VERBAL MEMORY PROCESSING AND FMRI: SYNTAX VERSUS SEMANTICS

by

COURTNEY L. BROWN

(Under the Direction of L. Stephen Miller)

ABSTRACT

This thesis examined semantic and syntactic components of verbal encoding in young adults. Participants were asked to judge phrases based on semantic and syntactic information. Recognition and recall tasks measured retention of words encoded using each strategy. FMRI BOLD signal was evaluated in predicted language regions of interest during verbal encoding and the correlation with behavioral data was examined. Results showed increased activation for semantically encoded words within the left (Brodmann's Area (BA) 21, BA 37, BA 45, and BA 47) and right hemisphere (BA 46). Significant activation was found within left BA 44 and BA 46 for semantic and syntactically encoded words. Correlations between fMRI activation and behavioral measures were not significant. Semantic processes appear to facilitate memory over syntactic processing in accordance with the levels of processing memory model (Craik & Lockhart, 1972) but no significant changes in fMRI activation correlate with rate of memory recall.

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

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CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

Language processing depends, in part, on memory for verbal information: this entails retrieval of information from short-term and long-term stores, as well as interaction of learned semantics and grammar rules, to facilitate formulation of organized thoughts. Difficulties with verbal processes, specifically verbal memory, appear in many psychological disorders, such as certain learning disorders of youth and Alzheimer's disease of older adulthood (Tijms, 2004; Korkman & Pesonen, 1994; Scahill, Hodges, & Graham, 2005). Verbal memory impairments have also been suggested to be indicative of a genetic risk of schizophrenia, being prodromally correlated with later development of psychosis in high risk samples (Pukrop et al, 2007; Bonner-Jackson, Csernansky & Barch, 2007).

Verbal memory entails interrelated language components working together to encode and retain information. These components include, but are not limited to: semantic processing (word meaning), and syntactic processing (grammar). Research examining the influence these processes exert on measures of verbal memory in healthy control samples could contribute to the foundation of verbal memory knowledge, as well as facilitate later explorations into verbal memory processes in clinical samples.

Verbal Memory Defined

Despite its scope of influence, the mechanism of verbal memory is not completely understood, being a complex issue among both clinical samples and the general population. It is comprised of various inter-related subsystems. Encoding information involves transforming presented information into a mental representation that can be stored in memory. Retrieval involves returning stored memories to conscious thought, allowing further manipulation. To distinguish these processes, memory is frequently tested by free recall (which load onto retrieval processes), as well as recognition (which load more on initial encoding processes) (Butters & Delis, 1995).

Memory begins formation in the form of short term memory, which holds information in place for several minutes after presentation, assuming a lack of interfering information in the interim. The amount of information held in short term memory is small, comprising of approximately 7 chunks of information. Rehearsal allows information to move towards long term memory. Once in long term memory, information will be stored despite distraction from the target information, and for indefinite periods of time (Butters & Delis, 1995). Long term memory can involve implicit memories for unconscious, procedural aspects of daily life, encoded by repeated exposure to this information. These memories are expressed through performance on a given task, rather than by active recollection of information (ex. tying one's shoe). Some have identified knowledge for the syntax of one's native language as falling under the umbrella of implicitly encoded information (Fabbro, 1999). Long term memory also consists of declarative memories for consciously manipulated facts, events, and rules (ex. dates of special occasions). A specific type of declarative memory is semantic memory, which involves general knowledge of the world and its organization. While some have argued for a mutually exclusive relationship to autobiographical memories, others indicate that autobiographical significance influences what semantic information is retained (Snowden, Griffiths, & Neary, 1996) or alternatively, that semantic relatedness can affect episodic memory for verbal material (McCloskey & Santee, 1981). Finally, a growing literature has focused on the process of actively manipulating and

maintaining verbal information in order to keep it "online" for a given experimental task, incorporating both memory skills as well as executive processes. This form of memory has been termed verbal working memory (D'Arcy, Ryner, Richter, Service, & Connelly, 2004). Syntax has been described as being a product of the working memory system, specifically through the process of phonological short term memory stores, which allow information to be efficiently rehearsed and integrated into long term stores of language information (Ellis & Sinclair, 1996).

Though some debate exists regarding specific cortical regions activated by verbal memory tasks, several researchers have implicated the left prefrontal cortex (Barde & Thompson-Schill, 2002; Baker et al, 2001). Some have isolated the left dorsolateral prefrontal cortex as important within short term verbal learning and suggest consolidation of information occurs within medial temporal areas (Elmer et al, 1999). Still others have proposed a potential lateralization depending, in part, on the strength of white matter in the corpus collosum; weaker connections could lead to verbal processing within the right inferior prefrontal gyrus in certain individuals (Putnam et al, 2008).

Models of Verbal Memory

The literature remains divided regarding the specific process of verbal memory, with various models that denote both the catalyst for activation and the specific cortical region being implicated within the verbal memory process. The most prominent models include the process model, materials model, levels-of-processing model, and the phonological loop model. Within working memory, a debate continues regarding single processing resource theories and separate language interpretation resource theories (Table 1.1).

The process model of verbal memory suggests that the specific areas activated by a memory task depend on the process initiated by the task itself (e.g. forced choice categorization,

inhibition of distracter choices) (Barde and Thompson-Shill, 2002). For example, researchers have examined potential distinctions between maintenance and manipulation of semantic information (ordering nouns by size and/or retaining noun information) versus phonological information (alphabetizing and/or remembering non-words). Both types of manipulation elicited greater dorsolateral and posterior activation than the control, maintenance task (Barde and Thompson-Shill, 2002). Discrepancies in cortical patterns of activation responding to the same stimuli using varying tasks to process stimuli (i.e., manipulating or maintaining information) support the theory that the process of encoding alters the cortical regions implicated in encoding.

In general, activation within verbal memory tasks have elicited left PFC (inferior frontal) activation. D'Esposito et al (1999) found similar areas of activation (ventrolateral and dorsolateral prefrontal cortex) during two distinct memory processes of letter sequences (pure maintenance of information versus manipulation of information). However, the dorsolateral areas elicited greater activity during manipulation tasks than the ventrolateral areas, suggesting a partially distinct area for processing task-specific information. Similar distinctions have been found in cerebellar areas as well. Fliessbach et al (2007) suggest that semantically processed words activate right cerebellar areas, and non-semantic tasks activate bilateral cerebellar areas. These findings suggest that, although verbal memory tasks often elicit similar cortical regions of action, the patterns of this activation in scope and/or intensity may vary based on the task being elicited.

By this model, the level of distinction in activation between memories for semantically and syntactically stored information would be driven by the level of difference between the processes. Although there is a lack of research comparing syntactic and semantic memories specifically, language comprehension research has illuminated BA 44 as syntax related (Frederici et al., 2003; Kang et al, 1999; Dapretto & Bookheimer, 1999; Newman, Ikuta, & Burns, 2010; Lee & Newman, 2009; Raettig, Friesch, Friederici, & Kotz, 2010) and BA 47 as related to semantic processing (Dapretto & Bookheimer, 1999; Newman, Ikuta, & Burns, 2010).

The material model suggests that verbal memory organization ought to be defined by differences in stimulus content (e.g. semantic versus phonological information, i.e. words versus non-words) (Barde and Thompson-Shill, 2002). This model arises out of evidence for the dorsal and ventral streams of cortical activation when processing visual-spatial versus visual-object information (Goldman-Rakic, 1987). Semantic processing researchers have found some support for this verbal information model. Through a semantic (abstract versus concrete) and structural (upper or lower case) encoding task, Baker, Sanders, Maccotta, & Buckner (2001) illustrated parallel regions of activation in response to verbal information, regardless of encoding process, citing success rate as correlated with intensity of activation (left fusiform gyrus and left inferior frontal gyrus). This pattern suggests the presence of a specific, task-independent, cortical network for processing of verbal material. Due to the integrated nature of semantic and syntactic information, this model would be a poor fit for questions related to isolating components of language within verbal memory.

The 'level-of-processing' model of Craik and Lockhart (1972) states that participants process similar material at varying degrees of encoding, from lower level structural (letter case) and lexical decision (word versus non-word) tasks, to higher level semantic categorization (animal versus tool) tasks. Higher level encoding requires more time and cortical resources to complete a task successfully (Craik & Lockhart, 1972, Bonner-Jackson, Csernansky & Barch, 2007). Cortically, higher level processing has been linked to left prefrontal activation (verbal memory area) and better recall on subsequent memory tasks. Researchers have found variations in left inferior frontal cortex activation for high and low levels of verbal processing (Bonner-Jackson, Csernansky & Barch, 2007). Others have found broader cortical regions differentially activated by semantic versus more shallow processing, including left inferior parietal regions (BA 39, 40), left middle temporal regions (BA 19, 21), and right supramarginal gyrus (BA 40) (Henson, Hornberger, & Rugg, 2005). It has been noted that within patients exhibiting semantic deficits (i.e. semantic dementia), lower level processes such as phonological and serial processing remain relatively preserved within short-term verbal memory (Majerus, Norris, & Patterson, 2007). In this manner, the level of processing for semantic versus syntactic memory could influence patterns of activation, though the specific outcome of this comparison has not been examined. However, in language comprehension, semantic processing has been utilized as a "deep" level of processing, suggesting a benefit of semantic processing in memory (Craik & Lockhart, 1972, Bonner-Jackson, Csernansky & Barch, 2007).

The phonological loop model was proposed by Baddeley and Hitch (1974). The model involves a lower level processing of presented information through sub-vocal rehearsal. For this reason, information will be more easily remembered if it is phonologically dissimilar from the stimuli it is grouped with (e.g., cat/hat will be more difficult than cat/hop). Similarity of meaning would become more important as long term memory is activated, but has no discernable effect within short term memory. Longer words have been shown to be more difficult to encode than shorter words (i.e. fewer syllables), which supports the theory of sub-vocal rehearsal during verbal encoding. In addition to the short-term phonological loop, participants maintained a "visual-spatial sketchpad" for visual storage and manipulation of stimuli. These two systems are

then organized and maintained by means of an executive control component (Baddeley, 2003). Due to the system's early activation and substantial feedback, phonological interference in word lists has been shown to hinder memory more so than semantic categorical interference (Chasse & Belleville, 2009). In contrast, syntactic comprehension appears to be benefited by the rehearsal component of the phonological loop (Papagno, Cecchetto, Reati, & Bello, 2007).

In 1992, Just & Carpenter put forth their single processing resource theory, describing a different verbal memory/ language interaction. They suggest that semantic processing, phonological, and syntactic processes load onto a single system of working memory, stating:

"We propose that individuals differ in the amount of activation they have available for meeting the computational and storage demands of language processing. This conceptualization predicts quantitative differences among individuals in the speed and accuracy with which they comprehend language." (p. 124).

However, increasing support exists for the alternative theory, the separate language interpretation resource theory. This theory separates language processing into an initial pass of discourse meaning of a sentence, and a second pass integrating semantic memory and reasoning. The second pass would then be the consciously controlled aspect of verbal working memory, while the first pass would be more implicitly driven (Waters & Caplan, 2004).

