-parietal activation for action judgments and lateral anterior inferotemporal activation for functional judgments. Further semantic subdivision is noted within anterior/ inferior temporal cortex for integrating perceptual information and lateral activation for functional aspects of nouns, both system impacting explicit and implicit object recognition (Canessa et. al, 2008). In identifying posterior left superior temporal activation in response to motion verbs, such activation could be viewed as a form of syntactic complexity assigned to that region, or as a form of semantic identification of stimuli as part of the category “motion verbs” (Bedny & Thompson-Schill, 2006). The anterior temporal lobe has been cited as a location of verbal unit integration, further connecting temporal semantic processes with syntactic counterparts (Visser et al., 2009).

Despite some evidence linking semantic and syntactic processing, evidence is building within the literature that these components of language may be disentangled. In a group of aphasic participants, left temporal regions related more to object naming (semantic) difficulties, while left frontal regions were implicated in action naming (syntactic) impairment (Perani et al, 1999). ERP temporal evidence supports syntactic processing occurring in left anterior regions as an early negativity and later positive waveform (i.e., 600ms), while semantic processing occurs more central parietally as a negative wave at 400ms (Kang et al., 1999; Holcomb, 1993; McPherson & Holcomb, 1999). When examining implicit language processing within a verb phrase anomaly reading task, frontal lateralization differences were noted, with syntax occurring in the left hemisphere (frontal lobe: BA 45, 46, 10), and semantic processing occurring within the right hemisphere (Kang, Constable, Gore, & Avrutin, 1999). Outside of the frontal spheres, research has implicated left anterior (basal ganglia region implicated in syntax and bilateral superior temporal regions as active for semantic processes; (Friederici et al, 2003). Others examine these differences through processing needs. Research has indicated that when words exhibit no inflection, semantic and syntactic input show equivalent activation of left frontal and temporal regions (Tyler, Bright, Fletcher, & Stamatakis., 2004). This could suggest a “morpho-syntactic” processing system in left inferior frontal regions. Support a levels-of-processing model of Craik & Lockhart (1972), inflected verbs would necessitate additional resources in this region due to complexity of tense, temporal input, and spatial information (Tyler et. al., 2004). Research also supports the procedural nature of syntax by implicating procedural syntax rules within the basal ganglia of the frontal cortex and those requiring full word processing rather than manipulation by learned rules (i.e., irregular verbs) activating temporal parietal regions (Ullman, 2001; Ullman et al., 1997).

Broca’s region maintains the claim of a semantic region (Newman, Ikuta, & Burns, 2010; Muller, Kleinhans, & Courchesne, 2003; Bedny & Thompson-Schill, 2006), though some relegate semantic processing to neighboring regions (Newman, Ikuta & Burns, 2010). It also maintains the claim of a syntactic region (Caplan et al., 2000, Caplan et al., 1998; Lee & Newman, 2010; Newman, Ikuta, & Burns, 2010; Raettig, Frisch, Friederici, & Kotz, 2010; Shetreet, Friedmann, & Hadar, 2009; Perani et al, 1999; Santi and Grodzinsky, 2007; Grodzinsky & Santi, 2008), and is fueled by evidence for selective PO and PT involvement in syntax within both western and eastern based languages (Suzuki & Sakai, 2003). Others suggest an integrative role combining grammar and word imaginability within inferior frontal left hemisphere (Bedny & Thompson-Schill, 2006). Others have suggested a role within processing both types of information, but a greater percent signal change in response to syntactic novelty among presented sentences rather than semantic novelty. Semantic novelty was noted to occur also within the right amygdala and the left hippocampus (Poppenk et al, 2008).

Substantial gains have been made in isolating activity related to semantic and syntactic processing. One viable method of doing so involves using identical verbal stimuli for both conditions, but having participants focus on only one aspect (semantic or syntactic) of the information being presented, such as pairs of sentences. Semantic decisions were isolated to left inferior frontal gyrus and syntax was isolated to Broca’s Area (Dapretto & Bookheimer, 1999). This is both supported and refuted by work that IFG is a region of semantic processing, but PO implicates verbal working memory and articulatory rehearsal and PT acts as a means for syntactic unification. This suggests a partially distinct unification system, akin to the separate language resource interpretation theory.

Language and Memory in Aging Populations

Some researchers have ventured to examine the effects that language components have within verbal memory, particularly within populations experiencing verbal memory deficits (e.g., older adult populations). Patterns of decline with deteriorating cognition become increasingly relevant as we conceptualize verbal memory within an aging population, as memory impairments within discourse language (involving syntax and semantic meaning) remain a motivating factor for initial neuropsychological screenings. When comparing the domains directly, within a healthy older adult sample, any form of organization (syntactic, semantic, or both) was found to benefit verbal memory (Nebes, Brady, & Jackson, 1989). However, further analysis reveals that differences may vary on the basis of semantic or syntactic contribution.

Semantics have been shown to exhibit deficits within cortical activity in older populations. Neuropsychological testing has shown increased use of semantic clustering techniques within verbal memory measures completed by younger adults, with no significant variability within the older adult sample. A semantic task, word finding, was found to facilitate prediction of immediate verbal memory (Jacobs et. al., 2001). Likewise, reduction in frontal (PT and IFG) activation diminished when participants were asked to focus on a semantic task rather than complete a superficial task (Logan et al, 2002). Semantic processing has been broken down into intentional (i.e., picture naming) and automatic processes (i.e., priming tasks). In comparing individuals with MCI or AD to HOA, intentional processes appear to show deficits within MCI only, while automatic deficits appear later in the progression of cognitive decline (AD; Duong, Whitehead, Hanratty, & Chertkow, 2006). Others have suggested over-reliance on semantic-focused encoding as cognition becomes impaired: in a learning task with semantically related word pairs, HOAs were shown to exhibit left frontal activation during encoding, and right frontal (IFG) and cingulate / left temporal activation during retrieval tasks, a pattern that was not replicated within a group of MCI individuals (left frontal activation only; Moulin, et al., 2007). Left ventrolateral prefrontal cortex (PFC) activation has been demonstrated to be reduced during semantic-focused verbal memory encoding in amnestic mild cognitively impaired (aMCI) participants, and was paired with behavioral data, corroborating difficulty with semantic encoding in this sample. In contrast, left PFC activation was positively correlated with recognition rates within healthy older adults (HOA) only. In addition to reduction in activation, shifts in activation have been shown within both a generalized semantic network and a more generalized language network. Left temporal regions showed increased generalized semantic activation with cognitive impairment, and category specific regions of displaced activation included left posterior left ventral temporal and frontal striatal regions (Grossman et al, 2003). Difficulties in semantic encoding were linked by authors to higher level executive processing impairing integration of information within the PFC (Dannhauser, 2008). Evidence exists that use of an acetylcholinesterase inhibitor improves both immediate and delayed recall of semantically processed words, but not words encoding using lower levels-of-processing (FitzGerald et al, 2008). Left hippocampal cells in particular have been implicated as impeding semantic decisions, compared with younger counterparts, when cells are hypocholinergic (Daselaar et. al, 2003).

While the deterioration of the semantic memory system within older adults is well supported, more debate exists regarding the status of syntax preservation in this population. Some have linked the level of cognitive deterioration with the number of syntactic errors made within speech more so than the types of errors produced (Altmann, Kempler, & Andersen, 2001). Others show conflicting findings, that though individuals experiencing cognitive decline exhibit semantic errors, their speech remains structurally accurate and complex (Kave & Levy, 2003). The integration of syntactic and semantic information becomes important as well, as some have highlighted difficulties with the semantic information embedded within verbs as more challenging with increasing levels of cognitive decline (Kemper, 1997). When engaging in language processing, older adults appear to pull compensatory cortical networks during syntax processing but not semantic processing. Comparing older to younger adults, patterns appeared similar during semantic prose processing (superior temporal gyrus, medial temporal gyrus). In processing abnormal syntax, older adults activated the left and right inferior frontal gyrus. No behavioral differences were observed in spite of older adult grey matter deficits. Within syntactic processing, left inferior and orbitofrontal activation, (PT and IFG) correlated with right frontal regions and bilateral medial temporal regions for older adult samples (Tyler et al, 2010).

Although the connection between executive functioning and processes within verbal memory have been discussed (Brooks, Weaver, & Scialfa, 2006), a distinction has been drawn between the processes of working memory and those used to process syntax implicit within verbally encoded material (Caplan, Dede, Waters, Michaud, & Tripodis, 2011; Dede, Caplan, Kemtes, & Waters, 2004; Waters & Caplan, 2002; Keptes & Kemper, 2009). Others disagree, however, linking poor syntactic skills with both white matter impairments and lower executive skills in a sample with at least mild dementia (Giovannetti et al, 2008). Related to executive skills, general frontal lobe function, has been shown to impact verbal memory when combined with age, or when relating to unorganized recall on the CVLT. The integration of frontal lobe functions within cognition makes it difficult to disentangle as a mutually exclusive entity (Simensky & Abeles, 2002).

Study Aims

Within daily life, older adults encounter verbal material to be retained for future recall or recognition. Although lists of single words frequently arise in the form of shopping lists, etc., more frequently verbal material is organized through the language that surrounds it, predominantly semantic and syntactic context. Any such form of organization has been demonstrated to benefit verbal memory within older adults (Nebes, Brady, & Jackson, 1989). However, these forms of organizational tools appear to be differentially impacted by the aging process. Syntactic processes appear to be preserved to a certain extent due to their implicit and over-learned nature (Kave & Levy, 2003; Nebes, Brady, & Jackson, 1989). Part of this observed preservation could be related to bilateral activation of frontal resources in line with the HAROLD model (Cabeza, 2002) benefiting behavioral syntactic processing performance. In contrast, semantic processing in more temporal regions does not always demonstrate this bilateral compensatory mechanism (Tyler et al, 2010). When observed within retrieval processes of verbal memory, semantic bilateral activation has been shown to diminish with increasing cognitive decline in some cases (Moulin, et al., 2007). In others, increased activation may still correlate with reduced behavioral benefit, as older adults may displace cortical semantic resources rather than recruit additional resources in addition to the expected regions (Dannhauser, 2008). Benefit of language processes have further been connected to semantic activation eliciting a greater scope of activation (Bonner-Jackson, Csernansky & Barch, 2007; Henson, Hornberger, & Rugg, 2005; Craik & Lockhart, 1972), and syntactic processes drawing on more efficient use of a smaller amount of cortical resources (Vos et. al., 2001). Research suggests that these resources could vary in efficiency based on their relationship to short term memory (syntactic processes; Perham, Marsh, & Jones, 2009) or long term memory (semantic processes; Buchsbaum, Padmanabhan, & Berman, 2010).

The broad aim of the current study was to examine the potentially increasing benefit of lower levels of verbal memory organization (i.e., syntax; Brown, 2011; Craik & Lockhart, 1972), as difficulties with higher level semantic processes intensify within an older adult population.

Due to dedifferentiation and lack of competition, difficulties in explicit semantic processing may be ameliorated by implicit syntactic processing recruiting explicit resources to benefit memory (Dennis & Cabeza, 2011). It was anticipated that as the benefit of semantic-focused encoding on verbal retention decreased, syntactic-focused encoding could act as a viable substitute and would facilitate verbal recall.

Behaviorally, we predicted that the benefit for semantic-focused encoding would be positively correlated with level of cognition: As total score on a brief measure of cognition increased, semantic-focused encoding benefit would increase, indicated by more semantically manipulated words retained after a delay. While retention of words that were semantically manipulated during an encoding task would exhibit a positive predictive relationship with cognitive status (RBANS Total Score), we hypothesized that verbal retention of syntactically manipulated words would exhibit a negative predictive relationship with cognitive status. As cognitive status declined (measured by lower RBANS score), benefit of syntactic-focused encoding would increase, measured by an increase in the number of syntactically manipulated words retained. Lower cognitive status may relate to these individuals experiencing degraded semantic networks paired with fairly intact syntax networks using appropriate compensatory mechanisms (Tyler et al, 2010).

Due to the implicit nature of syntactic encoding and its role within short term memory (Lombardi & Potter, 1992), we anticipated that syntactic-focused encoding would have a stronger benefit within immediate verbal memory than semantic encoding, which would benefit delayed retention to a greater extent. This pattern would be observed through a higher ratio of syntactically-encoded words recalled at immediate recall in comparison to after a delay, with the opposite pattern occurring in semantically-encoded words.

Following evidence that middle frontal and inferior frontal regions, and middle temporal regions were involved in deeper level processing (Henson, Hornberger, & Rugg, 2005), we predicted that semantic regions of verbal memory would include frontal and temporal regions within the left hemisphere (Brown, 2011). These regions included the middle temporal gyrus, the pars triangularis of the frontal lobe (anterior Broca's region), and the middle orbitofrontal regions, respectively. Implication of the orbitofrontal region aligns with previous research implicating the prefrontal cortex as an integrative region for higher level encoding processes (Dannhauser, 2008). We anticipated that the number of active voxels and the intensity of activation within these regions would be positively correlated with number of semantically manipulated words identified upon delayed recognition.

We further anticipated that this effect would be moderated by the role of semantic processing predominantly within long term retention. As such, the number of active voxels and the intensity of activation within these regions would be positively correlated with delayed but not immediate recall measures related to syntactic-focused encoding (as seen within the semantic – syntactic contrast).

In contrast, we anticipated that regions encompassing left inferior frontal (PO) and left middle frontal would yield greater levels of syntactic activation, in line with previous research (Brown, 2011). Our syntactic ROIs therefore included the left pars operculus of the frontal lobe (posterior Broca's region) and the left middle frontal gyrus, respectively. Although our prior study found both syntactic and semantic activation within these regions, this hypothesis remained in line with previous research linking inferior frontal (PO; Frederici et al., 2003; Kang et al, 1999; Dapretto & Bookheimer, 1999) and middle frontal (Perani et. at, 1999; Kang et al., 1999) regions within syntactic processing. We anticipated that the number of active voxels and the intensity of activation within these regions would be positively correlated with number of syntactically manipulated words identified upon delayed recognition.

We further anticipated that this effect would be moderated by the role of syntax with short term memory facilitating long term retention. As such, the number of active voxels and the intensity of activation within these regions would be positively correlated with both immediate and delayed recall measures related to syntactic-focused encoding (as seen within the syntactic – semantic contrast).

Finally, akin to Tyler et al, (2010), we expected a greater compensatory use of right hemisphere resources when processing verbal information through a syntactic lens. Greater bilateral activation of these regions within the syntactic – semantic contrast would correlate with higher retention scores for syntactic-focused encoding of words, a pattern that would not be replicated within the semantic-focused encoding condition (within the semantic – syntactic activation contrast). Specifically, we anticipated that the number of voxels activated and the intensity of activation within right hemisphere correlate ROIs would be related to immediate syntactic recall (syntactic – semantic contrast), but not immediate or delayed semantic-focused recall (semantic – syntactic contrast).

Although the current literature on expected regions of activity relating to language components of verbal recognition remains sparse, we predicted that patterns of language-based activation during a delayed recognition task would mirror the previous patterns discussed as being expected during verbal memory encoding. The directed use of language cues during encoding would likely lead to similar language regions being implicated during recognition of these words.

CHAPTER 2

METHODS

<u>Participant Recruitment</u>

Participants

Power Analysis

The current study included 32 participants, subsequent to the Desmond & Glover (2002) recommendations for verbal memory fMRI based experiments. Power was placed at .80 with an intra-subject variability estimated to be high (1.25%), secondary to potential variations within cognitive functioning, attention, and rate of fatigue development within the scanning environment. The within subjects design allowed for fixed inter subject variability, and percent voxel activity change was estimated at a conservative level (0.5%). Our time points per condition were estimated to be between 50- 100. The recommended number of participants for power above .80 for this range of time points, at a conservative two-tailed p = .002 was approximately 22- 28. However, we intentionally over-sampled from this estimate, to account for potential movement and/or high signal to noise ratio possibly occurring throughout the course of the study.

Inclusion and Exclusion criteria

The current experiment included 32 participants between the ages of 65- 85, drawn from the Athens, GA community. Recruitment was conducted by means of community fliers, psychoeducational talks regarding aging and memory, newspaper advertisements, and contacting previous Neuropsychology and Memory Assessment Laboratory participants who had expressed written interest in participating in future experiments within the laboratory. Inclusion criteria include right handed, native English speakers (no second language learned prior to age 5). Exclusion criteria included self-reported personal history of neurological disorder, self-reported immediate family history of psychosis, and self-reported personal history of psychosis or current treatment for mental illness. Participants further met medical safety criteria to enter the MRI environment: such restrictions include, but are not limited to, any question of the presence of ferromagnetic metallic material within the body, presence of a pacemaker, or self-reported significant claustrophobia. FMRI safety eligibility was reviewed upon initial screening, and confirmed by a certified MRI technician prior to placement within the fMRI environment. The project was approved by the University of Georgia Institutional Review Board.

Data Acquisition

Neurocognitive Measures

Participants completed the Wechsler Test of Adult Reading (The Psychological Corporation, 2001), a well validated estimate of premorbid intelligence that entails reading and pronouncing words of increasing difficulty, and correlating accuracy scores with demographic variables (The Psychological Corporation, 2001a). The combined WTAR/ Demographics estimate of full scale IQ was used to control for the potential confound of premorbid intelligence impacting between-subject verbal memory performance variance.

Cognitive functioning was assessed via the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998). This 30-minute neuropsychological battery assesses cognitive decline in older adults through 12 subtests generating 5 Index Scores and 1 Total Score. The indices include Visuospatial/Constructional, Attention, Language, Immediate Memory, and Delayed Memory (Randolph, Tierney, Mohr, & Chase, 1998).

fMRI Experimental Design

Each participant was trained regarding the structure and demands of the experimental encoding task following completion of neurocognitive measures. Participants completed a series of three distinct practice tasks (with two practice tasks programmed at a reduced speed, and allowing for multiple administrations) until they achieved an accuracy score greater than or equal to 80% of each practice task, including the final task set at a speed equivalent to that experienced within the scanner. Those that attained an accuracy rate of at least 80% on each practice run returned on a separate day to complete the fMRI experimental task.

The layout of the experimental paradigm is depicted within Figure 1. The experimental paradigm was an event-related, randomized design with variable ISIs across trials, to control for variations in the hemodynamic response function (HRF). The average ISI equaled 2 seconds, equivalent to the shortest stimulus duration within the paradigm. The mean ISI was informed by both previous research indicating shorter ISIs increase paradigm efficiency if they are variable (Dale, 1999), as well as research indicating that longer ISIs facilitate more effective encoding within the older adult population (Dehon, 2006). Of note, no significant differences in ISI were exhibited between encoding conditions of interest with the experimental paradigm ($p > .05$). ISI values fell on the continuum between 1 second and 3 seconds. ISI values deviated by factors of 100ms, with the exception that derivatives of the TR (1.5 seconds, 3 seconds), were not sampled. Stimuli included 80 phrases, with target nouns belonging to one of 2 categories: 40 man-made objects or entities, and 40 nouns occurring within nature. Words of equivalent length, concreteness, and frequency were generated through the MRC Psycholinguistic database (http://www.psy.uwa.edu.au/ mrcdatabase/uwa_mrc.htm; Wilson, 1988). Each phrase was constructed from one of these target nouns (presented in bold font) with the above parameters, one randomly generated verb, and an article (“the”), to form sensible subject phrases (*The* ***noun*** *verb*). Phrases were presented using E-Prime 2.0 Software (Psychology Software Tools, Inc., 2007) for 2 seconds, immediately followed by presentation of two categories for 3.5 seconds. The task involved classifying each phrase within one of the two subsequently presented categories, and remembering the bolded nouns for future recall and recognition. The choices varied based on the condition to which each phrase belonged: In the semantic condition, participants were asked to place a phrase into one of two aforementioned semantic categories, nature or man-made. In the syntactic condition, the participant was asked to judge the tense of the phrase by indicating if the preceding phrase was occurring currently or previously. There were also 40 trials of a baseline condition, which involved an active, non-verbal task. The participant was shown a “phrase” in which all letters were replaced by strings of Xs, approximating the varying lengths of verbal phrases (i.e., *XXX XXXX* ***XXXXX***). One string of letters was bolded to simulate the bolded word within the experimental conditions. The subsequent categories were an identical ‘X’ on each side of the screen. Each participant was asked to press the button that corresponds with the side of the screen where the string of bolded X’s appeared in the preceding screen (right or left position). Baseline “phrases” and choices were presented for 2 seconds and 3.5 seconds, respectively, to mimic durations of phrases and choices within experimental conditions. Target nouns were counterbalanced across 2 lists for condition of classification choice (semantic versus syntactic), and presentation within present or past tense. For all conditions, category choices were followed by variable ISIs, marked by a cross hair in the middle of the screen. As noted, ISI between semantic and syntactic categories did not significantly vary within either list, nor did ISI of any experimental condition significantly vary between lists. Neither experimental condition significantly varied with the baseline condition on either List 1 or List 2 ($p > .05$). Participants made all responses by means of a touch pad.