The models of verbal memory are extensive and their differences highlight the complexity that arises when encoding verbal material. Encoding may be influenced by the task posed to individual (process model), the actual stimuli used during the task (material model), and/or the depth of processing between aspects of the stimuli being processed (level of processing model). Other models implicate the role of executive functioning in integrating sub-rehearsal and visual memories (phonological loop model). A debate remains whether

semantic/syntactic processing occurs concurrently and is combined through working memory (single process resource theory) or whether lower level information is processed prior to semantic information, implicating verbal working memory integration (separate language interpretation resource theory). Despite differences, the nature of these verbal memory modes do appear to support a shared idea that semantic and syntactic processing could utilize at least partially distinct mechanisms for encoding information, allowing for the possibility of varying patterns of cortical activation. Several models also identify some variation of integrating aspects of verbal information during verbal encoding.

Semantic Processing

Semantic processing has been studied predominantly as it relates to discourse processing within the ERP and fMRI environments. Research in normal controls has conceptualized semantic processing in terms of the spread of activation model proposed by Collins and Loftus (1975). The model postulates that, in a healthy subject, the presentation of a word elicits mental representations of closely associated words in a semantic network. For example, the word dog might activate "dog," "cat," "animal," "Fido" and/or "furry." Building on the spread of activation, by the conceptual structure account, semantic concepts are represented by distributed, but inter-connected nodes of specific information regarding an object. Similar concepts activate similar pieces of information, and could potentially share cortical space. However, the patterns are not predetermined or predictable. Two broad categories of classification include nature (shared characteristics) and man-made objects (specifically tools; shared functions) (Devlin et al., 2002). Semantic processing has been proposed to take place in two phases. The first phase involves semantic processing in the presented modality, and another entails an amodal semantic system conceptualizing meanings of single words (Kuperberg et al., 2000). This model is

corroborated by ERP research indicating an amodal semantic processing system supplementing verbal or pictorial materials (West & Holcomb, 2002).

Semantic memory has been defined as, "... the capacity for recollecting concepts and general knowledge about the world" (Bartha et al, 2003, p. 339). It is important to note that semantic information is not confined to verbal processes. Covington et al (2005) remind us that "Not only words, but even thoughts are semantic. That is, they encode concepts and can refer to real world objects. There are also semantic relations between objects in the real world..." (p. 92). Supporting this idea is research implicating language-related EEG waveforms in the processing of pictures (McPherson & Holcomb, 1999) and videos of real world activities (Sitnikova et al, 2003). Several models for semantic memory exist within the literature, including the "perceptualfunctional" model of Warrington & Shallice (1984). This model states that nouns are processed by their salient characteristics. Information about living things typically loads onto perceptual characteristics to categorize. In contrast, information regarding types of tools may load more on the common functional properties of items, rather than perceptual features (Canessa et al, 2008). As previously mentioned, researchers support a semantic memory advantage under the levels of processing model, finding greater neural activation and increased behavioral performance in response to semantic-focused encoding compared to structural encoding (Baker et al., 2001).

It has been suggested that category-specific deficits exist, in particular between manmade artifacts versus nature-related objects (Forde & Humphreys, 1999). However, others have refuted this claim, stating that only the categories of 'animal' and 'tool' show distinct patterns of activation across studies. Proponents of this idea maintain a conceptual structure account: Networks of specific nodes of information create a protective factor for the preservation of broad conceptual understanding. Tasks asking for common, broad, conceptual information may yield greater success than those loading onto diverse, specific details, until neural damage develops to a point where the greater conceptual network of nodes deteriorates (Devlin et al., 2002). In this sense, nature may include more breadth of connections than animals. Likewise, man-made functional characteristics show greater diversity in connections than tool concepts, and the broader categories could be well-preserved.

Semantics- Neurocognitive Findings

As with verbal memory in general, a debate remains within the literature regarding the distribution of semantic memory processes in the brain. Akin to the process versus material debate in verbal memory, some speculate that semantic memory activation could be broken down into visual-feature based classification or functional-based classification. The alternative accounts propose a categorically non-specific semantic processing system, or several distinct but interconnected semantic systems within the brain. ERP work has shown differences in regions of activation between functionally dissimilar semantic categories, such as animals and tools, negating the non-specific theory of semantic processing (Sitnikova et al, 2005). In contrast, some have implicated the dorsolateral prefrontal cortex as integral in processing general verbal relationships (Murray & Ranganath, 2007), supporting a non-specific model. Further support for this broader semantic system includes research implicating bilateral medial temporal and inferior temporal activation within semantic tasks, regardless of handedness (Bartha et al, 2003), and research suggesting left medial temporal semantic activation, regardless of modality (Muller, Kleinhans, & Courchesne, 2003). Cassanto et. al. (2002) related such semantic-focused encoding to the levels of processing model. They illustrated increased performance on memory tasks correlated with left prefrontal, temporal parietal and bilateral medial temporal (word meaning) activation. Poorer performance was associated with right temporal-parietal activity.

One particular region suggested to support semantic processing includes Broca's area. This has been shown by increased activation in Brodmann's area 44 (BA 44) in response to comprehension probes, and a neighboring region, BA 47, activation correlating to processing relatedness of nouns (Newman, Ikuta, & Burns, 2010). Muller, Kleinhans, & Courchesne (2003) identify BA 44 and BA 45 as predominantly involved within semantic processing. Inferior frontal regions have also exhibited increased activation in response to nouns with lower imaginability ratings, an arguably semantic ambiguity (Bedny & Thompson-Schill, 2006). *Syntax Processing*

Another component of verbal memory involves syntax. Syntax can be defined as, "...the way that words are combined grammatically to form meaningful phrases or sentences" (Kircher, Oh, Brammer, & McGuire, 2005, p. 209). The predominance of syntax research focuses on sentence comprehension paradigms in both normal controls and clinical samples. In general, participants prefer syntactically simpler verb clauses (subject first rather than object first) due to the ease of role assignment of a noun to the verb information (Bahlmann, Roddriguez-Fornells, Rotte, & Munte, 2007). In addition to use of semantic memories, such as that of appropriate role assignment, syntactic processing involves taking smaller pieces of information and combining them into more complex forms through the process of syntactic unification (Hagoort, 2005). Some have suggested that if the first pass of processing, integrating information, is not effectively completed (due to ambiguities within the syntactic structure), the semantic aspects of the phrase in question are not evaluated in a second pass (Kuperberg et al., 2000).

Less research has involved the role of syntax in verbal memory. Waters & Caplan (2004) explored the relationship between syntactic complexity and working memory load. They found support for the separate language interpretation resource theory, indicating that syntactic processes could draw on a distinct working memory system rather than other language processes calculated by traditional measures of verbal working memory: Ease of online syntactic processing did not correlate with working memory measured by these means. Work with other groups also show a dichotomy between low working memory spans and intact syntactic processing, including individuals with history of stroke or diagnosis of Parkinson's (Waters & Caplan, 2004). Some research has lent support for a protective interaction of syntax on verbal memory. In work with Alzheimer's patients, memory increased at a rate equivalent to a normal aging sample as word lists increased approximation to discourse text. When processing full text, normal sentences were best remembered, while difficulties emerged when both semantic and syntactic errors were presented. This evidence suggests better memory with intact syntactic forms. The authors note the "over-learned" nature of reading, which is suggestive of the implicit nature of syntax acquisition (Nebes, 1989).

Syntax- Neurocognitive findings

Patterns of cortical activity have been shown to vary based on the complexity and nature of the syntactic task. Research points to ambiguity as one such level of complexity. A subjectfirst versus object-first sentence comprehension task elicited greater activity in the left supramarginal gyrus during ambiguous trials, and left inferior frontal gyrus activation during non-ambiguous trials (Bahlmann, 2007). Supporting these results, researchers have also shown decreased left anterior temporal activation to sentences with similar syntactic structures as opposed to novel structures, indicating the deeper processing of more infrequent phrases (Noppeney & Price, 2004). However, some debate exists regarding the left anterior temporal regions, as inconsistent findings suggest fMRI artifact potentially obscuring results in this region (Visser, Jeffries, & Lambon Ralph, 2009). The middle temporal gyrus, less susceptible to such artifacts, has demonstrated some syntactic processing effects (Visser, Jeffries, & Lambon Ralph, 2009; Shetreet, Friedmann, & Hadar, 2009, Christensen et al., 2010). Others have located syntactic processing within the left perisylvian fissure, in proximity to areas for non-verbal cognitive sequencing (Lelekov, Franck, Dominey, & Georgieff, 2000).

A handful of studies have illustrated the power of syntax distinctions in single word/ word triplet lexical decision/ passive reading paradigms. Positron Emission Tomography (PET) lexical decision (word versus non-word) research, asking participants to distinguish nouns and verbs, found increased dorsolateral frontal and medial temporal activation for verb processing, but no distinct areas for noun processing. The authors attribute this effect to verbs specifically accessing centralized syntactic information, secondary to its structural importance in sentences comprehension. Noun activity, being dispersed throughout semantic-focused areas of the brain, would not attain significant activation in any one area (Perani et al, 1999).

A growing literature has debated the potential role of Broca's area (BA 44 and 45) in syntactic processing. Despite the region's role in expressive language, it has been suggested that BA 44 and 45 play a role in syntactic processing beyond theorized sub-rehearsal of complex language generated by the phonological loop (Caplan, Alpert, Waters, & Olivieri, 2000; Papagno, Cecchetto, Reati, & Bello, 2007). Some researchers have identified BA 44 as one region of syntactic processing (Caplan, Alpert, & Waters, 1998; Lee & Newman, 2009; Newman, Ikuta, & Burns, 2010), with others isolating a specific process, verb-argument structure, to this region (Raettig, Frisch, Friederici, & Kotz, 2010). Some have isolated syntactic inflection to anterior areas and abstract syntax to ventral and dorsal regions (BA 44 and 47, respectively; Sahim et al, 2006). Others have pointed to BA 45 and neighboring BA 46 as implicated in processing complex syntactic sentences (BA 45: Shetreet, Friedmann, & Hadar, 2009; BA 45, 46: Perani et al, 1999). Santi and Grodzinsky (2007), have shown varying areas of activity for manipulation of subject versus object ("The *dog* walks" versus "Sally walks the *dog*") activation (posterior and superior areas) compared to manipulation of reflexive pronouns and their antecedents (e.g. "Sally saw *Bob* hurt *himself* rollerblading"), found in more anterior and inferior Broca's areas. In reviewing the role of Broca's area, Grodzinsky & Santi (2008) suggest syntactic movement (i.e. multiple phrases with varying subjects, rather than multiple phrases with one subject) has the largest impact on activity within Broca's region, citing syntactic complexity, working memory, and perception of action as other potential processes housed in this region.