Participants were asked to verbally recall as many presented bolded target nouns as possible immediately after the encoding portion of the experiment. After a delay of approximately 15 minutes, they were administered both a delayed verbal recall task and a delayed recognition task for the bolded target nouns. This task included presentation of 80 target words and a distracter being presented on each side of the screen for 3.5 seconds each. Following each recognition choice, the participant viewed a cross hair with variable ISIs, which mirrored the format described within the experimental paradigm above.

Image Acquisition

Images were acquired at the University of Georgia's Bioimaging Research Center (BIRC) using a General Electric 16-channel fixed-site Signa HDx 3.0 Tesla Magnetic Resonance Imaging (MRI) magnet. Participants underwent an initial T-1 weighted structural MRI scan (FOV = 240mm, slice thickness = 1.2mm, locs per slab = 154, TR= 7.8, TE = min full, matrix = 256 x 256) to establish a reference template for future images. Participants also underwent 3 T2*-weighted, single-shot echo planar sequence scans. Functional image acquisition occurred over 2 separate runs of the experimental paradigm with 7.5 minute durations (separated by a short break to prevent fatigue), and one delayed recognition paradigm with 7.5 minute duration. Functional scans included 30 interleaved (bottom-up) slices per volume, aligned to the inter-commissural line (AC-PC line) with: TR = 1.5 s, TE = 25ms, flip angle = 90°, slice thickness = 4mm, FOV = 220 x 220 mm, matrix = 64 x 64, and ASSET factor = 2. Functional images covered the cortex and cerebellum. Each encoding paradigm run consisted of 300 total volumes, and the recognition paradigm consisted of 294 total volumes. In each paradigm, 10 samples were discarded during the initial acquisition. Magnitude and phase map images were acquired for field map unwarping with the following parameters: T2 gradient echo, flip angle = 30°, TR = 750 ms, TE = 5 ms, FOV = 256 x 256 mm, slice thickness = 2 mm, matrix = 128 x 128, 60 interleaved slices and ASSET factor = 2.

Data Analysis

Preprocessing

FMRI data was preprocessed with Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm; Ashburner et al., 2010), through Matlab (The Math Works, Natick, MA) with the following parameters: TR = 1.5 s, Slice Order = interleaved bottom-up, Reference slice = 1. Run 1 and run 2 for each subject was analyzed separately and combined during the second level analysis stage, to allow first level analysis to account for variations in condition stimulus onset times between runs. To preprocess, images first underwent a slice timing correction to adjust for non-sequential acquisition (interleaved bottom-up). Anatomical, functional, magnitude, and phase images were then manually aligned to bring the AC-PC line of each image in line with the horizontal plane, and facilitate future alignment of images with each other. Images were realigned to the first image of the middle series scan (the first image of the second experimental paradigm run), correcting for participant movement. Scans were both realigned and unwrapped using individual fieldmaps as a measure of phase and magnitude variations in signal during a specific session. This process corrected distortions caused by motion or inhomogeneity in measured fields (e.g., varying densities of different tissue within the brain). Anatomical scans were coregistered to the first functional image of the second experimental paradigm, to align the anatomical data to the most representative positioning of functional data, the middle slice of all functional data collected. This structural image (set within fMRI space), along with all functional images, was then registered to the standardized T1 image (MNI space) in order to normalize images, or move all images to a common standardized space for between-subject comparisons. The anatomical scan was segmented to differentiate grey matter from white matter in order to better localize activation occurring within specified regions of interest located within grey matter of the cortex. Deformation fields, taking into account the locations of each type of matter, were applied to the functional images in order to match locations of activation to the corresponding types of matter. In the final step, scans were smoothed to decrease interfering noise in the signal-to-noise ratio.

Data Analysis

Data was analyzed using SPSS version 16.0 (SPSS, Chicago). Behavioral analyses addressing semantic versus syntactic encoding aims tested the hypotheses that semantic-focused encoding would be positively related to total cognition, while syntactic-focused encoding would be negatively related. Multiple regressions were completed, using Total RBANS score as the predicted variable and delayed syntactic recognition and delayed semantic recognition as predictor variables. Behavioral analyses aiming to compare immediate and delayed recall tested the hypotheses that more syntactically manipulated words would be recalled immediately following the encoding task, while more semantically manipulated words would be recalled upon delayed recall. Paired t-tests compared number of syntactically and semantically manipulated words recalled immediately in comparison to delayed recall. We further hypothesized that the previously discussed pattern of RBANS and recognition scores would extend to RBANS and recall scores: To test this, a repeated measures 2 (condition: syntactic, semantic) x 2 (time:

immediate, delayed) ANOVA used Total RBANS score as the dependent variable and recall scores as independent variables.

FMRI data was pre-processed and voxel activity within areas of interest, as determined by observed regions of activity during each condition, was evaluated. ROIs were defined by the automated anatomical atlas of the WFU PickAtlas (Maldjian, Laurienti, & Burdette, & Kraft, 2003; Maldjian, Laurienti, & Burdette, 2004; Tzourio-Manoyer & Landeau, 2002). Hypothesized regions of interest for the semantic condition included the left hemisphere middle orbitofrontal gyrus and left pars triangularis, as well as the left MTG. Regions of interest for the syntactic condition included left hemisphere pars operculus and left middle frontal gyrus (MFG). Right hemisphere correlates for all regions of interest were examined. Average BOLD signal and number of activated voxels within each ROI were calculated using SPM8. T-test contrasts were calculated through structural equation modeling functions of SPM8. Within-subject t-test contrasts included mean BOLD signal for each of the experimental conditions, within observed areas of interest. Contrasts for semantic versus syntax-focused encoding, semantic versus syntactic-focused delayed recognition, and right versus left hemisphere analyses were computed (i.e., semantic – syntactic activation and syntactic – semantic activation).

Behavioral performance and fMRI BOLD signal were then integrated for the final analyses, examining the impact of behavioral covariates with BOLD activation (i.e., syntactic - semantic and semantic – syntactic activation contrasts). First, RBANS Total scores were correlated with levels of left and right sided activation during the encoding task, and recognition task. This allowed us to address the hypothesis that level of cognition would relate to increased use of semantic networks (high cognition) or syntactic networks (lower cognition).

We next addressed aims regarding semantic versus syntactic manipulation during encoding. Hypotheses regarding activation within each condition, relating to number of condition-specific manipulated words retained, were tested using SPM. Cortical BOLD activation during the encoding task, within each condition of interest, was used as the predicted variable. Left syntactic ROI BOLD activation as predicted by the number of words recognized after syntactic manipulation was determined. Left semantic ROI BOLD activation, as predicted by the number of words recognized after semantic manipulations was calculated. The hypothesis that right hemisphere correlates would show this same predictive pattern only within the syntactic condition was then examined: Right hemisphere ROI correlated BOLD activation as predicted by the number of words recognized after syntactic manipulation during the encoding task, as well as recognized after semantic manipulation during the encoding task, was also calculated. As it was hypothesized that this pattern would be replicated within the recall based BOLD activation, these covariate analyses were repeated, replacing encoding task BOLD activation with recognition task activation.

To address aims regarding immediate versus delayed retention, hypotheses relating to immediate and delayed recall showing a positive relationship between condition-specific behavioral results and condition-specific BOLD activation was examined. BOLD activation during the encoding task, within each condition of interest, was used as the predicted variable. Left hemisphere syntactic ROI BOLD activation, as predicted by the number of manipulated words retained upon immediate free recall versus delayed free recall, was examined. Left hemisphere semantic ROI BOLD activation, as predicted by the number of words recalled following immediate free recall versus delayed free recall, was examined. To again test the hypothesis that bilateral compensation would occur predominantly within the syntactic condition, right hemisphere correlates were examined, using recall scores as behavioral covariates: Right hemisphere ROI BOLD activation by condition, as predicted by the number of words recalled following immediate free recall versus delayed free recall was examined.

Table 2.1: Target Phrase Examples

Nature Related Targets	
Present Tense	***Past Tense***
THE **ATOM** STABILIZES	THE **ATOM** STABILIZED
THE **BODY** HURTS	THE **BODY** HURT
THE **TAIL** WAGS	THE **TAIL** WAGGED
THE **CARBON** BONDS	THE **CARBON** BONDED
THE **MOSQUITO** ANNOYS	THE **MOSQUITO** ANNOYED
Man-Made Related Targets	
Present Tense	***Past Tense***
THE **ARMY** TRAINS	THE **ARMY** TRAINED
THE **LENS** REFINES	THE **LENS** REFINED
THE **CANDY** SWEETENS	THE **CANDY** SWEETENED
THE **ARROW** POINTS	THE **ARROW** POINTED
THE **VEHICLE** CRASHES	THE **VEHICLE** CRASHED

CHAPTER 3

LANGUAGE PROCESSES IMPLICATED WITHIN VERBAL MEMORY ACTIVATION AND RETENTION DURING OLDER ADULTHOOD[1]

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[1] Brown, C. & Miller, L.S. To be submitted to *NeuroImage*.

Abstract

Although verbal memory deficits of older adulthood have been long studied, the specific impact that contextual syntactic and semantic components have within this process are less clear. FMRI activation and behavioral retention measures for a verbal encoding/ categorization task were compared with neuropsychological measures of cognition. FMRI activation during subsequent delayed recognition task was also analyzed in a post-hoc analysis. Syntactic focused encoding yielded activation within bilateral middle temporal gyrus (MTG) and pars opercularis (PO). Semantic focused encoding regions including left hemisphere activation within PO, pars triangularis (PT), middle frontal gyrus (MFG), middle orbitofrontal gyrus (MOFG), and MTG. Right hemisphere activation included MFG, MOFG, and MTG. Significant recognition activation included left MFG and bilateral MTG during semantically manipulated words. Cognitive status demonstrated a significant relationship to semantic specific encoding activation within left MOFG, PO, and PT. Right hemisphere regions of significant for this contrast included MTG and PO at more liberal thresholds. Results are consistent with the levels of processing model of verbal memory (Craik & Lockhart, 1972), suggesting increased scope of semantic resources with increasing cognition in comparison to syntactic resources.

Index Words: verbal memory, fMRI, language, syntax, semantic, older adults

Introduction

Verbal memory has long been examined as problematic within the aging process, both in terms of healthy and pathological aging (APA, 2000). In order to better understand some of the variables that impact pathological aging, researchers first must explore these variables within a healthy aging population. Neuropsychologists generally examine memory utilizing list learning task (e.g., California Verbal Learning Test; CVLT) or contextual discourse memory tasks (e.g., Logical Memory subtest, WMS-IV). Contextual learning tasks have been shown to benefit diagnostic accuracy in isolating normal from pathological aging (Rabin et al., 2009). Even outside the realm of pathological aging, passively provided (Strangman et al, 2009) or actively contrived (Marshall & Smith, 1977) semantic relatedness benefits memory performance.

Cognitive difficulties of aging also include maintaining and filtering relevant information and processing information quickly (Li, Lindenberger, & Sikstrom, 2001). Cognitive slowing and attentional difficulties may impact verbal memory difficulties at higher levels of cognitive complexity such as recall over recognition (Lou & Craik, 2008) or semantic processing over lower level syntactic processing. Indeed, older adults experience deficits structuring language semantically (Jacobs et al., 2001), but fewer difficulties appear within more implicit/ procedural syntactic domains (Hoyte, Brownell, & Wingfield, 2009; Fabbro, 1999). Some have suggested that semantic comprehension and syntactic complexity hold diagnostic value differentiating individuals with dementia from those experiencing healthy aging (Emory & Breslau, 1988).

Research within the verbal memory field has likewise implicated aspects of language processing as conveying partially distinct levels of benefit. Most notably, the level-of-processing model (Craik & Lockhart, 1972) implicates complexity of processing with the need for additional cortical resources. Research in this field has categorized semantic processing as high complexity, requiring additional cortical resources and affording deeper encoding that benefits retention (Craik & Lockhart, 1972, Bonner-Jackson, Csernansky & Barch, 2007; Baker, Sanders, Maccotta, & Buckner, 2001). Specific cortical regions involved within higher level semantic encoding have been suggested within left inferior frontal, left prefrontal, left inferior parietal, middle temporal, and right supramarginal regions (Bonner-Jackson, Csernansky & Barch, 2007; Henson, Hornberger, & Rugg, 2005). Of note, as tasks at higher levels of complexity increase in difficulty, researchers have found preserved short term memory using lower levels of encoding complexity (Majerus, Norris, & Patterson, 2007). Although the specific comparative complexity between syntax and semantic process remains unclear, some research suggests that syntax manipulation and encoding utilizes procedural processes (Lombardi & Potter, 1992), and memory for syntax remains relatively preserved through procedural mechanisms in spite of cognitive difficulties (Ferreira, Bock, Wilson, & Cohen, 2008). These lines of research support syntactic processing being a lower level processing than semantic processing. Another explanation for this phenomenon is that syntax requires efficient use of, rather than additional, cortical resources (e.g., Vos, Gunter, Schriefers, & Friederici., 2001).

In addition to encoding, verbal memory also focuses attention on future retrieval of information. Retrieval has been isolated into recollection (free recall) and familiarity (recognition), with impaired function in both denoting encoding deficits, and intact familiarity paired with poor recollection denoting successful encoding (Lou & Craik, 2008; Anderson et al, 2011). Some have suggested that while memory strategies within healthy controls facilitate organization and reduce necessary encoding resources, these strategies do not reduce the resources required during retrieval of information (Arenth et al, 2008). Research correlates recognition with encoding activity in middle frontal regions (Ranganath, Johnson, & D’Esposito,

2000) and temporal regions (Henson, 2005) but isolates DLPFC as related more to the encoding process than recall or recognition per se (Turriziani et al, 2010). The right hemisphere has been suggested to be more active within recognition tasks (Johnson et al, 2001). Left IFG and hippocampus have been linked to successful recognition and recall, with greater resources allocated during recall tasks over recognition (Staresina & Davichi, 2006). Inferior temporal gyrus and occipital lobes have been related by some to recognition regardless of accuracy (Heun et al, 2004). Others break down recognition into higher confidence judgments (i.e., recollection) within the MTG and ventral posterior parietal cortex (PPC), with lower confidence judgments (i.e. familiarity) processed in the PFC and dorsal PPC (Kim & Cabeza, 2009). Of note, these regions likewise play a prominent role within language processing, with MTL related to semantic novelties and IFG related to syntactic novelties (Poppenk et al, 2008).

HAROLD and HERA models suggest that the key to maintaining cognitive function, such as these aspects of language and memory, lies within cortical reorganization (Cabeza, 2001). Imaging research has demonstrated such a link between cortical activation and verbal memory, with healthy controls showing increased activity in temporal and less activity in prefrontal regions than MCI participants during encoding and retrieval (Clement & Belleville, 2009). Others have related increased activity within PFC to increased memory accuracy (Lim el al, 2008). Hyperactive frontal regions have also been identified as potentially compensating for temporal deficits within the aging brain (Rajaha & MacIntosh, 2008). Recognition-specific activation has included right parahippocampal, parietal, prefrontal, and left precuneus activation in older adults. Left PFC and precuneus in particular have been linked to behavioral accuracy (Rajah & McIntosh, 2008).

Support for the HAROLD model has been found in particular within frontal regions (Cabeza et al, 1997) and when activation correlates to depth of memory encoding (Stebbins et al, 2002). One such domain of dedifferentiation occurs between implicit versus explicit resources: This shift should lead to decreased competition and decreased specialization between these resources within older adults (Dennis & Cabeza, 2011). Within the aging brain, explicit memory has been observed to be more impaired than implicit memory (Cabeza, 2001) and verbal memory more so than non-verbal memory. Part of these discrepancies lies in the left frontal pattern of degeneration in older adults, mapping onto regions that assist with verbal organization and semantic processing. It is because of this that verbal memory, particularly word learning and long delayed recall on the CVLT-II have been found to be predictive of pathological aging (Greenaway et al, 2006). Each 1 SD variation from the mean on short and long delay free recall tasks increases the risk of possible/probable AD by 8/3 times, respectively (Lange et. al, 2002). Accuracy and speed of response, as well as less specific distribution of cortical resources have also been observed within the aging population during a recognition task (Madden et al, 1999). Compensatory mechanisms have also been suggested for memory deficits such as frontal hypoactivation during memory encoding in older adults. Manipulation of verbal materials benefit memory (Logan et al, 2002), supporting the idea that using intact implicit/ procedural resources and semantic world knowledge could be a way to manipulate information using intact resources. Reduced specificity and context could be beneficial within this regard (Lou & Craik, 2008).

The goal of this study was to examine the benefit of varying levels of verbal organization within a sample of healthy aging adults (Brown, 2011; Craik & Lockhart, 1972). Specifically, we sought to examine whether the interaction of language and verbal memory was related to level of cognitive function. The well-established ‘levels of processing’ model suggests that semantic processing, being higher level, requires higher levels of cortical resources (Craik & Lockhart, 1972, Bonner-Jackson, Csernansky & Barch, 2007; Baker, Sanders, Maccotta, & Buckner, 2001). The current study sought to build on this prior work by examining whether lower level syntactic processing could benefit verbal memory as cognition declined, reducing resources available for higher level semantic processing. Previous work has suggested dedifferentiation of domains during cognitive decline, coupled with reduced competition for resources (Dennis & Cabeza, 2011), raising the question of whether implicit syntactic resources could facilitate memory when semantic resources decline. We aimed to examine this potential increasing benefit of syntax as difficulties with higher level semantic processes increase through both behavioral and neuroimaging variables.

Behaviorally, we hypothesized that the nature of language cues facilitating verbal memory would be influenced by level of cognition. Specifically, it was predicted that semantic focused encoding would correlate with cognition in a positive direction: As total cognition (measured by RBANS Total Scaled Score) increased, more semantically manipulated nouns would be retained (measured by number of semantically manipulated words identified at delayed recognition). In contrast, as cognition decreased, the benefit of semantic manipulation during encoding would decrease and the benefit of syntactic-focused manipulation would increase (measured by number of syntactically manipulated words identified at delayed recognition). Lower cognitive status could reflect degraded semantic networks allowing for increased compensatory use of dedifferentiated syntactic networks (Tyler et al, 2010). Lower RBANS scores would therefore correlate with greater number of syntactically manipulated words retained following a delay.