Syntax and Semantics

Several researchers have undertaken to compare semantics and syntax directly. Clinical samples have shown varying deficits in both semantic and syntactic processing. Aphasic studies have compared object naming (semantic) and action naming (syntactic) processing and found damage in left temporal areas for object naming impairment, and left frontal areas in syntactic impairment (Perani et al, 1999). In neuropsychological batteries, thought disordered participants with schizophrenia exhibited predicted deficits within the domain of semantic fluency, but no significant effects on tests of syntactic processes (Stirling, Hellewell, Blakely, & Deakin, 2006). Linguists have noted that even in extreme cases of thought disorder involving "word salad," syntactic components of speech remain intact (Covington et al, 2005). Prodromal linguistic deficits, but instead, a lack of syntactic complexity (Done, Leinonen, Crow & Sacker, 1998), a pattern retained in adulthood (Kircher et al, 2005). In dementia populations, when comparing speech samples of an Alzheimer's population to healthy aging controls, researchers have

observed preserved syntactic complexity and structure, but reduced amount of information expressed and increased semantic errors (Lai, Pai, & Lin, 2009). Syntactic processing appears preserved within early stages of the disorder, deteriorating only as a person progresses into more severe stages of dementia (Bickel, Pantel, Eysenbach, & Schroder, 2000). In contrast, the degradation of semantic networks, alongside explicit memory detriments, has been documented within Alzheimer's patients (Rogers & Friedman, 2008).

Syntax and Semantics: fMRI Findings

Some researchers incorporate syntactic processing as a subcomponent of semantic processing. Proponents state that even the organization of basic syntactic material (verbs) is ultimately rooted within semantic processing, as verbs are processed in semantic cortical areas for tool and action/imitation-based information (posterior medial temporal gyrus) (Davis et al, 2003). There has been support for this perceptual-function model of semantic processing when comparing responses to action decisions (left frontal-parietal cortex) and functional decisions (lateral anterior inferotemporal cortex). Researchers have suggested that medial portions of anterior and inferior temporal cortex may focus on integrating perceptual information, while lateral regions process abstract concepts such as functional aspects of nouns. Both types of information tend to load on the "lateral occipital complex," a region known for explicit and implicit object recognition (Canessa et al, 2008). Further incorporating syntax as part of semantic processing within the temporal lobe, some identify the anterior temporal lobe as potentially integrating strings of verbal information, similar to that occurring during sentence processing (Visser, Jeffries, & Lambon Ralph, 2009).

In contrast to research suggesting a yoked relationship between semantic and syntactic processing, there is substantial research illustrating various distinctions between semantic and

syntactic processing. ERP research has suggested that syntactic processing takes place predominantly as an early left anterior negativity, and a later positive wave at 600 ms, while semantic processing is marked by a centro-parietal N400 waveform (Kang et al., 1999; Holcomb, 1993; McPherson & Holcomb, 1999). Kang et al. (1999) examined implicit processing of syntax and semantic verb phrases (congruent versus anomalous). They found some lateralization differences within frontal areas during language processing (BA 45, 46, 10), with predominantly syntactic processing occurring within the left hemisphere, and semantic processing within the right hemispheres. Authors relate these differences to verb and noun activation levels, and the structure of their verb-phrase anomaly reading task (Kang et al, 1999). Furthering the verb/ noun distinction, when words are not inflected in some way (use noun/verb stem), semantic and syntactic input appears to activate left frontal and temporal areas to an equivalent extent during a semantic categorization of word triplets (Tyler et. al, 2001). The authors suggest this distinction could relate to a "morpho-syntactic" processing system within the left inferior frontal gyrus (LIFG). Inflected verbs would necessitate LIFG processing of tense, temporal information, and spatial movement information, in addition to categorical relationships inherent in semantic processing (Tyler et al, 2004).

However, these distinctions are blurred by the difficulty in completely isolating semantic and syntactic information. Indeed, studies examining distinct syntax and semantic activation have also illustrated areas of activation common to semantics and syntax. These areas are generally known for verbal fluency and integration, as well as visual imagery of concrete words (Kuperberg et al., 2000). Bedny & Thompson-Schill (2006) found increased activation in the posterior left superior temporal gyrus (LSTG), a region typically linked to syntactic complexity and errors, when participants responded to motion verbs. However, they caution that motion verbs also denote a semantic category, and this region could then be implicated in both functional semantic aspects of actions, and/or syntactic decisions. Friederici et al (2003) explored this potential distinction and found an internal modularity within language: Left anterior (basal ganglia) regions showed increased activation for syntax, and bilateral superior temporal regions showed increased activation for semantics. In line with prior concerns regarding the overlap of semantics and syntax, research has illustrated tasks implicated in the procedural memory for syntactic rules as activating regions of the frontal cortex, specifically the basal ganglia). Irregular verbs (processed by entire word rather than rule based) activated temporal parietal regions (Ullman, 2001; Ullman et. al., 1997).

As previously discussed, Broca's region remains a particular source of debate, being claimed as a semantic region by some (Newman, Ikuta, & Burns, 2010; Muller, Kleinhans, & Courchesne, 2003; Bedny & Thompson-Schill, 2006), and a syntactic area by others (Caplan, Alpert, Waters, & Olivieri, 2000, Caplan, Alpert, & Waters, 1998; Lee & Newman, 2009; Newman, Ikuta, & Burns, 2010; Raettig, Frisch, Friederici, & Kotz, 2010; Shetreet, Friedmann, & Hadar, 2009; Perani et al, 1999; Santi and Grodzinsky, 2007; Grodzinsky & Santi, 2008). In directly comparing processing of identical sentences for phonological, semantic, and syntactic decisions, Suzuki & Sakai (2003) found selective involvement of syntax within this region (BA 44 and 45), and note the universality of the effect within both western and eastern languages. Newman, Ikuta, & Burns (2010) identify a nearby region for semantic processing, but maintain that syntactic processing occurs within Broca's region (BA 44). Bedny & Thompson-Schill (2006) allude to an interaction of grammar and word imaginability within left inferior frontal regions, related to task demands and stimuli characteristics.

Despite a continued debate regarding the isolated regions or syntax and semantics, researchers have made gains in isolating these variables. Dapretto & Bookheimer (1999) isolated syntax and semantic effects by showing pairs of sentences to participants, and requiring participants to focus on either syntactic or semantic information to determine whether meaning was similar between sentences. Authors showed that examining differing aspects of the same stimuli created a viable option for distinguishing the effects of semantic and syntactic effects. They further showed activation proximal to Broca's area for semantic and syntactic decisions. Semantic decisions took place within Brodmann's Area 47 (left inferior frontal gyrus), while syntax was processed within Brodmann's Area 44. Uchiyama et al. (2008) also suggest BA 47 as a region of interest for semantic processing. However, they identify BA 44 as involved in verbal working memory and articulatory rehearsal of online information. The researchers identify BA 45 as an area involved in integrating semantic processes of BA 47 and working memory processes of BA 44 through syntactic unification. This area then would link the semantic and working memory systems with a partially distinct syntactic system, supporting the separate language resource interpretation theory.

Aims of Current Study

The overarching aim of this study is to examine specific subcomponents of verbal memory in the healthy brain, and to more accurately assess memory effects imposed by levels of language processing. More specifically, semantics and syntax are critical components utilized in daily language processing, with differential behavioral effects on memory performance. In participants with significant memory deficits (e.g., Alzheimer's disease), language processing difficulties involve content of speech rather than form of speech (Nebes et al., 1989). Researchers have shown distinct areas for semantic processing, verbal working memory, and syntactic unification areas within Brodmann's regions (BA 47, 44, and 45, respectively) (Uchiyama et al., 2008). It has been shown that by using identical stimuli but focusing attention on differing aspects of the stimuli, semantic and syntactic distinctions could be effectively examined (Dapretto & Bookheimer, 1999; Suzuki & Sakai, 2003).

The current study sought to identify the distinction that these processes have on facilitating verbal encoding of concrete nouns by varying the task associated with a list of subject and object phrases. Behaviorally, it was hypothesized that semantic processing would elicit better recall and recognition scores than the syntactic-focused encoding task, secondary to the level of processing model of verbal memory (Craik & Lockhart, 1972), in that syntactic decisions necessitate implementation of grammar based rules to the phrases, but not integration of word meaning.

It was hypothesized that fMRI BOLD signal would vary based on the type of task performed during verbal encoding (refer to Figure 1.1 and Table 1.2 for regions of interest). Both tasks would elicit verbal memory encoding processes, generating activity within the left frontal area (BA 45), an area implicated in both semantic and syntactic processes and suggested to be integrative in function (Kang et al., 1999; Dapretto & Bookheimer, 1999). Some have implicated Broca's area (BA 44/45) in processing of both semantic and syntactic information (Kang et al, 1999), but a distinction has arisen between BA 44 as syntax related (Frederici et al., 2003; Kang et al, 1999; Dapretto & Bookheimer, 1999; Newman, Ikuta, & Burns, 2010; Lee & Newman, 2009; Raettig, Friesch, Friederici, & Kotz, 2010) and BA 45 as an integrative area or a taskbased processing region (Frederici et al., 2003; Dapretto & Bookheimer, 1999).

Focusing on syntactic processes during verbal encoding would result in activity in more posterior regions, specifically within the left prefrontal (BA 44 as previously stated) and medial gyrus (BA 46), areas implicated in discourse processing. As stated previously, several researchers have implicated BA 46 in syntactic processing (Perani et. at, 1999; Kang et al., 1999). This hypothesis is in line with previous research utilizing simple conjugated verbs as the syntactic material, which activated the left basal ganglia regions, as opposed to temporal regions activated by irregular verbs (Frederici et al., 2003).

Focusing on semantic processing during encoding would be correlated with left inferior frontal areas previously linked to semantic processes (BA 47), in concordance with sentence processing findings of Dapretto & Bookheimer (1999), and Newman, Ikuta, & Burns, (2010). The phrase structure of the current stimuli should activate the left prefrontal cortex through participants' need to process information during encoding, and organize response information (Dannhauser, 2008). Temporal regions, in particular left medial temporal gyrus (BA 21/37) would show increased activation to semantic processing in verbal memory tasks when compared with syntactic counterparts (Bartha et al, 2003; Frederici et al., 2003; Muller, Kleinhans, & Courchesne, 2003). Finally, phrase level research has placed semantic retrieval and encoding in the left hemisphere, and episodic memory retrieval in the right hemisphere (Kang et al, 1999). However, it has been suggested that phrase level and/or event-related verbal stimuli may elicit more bilateral resources, and some support for semantic activation in the right hemisphere of the medial frontal gyrus has been found (Kang et al, 1999). For these reasons, although left BA 46 was hypothesized as a syntactic region, activation in the right medial frontal gyrus (BA 46) was hypothesized as a semantic region.

It was hypothesized that behavioral accuracy on the experimental categorization task during encoding within each condition would correlate positively with level of activation in targeted regions of interest for that task. In addition to behavioral accuracy, it was predicted that increased memory on recall and recognition tasks following the experimental task would correlate with higher levels of BOLD activation during the task itself, within the above described regions of interest for each condition.



Figure 1.1

Hypothesized Regions of Interest

Regions of interest included areas frequently implicated in semantic processing (Left BA 21, Left BA 37, Right BA 46), syntactic processing (Left BA 44 and Left BA 46), or both (Left BA 45). Slice A (X = 44, Y = 61, Z = 30) captures temporal regions BA 21 and BA 37, as well as inferior frontal regions BA 47 and BA 44. Slice B (X = 44, Y = 61, Z = 42) illustrates BA 21 and BA 44, as well as more superior frontal regions (Left BA 45, Left and Right BA 46).