Via functional neuroimaging, we examined regions of activation during encoding phase based on specific language context by shifting attention towards semantic or syntactic processing with an embedded forced choice language manipulation task. We hypothesized that regions of activation during this manipulation would align closely with regions previously suggested as engaged in predominantly semantic or syntactic processing. Please refer to Table 3.1 for regions of interest. Semantically, the MTG, PT of anterior Broca's region, and MOFG would be predominantly implicated in semantic manipulation during encoding phase. We hypothesized that the number of voxels activated and intensity of activation in these regions would be higher when subtracting syntactic activation from semantic activation than vice versa. Also, we hypothesized that this activation would be positively correlated with delayed recognition of semantically manipulated target words. Predictions for semantic regions of interest were in line with research on MFG, IFG, and MTG regions being involved in deeper processing, the PFC being involved in higher level integration (Dannhauser, 2008), as well as previous research within our lab (Henson, Hornberger, & Rugg, 2005; Brown, 2011).

Syntactic manipulation ROIs included the left pars operculus (PO) of posterior Broca's and the left MFG, in line with research relating inferior frontal (BA 44; Frederici, Ruschemeyer, Hahne, & Fiebach, 2003; Kang, Constable, Gore, & Avrutin, 1999; Dapretto & Bookheimer, 1999) and middle frontal (BA 46; Perani et. at, 1999; Kang, Constable, Gore, & Avrutin, 1999) regions within syntactic manipulation. This was in line with previous research isolating regions encompassing left IFG and left MFG with increased syntactic activation (Brown, 2011). We hypothesized that the number of voxels activated and intensity of activation in these regions would be higher when subtracting semantic activation from syntactic activation than vice versa.

Also, we hypothesized that this activation would be positively correlated with delayed recognition of syntactically manipulated target words.

Finally, on a more exploratory level, we hypothesized language-based activation during delayed recognition would mirror patterns discussed above as expected during encoding. Language encoding cues would likely activate similar language regions during recognition as were activated during encoding. Semantic recognition activation, when syntactic recognition activation was subtracted, would activate regions MTG, PT of anterior Broca's region, and MOFG, as measured by number of voxels activated, intensity of activation, and positive correlation of this activation with delayed recognition of semantically manipulated target words. Syntactic recognition activation, when semantic recognition activation was subtracted, would activate regions left pars operculus (PO) and the left MFG, as measured by the number of voxels activated, the intensity of activation, and positive correlation of this activation with delayed recognition of syntactically manipulated target words.

Methods

Participants

The current experiment included 32 older adults between the ages of 65- 85, drawn from a college-town community. Participants were recruited by means of fliers, psychoeducational memory talks, newspaper advertisements, and previous laboratory participants who expressed written interest in participating in future studies. Participants were right handed, native English speakers (no second language learned prior to age 5) who met safety criteria to enter the MRI environment. Exclusion criteria included self-reported personal history of neurological disorder, immediate family or personal history of psychosis or current self-reported treatment for mental illness. The project was approved by the University of Georgia Institutional Review Board.

Neurocognitive Measures

Participants completed the Wechsler Test of Adult Reading (The Psychological Corporation, 2001), an estimate of premorbid intelligence that is well validated and entails reading increasingly difficult words. The test allows for correlating accuracy with demographic information (The Psychological Corporation, 2001a). The combined WTAR/ Demographics estimate of full scale IQ was used to control for the potential confound of premorbid intelligence impacting between-subject verbal memory performance variance.

Cognitive functioning was assessed briefly via the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998). This neuropsychological battery assesses cognitive function through 12 subtests generating 5 Index Scores and 1 Total Score. Indices include Visuospatial/Constructional, Attention, Language, Immediate Memory, and Delayed Memory (Randolph, Tierney, Mohr, & Chase, 1998).

fMRI Experimental Design

Participants were trained for the experimental encoding task. Participants completed three practice tasks (two allowing for reduced presentation speed and multiple administrations). Those that attained an accuracy rate of at least 80% on the final practice run returned on a separate day for the fMRI task.

The layout of the experimental paradigm is depicted within Figure 3.1. The encoding paradigm was an event-related, randomized design with variable ISIs (average ISI = 2 seconds), equivalent to trial presentation durations. Mean ISI was informed by previous research indicating shorter and variable ISIs increase paradigm efficiency (Dale, 1999), while longer ISIs facilitate effective encoding within the older adults (Dehon, 2006). No significant ISI differences were exhibited between conditions of interest ($p > .05$). ISI ranged from 1 second to 3 seconds in duration and varied by factors of 100ms (durations equivalent to TR were not sampled: 1.5 seconds, 3 seconds). Stimuli included 80 phrases. Phrases included target nouns from 2 different categories: 40 man-made entities, and 40 entities occurring within nature. Words of equivalent concreteness, frequency and length were generated through the MRC Psycholinguistic database (http://www.psy.uwa.edu.au/ mrcdatabase/uwa_mrc.htm; Wilson, 1988). Each phrase was constructed from previously described target nouns (presented in bold font), a randomly generated verb, and the article ("the"), forming sensible phrases (*The* ***noun*** *verb*). Phrases were presented using E-Prime 2.0 Software (Psychology Software Tools, Inc., 2007). Duration of presentation was 2 seconds, followed by presentation category choices for 3.5 seconds. Participants were asked to: 1) classify each phrase within one of the categories presented; and 2) to remember the bolded nouns. In the semantic condition, participants placed phrases into one of the aforementioned semantic categories, nature or man-made. In the syntactic condition, participants judged the grammatical tense of the phrase by indicating if it was occurring currently or previously. There were 40 baseline trials involving an active, non-verbal task. Participants were presented "phrases" in which letters were replaced by strings of Xs, approximating varying lengths of words in verbal phrases (i.e., *XXX XXXX* ***XXXXX***). One string of letters was bolded to simulate the bolded word in each phrase. Subsequent categories were identical 'X's on each side of the screen. Participants pressed the button corresponding with the side of the screen on which bolded X's appeared (right or left position). Baseline "phrases" and choices were presented for 2 seconds and 3.5 seconds, respectively. Target words were counterbalanced (2 lists) for: classification choice (semantic versus syntactic), present or past tense presentation. Category choices were followed by variable ISIs, visualized by a centered cross hair. ISI between semantic and syntactic categories did not significantly vary within either list or between lists.

Experimental conditions did not significantly vary with the baseline condition ($p > .05$). Participants made responses by a touch pad.

After a delay of approximately 15 minutes, participants were administered a delayed recognition task for the bolded target nouns. A recognition format was utilized as it most accurately measures level of verbal material encoded, in comparison to recall measures, which could indicate retrieval deficits in spite of adequate encoding (Lou & Craik, 2008; Anderson et al, 2011). This task included presentation of 80 target words and a distracter being presented on each side of the screen for 3.5 seconds each. Following each recognition choice, the participant viewed a cross hair with variable ISIs, which mirrored the format described within the experimental paradigm above.

Image Acquisition

Images were acquired at the University of Georgia's Bioimaging Research Center (BIRC) using a General Electric 16-channel fixed-site Signa HDx 3.0 Tesla Magnetic Resonance Imaging (MRI) magnet. Participants underwent an initial T_1 weighted structural MRI scan (FOV = 240mm, slice thickness = 1.2mm, locs per slab = 154, TR= 7.8, TE = min full, matrix = 256 x 256) to establish a reference template for future images. Participants also underwent 3 T_2*-weighted, single-shot echo planar sequence scans. Functional image acquisition occurred over 2 separate runs of the experimental paradigm with 7.5 minute durations (separated by a short break to prevent fatigue), and one delayed recognition paradigm with 7.5 minute duration. Functional scans included 30 interleaved (bottom-up) slices per volume, aligned to the inter-commissural line (AC-PC line) with: TR = 1.5 s, TE = 25ms, flip angle = 90°, slice thickness = 4mm, FOV = 220 x 220 mm, matrix = 64 x 64, and ASSET factor = 2. Functional images covered the cortex and cerebellum. Each encoding paradigm run consisted of 300 total volumes, and the recognition paradigm consisted of 294 total volumes. In each paradigm, 10 samples were discarded during the initial acquisition to control for potential variability within the scanning environment during initiation of scan and allow for a steady state to be reached prior to data acquisition. Magnitude and phase map images were acquired for field map unwarping with the following parameters: T_2 gradient echo, flip angle = 30°, TR = 750 ms, TE = 5 ms, FOV = 256 x 256 mm, slice thickness = 2 mm, matrix = 128 x 128, 60 interleaved slices and ASSET factor = 2.

Preprocessing

FMRI data was preprocessed with Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm; Ashburner et al., 2010), through Matlab (The Math Works, Natick, MA) with the following parameters: TR = 1.5 s, Slice Order = interleaved bottom-up, Reference slice = 1. Run 1 and run 2 for each subject was analyzed separately and combined during the second level analysis stag, to allow first level analysis to account for variations in condition stimulus onset times between runs. To preprocess, images underwent slice timing correction, manual realignment of anatomical, functional, magnitude, and phase images, realignment of images to the first image of middle scan series (1st image of 2nd run), and realigned and unwrapped using individual fieldmaps. Anatomical scans were coregistered using the first functional image of the 2nd run as a reference. The structural image and functional images were registered to the standard T_1 MNI image. Anatomical scans were segmented and deformation fields were applied to functional imaging to match to the anatomical material. Finally, images were smoothed using a FWHM Gaussian filter.

Data Analysis

Data was analyzed using SPSS version 16.0 (SPSS, Chicago). Multiple regressions were completed using Total RBANS score as the predicted variable. Delayed syntactic recognition and delayed semantic recognition were entered as predictor variables.

Voxel activity within ROIs was evaluated. ROIs were defined by the automated anatomical atlas of the WFU PickAtlas (Maldjian, Laurienti, & Burdette, & Kraft, 2003; Maldjian, Laurienti, & Burdette, 2004; Tzourio-Manoyer et al, 2002). Hypothesized semantic manipulation ROIs included left hemisphere MOFG and left PT, as well as left MTG. Hypothesized syntactic manipulation ROIs included left hemisphere PO and left MFG. Right hemisphere correlates for ROIs were examined. Maximum BOLD signal and number of activated voxels within each ROI were calculated using SPM8. T-test contrasts included max BOLD signal for experimental conditions, within ROIs. Contrasts for semantic versus syntax-focused encoding and semantic versus syntactic-focused delayed recognition were also examined.

Behavioral performance and fMRI BOLD signal were integrated, examining the impact of behavioral covariates on cortical activation (i.e., syntactic - semantic and semantic – syntactic activation contrasts). First, RBANS Total scores were correlated with levels of left and right sided activation during the encoding task and recognition task.

Left syntactic ROI BOLD activation as predicted by words recognized after syntactic manipulation was calculated. Semantic ROI BOLD activation with the same predicting variables was also examined. Right hemisphere ROI correlates predicted by words recognized after syntactic manipulation and after semantic manipulation were also calculated. These covariate analyses were repeated, replacing encoding with recognition task activation.

Results

Sample Description

Participants had a mean age of 74.63 years (s.d. = 6.66), and a mean education of 17.54 years (s.d. = 2.76). The sample was split equally by gender (50% male, 50% female) and self-identified as Caucasian/Non-Hispanic (100%). Please refer to Table 3.2 for further sample descriptions.

Demographic Bivariate Correlations

Demographic correlations with behavioral measures of interest were determined. Age was found to have significant relationships with Immediate Total Recall ($r = -0.36$, $p < .05$), Delayed Semantic Recall ($r = -0.43$, $p < .05$), and Delayed Total Recall ($r = -0.41$, $p < .05$). Education was found to have significant relationships with WTAR/Demographics Predicted FSIQ ($r = 0.62$, $p < .01$), RBANS VisuoConstructional Index ($r = 0.39$, $p < .05$), RBANS Language Index ($r = 0.41$, $p < .05$), and RBANS Total Index ($p = 0.44$, $p < .05$). Gender was found to be significantly correlated to WTAR/ Demographics Predicted FSIQ (rho = -.36, $p < .05$) and Immediate Semantic Recall (rho = -0.37, $p < .05$) using Spearman’s rho. Race was not found to be significantly correlated with any behavioral measures of interest by means of the same method.

Estimate of Premorbid Intelligence

Scores on WTAR reflect standard scores (mean of 100 and standard deviation of 15; Table 3.2). Participants demonstrated a WTAR predicted FSIQ score of 115 (s.d. = 6.7). WTAR predicted FSIQ demonstrated significant bivariate correlation with Syntactic Paradigm Accuracy ($r = 0.46$, $p < .05$), Semantic Recognition Accuracy ($r = 0.45$, $p < .05$), RBANS Immediate Memory ($r = 0.42$, $p < .05$), RBANS VisuoConstructional Index ($r = 0.41$, $p < .05$), RBANS

Language Index ($r = 0.47$, $p < .05$), RBANS Delayed Memory Index ($r = 0.37$, $p < .05$), and RBANS Total Index ($p = 0.60$, $p < .05$).

Cognitive Functioning: RBANS

Scores on the RBANS were converted into standard scores (mean = 100, SD = 15). Based on normative scores on the RBANS, participants fell within the average range across indices (Table 3.2). This suggests no significant discrepancies between estimates of premorbid functioning (WTAR Predicted FSIQ), which fell within the high average range. It also suggests no significant discrepancies between baseline cognitive functioning within the current sample and that of the overall population, controlled for age.

Behavioral Results

fMRI Behavioral Paradigm Accuracy

Response accuracy reflects accuracy of categorizing phrases within the verbal encoding phase of the experiment. Number of correct syntactic manipulations ranged from 20 to 40 phrases (out of a possible 40 phrases), with a mean of 35 words and an SD of 4.41. Number of correct semantic manipulations ranged from 23 to 37 out of a possible 40 phrases (mean = 33 words, SD = 2.91). Number of correct baseline manipulations ranged from 1 to 40, with a mean of 38 out of 40 responses and an s.d. of 7.02. Of note, low ranges of baseline response related to infrequent slowed baseline response speed rather than poor effort during the task, as confirmed by delayed responses for baseline items. When delayed responses were taken into account, participants correctly answered an average of 39.68 baseline trials, with a s.d. of 0.54. As individuals showing low response rates within the given time frame demonstrated delayed responses, they were judged to be attending to the task and remained in the analyses. Total correct responses (Sum of target and baseline responses) demonstrated a mean of 89 out of a possible 120 responses, with a SD of 7.92. Total Correct Accuracy rates demonstrated a mean of 106 responses out of a possible 120, with a standard deviation of 9.50. Percent accuracy for the task showed a mean of 88.57% (s.d. = 7.92).

Delayed Recognition Accuracy

Following delayed recall, participants underwent a delayed recognition forced- choice task. Accuracy for syntactically manipulated words demonstrated a mean of 33 out of 40 words (s.d. = 4.06). Participants remembered a mean of 39 semantically manipulated words (out of a possible 40 words; s.d. = 3.96). They showed a mean total correct response of 67 out of 80 (s.d. = 7.30). Participants demonstrated a mean accuracy rate of 84.57% (s.d. = 9.35).

Regression Analyses: RBANS Total Scale Score

Multiple regressions were conducted to examine the role of semantic recognition accuracy and syntactic recognition accuracy in predicting RBANS Total Scale Score. Due to the significant bivariate relationship between education and RBANS Total Scale Score, years of education was controlled for within the model. Both semantic ($\beta = .376$, $t = 2.409$, $p < .05$) and syntactic ($\beta = .325$, $t = 2.043$, $p = .05$) delayed recognition accuracy significantly predicted RBANS Total Scale Score after education was accounted for. However, neither variable accounted for variance beyond the other when both were entered into the model after accounting for education.

fMRI Analyses

Individual Regions of Interest

To test our hypotheses regarding regions of interest and their relationship to semantic (MTG, PT, MOFG) or syntactic (PO, MFG) related manipulations, fMRI activation was examined using masks specific to each previously defined region of interest. It is important to note that these were apriori selected ROIs meant to test our specific hypotheses and that they were not influenced by the below described exploratory whole-brain analyses.

Activation during the encoding paradigm was assessed first. Syntactic – Baseline activation occurred within left MFG, PT, MTG, and PO ($p < .05$, FWER). Right hemisphere activation occurred within right MFG, MOFG, PT and PO ($p < .05$, FWER). In the Semantic – Baseline contrast, left hemisphere activation occurred within all regions of interest ($p < .05$, FWER), while left hemisphere activation occurred within all regions with the exception of MTG ($p < .05$, FWER). In the Syntactic – Semantic contrast, left hemisphere significant activation occurred within the syntactic PO at FWER $p < .05$ and MTG at an uncorrected $p < .001$. Right hemisphere activation displayed a similar pattern. In the Semantic – Syntactic contrast, left hemisphere significant activation occurred within all regions of interest, while right hemisphere activation occurred within MFG, MOFG, and MTG.

Activation during the recognition paradigm was assessed subsequently. In the Syntactic – Baseline contrast, Activation was found within semantic PT and MOFG at FWER $p < .05$, while syntactic MFG activation was observed at a more liberal, uncorrected $p < .001$. Right hemisphere activation was observed within MOFG and PO at FWER $p < .05$. Activation was observed within MFG and PT at uncorrected $p < .001$. Semantic – Baseline activation was observed within MOFG, PT, and PO in left hemisphere regions at FWER $p < .05$. Right hemisphere activation was observed at MFG, MOFG, PO, and PT at FWER $p < .05$. No significant activation in either hemisphere was observed within the Syntactic – Semantic contrast at conservative (FWER $p < .05$) or liberal (uncorrected $p < .001$) thresholds. Semantic – Syntactic activation was observed within left MFG and bilateral MTG at FWER $p < .05$.

Whole Brain Analyses

An initial whole brain analysis was conducted to identify regions of activation across contrasts within each encoding paradigm (Figure 3.2, Table 3.5). Unless otherwise stated, results reflect a family wise error correction with cluster threshold of 8 voxels ($p < .05$). Within the Syntax – Baseline condition activation across hemispheres, with clusters ranged in number from 10 voxels to 23,354 voxels. Activation within ROIs included bilateral pars triangularis, right middle frontal gyrus and right middle orbitofrontal gyrus. Regions of activation also encompassed right lingual, postcentral, superior frontal, insula, and pallidum. Left hemisphere regions included middle occipital, calcarine, occipital, supplemental motor, and inferior parietal regions. Bilateral involvement was observed within precentral regions. Semantic – Baseline regions of activation ranged in size from 11 voxels to 19245 voxels. Regions of interest activated included left inferior pars opercularis, left middle temporal gyrus, right pars triangularis, right middle orbitofrontal gyrus and right middle frontal gyrus. Other regions of activation included bilateral calcarine, right occipital, left precentral, left supplemental motor area, left parietal, left lentiform, right insula, right precentral, right superior frontal, and bilateral postcentral regions. When semantic activation was subtracted from syntactic activation (Syntactic – Semantic contrast), activation was observed within the right middle temporal region (voxels = 21). When syntactic activation was subtracted from semantic activation (Semantic – Syntactic contrast), cluster sizes ranged from 26 to 2787 voxels. Regions of interest activated included left middle temporal, left middle frontal, and left pars triangularis. Other regions of activation included left frontal, left angular, left parietal, left precuneus, and right angular regions.

A similar whole brain analysis was conducted for the contrasts within the delayed recognition task portion of the paradigm (Table 3.6). During the Syntactic – Baseline condition, no activation was observed at FWE correction (p < .05), but at uncorrected p < .001, cluster sizes varied from 10 voxels in volume to 933 voxels. Regions of interest implicated in this contrast included bilateral middle frontal, bilateral pars triangularis, right middle orbitofrontal and right pars opercularis. Other regions of activation included left postcentral, bilateral occipital, left parietal, left fusiform, left precentral, left supplemental motor area, right temporal, right frontal, and right cerebellar regions. Within the Semantic- Baseline contrast, a cluster of 10 voxels was observed within the right occipital region. No significant activation was observed within the Syntactic – Semantic contrast. Within the Semantic – Syntactic contrast, a cluster of approximately 106 voxels was observed within left angular regions.

Total Task Activation Across ROIs

Activated voxels within the encoding task across only ROIs were then examined. This allowed for increased sensitivity, in comparison to prior whole brain analyses, to facilitate isolating patterns in the distribution of activation across ROIs. Increasing power for this broad perspective was beneficial given the small size and close proximity of several ROIs. In addition, we sought to gauge whether activation found at the individual level sustained significance across all ROIs (Table 3.3). Within the Syntactic – Baseline contrast, activated clusters ranged from 11 voxels to 8038 voxels. Activated regions included bilateral pars triangularis, bilateral pars opercularis, left middle temporal gyrus, right middle frontal and right middle orbitofrontal regions (Figure 3.3). Within the Semantic – Baseline contrast, clusters ranged from 11 to 9688 voxels in size. Regions of activation encompassed left pars opercularis, bilateral pars triangularis, right middle frontal, right middle orbitofrontal and bilateral middle temporal (Figure 3.3). When semantic activation was subtracted from syntactic activation (Syntactic – Semantic contrast), a cluster of 151 voxels was observed within the right precuneus regions. When the reverse contrast was applied (Semantic- Syntactic contrast), activation ranging from clusters of 20 voxels to clusters of 1252 voxels was observed within left middle temporal, left middle frontal, left middle orbitofrontal, left pars triangularis and left middle temporal regions. Activation was also noted in more superior regions of the frontal lobe.

Identical contrasts were applied to the activation during the delayed recognition task (Table 3.4). During the Syntactic – Baseline task, a cluster of 11 voxels was observed within the right middle frontal gyrus. During the Semantic- Baseline task, no significant clusters were observed within the FWE correction ($p < .05$). At a more liberal, uncorrected threshold ($p < .001$), clusters ranging from 13 to 480 voxels were observed within the left pars triangularis, bilateral middle frontal gyrus, right middle orbitofrontal regions and right pars opercularis. No significant activation was observed at either a FWE correction or uncorrected threshold within the Syntactic – Semantic contrast. Within the Semantic – Syntactic contrast, a cluster of 63 voxels was observed within the left middle temporal lobe.

fMRI Activation Predicted by RBANS Total Scaled Score

To test the hypothesis that RBANS Total Scaled Score would be positively correlated with activation of semantic networks and negatively correlated with syntactic networks of activation, RBANS Total Scaled Scores were entered as covariates into the fMRI models of individual regions of interest. Because education was found to be significantly related to RBANS Total Scaled Score, this was entered into the model as a confounding variable.

Within the encoding condition, the first contrast involved Syntactic – Baseline activation. Syntactic MFG activation (cluster = 46 voxels, max $z = 3.48$, $p < .001$ uncorrected) occurred within the right hemisphere when RBANS Total Scale Score was accounted for. No activation occurred at a more conservative, FWE correction of .$p < .05$. In the Semantic – Baseline contrast, right hemisphere activation again occurred at a more liberal threshold, within the MTG (cluster = 8 voxels, max z – 3.18, p < .001 uncorrected). No significant activation occurred at conservative or liberal threshold within the Syntactic – Semantic contrast. Within the Semantic – Syntactic contrast, significant activation was found within left MOFG, left PO and left PT (cluster => 8 voxels, p < .05 FWER). At more liberal threshold (clusters => 8 voxels, p < .001 uncorrected) activation was also observed within right MTG and right PO regions (Figure 3.4).

No significant activation was observed within the recognition task using RBANS total score as a covariate and accounting for confounding level of education across any of the above mentioned contrasts.

fMRI Activation Predicted by Syntactic and Semantic Recognition Scores

The hypotheses that BOLD activation during recognition would relate to behavioral recognition performance was tested, including the hypothesis that right hemisphere resources would be most prevalent within the syntactic condition. No significant activation was observed at conservative or liberal thresholds discussed above within the recognition task using behavioral accuracy rates related to either condition in predicting condition specific activation.

Discussion

The current study sought to isolate the role of language components within the verbal memory cortical network. In particular, within the older adult population, explicit memory components (i.e. semantic memory) have been shown to degrade in the face of intact implicit memory components (i.e. syntactic memory; Cabeza, 2001). As such, behaviorally we predicted that semantic focused encoding would correlate positively with cognition (observed through RBANS Total Scaled Scores). As RBANS Total Scaled Score increased, more semantically related target words would be retained. As predicted, number of semantically encoded words later recognized did significantly predict RBANS Total Scaled Score within regression analyses in a positive direction. These results support the hypothesis that use of semantic manipulation increases as cognition increases. This supports the levels of processing model (Craik & Lockhart, 1972) in suggesting that semantic processing benefits from additional resources and additional resources benefit memory as a result of this type of encoding.

We also hypothesized that the contrasting situation would occur with syntactically related target words, which would demonstrate a negative predictive relationship with cognition. As RBANS Total Scaled Score decreased, the number of syntactically manipulated words would increase. Syntactic recognition did predict RBANS Total Scale score. However, this occurred within the opposite direction to what was anticipated. Cognition increased as syntactic words recognized at a later point increased. Of note, when both were included in the model, neither semantic nor syntactic words recognized significantly predicted RBANS Total Scaled score above and beyond the other. These results do not support the hypothesis that use of syntactic manipulation increases as cognition decreases. One reason for this discrepancy could relate to flexibility in memory tools used by older adults. Even without significant impairments, research has suggested that older adults perceiving increased difficulties in a task will use more tools, including time and effort, to maintain baseline memory functioning (Garrett, Grady, & Hasher, 2010). It is possible that individuals benefiting more from semantic cues increased resources or elicited memory tools that benefited them during the syntactic task. It is also possible that with intact functioning, older adults are able to utilize a variety of contextual input (e.g., semantic or syntactic) to facilitate organizing verbal information in a way that is meaningful and therefore beneficial to verbal memory. A greater discrepancy between benefit of “higher” and “lower” levels of processing may occur more within pathological aging, when cognitive resources for "higher" levels of processing potentially become impaired.

To better understand the behavioral mechanisms at play in these situations, we turn to the imaging data examining regions active during these times. When imaging data was masked for apriori ROIs, semantic and syntactic regions demonstrated overlap in activation, including left pars opercularis, bilateral pars triangularis, left middle temporal, right middle frontal and right middle orbitofrontal regions. Syntactic activation that was significant after subtracting out semantic activation during the encoding task included right precuneus regions. Regions significant for semantic activation after accounting for syntactic activation included left hemisphere MTG, MFG, MOFG, and PT regions. Thus, the levels of processing model (Craik & Lockhart, 1972) is supported by the breadth of regions specific to semantic manipulations in comparison with those specific to syntactic activation. This is consistent with prior research implicating higher activation with higher level encoding (Baker, Sanders, Maccotta, & Buckner, 2001). These findings support the idea that semantic processing, being an explicit process, would be a higher level process when compared to a more implicit process of syntactic processing. The prominence of the left MTG in semantic-specific processing when syntactic process has been subtracted fits within prior research implicating the MTL with the explicit memory system (Dennis & Cabeza, 2011). The current results do not support this region's dedifferentiation, but encoding activation would suggest dedifferentiation of semantic and syntactic regions subsequent to the overlapping activation in frontal regions, some of which did not survive subtraction within either contrast. Encoding tasks did show bilateral activation within manipulation minus baseline contrasts, and though they did not survive contrast-specific subtractions, this pattern still supports the HAROLD model of Cabeza (2002). This model would suggest that intact behavioral performance would be subsequent to increasing bilateral resources being implicated by the syntactic and semantic systems, which occurred within these activation contrasts. Cabeza (1997) found particular evidence for this within orbitofrontal regions (identified as BA 47), supported by our results that right middle orbitofrontal regions were implicated in both the semantic minus baseline contrast, as well as the syntactic minus baseline contrast.

A similar pattern was observed within the recognition task activation, which illustrated activation within the left middle temporal lobe during semantic activation (subtracting syntactic activation). No areas of activation were found for the reverse contrast at either conservative or liberal contrasts. This corresponds to data implicating temporal regions in both recognition and encoding (Henson, 2005) and DLPFC more to encoding specific processes (Turriziana et al, 2010). It also relates to research describing similar patterns of middle frontal activation between tasks of encoding and that of recognition (Ranganath, Johnson, & D'Esposito, 2000). The MTG has also been implicated in higher confidence judgments rather that prefrontal low confidence judgments (Kim & Cabeza, 2009). It is possible that semantic processes yield higher confidence than syntactic encoding, due to deeper levels of processing, accounting for the temporal skew to activation within this region.

When individual regions were isolated, we observed activity within the syntactic minus baseline contrast in bilateral MFG and PO, consistent with our hypothesis that syntactic activation would occur within these regions. This supports previous research finding left IFT and MFG activation within semantic manipulation encoding tasks (Brown, 2011), as well as research implicating inferior frontal activation and middle frontal regions in this task (Frederici et al., 2003; Kang et al, 1999; Dapretto & Bookheimer, 1999; Perani et. at, 1999).

However, significant activation was also observed within other regions of interest hypothesized to be semantic in nature. Although it does not support our hypothesis that these regions were specific to syntactic processing, it does support previous research that cortical regions become less specialized within older adulthood as a coping mechanism for cognitive function (Dennis & Cabeza, 2011; Stebbins et al., 2002; Cabeza, 2002).

When the reverse contrast was completed, semantic activation also occurred within both semantic and syntactic regions of interest during the manipulation/ encoding task. This remains in line with research implicating MFG, IFG, and MTG in deeper processing (Henson, Hornberger, & Rugg, 2005; Brown, 2011). It supports research that MTG, PT, and MOFG would be implicated in semantic encoding (Dannhauser et al., 2008). A similar pattern was observed within the recognition task in that each contrast illustrated activation specific to ROIs that both supported and did not support the hypothesized contrast specific regions. Increased resources may not necessarily correlate with improved use of resources: Research has found that with syntactic processing, fewer resources reflect more efficient use of these resources (Vos et al, 2001). In this manner, the additional resources activated by semantic processing may not yield greater effectiveness of this tool over syntactic context.

When activation was compared to cognition, significant activation was observed within the semantic minus syntactic contrast within hypothesized semantic regions left MOFG and left PT, as well as hypothesized syntactic region left PO. The same pattern was not observed during the syntactic minus semantic contrast, in which no regions of significant activation were observed. This supports our hypothesis that cognition would have a positive relationship with semantic but not syntactic manipulation during verbal memory encoding.

The same pattern was not observed during a recognition task, suggesting the role of cognition on these processes may be more specific to encoding rather than also significantly impacting recognition. This was further emphasized by the lack of significant results obtained when recognition scores were used to predict activation during the recognition task. These results would not support prior research suggesting a role for associative information both within the encoding phase as well as the retrieval phase (Atkinson & Shiffrin, 1971). The current results would rather suggest that the bulk of processing occurs during the encoding phase in manipulating language. In this manner, context may have a greater impact on verbal memory during learning rather than retrieval. However, the recognition phase did not include an explicit cue connecting the task to either semantic or syntactic processes. Research has shown that older adults show increased struggle in self-initiating cognitive processes, but benefit from more directive cues (Lou & Craik, 2008). This has been observed on neuropsychological testing in the form of semantic clustering being reduced when compared with younger samples, but semantic tasks being found to predict immediate verbal memory (Jacobs et al, 2001). This was supported by the current lack of activation in language regions during non-contextual recognition. It is possible though that cues during manipulated encoding facilitated maintenance of information in long term memory, if not benefiting memory through an active retrieval cue (Cameron, Haarmann, Grafman, & Ruchkin, 2005). Individuals may have used a familiarity-based method during recognition. Therefore, once effectively encoded with contextual organization, verbal information storage may have been effective enough for future familiarity tasks. As an exploratory analysis within the current study, the role of context on recognition warrants future research.

The results of this study are framed by limitations. Future research could work to isolate the language mechanisms utilized by individuals without direct contextual cuing. Also, given the relatively high level of functioning in our community sample, work with individuals of greater differing levels of cognitive impairment would facilitate building upon the current research. Specifically, these paradigms could be helpful in adding to the research on MCI and progression to Alzheimer's disease. Furthermore, future studies could also examine the implicit and explicit memory systems as they relate to non-verbal forms of memory, to contrast visual memory mechanisms with those of verbal mechanisms. Finally, better understanding variables that impact these language mechanisms, such as varying durations of delay and scope of hemispheric asymmetry during memory tasks could prove beneficial.

As the population increases in number of older adults, it becomes increasingly essential to better understand how cognitive mechanisms change as we age. The results of this study suggest that in a healthy older adult sample, different cortical patterns of activation lead to adequate memory for verbal material framed with implicit syntactic and explicit semantic context. Use of semantic and syntactic manipulation significantly predicted level of cognition in a similar direction. More information remains necessary to fully understand how use of these mechanisms differs with greater levels of cognitive impairment. As it stands, both semantic and syntactic cues appear beneficial in facilitating verbal memory mechanisms within older adults, and show promise as potential tools to maintain baseline function further into older adulthood.

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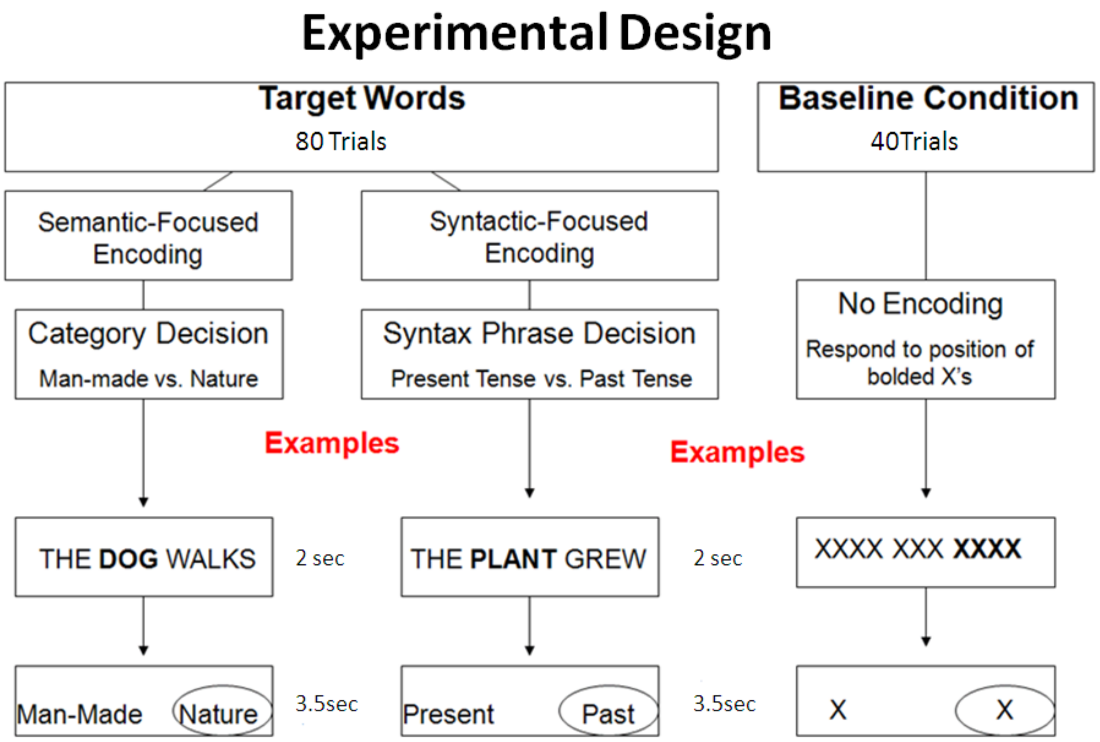

Figure 3.1

Experimental Design

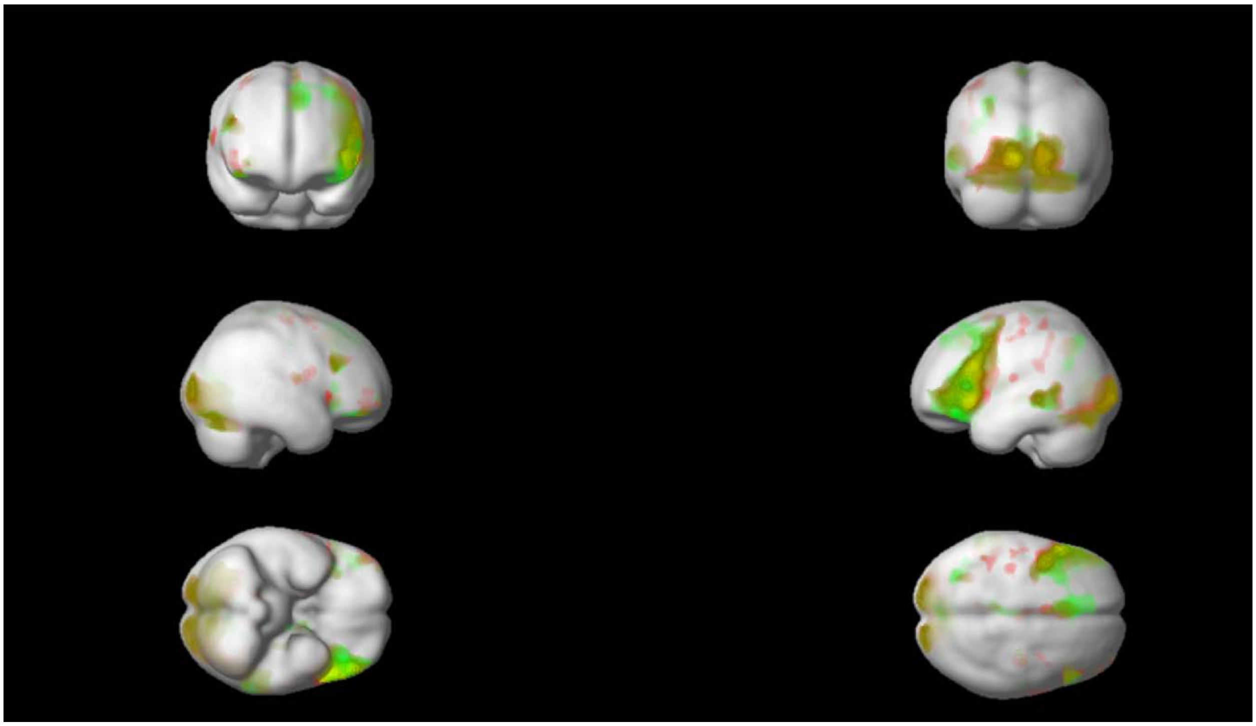

Figure 3.2

Whole Brain Analysis of Encoding Paradigm

Syntactic – Baseline (Red) and Semantic – Baseline (Green) present within frontal, temporal, and occipital regions.