Table 1.1

Verbal Memory Model	Process Model	Material Model	Level of Processing	Phonological Loop	Single Process Resource	Separate Language Interpretation Resource
Activation Determined by	Process initiated by task	Difference in stimulus content	Cortical resources needed for task	Level of phonological similarity	Integration of language components	"Second pass" processing integrating discourse language
Areas of Activation Implicated	Dorsolateral and ventrolateral PFC Cerebellum	PFC, MTC, Left Fusiform, ITG	Left PFC (inferior frontal cortex)	N/A	N/A	N/A

Verbal Memory Model Regions of Interest

Table 1.2

Hypothesized Regions of Interest

Brodmann's	Hypothesized Predominant	Region	
Area	Condition of Interest	-	
Left BA 21	Semantic	Left Temporal	
Left BA 37	Semantic	Left Temporal	
Left BA 47	Semantic	Left Frontal	
Right BA 46	Semantic	Right Frontal	
Left BA 44	Syntactic	Left Frontal	
Left BA 46	Syntactic	Left Frontal	
Left BA 45	Semantic and Syntactic	Left Frontal	

CHAPTER 2

METHODS

Participants

Power Analysis

A power analysis was conducted using the fMRI specifications set forth by Desmond & Glover (2002) for fMRI group analyses using cognitive tasks, such as verbal working memory. These specifications included a medium effect size (percent voxel activation change = 50%), power = .80, and an estimate of high intra-subject variability. At the traditional p = .05 level, the power analysis yielded N = 14. At a more conservative estimate appropriate for multiple comparisons, p = .002, N = 28.

The current sample included 32 participants drawn from the University of Georgia's Psychology Research Participant Pool, campus flyer advertisements, and the UGA graduate student email list-serve. Participation criteria entailed right handed, native English speakers, with no self-reported history of neurological disorder and no personal or family history of mental illness. In addition, participants met safety criteria for the MRI environment: this excluded those with any question of a pacemaker, metal in the body, or self-reported pregnancy. A pregnancy test was given to potential female participants prior to the fMRI scan, to afford them the option of confirming pregnancy status in private, and withdrawing from study should the question of pregnancy exist. The project was approved by the University of Georgia Institutional Review Board. All participants provided written consent and received course credit (Psychology Research Pool participants) or a structural image of their brain (participants who were not involved within the Psychology Research Pool).

Neurocognitive Measures

Participants completed the Wechsler Test of Adult Reading (The Psychological Corporation, 2001), a widely used and validated test of estimated intelligence involving reading words of increasing difficulty and correlating this information with predictive demographic variables (The Psychological Corporation, 2001a). The WTAR/ Demographics Full Scale IQ was assessed through this verbal based task, in order to confirm that overall intelligence differences did not influence memory for task stimuli.

They also completed a neurocognitive measure of verbal memory. The Rey Auditory Verbal Learning Test (RAVLT, Rey, 1941) is a widely used test of verbal memory and learning, involving listening to a list of categorically distinct words and measuring number of words recalled on each trial, number of words recalled on a distracter list, immediate and delayed recall of learned list, and recognition of both lists (Strauss, Sherman, & Spreen, 2006). It shows strong ecological validity as well as comparative validity to other commonly used neuropsychological measures of verbal memory, namely, the California Verbal Learning Test (Strauss, Sherman, & Spreen, 2006; Crossen & Wiens, 1994). Overall verbal learning was assessed to identify whether differences in participants' baseline ability to encode verbal information influenced their ability to remember target words within task stimuli.

fMRI Experimental Design

After initial neurocognitive testing, participants completed a short practice trial of the experimental task. Each participant completed up to three distinct practice runs, until an accuracy score of at least 80% on a single practice run was achieved. For those participants who did not

meet this accuracy requirement, experimental participation ended at this point. Those who met the accuracy requirement participated in the MRI paradigm, with a minimum of 1 day separating neuropsychological tasks and experimental paradigm, in order to prevent RAVLT or practice word interference effects on memory during the experimental paradigm. MRI safety compatibility was again confirmed at this time by a certified MRI technician before entering the MRI environment for the experimental task.

The experimental paradigm was an event-related design, randomized across conditions. Stimuli included a list of 76 nouns, with 38 nouns in each of 2 conditions, semantic-focused encoding and syntactic-focused encoding. Stimuli were presented using E-Prime 2.0 Software (Psychology Software Tools, Inc., 2007). Words of equivalent length, concreteness, and frequency were generated through the MRC Psycholinguistic database (Wilson, 1988; http://www.psy.uwa.edu.au/mrcdatabase/uwa mrc.htm). Phrases were constructed from 1 target noun with the above parameters, 1 randomly generated verb, and the article "the," to form sensible subject phrases (the-noun-verb) and object phrases (verb-the-noun). Prior to the task, participants were asked to remember the bolded nouns for a future memory task. Phrases were presented on the screen for 1 second, immediately followed by presentation of two category choices for 2 seconds. The task involved classifying the phrase within the most appropriate category presented. The choice of specific category varied by condition (Figure 2.1): In the semantic condition, the choice involved placing the phrase into one of two semantic categories (i.e., nature or man-made). In the syntactic condition, the subject classified the phrase as occurring in the present tense or past tense. Choice categories were counterbalanced across subjects, so that each phrase was encoded using a focus on semantic and syntactic information. Target words were counterbalanced for phrase type (subject versus object), condition (semantic

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versus syntactic decision), and grammar (present tense versus past tense) across participants (Figure 2.2). In addition, there were 164 baseline trials, which involved non-verbal strings of x's in place of words, approximating lengths of experimental stimuli (e.g., xxx xxxx xxxx) and controlled for length of letter strings. One string of letters in each non-verbal "phrase" was bolded, and the bolded string was balanced between the first and last group of X's in the three string series). These x's were immediately followed by presentation of two identical x's in the positions of the two categorical options. The participant was asked to choose the position of the previously presented bolded x's (i.e., right or left on screen). Responses were counterbalanced for position on the screen within target word and baseline conditions. For all conditions, participants responded to the classification task by means of a touch-pad. Responses occurring within 1000 ms post offset of response screen were counted within behavioral totals. After fMRI testing, participants were removed from the MRI scanner and given a recall and then recognition test for the presented words. The un-timed recall task entailed the participant being asked to list as many bolded words as they could remember from the task, following a 20 minute delay. The recognition task was a forced choice, un-timed task involving presentation of all 76 nouns matched with a distracter word and counterbalanced for position on the screen.

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. Two localizing scans were utilized to appropriately center the brain within the field of view (gradient echo images with interleaved bottom-up acquisition, FOV = 24 mm, slice thickness = 10 mm, slice spacing = 5 mm, matrix = 256 x 128) and an ASSET calibration scan was utilized to prepare the scanner for parallel image acquisition (gradient echo
images, FOV = 30 mm, slice thickness = 6 mm). Participants underwent an initial T-1 weighted structural MRI scan (FOV = 24mm, slice thickness = 1.0 mm, locs per slab = 184, TE = min full, matrix = 256 x 256) to establish a reference template. Functional image acquisition occurred over 2 runs with approximately 6 minute durations, separated by a short break to prevent fatigue (38 slices with interleaved bottom-up acquisition, 4 mm slice thickness, slice orientation aligned to Anterior Commissure- Posterior Commissure (AC-PC) line, matrix = 64 x 64, in-plane resolution of 3.44 mm, TR = 2 seconds, TE = 25 msec, flip angle = 90, FOV = 22 mm). The conditions from the first session were permutated to attain the design for the second session. This event-related design was structured to maximally account for potential variations in HRF when examining 1-second stimulus presentation, 2-second response time, or combined 3-second presentation time (time-to-peak = 7.5 seconds, and time-to-onset = 1 second, corresponding to a possible HRF for a 2 second stimulus). The design achieved 94% of maximal detection power and maximal estimation efficiency (J. Kao, personal communication; Kao, Mandal, Lazar, & Stufken, 2009). Inter-stimulus interval was 6 seconds.

Preprocessing

FMRI data were preprocessed with FMRIB Software Library, version 4.1 (FSL, Analysis Group at the Oxford Centre for Functional MRI of the Brain, Oxford, UK; http://www.fmrib.ox.ac.uk/fsl; Smith et. al, 2004; Woolrich et al, 2009), using FMRI Expert Analysis Tool (FEAT Version 5.98). The middle slice (37) was used as the reference slice during preprocessing. Run 1 and run 2 for each subject were processed separately within a first level mixed effects analysis, and then combined within a second level, fixed effects analysis. To preprocess, images were realigned to the reference slice), correcting for any participant movement. Scans were realigned and unwrapped to correct distortions caused by motion or inhomogeneity in measured fields (e.g., varying densities of different tissue within the brain) using a non-linear transformation. Individual participant fieldmaps were utilized to account for inhomogeneities in magnet strength and reduce potential artifacts that arise from these variations. A high pass filter (100s) was applied in order to reduce noise created by scanner signal drift during data collection. Data were coregistered to the subject's structural MRI image to match functional activity to anatomical location of neural structures. In order to compare individualized data to other subjects, the scans were normalized, or mapped, to a standardized anatomical template, Montreal Neurological Institute (MNI) space, for the purposes of effective group comparisons between specific cortical regions of interest. The scans were also smoothed (Original voxel size = $3.44 \times 3.44 \times 4$ mm, Full Width Half Max (FWHM) = $6.88 \times 6.88 \times 8$ mm): Smoothing entails the application of a Gaussian kernel to the activation, improving signal to noise ratio of the data by reducing the number of statistical comparisons. It does so by joining discrete, adjacent voxels into a cohesive region of activation. Temporal derivatives were incorporated into the preprocessing model to supplement the standard canonical hemodynamic response function (HRF) and provide an informed basis for analyses, accounting for individual variations. Temporal derivatives account for individual differences (within 1 second) in latency of the peak HRF following presentation of a stimulus (Ashburner et al, 2010).

Data Analysis

Data were analyzed using FSL version 4.1. Behavioral analyses included a repeated measure ANOVA: a 2 (encoding: semantic, syntactic) x 2 (memory: recall, recognition) design. As a manipulation check, the ratio of total words retained encoded within present and past tense phrases, were analyzed through a 2: (grammar tense: present, past) x (2: memory task: recall, recognition) repeated measures ANOVA.

FMRI data were pre-processed at the first level using a whole brain analysis. At higher level analyses, whole brain activation and voxel activity within the 7 areas of interest were evaluated. Within-subject z-score contrasts included mean BOLD signal for each of the two experimental conditions, subtracting out baseline activation from condition specific activation. Subsequent contrasts were conducted for semantic processing (total semantic activation- baseline activation) versus syntactic processing (total syntactic activation- baseline activation). Average BOLD signal for these areas and z-score contrasts were calculated using FSL. Between-subjects z-scores consisted of the average activation found within the four above mentioned individual analyses for both runs of the 32 participants, within the 7 regions of interest. Higher level analyses included a whole brain analysis and a masked analysis including all regions of interest (Left BA 44, 45, 46, 47, 21, 37; Right BA 46), to limit executed voxel comparisons between subjects. This mask allowed for analyses only within the 7 regions of interest at the between-subjects level. Approximately 4.56% of total brain voxels, based on a standardized MNI (Montreal Neurological Institute) brain, were included within this analysis. In addition to a joint mask, activation within each region of interest was calculated in the same manner and the above z-score contrasts were reproduced for each of the 7 regions of interest (range = 0.27-1.28% of the total MNI brain utilized within each analysis). Regions of interest for the semantic condition included the right hemisphere MFG (BA 46), left hemisphere IFG (BA 47), and left hemisphere posterior MTG (BA 21, 37). Regions of interest for the syntactic condition included left hemisphere posterior IFG and MFG (BA 44, 46, respectively). Regions expected to be active in both conditions included portions of the left hemisphere IFG (BA 45). Masks were generated using WFU PickAtlas (Maldjian, Laurienti, Burdette & Kraft, 2003; Maldjian, Laurienti, & Burdette. 2004) within the Statistical Parametric Mapping software (SPM-8: Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm), through Matlab (The Math Works, Natick, MA).