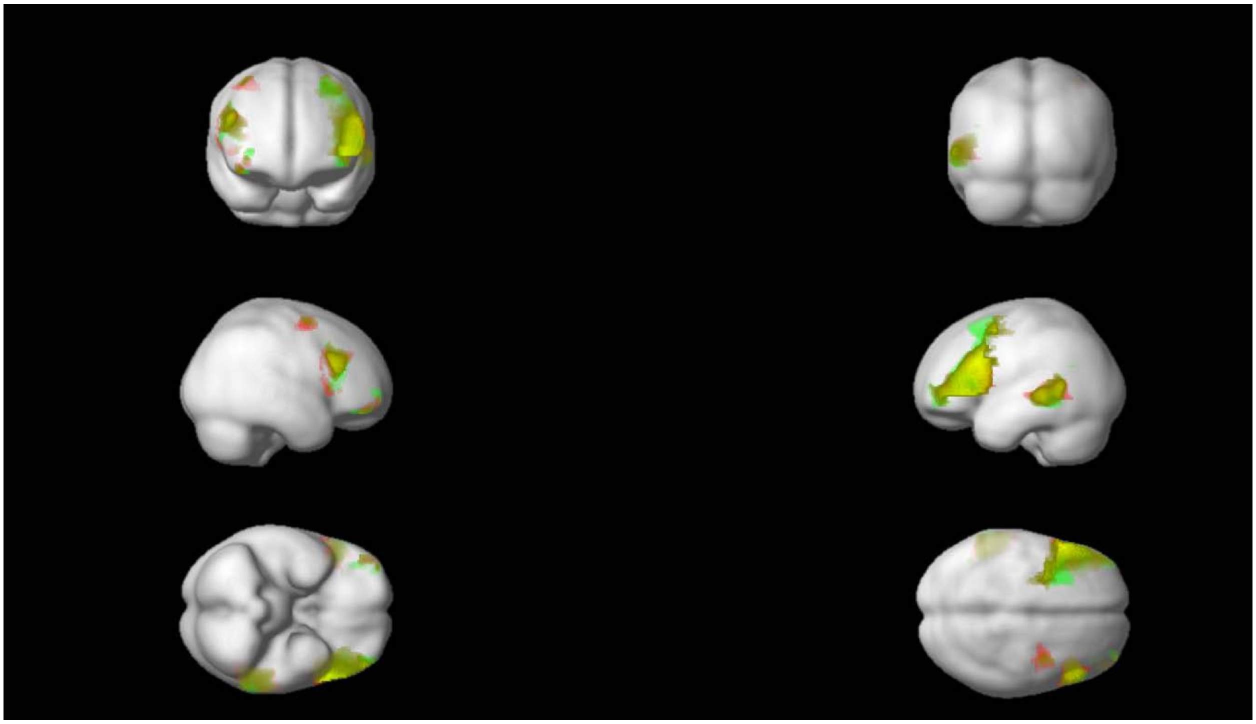

Figure 3.3

Analysis of Encoding Paradigm across ROI

Syntactic – Baseline (Red) and Semantic – Baseline (Green) present across temporal and frontal regions of interest in both hemispheres.

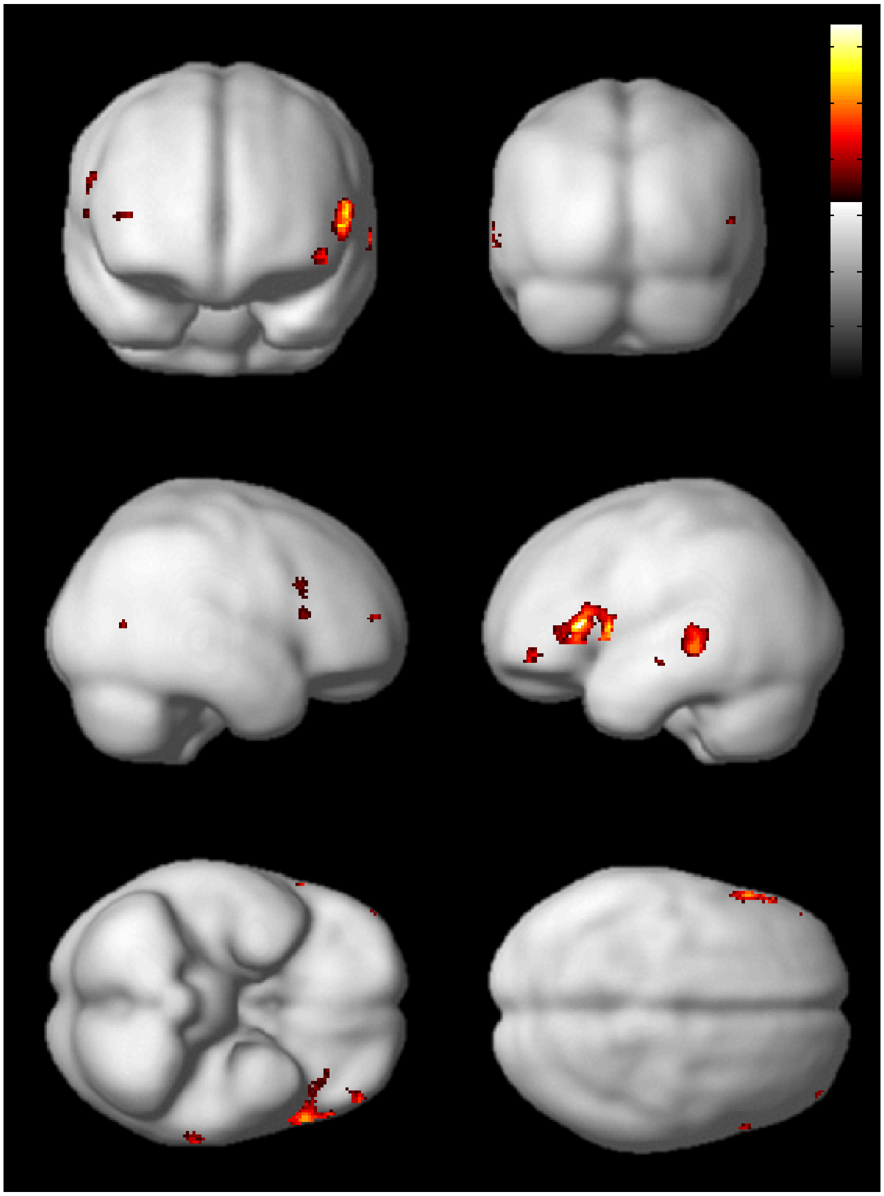

Figure 3.4

Correlation of fMRI BOLD Activation and Cognition

When correlated with RBANS total score, significant activation occurs with the Semantic – Syntactic condition at the liberal threshold ($p < .001$) predominantly within the left hemisphere, with some correlates in the right hemisphere active as well.

Table 3.1

Hypothesized Regions of Interest

Hypothesized Predominant Condition of Interest	**Region**	**Hemisphere**
Semantic- Focused Encoding	Middle Temporal Gyrus	Left
	Pars Triangularis (Anterior Broca's)	Left
	Middle orbitofrontal region	Left
Syntactic-Focused Encoding	Pars Operculus (Posterior Broca's)	Left and Right
	Middle Frontal Gyrus	Left and Right

Table 3.2

Demographics

	n	% of Total Sample
Gender		
Male	16	50
Female	16	50
Race/Ethnicity		
Caucasian/Non-Hispanic	32	100
	Mean	**SD**
Age	74.6	6.6
Years Education	17.5	2.8
WTAR/ Demo Predicted FSIQ	115	6.7
RBANS Immediate Memory	105	10.7
RBANS VisuoConstructional	96	13.6
RBANS Language	106	10.8
RBANS Attention	108	15.4
RBANS Delayed Memory	102	14.2
Total RBANS Standard Score	104	11.1

Table 3.3

Activation by Regions of Interest: Encoding Paradigm

Cluster List	Voxels	Region	Max z score	X	Y	Z
Syntactic-Baseline						
Lmfg	1589	Left Middle Frontal Gyrus	6.86	-39	6	36
Lmfg	0	Left Middle Frontal Gyrus	6.76	-39	2	49
Lmfg	0	Left Middle Frontal Gyrus	5.97	-52	14	36
Lmfg	369	Left Middle Frontal Gyrus	6	-44	47	0
Lmfg	0	Left Middle Frontal Gyrus	4.71	-40	44	7
Lmfg	0	Left Middle Frontal Gyrus	4.18	-39	57	6
Lmfg	53	Left Middle Frontal Gyrus	4.49	-45	38	16
Lmfg	0	Left Middle Frontal Gyrus	4.25	-39	33	19
Lmofg	333	Left Pars Triangularis	5.87	-45	44	-2
Lmtg	3175	Left Middle Temporal	6.16	-56	-49	3
Lmtg	0	Left Middle Temporal	5.98	-57	-36	0
Lpo	2189	Left Pars Opercularis	7.1	-38	5	28
Lpo	0	Left Pars Opercularis	7.08	-44	14	21
Lpo	0	Left Pars Opercularis	6.47	-52	14	33
Lpt	4824	Left Pars Triangularis	7.19	-51	20	25
Lpt	0	Left Pars Triangularis	6.89	-42	15	22
Lpt	0	Left Pars Triangularis	6.39	-45	30	13
Rmfg	.0	Right Middle Frontal	5.0600	46.0	21.0	31.0
Rmfg	.0	Right Middle Frontal	4.2700	51.0	20.0	40.0
Rmfg	62.0	Right Middle Frontal	5.8300	44.0	27.0	22.0
Rmfg	.0	Right Middle Frontal	4.2200	54.0	33.0	22.0
Rmfg	653.0	Right Middle Frontal	5.7400	36.0	2.0	63.0
Rmfg	.0	Right Middle Frontal	5.2900	44.0	2.0	57.0
Rmfg	.0	Right Middle Frontal	5.1300	28.0	-4.0	55.0
Rmfg	30.0	Right Middle Frontal	4.3000	46.0	56.0	4.0
Rmfg	77.0	Right Middle Orbitofrontal	4.0400	39.0	5.0	37.0
Rmfg	11.0	Right Middle Frontal	3.8000	39.0	62.0	.0
Rmofg	619.0	Right Middle Orbitofrontal	5.1400	44.0	51.0	-15.0
Rmofg	.0	Right Middle Orbitofrontal	4.7100	38.0	62.0	-6.0
Rmofg	.0	Right Middle Orbitofrontal	3.7500	27.0	50.0	-17.0
Rpo	1325.0	Right Pars Opercularis	5.6800	54.0	24.0	31.0
Rpo	.0	Right Pars Opercularis	5.2100	46.0	20.0	30.0
Rpo	.0	Right Pars Opercularis	5.0300	63.0	12.0	22.0
Rpt	1928.0	Right Pars Triangularis	6.0700	44.0	24.0	24.0
Semantic-Baseline						
Lmfg	335.0	Left Middle Frontal Gyrus	7.1900	-45.0	44.0	.0
Lmfg	.0	Left Middle Frontal Gyrus	4.8000	-42.0	45.0	7.0
Lmfg	2850.0	Left Middle Frontal Gyrus	7.0500	-39.0	8.0	34.0
Lmfg	.0	Left Middle Frontal Gyrus	7.0100	-39.0	2.0	52.0
Lmfg	.0	Left Middle Frontal Gyrus	6.3400	-51.0	14.0	36.0
Lmfg	90.0	Left Middle Frontal Gyrus	5.6600	-45.0	38.0	16.0
Lmfg	.0	Left Middle Frontal Gyrus	5.1600	-39.0	33.0	19.0
Lmofg	609.0	Left Pars Triangularis	7.3400	-45.0	44.0	-2.0
Lmofg	.0	Middle Orbitofrontal Gyrus	4.7800	-33.0	33.0	-14.0
Lmofg	.0	Middle Orbitofrontal Gyrus	4.6100	-34.0	39.0	-8.0
Lmofg	18.0	Middle Orbitofrontal Gyrus	4.4900	-28.0	33.0	-18.0
Lmtg	3089.0	Left Middle Temporal	6.5800	-57.0	-36.0	.0
Lmtg	.0	Left Middle Temporal	6.2600	-58.0	-49.0	3.0
Lmtg	.0	Left Middle Temporal	4.4000	-44.0	-61.0	22.0
Lpo	2132.0	Left Pars Opercularis	.0000	-46.0	15.0	22.0
Lpo	.0	Left Pars Opercularis	7.7000	-39.0	6.0	28.0
Lpo	.0	Left Pars Opercularis	6.8900	-52.0	17.0	31.0
Lpt	4773.0	Left Pars Triangularis	.0000	-48.0	17.0	24.0
Lpt	.0	Left Pars Triangularis	7.5200	-46.0	32.0	12.0
Lpt	.0	Left Pars Triangularis	7.5000	-45.0	41.0	-2.0
Rmfg	219.0	Right Middle Frontal	6.2100	52.0	29.0	31.0
Rmfg	.0	Right Middle Frontal	4.6600	51.0	20.0	42.0
Rmfg	74.0	Right Middle Frontal	5.6800	44.0	27.0	22.0
Rmfg	.0	Right Middle Frontal	4.9700	54.0	33.0	22.0
Rmfg	181.0	Right Middle Frontal	5.0600	38.0	3.0	61.0
Rmfg	.0	Right Middle Frontal	3.7500	46.0	9.0	52.0

Rmfg	238.0	Right Middle Frontal	4.7000	34.0	58.0	.0
Rmfg	.0	Right Middle Frontal	4.0900	45.0	57.0	6.0
Rmofg	520.0	Right Middle Orbitofrontal	5.4800	45.0	46.0	-17.0
Rmofg	.0	Right Middle Orbitofrontal	4.6800	42.0	56.0	-14.0
Rmofg	.0	Right Middle Orbitofrontal	4.6200	34.0	58.0	-2.0
Rmofg	.0	Right Middle Orbitofrontal	4.4100	38.0	62.0	-6.0
Rmofg	.0	Right Middle Orbitofrontal	3.2600	27.0	48.0	-17.0
Rpo	102.0	Right Pars Opercularis	4.3000	45.0	18.0	6.0
Rpo	.0	Right Pars Opercularis	4.0900	45.0	18.0	.0
Rpo	.0	Right Pars Opercularis	3.7800	45.0	20.0	16.0
Rpt	1758.0	Right Pars Triangularis	6.5400	54.0	29.0	28.0
Rpt	.0	Right Pars Triangularis	4.9500	62.0	22.0	7.0
Rpt	.0	Right Pars Triangularis	4.5500	60.0	28.0	13.0
Rpt	13.0	Right Pars Triangularis	4.2000	36.0	27.0	1.0
Syntactic- Semantic						
Lpo	45.0	Left Pars Opercularis	3.6600	-56.0	6.0	6.0
Rmtg	475.0	Right Middle Temporal	4.7300	58.0	-49.0	6.0
Rpo	22.0	Right Pars Opercularis	3.3800	52.0	9.0	9.0
Semantic- Syntactic						
Lmfg	1990.0	Left Middle Frontal Gyrus	6.0100	-27.0	17.0	49.0
Lmfg	.0	Frontal Superior Gyrus	5.3000	-20.0	29.0	49.0
Lmfg	.0	Left Middle Frontal Gyrus	4.3200	-45.0	18.0	43.0
Lmfg	11.0	Left Middle Frontal Gyrus	3.8500	-44.0	48.0	.0
Lmofg	592.0	Middle Orbitofrontal Gyrus	5.6100	-34.0	36.0	-14.0
Lmofg	.0	Middle Orbitofrontal Gyrus	4.8200	-44.0	48.0	-11.0
Lmtg	341.0	Left Middle Temporal	6.3400	-45.0	-61.0	22.0
Lmtg	251.0	Left Middle Temporal	4.8100	-62.0	-45.0	-12.0
Lmtg	69.0	Left Middle Temporal	4.4100	-60.0	-6.0	-21.0
Lpo	74.0	Left Pars Triangularis	5.2100	-38.0	18.0	21.0
Lpo	.0	Left Pars Opercularis	3.3900	-50.0	18.0	10.0
Lpo	182.0	SubGyral	4.1700	-34.0	17.0	25.0
Lpo	.0	Left Pars Opercularis	4.0600	-44.0	18.0	31.0
Lpt	1866.0	Left Pars Triangularis	5.3000	-38.0	20.0	21.0
Lpt	.0	Left Pars Triangularis	4.9300	-48.0	32.0	10.0
Rmfg	11.0	Right Middle Frontal	3.6500	36.0	21.0	52.0
Rmofg	36.0	Right Middle Orbitofrontal	3.8500	36.0	38.0	-14.0
Rmtg	8.0	Right Middle Temporal	3.6400	51.0	-61.0	22.0

Note: Activation shown at FWER, $p < .05$

Table 3.4

Activation by Regions of Interest: Recognition Paradigm

Cluster List	Voxels	Region	Max z score	X	Y	Z
Syntactic-Baseline						
Lmofg	13.0	Middle Orbitofrontal Gyrus	3.4600	-44.0	54.0	-2.0
Lpt	43.0	Left Pars Triangularis	3.8900	-50.0	33.0	25.0
Rmofg	100.0	Right Middle Orbitofrontal	4.0000	24.0	56.0	-14.0
Rmofg	.0	Right Middle Orbitofrontal	3.2000	30.0	48.0	-17.0
Rmofg	43.0	Right Middle Orbitofrontal	3.5500	36.0	60.0	-2.0
Rpo	9.0	Right Pars Opercularis	3.6600	57.0	20.0	33.0
Rpo	13.0	Right Pars Opercularis	3.4200	50.0	20.0	-2.0
Semantic- Baseline						
Lmofg	15.0	Middle Orbitofrontal Gyrus	3.5300	-39.0	60.0	-2.0
Lpo	12.0	Left Pars Opercularis	3.1800	-54.0	15.0	34.0
Lpt	52.0	Left Pars Triangularis	3.8300	-50.0	33.0	25.0
Rmfg	36.0	Right Middle Frontal	3.9300	40.0	58.0	3.0
Rmofg	201.0	Right Middle Orbitofrontal	4.1600	22.0	54.0	-14.0
Rmofg	.0	Right Middle Orbitofrontal	3.4900	38.0	60.0	-2.0
Rmofg	.0	Right Middle Orbitofrontal	3.4300	42.0	44.0	-17.0
Rmofg	23.0	Right Middle Orbitofrontal	3.4300	44.0	54.0	-14.0
Rpo	46.0	Right Pars Opercularis	3.8900	50.0	18.0	-2.0
Rpo	9.0	Right Pars Opercularis	3.5500	57.0	20.0	33.0
Rpt	11.0	Right Pars Triangularis	3.4700	51.0	32.0	30.0
Syntactic- Semantic						
Semantic-Syntactic						
Lmfg	75.0	Left Middle Frontal Gyrus	3.9100	-45.0	18.0	42.0
Lmtg	187.0	Left Middle Temporal	4.5800	-48.0	-63.0	22.0
Lmtg	38.0	Left Middle Temporal	4.1400	-56.0	3.0	-27.0
Rmtg	10.0	Right Superior Temporal	3.6000	54.0	-57.0	21.0

Note: Activation shown at FWER, p < .05

Table 3.5

Whole Brain Encoding Activation by Regions of Interest

Cluster List	Voxels	Region	Max z score	X	Y	Z
Syntactic-Baseline						
	23354	Right Lingual	Inf	15	-90	-5
		Left Calcarine	Inf	-15	-97	-5
		Left Inferior Occipital	Inf	-26	-91	-11
	21429	Left Precentral	7.51	-42	3	40
		Left Supplemental Motor	7.49	-6	11	46
		Left Pars Triangularis	7.19	-51	20	25
	289	Right Precentral	6.3	64	6	21
		Right Postcentral	4.94	68	-6	16
		Right Postcentral	4.79	68	-9	24
	1080	Right Pars Triangularis	6.07	44	24	24
		Right Middle Frontal	5.92	52	29	31
	2579	Left Inferior Parietal	6.06	-28	-58	45
		Left Inferior Parietal	5.98	-42	-42	36
		Left Inferior Parietal	5.87	-28	-64	39
	1202	Right Frontal Supplemental	5.91	40	-12	63
		Right Middle Frontal	5.74	36	2	63
		Right Precentral	5.53	33	-15	69
	533	Right Insula	5.5	33	26	-2
		Right Pars Triangularis	4.71	45	18	1
	146	Right Pallidum	5.45	18	-4	-3
	493	Left Middle Occipital	5.39	-18	-3	12
	36	Right Middle Orbitofrontal	5.14	44	51	-15
	10	Right Middle Frontal	4.94	38	62	-8
	14	Right Precentral	4.92	57	-10	46
	60	Left ExtraNuclear	4.87	-27	-24	-3
	20	Right Precentral	4.84	51	-15	54
Semantic- Baseline						
	19245	Right Calcarine	Inf	15	-90	-3
		Left Calcarine	Inf	-9	-91	-3
		Right Superior Occipital	7.72	24	-97	10
	16571	Left Pars Opercularis	Inf	-46	15	22
		Left Pars Opercularis	7.7	-39	6	28
		Left Precentral	7.57	-46	3	48
	3965	Left Supplemental Motor	7.63	-8	14	46
		Left Supplemental Motor	6.91	-10	24	49
		Left Supplemental Motor	6.29	-3	3	55
	2373	Left Middle Temporal	6.58	-57	-36	0
		Left Middle Temporal	6.26	-58	-49	3
	1039	Right Pars Triangularis	6.54	54	29	28
		Right Middle Frontal	4.66	51	20	42
	1778	Left Inferior Parietal	6.52	-30	-67	43
		Left Superior Parietal	6.09	-28	-58	43
		Left Temporal	5.23	-34	-60	28
	499	Right Insula	6.19	33	24	-6
	843	Left Lentiform	5.67	-15	0	7
	180	Right Precentral	5.57	33	-16	69
	72	Right Precentral	5.55	64	6	24
		Right Precentral	4.8	62	8	31
	267	Left Inferior Parietal	5.52	-46	-45	48
	101	Right Middle Orbitofronal	5.48	45	46	-17
	33	Right Precentral	5.31	57	-12	46
	100	Left ExtraNuclear	5.2	-26	-25	-5
	109	Left Brainstem	5.18	-10	-15	-14
		Left Brainstem	4.68	-4	-24	-6
	42	Right Middle Frontal	5.06	38	3	61
		Right Superior Frontal	4.8	30	-1	67
	20	Right Pars Triangularis	4.95	62	22	7
	129	Left Postcentral	4.84	-39	-22	49
	14	Right Postcentral	4.73	68	-6	16
	11	Right Middle Frontal	4.7	34	58	0

Syntactic- Semantic						
	21	Right MTG	4.73	58	-49	6
Semantic-Syntactic						
	873	Left Inferior Orbitofrontal	6.45	-36	32	-20
	1390	Left Middle Temporal	6.34	-45	-61	22
		Left Angular	6.13	-45	-66	33
		Left Inferior Parietal	5.62	-36	-73	42
	2787	Left Superior Frontal	6.13	-15	36	51
		Left Middle Frontal	6.01	-27	17	49
		Left Superior Frontal	5.85	-14	44	46
	102	Left Precuneus	5.31	-6	-52	10
	162	Left Pars Triangularis	5.3	-38	20	21
	26	Right Angular	5.1	54	-61	34
	80	Left Precuneus	4.96	-3	-58	34
	120	Left Pars Triangularis	4.93	-48	32	10
	58	Left Middle Temporal	4.81	-62	-45	-12

Note: Activation shown at FWER, $p < .05$

Table 3.6

Whole Brain Recognition Activation by Regions of Interest

Cluster List	Voxels	Region	Max z score	X	Y	Z
Syntactic-Baseline						
Semantic- Baseline	10	Right Occipital	4.77	34	-88	-15
Syntactic- Semantic						
Semantic-Syntactic						
	106	Left Angular	4.76	-46	-61	30
		Left Angular	4.53	-44	-67	39

Note: Activation shown at FWER, p < .05

CHAPTER 4

ROLE OF BILATERAL DEDIFFERENTIATION AND DURATION ON THE CONTEXTUAL SEMANTIC AND SYNTACTIC IMPACT WITHIN VERBAL MEMORY[2]

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[2] Brown, C. & Miller, L.S. To be submitted to *Journal of Applied Gerontology*.

Abstract

The role of language as a contextual framework for verbal memory has been previously examined by this and other groups. The interaction that retention duration and bilateral dedifferentiation within older adults plays on this process is less understood. FMRI activation was measured during an encoding task involving asking older adults to manipulate short phrases by a semantic or syntactic judgment. Immediate and delayed recall behavioral measures were contrasted with each other, as well as with BOLD activation. Semantic-focused encoding demonstrated a benefit over syntactic-focused encoding at the delayed duration. Total activated voxels across regions of interest did not vary between left and right hemisphere. Results suggest that dedifferentiation does not occur primarily within one component of language over another in healthy older adults, but that observed bilateral activation may have a stronger benefit within semantic processing at a delayed time point, in comparison with syntactic processing or more short term retention durations.

Index Words: verbal memory, fMRI, language, older adults, retention duration, bilateral dedifferentiation

Introduction

The semantic meaning of words and syntactic organization of phrases impart context that facilitate verbal memory within older adults (Brown et al, 2011). However, variables that impact the effectiveness of this context in facilitating memory are less clear. Semantic processing and syntactic processing within verbal memory are impacted by both the duration of memory delay and the scope of cortical resources activated during each task. Several well validated tasks of verbal learning allow comparison between immediate and delayed free recall tasks (e.g., California Verbal Learning Test, WMS-IV Logical Memory). The distinction between short and long delay however is not always purely duration: In the realm of verbal memory, various forms of language context predominate at different time points. Furthermore, varying scopes of cortical region activate during information encoding (Tyler et al., 2010), but the specific impact on the language and memory interaction remains unclear. The current experiment sought to explore these interactions. This study aimed to examine the nature of memory delay duration, scope of hemispheric asymmetry, and their relationship to verbal memory processes within a sample of older adults.

Research regarding the role of language within verbal memory has suggested that it varies by subcomponent, with semantic processes implicated in episodic forms of memory (McCloskey & Santee, 1981), and syntax maintained by implicit, procedural mechanisms (Fabbro, 1999). Associative information works either during encoding as organizational context for the target information, or during retrieval as a cue to isolate long term stores of information. Research has suggested that such information need not be mutually exclusive: Associative semantic information has been described as both a tool for both initial organization during encoding and a retrieval cue following a delay (Atkinson & Shiffrin, 1971), which has been supported by ERP research of semantic networks during both short term encoding and long term maintenance (Cameron, Haarmann, Grafman, & Ruchkin, 2005).

Information transfers between these short term (being imminently manipulated) and long term stores. Many have equated short term stores with verbal working memory, secondary to the easily accessible information for active manipulation, contrasted with more permanent memory embedded within long term stores (Atkinson & Shiffrin, 1971). It has been suggested that left inferior frontal activation increases as a function of delay duration, as the need for top down retrieval mechanisms increase to move information from short term store into long term store (Buchsbaum, Padmanabhan, & Berman, 2010). Researchers have pointed to interference as playing a large role in the degradation of information within the short term store, preventing this movement into long term memory (Berman, Jonides, & Lewis, 2009). However, tools have also been identified in the short term store that facilitate top down encoding to benefit long term memory, including rehearsal, coding information into a memorable context, and visual imagery (Atkinson & Shiffrin, 1971).

Researchers suggest that the extent of language component involvement may also change as a function of short term versus long term memory. Within the short term (15 second delay), correct syntactic order has been shown to facilitate memory (Perham, Marsh, & Jones, 2009). Syntactic memory has further been shown to benefit listening comprehension, further benefiting encoding (Call, 1985). Research has also implicated syntax within the phonological loop model of working memory through the need for syntactic regeneration (Baddeley, 2003; Chasse & Belleville, 2009; Papagno, Cecchetto, Reati, & Bello, 2007), which has been supported as implicating Broca’s area through the articulatory process required for recoding perceived visual information (Henson, Burgess, & Frith, 2000). Researchers have contrasted this implicit regeneration within short term memory to semantic explicit maintenance within long term memory (Lombardi & Potter, 1992; Ferreira, Bock, Wilson, & Cohen, 2008). Semantic processes have been linked to more long term stores through the ‘spread of activation’ model, connecting stores of information more strongly with related concepts (Collins & Loftus, 1975). Verbal memory using more in depth forms of processing, such as these semantic networks, has been demonstrated to correlate with behavioral verbal memory improvements (Craik & Lockhart, 1972; Bonner-Jackson, Csernansky & Barch, 2007; Baker, Sanders, Maccotta, & Buckner, 2001). Within healthy adults, it has been shown that increased delays lead to a semantic cue shift during retrieval (Buchsbaum, Padmanabhan, & Berman, 2010). It has also been suggested that in the face of these higher level processes experiencing impairments, lower levels preservation occurs within short term memory function (Majerus, Norris, & Patterson, 2007).

In conjunction with functional processes, activated cortical regions have also been shown to vary based on duration of delay. Some have suggested that short term memory implicates posterior superior temporal and inferior parietal regions (related to phonological working memory), while long term memory uses more inferior frontal. Short term cortical regions include posterior superior temporal and inferior parietal regions (Murray & Ranganath 2007). In contrast, long term memory has implicated predominantly frontal regions, with greater debate surrounding specific roles of various regions. Left inferior frontal regions in particular have been noted to increase in activation as a function of duration to memory task (Buchsbaum, Padmanabhan, Berman, & 2010). The pars triangularis has been linked to greater activation as a function of longer delays, with a negative behavioral correlation. In contrast, the ventrolateral prefrontal cortex (VLPFC) has been shown to have a positive relationship with behavioral memory performance and hold a role within long term memory store memory, with relationship-based memory occurring within the dorsolateral prefrontal cortex (DLPFC; Murray & Ranganath, 2007). Others implicate the left mid/ DLPFC and bilateral posterior parietal cortex (PPC), including its role within mnemonic representations, within long term memory (Staresina & Davichi, 2006). These regions overlap with cortical regions identified as holding involvement within semantic encoding, including: left inferior frontal/ prefrontal, inferior parietal, middle temporal, and right supramarginal regions (Bonner-Jackson, Csernansky & Barch, 2007; Henson, Hornberger, & Rugg, 2005).

Older adults have demonstrated a broader scale of cortical activation variance not only based on delay duration but also by language processes, particularly within older adults. It has been suggested that while semantic material requires a greater distribution of cortical activation (Bonner-Jackson, Csernansky & Barch, 2007; Henson, Hornberger, & Rugg, 2005; Craik & Lockhart, 1972), syntactic processes as require resource efficiency over quantity (Vos et. al., 2001). In accordance with the HAROLD model positing a reduction in hemispheric asymmetry within older adults (Cabeza, 2002), stroke victims were shown to exhibit language recovery correlated with bilateral activation of resources (Cao et al., 1999). Research has suggested that semantic information becomes impaired during aging, particularly pathological aging, while syntactic complexity remains intact until severe stages of dementia (Lai, Pai, & Lin, 2009; Bickel, Pantel, Eysenbach, & Schroder, 2000). Specifically, syntactic processes being over-learned and better preserved throughout the aging process (Kave & Levy, 2003; Nebes, Brady, & Jackson, 1989), potentially relate to increased bilateral frontal activation in line with the HAROLD model (Cabeza, 2002). In contrast, semantic temporal regions do not demonstrate the same level of bilateral compensatory mechanisms (Tyler et al, 2010) and bilateral activation has been shown to reduce with increasing cognitive decline (Moulin et al., 2007). In line with these theories, left temporal areas have shown increased semantic generalization with increased impairment, with category specific displacement occurring within left posterior, left ventral temporal, and frontal striatal regions (Grossman et al, 2003). Compensatory mechanisms occur more frequently for syntactic processes, as research has shown this within left and right IFG syntactic activation but no changes within semantic STG or MTG and no correlating behavioral differences. Left IFG and OFG and MTG showed bilateral activation (Tyler et al., 2010).

Study Aims

Semantic and syntactic resources are two options for mechanisms to facilitate memory processes, though variables impacting their interaction with verbal memory, namely hemispheric asymmetry and delay duration, have yet to be fully understood. The aims of this study were to examine variables that impact the effectiveness of language context on verbal memory benefit. We examined the implicit nature of syntactic encoding within short term memory using bilateral activation. We further examined the explicit nature of semantic encoding within long term memory using fewer bilateral resources. We anticipated that at all levels of cognition, syntactic focused encoding would benefit immediate verbal memory recall, due to the implicit syntactic regeneration within short term memory (Lombardi & Potter, 1992, Ferreira, Bock, Wilson, & Cohen, 2008). We hypothesized that semantic focused encoding would have a stronger benefit at delayed recall, based on research linking explicit semantic maintenance to long term memory (Lombardi & Potter, 1992; Ferreira, Bock, Wilson, & Cohen, 2008). Specifically, we predicted that more syntactically manipulated target words would be recalled following an immediate delay, in comparison to semantically manipulated target words. The opposite pattern would occur after a delay; with more semantically manipulated target words being better recalled after a 20 minute delay in comparison to syntactically manipulated target words. Due to cortical dedifferentiation within older adults (Dennis & Cabeza, 2011), we further predicted that when cognition was examined (measured by RBANS total score), greater cognitive decline (lower RBANS total score) would relate to greater benefit of syntactic focused encoding (measured by number of syntactically manipulated words recalled) at both time points. This would be more prominent than that found within previous research within this lab focused on recognition tasks (Brown et al, unpublished) due to the higher sensitivity of recall to cognitive decline over those recognition tasks (Lou & Craik, 2008).

We predicted that activation differences during verbal encoding (measured by number of voxels activated within each cluster and the intensity of activation) within semantic regions of interest (middle temporal regions (MTG), anterior Broca's region (pars triangularis; PT) and middle orbitofrontal regions (MOFG); Brown et al, in prep; Brown et al, unpublished) would be positively correlated with immediate and delayed recall measures (semantic – syntactic activation). Right hemisphere correlates of regions of interest would not show significant activation within this contrast. Syntactic ROIs (left pars opucularis (posterior Broca's), left middle frontal gyrus (MFG); Brown et al, 2011) would be positively correlated with both immediate and delayed recall measures (syntactic – semantic contrast). Akin to Tyler et al, (2010), greater compensatory right hemisphere activation across regions of interest (ROIs) during syntactic encoding would occur and relate to improved recall scores. It was anticipated that right hemisphere encoding activation (number of voxels activated, intensity of activation) would demonstrate positive correlation within the number of syntactically manipulated words identified at immediate recall, with no significant correlation occurring between the numbers of semantically manipulated words recalled at either time point with right hemisphere encoding activation.

Additionally, we sought to examine variance within cortical organization based on language context interacting with verbal memory. Secondary to dedifferentiation and lack of resource competition, explicit semantic difficulties frequently observed during cognitive decline could potentially be ameliorated by implicit syntactic resources acting as explicit memory aids as semantic resources decreased (Dennis & Cabeza, 2011). In light of research linking syntactic resources to more bilateral compensation than higher level and more temporal semantic networks (Cabeza, 2002; Tyler et al, 2010), we hypothesized that syntactic encoding would elicit more bilateral activation than semantic encoding across identified language regions of interest (MTG, PT of anterior Broca's region, MOFG, left pars operculus (PO) and the left MFG; Brown et al, unpublished). This pattern would be observed through increased intensity of voxel activation and numbers of voxels activated when semantic encoding activation was subtracted from syntactic encoding activation in both left and right correlates of the ROIs, in comparison to the reverse contrast.

Methods

Participants

The current study included 32 participants, ages 65- 85, drawn from a community sample. Recruitment was conducted through community fliers, psychoeducational community talks, newspaper advertisements, and prior research participants. Individuals were included who were right handed, native English speakers (defined as no second language learned before age 5), and met safety criteria to enter the MRI environment. Exclusion criteria included self-report of neurological disorder, family/ personal history of psychosis or current mental health treatment. The project was approved by the University of Georgia Institutional Review Board.

Neurocognitive Measures

Participants completed a well validated reading test as an estimate of premorbid intelligence, the Wechsler Test of Adult Reading (The Psychological Corporation, 2001), which correlates accuracy scores with demographic variables (The Psychological Corporation, 2001a). This measure helped to control for the potential confound of premorbid intelligence influencing verbal memory performance between subjects. The estimate of Full Scale IQ based on both WTAR and demographics information was utilized for this purpose.

Cognitive functioning was measured using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998). This brief neuropsychological battery assesses cognitive decline through 12 subtests generating 5 Index Scores and 1 Total Score. The indices include Visuospatial/Constructional, Attention, Language, Immediate Memory, and Delayed Memory (Randolph, Tierney, Mohr, & Chase, 1998).

fMRI Experimental Design

Participants were trained for the structure and demands of the experimental task. Participants completed a series of three distinct practice tasks (two allowing for multiple administrations and reduced speed) until each achieved an accuracy score greater than or equal to 80% on each task. Those that qualified based on the practice exam returned on a separate day for the fMRI experimental task.

Please refer to Figure 1 for experimental paradigm layout. The paradigm was an event-related, randomized design with variable ISIs (mean ISI = 2 seconds). The mean ISI was equivalent to the shortest stimulus duration. The mean ISI was informed by research indicating shorter variable ISIs increase paradigm efficiency (Dale, 1999) and research suggesting that longer ISIs facilitate effective encoding within older adults (Dehon, 2006). Of note, encoding conditions demonstrated no significant differences in ISI (p > .05). ISI values ranged from 1 second and 3 seconds and deviated by factors of 100ms, with the exception that TR derivatives (1.5 seconds, 3 seconds), were not sampled. Stimuli included 80 phrases, with target nouns within 2 categories: 40 man-made objects or entities, and 40 nouns occurring within nature. Words of equivalent concreteness, length and frequency were identified through the MRC Psycholinguistic database (http://www.psy.uwa.edu.au/ mrcdatabase/uwa_mrc.htm; Wilson, 1988). Phrases were constructed from one target noun (bold font), one verb (randomly generated), and an article ("the"), forming sensible subject phrases (*The **noun** verb*). Phrases were presented using E-Prime 2.0 Software (Psychology Software Tools, Inc., 2007) software for 2 seconds, followed by presentation of category choices for 3.5 seconds. The task involved classifying phrases into one of the two categories, and remembering bolded nouns for future recall. In the semantic condition, participants categorized phrases as related to nature or as man-made. In the syntactic condition, participants judged the tense of the phrase by indicating if it was occurring currently or previously. There were 40 trials of a baseline condition, which involved an active, non-verbal task. The participant was shown a "phrase" in which letters were replaced by Xs, approximating the varying lengths of words in phrases (i.e., *XXX XXXX **XXXXX***). One string of letters was bolded to simulate the bolded word within experimental conditions. Subsequent categories entailed an identical 'X' on each side of the screen. Participants were asked to press the button corresponding to the side of the screen where the bolded X's appeared (right or left). Baseline "phrases" and choices were presented for 2 seconds and 3.5 seconds, respectively, identical to experimental condition trials. Target nouns were counterbalanced across 2 lists for: classification condition (semantic versus syntactic), and grammatical tense of presentation (present or past). All category choices were followed by variable ISIs, marked by a centered cross hair. ISI between semantic and syntactic categories did not significantly vary within list or between lists. Neither experimental condition significantly varied with the baseline condition on either list ($p > .05$). Participants made responses by touch pad. Participants were asked to verbally recall presented bolded target nouns immediately after encoding and after a delay of approximately 15- 20 minutes. A verbal recall format was utilized within this experiment so as to accurately compare immediate versus delayed retention without the confound of multiple visual presentations of verbal material.

Image Acquisition

Images were acquired at the University of Georgia's Bioimaging Research Center (BIRC) using a General Electric 16-channel fixed-site Signa HDx 3.0 Tesla Magnetic Resonance Imaging (MRI) magnet. Participants underwent an initial T-1 weighted structural MRI scan (FOV = 240mm, slice thickness = 1.2mm, locs per slab = 154, TR= 7.8, TE = min full, matrix = 256 x 256) to establish a reference template for future images. Participants also underwent 3 T2*-weighted, single-shot echo planar sequence scans. Functional image acquisition occurred over 2 separate runs of the experimental paradigm with 7.5 minute durations (separated by a short break to prevent fatigue), and one delayed recognition paradigm with 7.5 minute duration. Functional scans included 30 interleaved (bottom-up) slices per volume, aligned to the inter-commissural line (AC-PC line) with: TR = 1.5 s, TE = 25ms, flip angle = 90°, slice thickness = 4mm, FOV = 220 x 220 mm, matrix = 64 x 64, and ASSET factor = 2. Functional images covered the cortex and cerebellum. Each run consisted of 300 total volumes. Ten initial samples within each run were discarded to facilitate attainment of steady state before data acquisition. Magnitude and phase map images were acquired for field map unwarping with the following parameters: T2 gradient echo, flip angle = 30°, TR = 750 ms, TE = 5 ms, FOV = 256 x 256 mm, slice thickness = 2 mm, matrix = 128 x 128, 60 interleaved slices and ASSET factor = 2.