Behavioral and fMRI BOLD signal were then integrated for the final analyses. A series of analyses were completed, using behavioral scores as covariates for fMRI activation. In order to test our hypothesis that levels of behavioral accuracy would correlate positively with level of activation within each region of interest, a series of analyses were completed using accuracy on semantic and syntactically encoded trials as covariates for fMRI activation. Activation which was significantly higher as accuracy scores increased was recorded, as well as the contrasts between semantic and syntactic-focused encoding with accuracy covariates. To test our hypothesis that semantic-focused encoding would elicit higher-level processes necessitating additional cortical resources, consistent with the levels-of-processing memory model (Craik & Jackson, 1972), the number of syntactic and semantic encoded words recalled for each participant was entered as a demeaned regressor within FSL. Activation which was significantly higher as recall scores increased was recorded, as well as the contrasts between semantic and syntactic domain.

Post-hoc Analyzes

Post-hoc bivariate analyses were performed to examine the relationship between behavioral measures and percent signal change mean and max value within the 7 pre-defined regions of interest.



Figure 2.1

Experimental Design

Experimental paradigm involved 2 conditions (semantic and syntactic-focused encoding), in addition to an active baseline condition replacing nouns and verbs with strings of x's (bolding 1 set of X's to denote the target position).



Figure 2.2

Experimental Protocol Counterbalancing

Counterbalancing occurred for target word condition (semantic versus syntactic), syntactic choice (present tense versus past tense) and phrase type (subject versus object). Stimuli were counterbalanced across participants.

CHAPTER 3

RESULTS

Sample Description

Participants had a mean age of 20.47 years (s.d. = 1.93), and a mean education of 14.19 years (s.d. = 1.90). The majority of the sample was female (71.9%) and self-identified as Caucasian/Non-Hispanic (90.6%). Please refer to Table 3.1 for further information. Demographic variables demonstrated no significant bivariate correlations with behavioral measures of interest, and therefore were not included in subsequent analyses.

Predicted Intelligence

Scores on WTAR were converted into standard scores, with a mean of 100 and a standard deviation of 15 points (Table 3.1). Participants demonstrated a WTAR/ Demographics predicted FSIQ score of 109.22 (s.d. = 5.97). WTAR/ Demographics predicted FSIQ demonstrated no significant bivariate correlation with behavioral measures of interest, and therefore was not included in subsequent analyses.

Learning and Memory: RAVLT

Scores on the RAVLT were converted into standard scores, with a mean of 100 and a standard deviation of 15 points (Table 3.1). On the RAVLT, participants earned a mean total learning standardized score of 99 (s.d. = 12.4). Participants had a mean of 97 (s.d. = 15.7) on the RAVLT immediate memory task. RAVLT delayed recall memory scores showed a mean of 104 (s.d. = 14.2), and participants had a mean of 89 (s.d. = 26.7) on the subsequent RAVLT recognition memory task for the learned list of words. Based on standardized normative scores,

participants performed within the low average range of recognition, and within the average range in other RAVLT reported tasks. This suggests no significant discrepancies between baseline verbal memory abilities of this sample and the overall population, controlled for age and gender. *Behavioral Results*

fMRI Behavioral Paradigm Accuracy

Response accuracy, namely level of accuracy categorizing phrases during the experimental task, is displayed in Figure 3.1. Participants achieved a mean of 223.03 correct responses during the fMRI behavioral task (s.d. = 14.97), for a mean of 92.92% behavioral accuracy (s.d. = 6.04). Total accuracy for target items demonstrated a mean of 62.38 (s.d. = 6.01), for a mean target accuracy rate of 82.07%. Accuracy rates were comparable for items within both conditions (syntactic: mean = 31.25, s.d. = 3.37; semantic mean = 31.13, s.d. = 4.14). Participants correctly responded to an average of 160.66 baseline items (s.d. = 13.70).

Experimental Memory Task

Post-experimental task recall and recognition scores for previously encoded target nouns are displayed in Figure 3.2. Following completion of the fMRI paradigm, participants recognized more words than they recalled (recognition mean = 61.84 words, s.d. = 7.74; recall mean = 5.53 words, s.d. = 4.31). When broken down by condition, participants recalled more semantically encoded words (syntactic recall: mean = 1.53, s.d. = 1.90; semantic recall: mean = 4.0, s.d. = 2.98) and recognized more semantically encoded words in comparison to syntactically encoded words (syntactic recognition: mean = 29.25, s.d. = 3.95; semantic recognition: mean = 32.59, s.d. = 4.22).

Analysis of Variance: Encoding focus (Syntactic, Semantic) by Memory (Recall, Recognition)

A repeated measures ANOVA was conducted to compare the effects of encoding focus (syntactic versus semantic) and memory task (recall versus recognition) on learning words during the fMRI behavioral paradigm. Results demonstrated a significant main effect of encoding focus (F (1, 31) = 76.36, p < .001, partial eta squared = .71), and memory task (F (1, 31) = 2396.06, partial eta squared = .99). Participants recognized significantly more words than they recalled, and remembered significantly more semantically encoded words than syntactically encoded words. No significant interaction between condition and memory task existed (p > .05).

Analysis of Variance: Grammar (Present, Past) by Memory (Recall, Recognition)

The ratio of total words remembered that were originally encoded within present and past tense phrases, were analyzed through a 2 (grammar tense: present, past) x 2 (memory task: recall, recognition) repeated measures ANOVA. Again, a significant main effect of memory occurred (F (1, 31) = 2444.75, p < .001), with participants recognizing significantly more words than they recalled. No main effect for grammar tense of words encoded, nor interaction between grammar tense and memory task occurred (p > .05).

fMRI Results

Whole brain analysis

An initial set of whole brain analyses were conducted in order to identify regions in which syntactic activation differed from baseline, semantic activation differed from baseline, and regions where these contrasts differed from each other (i.e., syntactic-semantic activation, semantic-syntactic activation). A cluster z threshold of z > 2.3, p < .05 was used for all analyses. Within the syntactic-baseline condition, pervasive activation was observed throughout the brain, including frontal and temporal regions. This pervasive activation coagulated into 1 large cluster of activation (122508 voxels), with local maxima z scores occurring within occipital (BA 17, BA 18, BA 19) and cerebellar regions. In response to the observed activation being masked by intense occipital and cerebellar activation, whole brain activation within specific regions of interest were measured. All regions (left frontal, right frontal, left temporal) demonstrated significantly activated voxels within the syntactic-baseline contrast (Table 3.2), though contiguous voxels with occipital regions prevented them from being identified as distinct clusters. With the semantic – baseline condition, 1 large cluster of significance occurred (122206 voxels) occurred, with local maxima z scores in the occipital region (BA 18, BA 19), cerebellar regions, and one frontal region of interest (BA 44). Again, all regions (left frontal, right frontal, left temporal) demonstrated significantly activated voxels within the semantic-baseline contrast (Table 3.2).

When semantic activation was subtracted from syntactic activation (both controlling for baseline activation; Figure 3.3), 4 significant clusters were seen:1 with a maximum z score within the cerebellum (1329 voxels), 1 with a maximum z in occipital regions (1090 voxels), 1 with a maximum z value in right frontal regions (1065 voxels), and 1 with a maximum z value in right parietal regions (13972 voxels). Local maxima z scores within these larger clusters occurred in right and left frontal regions, subcortical regions, left parahippocampal regions, right and left parietal regions, and occipital and cerebellar regions. When whole brain activation within specific regions of interest was measured, the syntactic-semantic contrast yielded significantly activated voxels activation in all regions except right BA 46, left BA 45 and left BA 47 (Table 3.2). Of note, within the left BA 21 region, this activation consisted of a small number of voxels (2 significant voxels; max z = 2.47, X = -40, Y = -2, Z = -8). The contrast was

reversed, and semantic-syntactic activation (Figure 3.3) exhibited significant clusters with maximum z scores occurring in: the right cerebellum (2708 voxels), left limbic area (2072 voxels), left temporal regions (2225 voxels), left medial temporal regions (3229 voxels), right MFG (1048 voxels), and left MFG (19858 voxels). Local maxima z scores within these clusters were identified in bilateral IFG and MFG, left limbic regions, left temporal regions, left MTG, left parietal, bilateral occipital, and right cerebellar regions. All regions (left frontal, right frontal, left temporal) demonstrated significant voxels of activation within the semantic-syntactic contrast (Table 3.2).

Total task activation across ROIs

To test our hypothesis that semantic-focused encoding would also elicit additional BOLD activation when compared to the syntactic condition, a joint mask encompassing all 7 regions of interest was used. Activation in the semantic and syntactic-focused encoding conditions was compared within the masked region, with significance denoted by clusters of voxels obtaining z > 2.3 and p < .05 (Table 3.3). The syntactic-focused encoding condition demonstrated significantly increased activation when compared with that of the baseline condition (max z = 11.4, p < .05). Semantic activation exhibited increased activation as well (max z = 12.2, p < .05). When these contrasts were directly compared, syntactic activation –semantic activation did not elicit significant post-threshold voxels (p > .05). Semantic- syntactic activation (max z = 8.59, p < .05) did show significant differences. Activation occurred within both temporal and frontal ROIs, and within left and right frontal cortical regions of interest.

Individual regions of interest analysis

To test our hypothesis that patterns of activation would vary within the brain based on the focus for encoding, fMRI data were examined using disjoined masks for each specifically

defined ROI (Table 3.4). First, syntactic activation was contrasted with baseline BOLD activation, and all regions of interest exhibited clusters of significance (z > 2.3, p < .05; Figure 3.4). When semantic information was contrasted with baseline activation, a similar pattern emerged (Figure 3.5).