Preprocessing

FMRI data was preprocessed with Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm; Ashburner et al., 2010), through Matlab (The Math Works, Natick, MA) with the following parameters: TR = 1.5 s, Slice Order = interleaved bottom-up, Reference slice = 1. Run 1 and run 2 for each subject was analyzed separately and combined during the second level analysis stage, to allow first level analysis to account for variations in condition stimulus onset times between runs. Preprocessing included a slice timing correction (interleaved bottom-up), manual alignment of anatomical, functional, magnitude, and phase images to the AC-PC line. Images were realigned to the first image of the middle series scan (first image of second run). Scans were realigned and unwrapped using individual fieldmaps. Anatomical scans were coregistered to the first functional image of the second run. The structural image (within fMRI space), along with all functional images, was then registered to the standardized T1 image (MNI space). The anatomical scan was segmented. Deformation fields were applied to functional images and scans were smoothed.

Data Analysis

Data was analyzed using SPSS version 16.0 (SPSS, Chicago). Paired t-tests compared number of syntactically and semantically manipulated words recalled immediately and following a delay. A repeated measures 2 (condition: syntactic, semantic) x 2 (time: immediate, delayed) ANOVA used Total RBANS score as the dependent variable and recall scores (Immediate and Delayed) as independent variables.

FMRI data was pre-processed and voxel activity within areas of interest, as determined by observed regions of activity during each condition, was evaluated. ROIs were defined by the automated anatomical atlas of the WFU PickAtlas (Maldjian, Laurienti, & Burdette, & Kraft, 2003; Maldjian, Laurienti, & Burdette, 2004; Tzourio-Manoyer et al., 2002). Maximum BOLD signal and number of activated voxels within ROIs were calculated. Within-subject t-test contrasts included mean BOLD signal for each of the experimental conditions. Contrasts for semantic versus syntax-focused encoding, semantic versus syntactic-focused delayed recognition, and right versus left hemisphere analyses were computed (i.e., semantic – syntactic activation and syntactic – semantic activation).

Behavioral performance and fMRI BOLD signal were then integrated for the final analyses, examining the impact of behavioral covariates on BOLD activation (i.e., syntactic - semantic and semantic – syntactic activation contrasts).

BOLD activation during the encoding within each condition was used as the predicted variable. Left hemisphere syntactic ROI BOLD activation, as predicted by the number of words retained upon immediate versus delayed free recall was examined. Left hemisphere semantic ROI BOLD activation, as predicted by the number of words recalled following immediate versus delayed free recall was examined. To test the hypothesis that bilateral compensation would occur within predominantly the syntactic condition, right hemisphere correlates were examined using behavioral covariate recall scores: Right hemisphere ROI BOLD activation by condition, as predicted by the number of words recalled following immediate free recall versus delayed free recall was examined.

Results

Sample Description

Participants had an average age of 74.63 years (s.d. = 6.66), and mean education of 17.54 years (s.d. = 2.76). Gender of the sample was evenly split (50% male, 50% female) and participants self-identified as Caucasian/Non-Hispanic (100%). Please refer to Table 4.1 for further information. Participants exhibited an average WTAR standard score of 115 (s.d. = 6.7).

Cognitive Functioning: RBANS

Scores on the RBANS reflect standard scores (mean = 100, SD = 15). Based on normative scores, participants fell within the average range across indices (please refer to Table 4.2). No significant discrepancies existed between measures of cognition and estimates of premorbid functioning (WTAR), which fell within the high average range. No significant discrepancies existed between baseline cognitive functioning within the current sample and that of the overall population, controlled for age.

Demographic Bivariate Correlations

As previously reported in our earlier work (Brown, unpublished), age was significantly related to Immediate Total Recall ($r = -0.36$, $p < .05$), Delayed Semantic Recall ($r = -0.43$, $p < .05$), and Delayed Total Recall ($r = -0.41$, $p < .05$); Education was related to WTAR ($r = 0.62$, $p < .01$), RBANS VisuoConstructional Index ($r = 0.39$, $p < .05$), RBANS Language Index ($r = 0.41$, $p < .05$), and RBANS Total Index ($p = 0.44$, $p < .05$); and Gender correlated significantly with WTAR (rho = -.36, $p < .05$) and Immediate Semantic Recall (rho = -0.37, $p < .05$) using Spearman’s rho. Race did not significantly correlate with behavioral measures of interest using Spearman’s rho method.

Behavioral Results

Immediate Recall Accuracy

Recall for words was measured immediately following presentation of complete list of phrases. Participants recalled an average of 2 syntactically encoded words (s.d. = 1.82), 3 semantically encoded words (s.d. = 2.28), and 5 total words (s.d. = 3.53). They generated an average of 2 errors of commission (s.d. = 1.56). Total attempts (words generated, regardless of accuracy) ranged from 0 to 15 words, with an average of 6 attempts per individual (s.d. = 3.54).

Delayed Recall Accuracy

Recall after a 15- 20 minute delay following immediate recall was measured. Participants recalled an average of 2 syntactically encoded words following a delay (s.d. = 1.98), 3 semantically encoded words (s.d. = 2.29), for a total of 5 correctly recalled words (s.d. = 3.84). They made an average of 3 errors of commission (s.d. = 3.03). Total attempts ranged from 0 to 21 words, with an average of 8 attempts per individual (s.d. = 5.11).

Repeated Measures ANOVA:

Immediate and delayed recall scores for each manipulation type were entered into repeated measures ANOVA with RBANS Total Scale Score. Significant differences were seen between semantic and syntactic manipulation, with a benefit towards semantic manipulation ($F(1, 13) = 6.027$, $p < .05$). No significant differences were found between memory time points. No significant differences were seen within interactions of manipulation and memory or either/both with RBANS Total Scale Score. When regression analyses were run to predict the RBANS total score, education was entered as a potential confounding variable with RBANS total score. No significant predictive value was found for immediate or delayed semantic recall. For syntactic recall, trend level significance occurred for the delayed syntactic recall ($\beta = .48$, $t = 1.99$, $p = .056$).

Paired T-Tests

Paired T-tests were conducted to compare syntactic and semantic recall across immediate and delayed time points, as well as against each other at each time point. No significant differences were found across time points, consistent with repeated measures ANOVA. Within time points, no differences between manipulation conditions were found at the immediate memory time point. After a delay, significantly more semantic words were recalled over syntactic words in comparison to those remembered at immediate recall ($t = -4.139$, $p < .05$).

Total Activation across hemispheres

Within previous work (Brown et al, 2011), we examined the pattern of activation across ALL current ROIs within post-hoc analyses (i.e., numbers reflect activation using 1 mask to include both left and right sided ROIs within analysis). In the current analysis, we sought to take this prior analysis a step further by directly comparing the level of activation across left-hemisphere ROIs with those of right-hemisphere ROIs. Therefore, in contrast to the single mask activation reported previously (Brown et al, 2011), the current numbers reflect activation when one mask was utilized to measure all left-sided ROIs, and another analysis when 1 mask was used to measure all right-sided ROIs. Within the encoding paradigm, activation occurred across hemispheres (Table 4.2).

First, a mask was used to isolate activation occurring across left-hemisphere ROIs. Within the Left Syntactic – Baseline contrast, activation included PO/PT activation (cluster size = 8465 voxels, max $z = 7.19$, $p < .05$ FWER) and MTG activation (cluster size = 2857 voxels, max $z = 6/16$, $p < .05$ FWER). Within the Left Semantic – Baseline contrast, activation occurred with predicted syntactic region PO (cluster size = 10019 voxels, max z = 7.70, $p < .05$ FWER), as well as predicted semantic region MTG (cluster size = 2723 voxels, max z = 6.58, $p < .05$ FWER). Within the Left Syntactic – Semantic contrast, no significant clusters were seen at FWER $p < .05$ (Figure 4.2). At a more liberal threshold of $p < .001$ uncorrected, activation was observed within syntactic PO (cluster size = 62 voxels, max z = 3.66, $p < .001$ uncorrected) and semantic MTG (cluster size = 67 voxels, max z = 3.60, $p < .001$ uncorrected). Within the Left Semantic – Syntactic contrast, activation was observed within semantic MTG (cluster size = 284 voxels, max z = 6.34, $p < .05$ FWER), MOFG (cluster size = 251 voxels, max z = 5.61, $p < .05$ FWER), and syntactic MFG (cluster size = 2725 voxels, max z = 6.01, $p < .05$ FWER; Figure 3).

Secondly, a mask was used to isolate activation occurring across right-hemisphere ROIs. Within the Right Syntactic-Baseline contrast, activation included PT (cluster size = 2135 voxels, max z = 6.07, $p < .05$ FWER), MFG (cluster size = 569 voxels, max z = 5.74, $p < .05$ FWER), MOFG (cluster size = 211 voxels, max z = 5.14, $p < .05$ FWER), and PO (cluster size = 63 voxels, max z = 4.10, $p < .05$ FWER). Within the Right Semantic – Baseline contrast, activation occurred within semantic PT (cluster size = 1810 voxels, max z = 6.54, $p < .05$ FWER), MOFG (cluster size = 388 voxels, max z = 5/48, $p < .05$ FWER), and syntactic MFG (cluster size = 120 voxels, max z = 5.06, $p < .05$ FWER). Within the Right Syntactic – Semantic contrast, activation was observed within the semantic MTG (cluster size = 260 voxels, max z = 4.73, $p < .05$ FWER). Within the Right Semantic – Syntactic contrast, activation included MOFG (cluster size = 36 voxels, max z = 3.85, $p < .05$ FWER), MTG (cluster size = 72 voxels, max z = 3.64, $p < .05$ FWER), and MFG (cluster size = 18 voxels, max z = 3.29, $p < .05$ FWER).

Finally, following observation of activation patterns within ROIs of each hemisphere, the number of voxels activated within each hemisphere was compared. The number of voxels activated within all left hemisphere ROIs compared to all right hemisphere ROIs did not significantly vary in either the syntactic – semantic contrast, or the semantic- syntactic contrast.

fMRI Activation Predicted by Syntactic and Semantic Immediate Recall

The relationship between paradigm activation and future free recall was examined by covarying immediate recall scores for each condition with condition specific information within both conditions. Gender and Age were entered as confounding variables, in response to significant correlation immediate recall scores. No voxels of significance were observed in the syntactic condition at either conservative or liberal thresholds. Temporal regions of the right hemisphere were activated significantly within the Semantic – Baseline condition, but only at more liberal thresholds (cluster = 69 voxels, max $z = 3.55$, $p < .001$ uncorrected). When syntactic – semantic activation was examined, no clusters of voxels reached significance at either the conservative or liberal threshold. The semantic – syntactic contrast was significant at the liberal threshold ($p < .001$, uncorrected) for the right hemisphere ROIs (cluster = 25 voxels, max $z = 3.02$) and for the right pars triangularis (cluster = 10 voxels, max $z = 3.36$). The right pars opercularis was significant at the conservative threshold ($p < .05$, FWER; cluster size = 8, max $z = 3.42$).

fMRI Activation Predicted by Syntactic and Semantic Delayed Recall

The relationship between activation during paradigm task and future free recall was examined by co-varying delayed recall scores for each condition with condition specific information within both conditions. Gender and Age were entered as confounding variables, in response to significant correlation delayed recall scores. Within the syntactic condition, no significant activation was observed in either in right or left hemispheres at conservative or liberal significance thresholds. In the semantic condition, significant activation was found within right hemisphere temporal regions at liberal thresholds (p < .001 uncorrected), but no significant activation was found at more conservative, FWER correction p < .05. When comparing syntactic – semantic activation, no significant activation was found at liberal or conservative thresholds. In the alternative contrast (semantic – syntactic activation), activation was found at liberal thresholds (p < .001, uncorrected) within the right MFG (cluster = 4 voxels, max z = 3.27). The cluster was significant at the hemisphere level and across all ROIs at the above stated liberal threshold.

Discussion

Semantic and syntactic resources have recently been examined as aspects of verbal memory (Brown, 2011), but the impact of component parts of verbal memory, namely delay duration and cortical hemisphere asymmetry, remain less clear. The current study examined the interaction of discourse language and their impact on behavioral and fMRI activation during a task of verbal memory.

No significant differences were observed between immediate and delayed recall, suggesting that individuals retained words that they originally encoded, regardless of level of cognition or delay duration. In this way, the benefit of context was maintained across immediate and delayed verbal memory durations, supporting the use of contextual organization as an encoding tool. No significant relationship occurred between semantic immediate and delayed recall predictors and cognition, observed through RBANS Total Scaled Score. A trend level relationship occurred between delayed syntactic recall and RBANS Total Scale Score, but not in the hypothesized direction. Research implicates increased difficulties with cognition in lower levels of encoding benefiting memory (Majerus, Norris, & Patterson, 2007). It is possible that the current sample did not experience difficulties significant enough to require exclusive use of lower levels of verbal memory encoding. It could also reflect that resources may have shifted but maintained adequate power to manipulate and encode information effectively (Cabeza, 2002).

As expected, individuals recalled more semantically encoded words than syntactically encoded words after a delay. This is consistent with prior evidence that semantic representations benefit maintenance of verbal information in long term stores by sustaining high levels of activations (Cameron et al., 2005) as well as evidence that contextual information impacts both encoding and retrieval phases of verbal memory (Atkinson & Shiffrin, 1971). It is also consistent with prior research from this lab (Brown et al, 2011). Not anticipated was the lack of relationship between the numbers of syntactically recalled words at the immediate memory time point in comparison to the delayed time point. This is inconsistent with prior research demonstrating the role of short-term memory regeneration in processing syntactic information, which would implicate this process within immediate more so than delayed recall (Lombardi & Potter, 1992; Papagno, Cecchetto, Reati, & Bello, 2007). Lack of significant effect could relate to inefficient use of syntactic resources not driving an effect at the immediate time point (Vos et al, 2001), or it is also likely that use of these resources were not defective but rather equivalently intact with short term semantic manipulation processing. These results suggest that while delay does not impact the overall amount of information recalled, it may impact the type of context most utilized in verbal memory tasks following such a delay. In this manner, either form of context could be beneficial at immediate delay, but the semantic benefit would be more likely to extend to more long term verbal memory stores.

In comparing activation between left-hemisphere ROIs and right-hemisphere ROIs, both semantic and syntactic focused contrasts identified significant activation for predicted syntactic regions as well as predicted semantic regions, in line with previous research integrating hemispheres into one analysis (Brown et al, 2011). The greater number of right sided regions occurring within the semantic – syntactic contrast compared to syntax – semantic contrast supports research implicating bilateral use of resources within deeper levels of verbal memory encoding (Stebbins et al, 2002) and falls in line with the model that implicit and explicit systems may become less specialized within older adulthood (Dennis & Cabeza, 2011). It is inconsistent with our hypothesis that frontal syntactic processes would elicit more bilateral resources than temporal semantic processes, as significant bilateral activation was also seen within temporal regions. Furthermore, the number of total voxels across ROIs did not significantly vary across hemisphere within either contrast. This suggests that syntactic processes may be implicating an equal number of voxels in a more specific region (rather than fewer voxels across the entirety of language regions examined), supporting the theory of Vos et al, (2001) that syntactic processes benefit more from efficient implication of cortical resources rather than only number of resources implicated. It is possible that due to this efficiency, bilateral activation was not needed for processing syntactic context. Higher levels of processing may have implicated additional bilateral resources as a form of compensation. Furthermore, results suggest that higher level processes may be implicating a greater number of regions, more so than activating a greater number of total voxels. In this way, levels of processing (Craik & Lockhart, 1972) may be viewed both in amount of activation, but also by the number of regions implicated in this activation.

When examining activation adjusting for the number of words recalled immediately, no clusters reached significance for syntactic specific voxels, subtracting out semantic voxels. In the semantic contrast, the right hemisphere PT (semantic region; Brown et al, 2011) and PO reached significance (syntactic region; Brown et al, 2011). As semantic memory was improved at the delay in comparison to syntactic memory, this supports research suggesting ventrolateral prefrontal cortex activation predicts success of long term behavioral memory (Murray & Ranganath, 2007). It is interesting that semantic activation was not lateralized within these frontal regions, as an increased recruitment of frontal resources over temporal resources have been observed within clinical samples (Trivedi et al, 2008). Frontal regions have been implicated to a greater extent within long term memory and shifts to semantic functions (Buchsbaum, Padmanbahn, & Berman, 2010). However, we predicted that the syntactic contrast would elicit more bilateral activation, which did not occur. This supports the levels of processing model (Craik & Lockhart, 1972; Bonner-Jackson, Csernarnsky & Barch, 2007) and also other models that suggest that syntactic processing facilitates memory when it is more efficient rather that engaging greater cognitive resources. Semantic processing was not significantly greater than syntactic memory at this time point, which would again support the idea that both were equally effective with differing amounts of cortical resources (Vos et al, 2001).

When examining activation, adjusting for words recalled following a delay, semantic activation (semantic – syntactic contrast) was seen within hypothesized syntactic right MFG. This was not the case when the reverse contrast was completed. More semantic words were recalled in comparison to syntactic words, consistent with prior research from this lab (Brown et al, 2011). This pattern of behavioral and BOLD results supports the levels of processing theory that activation relates to the behavioral accuracy (Craik & Lockhart, 1972; Bonner-Jackson, Csernarnsky & Barch, 2007). It further supports work suggesting that semantic context benefits memory in the long term by maintaining greater levels of activation (Atkinson & Shiffrin, 1971), and that with increasing delays the cortex tends to shift to semantic forms of retrieval (Buchsbaum, Padmanabhan, & Berman, 2010). The middle frontal cortex is proximal to mid/dorsolateral PFC regions identified as recall specific regions, specifically long term memory success (Staresina & Davichi, 2006).

Although the current activation was measured during the manipulation/ encoding task, it remains interesting that activation occurs in the context of future behavioral recall benefit. It is also significant that this pattern occurs during encoding, as left hemisphere has typically been relegated for encoding with right hemisphere for recall (Johnson, Saykin, Flashman, McAllister, & Sparling, 2001). Part of the discrepancy could arise from the HAROLD model implicating additional resources within older adults (Cabeza, 2001). It is possible that this reflects some of the dedifferentiation discussed within the model, and the use of additional resources to account for aging related decline in grey matter. This pattern corresponds with some literature coming out of the MCI research, which implicates use of additional frontal resources in successful recognition as opposed to the traditional semantic MTG networks (Trivedi et al, 2008). This could relate to frontal networks being more involved than temporal networks when making lower confidence judgments on ambiguous stimuli (Kim & Cabeza, 2009).

This study is framed by several limitations. Due to potential noise secondary to muscle movement, participants were not scanned during immediate and delayed recall tasks, and we are unable to comment on cortical activation during the retrieval phase of verbal memory. The older adult sample was fairly homogenous, and future research detailing patterns of activity within individuals along the full spectrum of pathological aging would be beneficial. Despite this limitation however, it remains critical to understand verbal memory mechanisms within a healthy older adult sample prior to effectively gauging difficulties that occur within pathological aging.