In comparing syntactic activation and semantic activation directly, first semantic activation was subtracted from syntactic activation (Figure 3.6). Regions close to the left temporal lobe BA 37 exhibited increased activation to syntactic-focused encoding over semanticfocused encoding ($z \max = 5.45$, p < .05). Brodmann's area 44 ($z \max = 4.60$, p < .05) and left BA 46 ($z \max = 4.04$, p < .05) also demonstrated statistical significance of syntactic over semantic activation. Temporal BA 21, left frontal BA 45 and BA 47, as well as right frontal BA 46 did not show significant clusters that survived thresholding (p > .05). When syntactic activation was subtracted from semantic activation, all regions showed clusters of significance (Figure 3.7). Of note, this included regions exhibiting clusters of higher significance in the syntactic - semantic condition (BA 37, BA 44, and BA 46). When coordinates of maximum activation were compared, BA 37 activation within the semantic- syntactic contrast appeared to have a more lateral, anterior inferior location than the maximum within the syntactic - semantic condition. For BA 44, the semantic - syntactic condition elicited a maximum z score at a region more medial, anterior, and superior than was the syntactic - semantic counterpart. BA 46 demonstrated a more lateral, posterior, inferior location of highest activation when compared with the semantic - syntactic contrast.

fMRI activation: Relationship of behavioral accuracy to fMRI activation

In order to test our hypothesis that levels of behavioral accuracy would correlate positively with level of activation within each region of interest, a series of analyses were completed using accuracy on semantic and syntactically encoded trials as covariates for fMRI activation. Within these ROI analyses, there was no significant correlation between levels of accuracy and fMRI activation in any ROI. Specifically, no increase in activation occurred with increasing levels of behavioral accuracy (p > .05). This lack of effect was seen within both syntactic and semantically encoded conditions, and within each of the seven regions of interest.

fMRI activation: Relationship of Recall and Recognition on fMRI activation

In order to test our hypothesis that accuracy on recall and recognition tasks would correlate positively with level of activation within each ROI, a series of analyses were completed, using semantic and syntactic recall and recognition rates as covariates for fMRI activation. Separate analyses were run for recall and recognition tasks. No significant correlation between semantic or syntactic recall and fMRI activation occurred within any predefined region of interest (p > 0.5). A similar pattern occurred with the recognition condition, and no significant increases in fMRI BOLD activation were observed to correlate with increased performance on the recognition task in either encoding condition.

Post-hoc Analyses

Post-hoc analyses further examined the relationship between behavioral measures and percent signal change mean and max value within the 7 pre-defined regions of interest. When behavioral measures were compared with ROI percent change activation, recognition appeared to significantly correlate with specific regions. Specifically, the mean percent change of syntactic-focused encoding in BA 47 demonstrated a positive correlation with recognition of syntactically encoded words (r = .477, p < .01). A similar positive correlation was found when the mean percent change activation was replaced with the maximum percent change within BA 47 syntactic-focused encoding in this region (r = .373, p < .05). When semantic recognition was

examined, BA 47 showed a positive correlation of percent change mean activation during syntactic-focused encoding and number of semantically encoded words that were recalled (r = .352, p < .05). The number of semantic words recalled showed a negative correlation with the mean semantic percent change activation in BA 44 (r = ..382, p < .05).





Behavioral Accuracy on a fMRI Verbal Memory Task

Accuracy rates overall reached a mean of 92.92%, with comparable rates between semantic and syntactic-focused encoding (Syntactic: mean = 31.25, s.d. = 3.37; Semantic: mean = 31.13, s.d. = 4.14). Mean accuracy for target items = 62.38 (s.d. = 6.01, mean target accuracy = 82.07%), and total mean accuracy = 223.03 correct responses (s.d. = 14.97, mean accuracy = 92.92%).



Figure 3.2

Behavioral Delayed Memory Scores

Each participant was scored on number of semantically and syntactically recalled and recognized words identified. Recognition rates exceeded recall rates overall and semantic words showed a significant advantage over syntactic words in delayed recall and recognition.





Whole Brain Activation: Syntactic - Baseline versus Semantic - Baseline Red represents syntactic - semantic activation and blue represents semantic - syntactic activation. Semantic activation displays a temporal and frontal pattern of activation, while syntactic appears to elicit parietal regions to a greater extent, and frontal regions to a lesser extent. Three ROIs (BA 37, 44, and 46) showed significance within both contrasts. Cluster z threshold = 2.3, p < .05.



Figure 3.4

Syntactic - Baseline Activation in 7 Regions of Interest

Activation is seen across 3 of the 7 ROIs: BA 37 = copper/tan, BA 44 = yellow, BA 46 = royal

blue.





Semantic - Baseline Activation in 7 Regions of Interest

Activation is seen across all seven ROIs: BA 21 = light blue, BA 37 = copper/tan, BA 44 =

yellow, BA 45 = green, BA 46 = royal blue, BA 47 = red.





Syntactic - Baseline minus Semantic - Baseline Activation in 7 Regions of Interest Significant activation is seen across 4 of the 7 ROIs: BA 37 = copper/tan, BA 44 = yellow, BA 46 = royal blue.





Semantic - Baseline minus Syntactic - Baseline Activation in 7 Regions of Interest Activation is seen across all seven ROIs: BA 21 = light blue, BA 37 = copper/tan, BA 44 = yellow, BA 45 = green, BA 46 = royal blue, BA 47 = red. Table 3.1: Demographics

	n	% of Total Sample
Gender		
Male	9	28.1
Female	23	71.9
Race/Ethnicity		
Caucasian/Non-Hispanic	29	90.6
Hispanic/ Latino	1	3.1
Asian/ Pacific Islander	1	3.1
Other	1	3.1
	Mean	SD
Age	20.5	1.9
WTAR/ Demo Predicted FSIQ	109	1.9
RAVLT Total Learning	99	6.0
RAVLT Immediate Memory	97	15.6
RAVLT Delayed Memory	104	14.2
RAVLT Recognition A (Learned List)	89	26.7

Contrast	BA	# voxels	max z	std dev	Х	Y	Ζ
Syntactic-Baseline							
	L21	440	6.42	0.8461	-52	-44	6
	L37	1363	8.557	1.756	-42	-54	-24
	L44	610	8.043	1.015	-40	12	10
	L45	791	7.984	1.291	-54	14	22
	L46	1213	7.345	1.009	-42	30	20
	R46	876	5.577	0.8109	42	46	26
	L47	1184	7.44	1.346	-32	18	-2
Semantic-Baseline							
	L21	860	6.584	0.9732	-52	-44	4
	L37	1392	8.261	1.695	-42	-52	-24
	L44	602	8.961	1.251	-52	12	22
	L45	830	8.961	0.8593	-52	12	22
	L46	1165	8.211	1.413	-46	30	20
	R46	793	5.992	0.9578	50	32	24
	L47	1932	7.828	1.177	-48	30	0
Syntactic-Semantic							
	L21	2	2.471	0.00123	-40	-2	-8
	L37	204	5.003	0.6646	-48	-76	-2
	L44	151	4.242	0.5072	-56	4	12
	L45	0	0	0	92	-128	-74
	L46	124	3.716	0.3295	-42	42	30
	R46	0	0	0	92	-128	-74
	L47	0	0	0	92	-128	-74
Semantic-Syntactic							
	L21	1525	6.279	0.9518	-62	-48	-4
	L37	533	6.194	1.144	-58	-52	-12
	L44	150	5.569	0.8285	-48	18	16
	L45	691	6.337	0.9442	-52	28	10
	L46	681	6.264	0.9748	-52	26	12
	R46	110	3.225	0.2255	50	30	24
	L47	1650	6.962	1.19	-38	38	-10

Table 3.2: ROI Activation within Whole Brain Analysis

Cluster List	Voxels	BA	Max z score	X	Y	Z
Syntactic-Baseline						
Left IFG	3568	44	10.9	-52	12	22
Left Temporal	1174		11.4	-42	-60	-18
Right MFG	981	45	7.42	54	34	24
Semantic-Baseline						
Left IFG	4138	44	12.2	-52	12	22
Left Temporal	2136		11.5	-44	-56	-22
Right MFG	910	45	8.31	50	34	24
Syntactic- Semantic						
None						
Semantic-Syntactic						
Left Frontal MFG	2919		8.59	-40	38	-10
Left MFG	2000		7.97	-62	-48	-6

Table 3.3: Joint Mask Analysis

Brodmann's	Voxels	Max z stat	Max X (z stat)	Max Y (z stat)	Max Z	Region
Syntactic Activation (Syntactic-Baseline)						
L-21	362	8.35	-52	-44	6	Left Middle Temporal Gyrus
L-37	1445	11.41	-42	-60	-18	Left Fusiform Gyrus
L-44	610	10.88	-52	12	22	Left Inferior Frontal Gyrus
L-45	828	10.88	-52	12	22	Left Inferior Frontal Gyrus
L-46	1215	10.06	-44	30	20	Left Middle Frontal Gyrus
L-47	1359	9.78	-28	22	-2	Left Sublobar
R-46	1022	7.421	54	34	24	Right Middle Frontal Gyrus
Semantic Activa	tion (Sema	ntic-Basel	ine)			
L-21	938	8.933	-52	-44	4	Left Middle Temporal Gyrus
L-37	1474	11.46	-44	-56	-22	Left Culmen
L-44	606	12.16	-52	12	22	Left Inferior Frontal Gyrus
L-45	830	12.16	-52	12	22	Left Inferior Frontal Gyrus
L-46	1180	11.31	-46	30	20	Left Middle Frontal Gyrus
L-47	1966	10.56	-48	30	0	Left Inferior Frontal Gyrus
<i>R-46</i>	949	8.307	50	34	24	Right Middle Frontal Gyrus
Syntactic- Sema	ntic Activa	tion (Synt	actic-Basel	ine – Sema	ntic-Baseli	ne)
L-21		0				
L-37	202	5.447	-48	-76	-2	Left Middle Occipital Gyrus
L-44	182	4.599	-56	4	12	Left Precentral Gyrus
L-45		0				
L-46	129	4.04	-42	50	18	Left Middle Frontal Gyrus
L-47		0				
R-46		0				
Semantic-Syntae	ctic Activat	tion (Sema	ntic-Baseli	ne – Synta	ctic-Baselir	ie)
L-21	1632	7.975	-62	-48	-6	Left Middle Temporal Gyrus
L-37	565	7.641	-62	-50	-4	Left Middle Temporal Gyrus
L-44	165	6.431	-48	18	16	Left Frontal Sub-Gyral
L-45	705	7.913	-50	28	10	Left Inferior Frontal Gyrus
L-46	713	7.723	-52	26	14	Left Inferior Frontal Gyrus
L-47	1686	8.591	-40	38	-10	Left Middle Frontal Gyrus
R-46	194	3.853	50	30	24	Right Middle Frontal Gyrus

Table 3.4: Regions of Interest Maximum Activation

z > 2.3, p < .05

CHAPTER 4

SEMANTIC SPECIFIC AND SEMANTIC – SYNTACTIC INTEGRATION REGIONS ENGAGED BY VERBAL MEMORY PROCESSES AND THE SEMANTIC ENCODING ADVANTAGE¹

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Abstract

The impact of language components on verbal memory has yet to be fully understood. The current study examined semantic and syntactic components of verbal encoding in a young adult sample. Participants were asked to judge phrases using semantic processing (categorical choice) and syntactic processing (grammatical choice). Recognition and recall tasks measured retention of words encoded using each strategy. BOLD activation within predicted language-related regions of interest during encoding, as well as its correlation with verbal retention, was examined. Results showed increased activation for only semantic over syntactic-focused encoding within left hemisphere Brodmann's areas (BA) 21, 45, and 47, and right hemisphere BA 46. Significant activation was found for both semantic over syntactic as well as syntactic over semantic-focused encoding within left BA 37, 44, and 46. Correlations between fMRI activation and word retention were not significant. Results suggest an advantage for semantic over syntactic cues in facilitating verbal memory encoding within the healthy brain and support cortical regions with specialized function for integration of syntactic and semantic information.

Keywords: fMRI, syntax, semantic, verbal memory, Broca's area

Introduction

Verbal memory involves the interrelated language components of syntactic and semantic meaning working together to encode and retain information. Differences between extensive verbal memory models highlight the complexity that arises when encoding verbal material. Verbal memory models support a shared idea that semantic and syntactic processing could utilize at least partially distinct mechanisms for encoding information, allowing for varying cortical patterns of activation (Barde & Thompson-Schill, 2002, Goldman-Rakic, 1987, Craik & Lockhart, 1972). Within the episodic domain, semantic relatedness has demonstrated an impact on episodic memory for verbal material (McCloskey & Santee, 1981). Syntax has been described as a product of the working memory system (Just & Carpenter, 1992, Waters & Caplan, 2004), specifically through phonological short term memory, which allows information to be efficiently rehearsed and integrated into long term stores of language information (phonological loop model: Baddeley & Hitch, 1974; Ellis & Sinclair, 1996).

Broca's region remains a particular source of debate, being claimed as a semantic region by some (Newman, Ikuta, & Burns, 2010; Muller, Kleinhans, & Courchesne, 2003; Bedny & Thompson-Schill, 2006), and a syntactic area by others (Caplan, Alpert, Waters, & Olivieri, 2000, Caplan, Alpert, & Waters, 1998; Lee & Newman, 2009; Newman, Ikuta, & Burns, 2010; Raettig, Frisch, Friederici, & Kotz, 2010; Shetreet, Friedmann, & Hadar, 2009; Perani et al, 1999; Santi and Grodzinsky, 2007; Grodzinsky & Santi, 2008). The semantic role in the region has been supported by increased activation in Brodmann's area 44 (BA 44) in response to comprehension probes, and within a neighboring region, BA 47 (Dapretto & Bookheimer, 1999; Newman, Ikuta, & Burns, 2010), potentially correlating relatedness of nouns (Newman, Ikuta, & Burns, 2010). Inferior frontal regions have also exhibited increased activation in response to nouns with lower imaginability ratings, an arguably semantic ambiguity (Bedny & Thompson-Schill, 2006). Semantic left prefrontal activation holds significance with verbal memory by being linked to better recall on subsequent verbal memory tasks (Bonner-Jackson, Csernansky & Barch, 2007). Researchers have pointed to the spread of cortical activation as related to depth of processing, with semantic processing activating more regions (parietal, temporal, supramarginal) than lower level processes (Henson, Hornberger, & Rugg, 2005).

Others have focused on the role of Broca's area (BA 44 and 45) in syntactic processing over semantic processing, suggesting a universal, cross-cultural component to this effect (Suzuki & Sakai, 2003). It has been suggested that the role BA 44 and 45 play in syntactic processing extends beyond theorized sub-rehearsal of complex language generated by the phonological loop (Caplan, Alpert, Waters, & Olivieri, 2000; Papagno, Cecchetto, Reati, & Bello, 2007). Several researchers have identified BA 44 as syntax related (Caplan, Alpert, & Waters, 1998; Frederici et al., 2003; Kang et al, 1999; Dapretto & Bookheimer, 1999; Newman, Ikuta, & Burns, 2010; Lee & Newman, 2009; Raettig, Friesch, Friederici, & Kotz, 2010), or more specifically verb-argument structure related (Raettig, Frisch, Friederici, & Kotz, 2010). Others have broken down the process to assign syntactic inflection to BA 44 and abstract syntax to BA 47 (Sahim et al, 2006). The latter is supported by research suggesting inflected verbs necessitate LIFG processing of tense, temporal information, and spatial movement, in addition to categorical relationships inherent in semantic processing (Tyler et al, 2004).

It has been suggested that syntactic movement, as well as syntactic complexity, working memory, and perception of action, have the largest impact on activity within Broca's region (Grodzinsky & Santi, 2008). Research has pointed to BA 45 and neighboring BA 46 as implicated in processing complex syntactic sentences (BA 45: Shetreet, Friedmann, & Hadar,

2009; BA 45, 46: Perani et al, 1999). Santi and Grodzinsky (2007), have shown varying areas of activity for manipulation of subject versus object ("The *dog* walks" versus "Sally walks the *dog*") activation (posterior and superior areas) compared to manipulation of reflexive pronouns and their antecedents (e.g. "Sally saw *Bob* hurt *himself* rollerblading"), found in more anterior and inferior Broca's areas. Uchiyama et al. (2008) identified BA 44 as involved in verbal working memory and articulatory rehearsal of online information and BA 45 as involved in integrating semantic processes of BA 47 and working memory processes of BA 44 through syntactic unification. This area then would link semantic and working memory systems with a partially distinct syntactic system.

Despite a continued debate regarding the integrated regions of syntax and semantics, researchers have made gains in isolating these variables. By focusing attention on differing aspects of the stimuli (e.g., syntactic or semantic information within sentences), semantic and syntactic distinctions may be effectively examined (Dapretto & Bookheimer, 1999; Suzuki & Sakai, 2003). Such differential effects and their impact on verbal memory performance have been observed within some clinical populations: in participants with significant memory deficits (e.g., Alzheimer's disease), language processing difficulties involve content of speech rather than form of speech (Nebes et al., 1989). The current study sought to identify the patterns of cortical activation elicited by semantic and syntactic processes during verbal encoding and their relationship with future retention of verbal information. This was accomplished by varying the task associated with encoding concrete nouns embedded within subject and object phrases and relating cortical activation to performance on delayed recall and recognition tasks.

It was hypothesized that fMRI BOLD signal would vary based on the type of task performed during verbal encoding. The phrase structure of the current stimuli would activate the left prefrontal cortex through participants' need to process information during encoding, and organize response information (Dannhauser et al, 2008). Both semantic and syntactic tasks would elicit verbal memory encoding processes, generating activity within the left frontal area (BA 45), an area implicated in both processes and suggested to be integrative in function (Kang et al., 1999; Dapretto & Bookheimer, 1999). Some have implicated Broca's area (BA 44/45) in processing of both semantic and syntactic information (Kang et al, 1999), but a distinction has arisen between BA 44 as syntax related (Frederici et al., 2003; Kang et al, 1999; Dapretto & Bookheimer, 1999; Newman, Ikuta, & Burns, 2010; Lee & Newman, 2009; Raettig, Friesch, Friederici, & Kotz, 2010) and BA 45 as an integrative area or a task-based processing region (Frederici et al., 2003; Dapretto & Bookheimer, 1999).

Syntactic processes in verbal encoding would result in activity in more posterior regions related to discourse processing, specifically within the left prefrontal (BA 44 as previously stated) and medial gyrus (BA 46). As stated previously, several researchers have implicated BA 46 in syntactic processing (Perani et. at, 1999; Kang et al., 1999). Semantic-focused encoding would be correlated with left inferior frontal areas previously linked to semantic processes (BA 47), in concordance with sentence processing findings of Dapretto & Bookheimer (1999) and Newman, Ikuta, & Burns, (2010). Temporal regions, in particular left medial temporal gyrus (BA 21/37) would show increased activation to semantic processing in verbal memory tasks when compared with syntactic counterparts (Bartha et al, 2003; Frederici et al., 2003; Muller, Kleinhans, & Courchesne, 2003). Finally, it has been suggested that phrase level and/or event-related verbal stimuli may elicit more bilateral resources, and some support for semantic activation in the right hemisphere of the medial frontal gyrus has been found (Kang et al, 1999).

For these reasons, activation in the right medial frontal gyrus (BA 46) was hypothesized as a semantic region.

Finally, the 'level-of-processing' model of Craik and Lockhart (1972) states that participants process similar material at varying degrees of encoding, from lower level structural (letter case) and lexical decision (word versus non-word) tasks, to higher level semantic categorization (animal versus tool) tasks. Higher level encoding requires more time and cortical resources to complete a task successfully (Craik & Lockhart, 1972; Bonner-Jackson, Csernansky & Barch, 2007). Accordingly, it was predicted that semantic-focused encoding would show a higher retention rate than syntactically encoded words. It was further predicted that increased memory on recall and recognition tasks following the experimental task would positively correlate with levels of BOLD activation during the task itself, within the above described regions of interest for each condition.

Methods

Participants

The current sample included 32 participants drawn from a university undergraduate and graduate community. Participation criteria entailed right handed, native English speakers, with no self-reported history of neurological disorder and no personal or family history of mental illness. In addition, participants met safety criteria for the MRI environment. A pregnancy test was given to female participants prior to the fMRI scan, to afford them the option of confirming negative pregnancy status. 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), a widely used and validated test of estimated intelligence involving reading words of increasing difficulty and correlating this information with predictive demographic variables (The Psychological Corporation, 2001a). The WTAR/ Demographics Full Scale IQ was generated through this verbal based task in order to confirm that overall intelligence differences did not influence memory for task stimuli.

Participants also completed a neurocognitive measure of verbal memory. The Rey Auditory Verbal Learning Test (RAVLT, Rey, 1941) is a widely used test of verbal memory and learning, involving listening to a list of categorically distinct words and measuring number of words recalled on each trial, number of words recalled on a distracter list, immediate and delayed recall of learned list, and recognition of both lists (Strauss, Sherman, & Spreen, 2006). It shows strong ecological validity as well as comparative validity to other commonly used neuropsychological measures of verbal memory, namely, the California Verbal Learning Test (Strauss, Sherman, & Spreen, 2006; Crossen & Wiens, 1994). Overall verbal learning was assessed to identify whether differences in participants' baseline ability to encode verbal information influenced their ability to remember target words within task stimuli.

fMRI Experimental Design

Each participant completed up to three distinct practice runs of the experimental task, until an accuracy score of at least 80% on a single practice run was achieved. Those who met the accuracy requirement participated in the MRI paradigm, with a minimum of 1 day separating neuropsychological tasks and experimental paradigm.

The experimental paradigm was an event-related design, randomized across conditions. Stimuli included a list of 76 nouns, with 38 nouns in each of 2 conditions, semantic-focused encoding and syntactic-focused encoding. Stimuli were presented using E-Prime 2.0 Software (Psychology Software Tools, Inc., 2007). Words of equivalent length, concreteness, and frequency were generated through the MRC Psycholinguistic database (Wilson, 1988; http://www.psy.uwa.edu.au/mrcdatabase/uwa mrc.htm). Phrases were constructed from 1 target noun with the above parameters, 1 randomly generated verb, and the article "the," to form sensible subject phrases (the-noun-verb) and object phrases (verb-the-noun). Prior to the task, participants were asked to remember the bolded nouns for a future memory task. Phrases were presented on the screen for 1 second, immediately followed by presentation of two category choices for 2 seconds. The task involved classifying the phrase within the most appropriate category presented. The choice of specific category varied by condition (Figure 4.1): In the semantic condition, the choice involved placing the phrase into one of two semantic categories (i.e., nature or man-made). In the syntactic condition, the subject classified the phrase as occurring in the present tense or past tense. Choice categories were counterbalanced across subjects, so that each phrase was processed using semantic and syntactic-focused encoding. Target words were counterbalanced for phrase type (subject versus object), condition (semantic versus syntactic decision), and grammar (present tense versus past tense) across participants. In addition, there were also 164 baseline trials, which involved non-verbal strings of x's in place of words, approximating lengths of experimental stimuli (e.g., **xxx** xxxx xxxx) and controlled for length of letter strings. One string of letters in each non-verbal "phrase" was bolded, and the bolded string was balanced between the first and last group of X's in the three string series). These x's were immediately followed by presentation of two identical x's in the positions of the

two categorical options. The participant was asked to choose the position of the previously presented bolded **x**'s (i.e., right or left on screen). Responses were counterbalanced for position on the screen within target word and baseline conditions. For all conditions, participants responded to the classification task by means of a touch-pad. Responses occurring within 1000 ms post offset of response screen were counted within behavioral totals. After fMRI testing, participants were removed from the MRI scanner and given a recall and then recognition test for the presented words. The un-timed recall task entailed the participant being asked to list as many bolded words as they could remember from the task, following a 20 minute delay. The recognition task was a forced choice, un-timed task involving presentation of all 76 nouns matched with a distracter word and counterbalanced for position on the screen.