Future research could examine encoding and retrieval activation to compare the role of regions at different stages of the verbal memory process. This would benefit our understanding of individuals in which the breakdown in verbal memory does not occur at the encoding phase, but rather the retrieval phase. It would also benefit the body of literature for future research to explore both direct memory cues as presented within the current paradigm, compared with more unstructured approaches to memory tasks, to better understand the mechanisms that occur naturally and how directive cuing influences memory above and beyond innate memory tools.

Verbal memory has a strong impact on the daily lives of older adults, and a detrimental effect in pathological aging when related language mechanisms do not function as desired. The current study aimed to examine the variables that impact language mechanisms in facilitating verbal memory, specifically duration of memory and scope of related cortical activation. It is possible that syntactic memory was benefited more by efficient use of resources rather than number of resources required by semantic processing to yield a similar performance on verbal memory measures. Framed by the memory mechanisms impacting implicit syntax and explicit semantic information, the current results paint a complicated picture of verbal memory and the role language plays in facilitating these processes.

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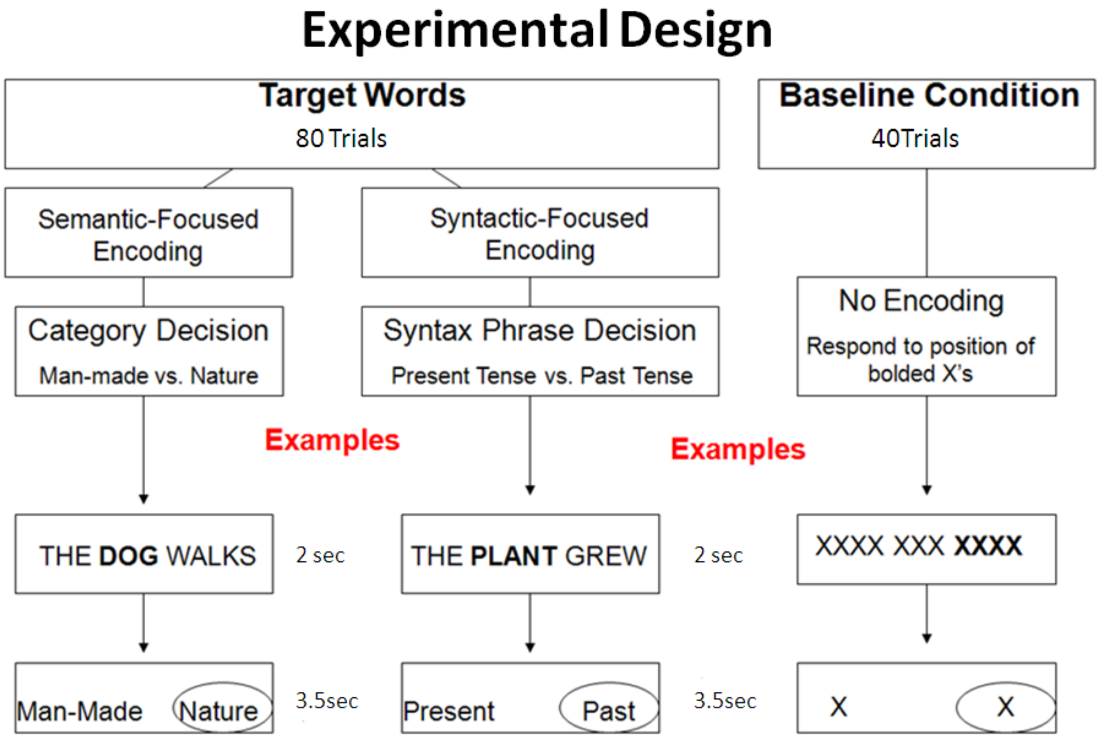

Figure 4.1

Experimental design

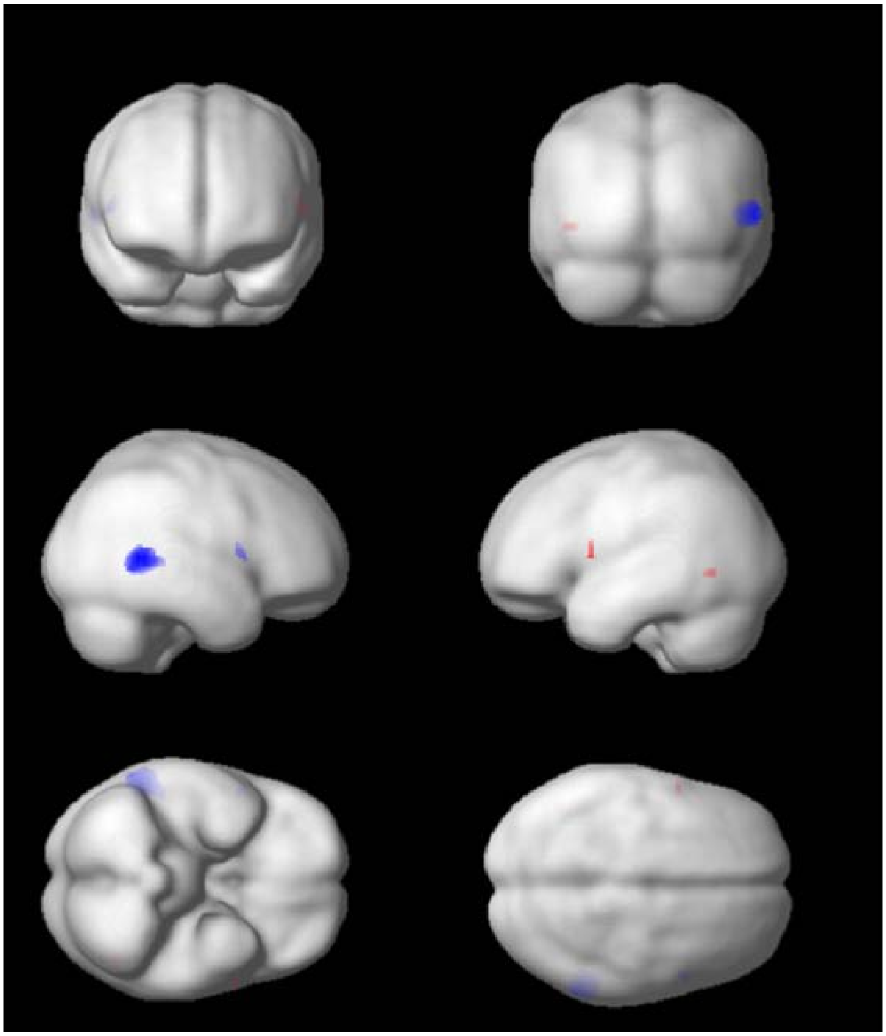

Figure 4.2

Left (red) versus Right (blue) activation for Syntactic – Semantic contrast

Right activation surpasses left activation, but occurs within similar frontal and temporal regions.

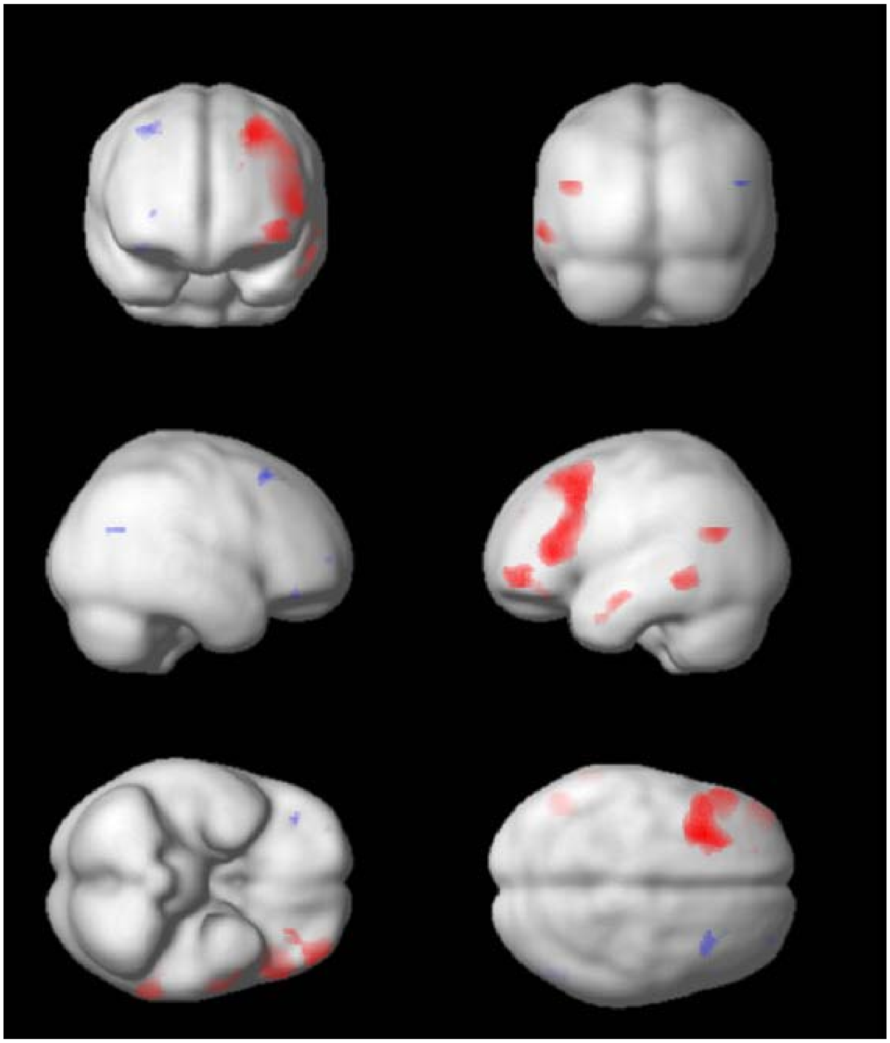

Figure 4.3

Left (red) versus Right (blue) activation for Semantic – Syntactic activation contrast

Left activation surpasses right activation, but again occurs within similar frontal and temporal regions.

Table 4.1

Demographic and Behavioral Scores

	Mean	**SD**
Age	74.6	6.6
Years Education	17.5	2.8
WTAR/ Demo Predicted FSIQ	115	6.7
RBANS Immediate Memory	105	10.7
RBANS VisuoConstructional	96	13.6
RBANS Language	106	10.8
RBANS Attention	108	15.4
RBANS Delayed Memory	102	14.2
Total RBANS Standard Score	104	11.1
Paradigm- Syntactic Accuracy	35.41	4.41
Paradigm- Sematnic Accuracy	32.69	2.91
Paradigm- % Behavioral Accuracy	88.57	7.91
Immediate Syntactic Recall	2.13	1.83
Immediate Semantic Recall	2.66	2.28
Delayed Syntactic Recall	1.88	1.98
Delayed Semantic Recall	3.25	2.29

Table 4.2

Left versus Right hemisphere Activation across ROIs

Cluster List	Voxels	Region	Max z score	X	Y	Z
Left Syntax- Semantic						
	62	Pars Opercularis	3.66	-56	6	6
	67		3.60	-45	-63	-3
Left Semantic- Syntax						
	460	MTG	6.3400	-45	-61	22
	5070	MFG	6.0100	-27	27	39
		Frontal Superior Gyrus	5.3000	-20	29	49
		Pars Triangularis	5.3000	-38	20	21
	665	MOFG	5.6100	-34	36	-14
		MOFG	4.8200	-44	48	-11
	407	MTG	4.8100	-62	-45	-12
		MTG	3.2000	-52	-39	-9
	213	MTG	4.4100	-60	-6	-21
		MTG	3.7300	-54	5	-30
	12	Frontal Superior Gyrus	3.8100	-20	50	33
Right Syntax – Semantic						
	919	MTG	4.73	58	-49	6
	64	Pars Opercularis	3.38	52	9	9
Right Semantic - Syntax						
	36	MOFG	3.85	36	38	-14
	161	Frontal Superior Gyrus	3.69	27	23	57
		MFG	3.65	36	21	52
	72	Frontal Superior Gyrus	3.38	27	32	51
	18	MTG	3.64	51	-61	22

Note: Activation shown at uncorrected, p < .001

CHAPTER 5

DISCUSSION

General Discussion

The current experimental endeavor examined the interaction of verbal memory processes within older adults and the very language processes that inevitably are paired with verbal material during mundane encoding. Neuropsychologists frequently use both rote word memory lists (i.e., CVLT-II) and contextual story memory (i.e., WMS-IV Logical Memory) to isolate difficulties at increasing levels of verbal organization. The diagnostic benefit of isolating these variables has been identified within MCI samples (Rabin et al, 2009). The current study sought to isolate components of verbal contextual organization to determine if the mechanism of its benefit vary based on level of cognitive impairment. Specifically, we examined whether lower levels of language organization would be easier to process with individuals displaying greater cognitive difficulties. We further sought to deconstruct variables that may be impacting language processes on verbal memory within older adults, specifically duration of memory delay and scope of cortical activation. The specific findings have been discussed previously within the manuscripts. The main themes within these specific findings are presented below:

Semantic versus Syntactic Processing

One overarching question within the current evaluation involved whether semantic processing would be of greater benefit with increasing levels of cognitive ability. The question stemmed from prior research implicating explicit memory difficulties with earlier degradation during cognitive decline than implicit memory (Cabeza, 2001). This hypothesis was supported by the finding that semantic (i.e., explicit) manipulation of phrases during encoding significantly and positively predicted RBANS Total Scaled Score more so than syntactic (i.e. implicit) manipulation. The hypothesized pattern of increased use of syntactic manipulations benefiting verbal memory at lower levels of cognition did not occur, and in fact, the opposite direction of significance was found within this relationship. Within the current sample then, both forms of contextual organization benefitted older adults. One factor playing into this could involve the homogeneity of the final sample's cognition. These results would suggest that at higher levels of cognition, contextual organization of any kind benefits verbal memory in older adults. Within intact functioning then, individuals are able to use context of either semantic or syntactic varieties to organize information in a meaningful way, despite semantic processing necessitating "higher/ deeper" processing load. In light of this, it is possible that greater distinctions between benefit at higher and lower processing loads would be observed within more pathological forms of aging, during which cognitive decline may elicit greater impairment within higher forms of contextual processing. Another potential option would be intact cognitive flexibility facilitating increased efficient use of cortical resources within both forms of manipulation (Garrett, Grady, & Hasher, 2010). This is supported by the imaging data demonstrating dedifferentiation of semantic versus syntactic frontal resources. Overall, semantic resources showed greater breadth of activation, supporting the levels of processing model (Craik & Lockhart, 1972). Voxel analysis further suggested that syntactic activation was occurring in an equal number of voxels as semantic encoding, but within a more specific region. This also supports research implicating syntactic resources as benefiting from efficiency over scope of activation (Vos et al, 2001). Results suggest that rather than syntactic processing requiring fewer resources as a "lower" form of processing, the same number of resources would be activated in a more isolated region. In this manner results illustrate that the quantity of regions implicated may not be equivalent to the number of resources implicated within cortical processes. Thus, the levels of processing model (Craik & Lockhart, 1972) ought to be viewed in terms of spread of activation across regions, as well as the number of voxels activated within particular regions and across the cortex. When comparing activation to cognitive function, significant activation was demonstrated within the semantic- syntactic contrast. As the reverse contrast was not observed for syntactic activity, results demonstrate that higher levels of semantic processes relate to higher levels of cognition. In this manner, levels of processing may be thought of more as a ratio of significant difference in activation between two types of processes, more so than a comparison between number of regions or number of voxels activated by each process. This form of comparison becomes increasingly important when examining processes such as syntax and semantics, which are by no means mutually exclusive to the other.

Short Term versus Long Term Memory

No notable differences were identified between immediate and delayed recall, or in time point variables predicting RBANS Total Scale Score. This suggests that individuals within this sample of older adults recalled at a delay what was encoded at the immediate time-point, regardless of level of cognition. These results support the argument noted above regarding the effective use of context as a coping mechanism to account for difficulties within the task. Benefit at immediate recall was largely carried over into delayed recall. This pattern supports the use of organizational tools at encoding, as the benefit may extend into the delayed time point. More semantically encoded words were recalled when compared to syntactically encoded words, specifically at the delayed recall time point. This could relate to research reflecting that semantic information in particular facilitates maintenance of encoded information within long term stores.

In this respect, time does not have an impact on overall memory for verbal information once encoded with context, but it may have an impact on the type of context an individual most utilizes during delayed recall. A specific PT/PO semantic based activation was observed at encoding, supporting a potential ventrolateral prefrontal predictive power of long term memory benefit (Murray & Ranganath, 2007). In this regard, the benefit for semantic information comes from engaging the information at encoding to maximize the benefit at long term delayed recall. It also supports research implicating frontal regions with long term memory and semantic functions (Buschsbaum, Padmanabahn, & Berman, 2010). The benefit of syntactic processing within short term memory was not identified within the current experimental sample. This could relate to inefficiencies within syntactic encoding, or conversely, equivalent processing when compared to semantic encoding at this time point. In either case, the results suggest that older adults would benefit by either form of processing in the short term, but the semantic benefit may be more likely to extend into the delayed recall durations and thus more permanent memory.

Encoding versus Recognition

The recognition activation demonstrated similar patterns of activation to that of the encoding manipulation: Left middle temporal lobe activation was prominent during the semantic more so than the syntactic manipulation, supporting research implicating this region with both encoding and retrieval processes (Henson, 2005) and to higher confidence judgments potentially elicited by deeper levels of encoding (Kim & Cabeza, 2009). The direct correlations between significant regions of activation being related to level of cognition was not observed within the recognition manipulation as it was within the encoding manipulation. The distinction may have arisen from the lack of explicit cues to use semantic or syntactic encoding within the recognition task, as explicit cues benefit directing cognitive function within older adults (Lou & Craik, 2008). It could also point to context as being most directly implicated with the learning process rather than the retrieval process. Once encoded by whatever means available, the information was stored effectively enough for tasks of familiarity. As recognition was an exploratory analysis, more specific lines of research could be helpful in fleshing out the relationship of recognition to different forms of contextual organization.

Right Hemisphere versus Left Hemisphere

The pattern of left lateralized activation during encoding and right activation during recall did not occur within the current sample (Johnson, Saykin, Flashman, McAllister, & Sparling, 2001). Regarding previous research supporting bilateralization of cortical activation during aging (Cabeza, 2002), bilateralization was observed within the current findings, specifically within frontal regions more so than temporal lobed based activation. This suggests that with older adults, use of higher levels of processing may be different in terms of activating more bilateral resources to achieve the same results. Due to the efficiency of syntactic resources (Vos et al, 2001), this may not have been needed to the same extent for information processed in this manner. Frontal activation rather than temporal could relate to organizational processes being more associated with the frontal lobes, and therefore interfacing with contextual information at these junctures. Bilateral activation was particularly salient during the semantic over syntactic manipulation task, supporting prior research reflecting greater dedifferentiation within frontal regions (Cabeza, 2002; Tyler et al, 2010). Although we anticipated syntactic information to yield greater dedifferentiation in frontal regions, greater semantic dedifferentiation could relate to an increased number of previously centralized cortical activation relating to semantic processing activation or displacement (Moulin et al, 2007; Dannhauser, 2008). In this manner, the levels of processing (Craik & Lockhart, 1972) could be reflective of the number of regions pulled into processing a given set of information, more so than the number of voxels activated within both contextual conditions.

Conclusion

The current study demonstrates support for semantic processing eliciting greater dedifferentiation within frontal regions during older adulthood, specifically during a verbal memory encoding task involving a language-based manipulation. Future research evaluating the role of these language-based contextual tools within individuals experiencing varying levels of cognitive impairment could further isolate the extent of influence that various forms of context have on improving memory performance as we age. In general, this organizational context appears to benefit individuals and elicit a wide range of cortical activation in processing information. The prominent role of verbal memory within deficits of aging, and the pervasiveness of the very language we encode during verbal memory lends itself well to continued research. Continued contributions to the empirical literature in this regard will facilitate clinical recommendations for individuals at varying levels of cognitive impairment.

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