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 = 24mm, slice thickness = 1.0 mm, locs per slab = 184, TE = min full, matrix = 256 x 256) to establish a reference template. Functional image acquisition occurred over 2 runs with approximately 6 minute durations (38 slices with interleaved bottom-up acquisition, 4 mm slice thickness, slice orientation aligned to AC-PC line, matrix = 64 x 64, in-plane resolution of 3.44 mm, TR = 2 seconds, TE = 25 msec, flip angle = 90, FOV = 22 mm). The conditions from the first session were permutated to attain the design for the second session. This event-related design was structured to maximally account for potential variations in HRF when examining 1second stimulus presentation, 2-second response time, or combined 3-second presentation time (time-to-peak = 7.5 seconds, and time-to-onset = 1 second, corresponding to a possible HRF for a 2 second stimulus). The design achieved 94% of maximal detection power and maximal estimation efficiency (M-H. Kao, personal communication; Kao, Mandal, Lazar, & Stufken, 2009). Inter-stimulus interval was 6 seconds.

Preprocessing

FMRI data were preprocessed with FMRIB Software Library, version 4.1 (FSL, Analysis Group at the Oxford Centre for Functional MRI of the Brain, Oxford, UK; http://www.fmrib.ox.ac.uk/fsl; Smith et. al, 2004; Woolrich et al, 2009), using FMRI Expert Analysis Tool (FEAT Version 5.98). The middle slice (37) was used as the reference slice during preprocessing. Run 1 and run 2 for each subject were processed separately within a first level mixed effects analysis, and then combined within a second level, fixed effects analysis. To preprocess, images were realigned and unwrapped using a non-linear transformation. Individual participant fieldmaps and a high pass filter (100 Hz) were utilized to reduce noise. Data were coregistered to the subject's structural MRI image, normalized and smoothed (FWHM = 6.88 x 6.88 x 4 mm). Temporal derivatives were incorporated into the preprocessing model.

Data Analysis

Behavioral analyses included a repeated measure ANOVA: a 2 (encoding: semantic, syntactic) x 2 (memory: recall, recognition) design. FMRI data were analyzed using FSL version 4.1. FMRI data were pre-processed at the first level and higher levels using a whole brain analysis. Activity in all regions of interest was then compared between conditions using a joint mask, allowing for analyses only within the 7 regions of interest at the between-subjects level (4.56% of the total MNI standard brain template). In addition to a joint mask, activation within each region of interest was calculated in the same manner and the above z score contrasts were reproduced for each of the 7 regions of interest (range = 0.27- 1.28% of the total MNI brain
utilized within each analysis). Masks were generating using WFU PickAtlas (Maldjian, Laurienti, Burdette & Kraft, 2003; Maldjian, Laurienti, & Burdette. 2004) within the Statistical Parametric Mapping (SPM-8) software (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm), through Matlab (The Math Works, Natick, MA). Contrasts included clusters of voxels within each of the two experimental conditions that passed a pre-determined thresholding value after subtracting baseline activation from each condition (semantic- baseline, syntactic- baseline: z > 2.3, p < .05). Subsequent contrasts included each condition of interest contrasted with the other (controlling for baseline activation: syntacticsemantic, semantic- syntactic). Within-subject BOLD signal and z scores were calculated using FSL. Between-subjects z scores consisted of significant clusters (cluster z > 2.3, p < .05) and corresponding maximum z score within these clusters for each of the above mentioned individual analyses within the 7 regions of interest.

Behavioral and fMRI BOLD signal were then integrated for the final analyses. A series of analyses were completed, using syntactic and semantic recall and recognition rates as covariates for fMRI activation. The number of syntactic and semantic encoded words recalled for each participant was entered as a demeaned regressor within FSL. Activation which was significantly higher as scores increased was recorded, as well as the contrasts between semantic and syntactic processing with recall covariates. The same process was repeated for recognition scores within the semantic and syntactic domain.

Results

Sample Description

Participants demonstrated a mean age of 20.47 years (s.d. = 1.93), and a mean education of 14.19 years (s.d. = 1.90). The majority of the sample was female (71.9%) and self-identified

as Caucasian/Non-Hispanic (90.6%). Demographic variables demonstrated no significant bivariate correlations with behavioral measures of interest, and therefore were not included in subsequent analyzes.

Predicted Intelligence

Participants demonstrated a WTAR/ Demographics predicted standardized FSIQ score of 109.22 (s.d. = 5.97). WTAR/ Demographics predicted FSIQ demonstrated no significant bivariate correlation with behavioral measures of interest, and therefore was not included in subsequent analyzes.

Learning and Memory: RAVLT

On the RAVLT, participants earned a mean total learning standardized score of 99.03 (s.d. = 12.39). Participants demonstrated a mean of 97 (s.d. = 15.7) on the RAVLT immediate memory task. RAVLT delayed recall memory scores showed a mean of 104 (s.d. = 14.2), and participants demonstrated a mean of 89 (s.d. = 26.7) on the subsequent RAVLT recognition memory task for the learned list of words. Based on standardized normative scores, participants performed within the low average range of recognition, and within the average range in other RAVLT reported tasks. This indicates no significant discrepancies between verbal memory abilities within this sample and the overall population, controlled for age and gender.

Behavioral Results

fMRI Behavioral Paradigm Accuracy

Participants achieved a mean of 223.03 correct responses during the fMRI behavioral task (s.d. = 14.97), for a mean of 92.92% behavioral accuracy (s.d. = 6.04). Total accuracy for target items demonstrated a mean of 62.38 (s.d. = 6.01), for a mean target accuracy rate of 82.07%. Accuracy rates were comparable for items within both conditions (syntactic: mean =

31.25, s.d. = 3.37; semantic mean = 31.13, s.d. = 4.14). Participants correctly responded to an average of 160.66 baseline items (s.d. = 13.70).

Experimental Memory Task

Following completion of the fMRI paradigm, participants recognized more words than during free recall (recall mean = 5.53 words, s.d. = 4.31; recognition mean = 61.84 words, s.d. = 7.74). When broken down by condition, participants recalled more semantically encoded words (syntactic recall: mean = 1.53, s.d. = 1.90; semantic recall: mean = 4.0, s.d. = 2.98) and recognized more semantically encoded words in comparison to syntactically encoded words (syntactic recognition: mean = 29.25, s.d. = 3.95; semantic recognition: mean = 32.59, s.d. = 4.22).

Analysis of Variance: Encoding (Syntactic, Semantic) by Memory (Recall, Recognition)

A repeated measures ANOVA was conducted to compare the effects of encoding (syntactic versus semantic) and memory task (recall versus recognition) on learning words during the fMRI behavioral paradigm. Results demonstrated a significant main effect of encoding (F (1, 31) = 76.36, p < .001, partial eta squared = .71), and memory task (F (1, 31) = 2396.06, partial eta squared = .99). Participants recognized significantly more words than they recalled, and remembered significantly more semantically encoded words than syntactically encoded words. No significant interaction between condition and memory task existed (p > .05). *fMRI Results*

Semantic and syntactic conditions within the following discussion indicate activation found specific to each condition, after subtracting baseline activation (i.e., syntactic activation = total activation during syntactic-focused encoding- activation during baseline trials, semantic activation = total activation during semantic-focused encoding- activation during baseline trials).

Whole brain analysis

An initial set of whole brain analyses were conducted in order to identify regions in which syntactic activation differed from baseline, semantic activation differed from baseline, and regions where these contrasts differed from each other (i.e., syntactic-semantic activation, semantic-syntactic activation). A cluster z threshold of z > 2.3, p < .05 was used for all analyses. Within the syntactic-baseline condition, pervasive activation was observed throughout the brain, including frontal and temporal regions. This pervasive activation coagulated into 1 large cluster of activation (122508 voxels), with local maxima z scores occurring within occipital (BA 17, BA 18, BA 19) and cerebellar regions. In response to the observed activation being masked by intense occipital and cerebellar activation, whole brain activation within specific regions of interest were measured. All regions (left frontal, right frontal, left temporal) demonstrated significantly activated voxels within the syntactic-baseline contrast, though continguous voxels with occipital regions prevented them from being identified as distinct clusters. With the semantic – baseline condition, 1 large cluster of significance occurred (122206 voxels) occurred, with local maxima z scores in the occipital region (BA 18, BA 19), cerebellar regions, and one frontal region of interest (BA 44). Again, all regions (left frontal, right frontal, left temporal) demonstrated significantly activated voxels within the semantic-baseline contrast.

When semantic activation was subtracted from syntactic activation (both controlling for baseline activation), 4 significant clusters were seen: 1 with a maximum z score within the cerebellum (1329 voxels), 1 with a maximum z in occipital regions (1090 voxels), 1 with a maximum z value in right frontal regions (1065 voxels), and 1 with a maximum z value in right parietal regions (13972 voxels). Local maxima z scores within these larger clusters occurred in right and left frontal regions, subcortical regions, left parahippocampal regions, right and left

parietal regions, and occipital and cerebellar regions. When whole brain activation within specific regions of interest was measured, the syntactic-semantic contrast yielded significantly activated voxels activation in all regions except right BA 46, left BA 45 and left BA 47. Of note, within the left BA 21 region, this activation consisted of a small number of voxels (2 significant voxels; max z = 2.47, X = -40, Y = -2, Z = -8). The contrast was reversed, and semantic-syntactic activation exhibited significant clusters with maximum z scores occurring in: the right cerebellum (2708 voxels), left limbic area (2072 voxels), left temporal regions (2225 voxels), left medial temporal regions (3229 voxels), right MFG (1048 voxels), and left MFG (19858 voxels). Local maxima z scores within these clusters were identified in bilateral IFG and MFG, left limbic regions, left temporal regions, left MTG, left parietal, bilateral occipital, and right cerebellar regions. All regions (left frontal, right frontal, left temporal) demonstrated significant voxels of activation within the semantic-syntactic contrast.

Total task activation across ROIs

Activation in the semantic and syntactic-focused encoding conditions was compared within the joint masked region, with significance denoted by clusters of voxels obtaining z > 2.3and p < .05 (Table 4.1). The syntactic-focused encoding condition demonstrated significantly increased activation when compared with that of the baseline condition (max z = 11.4, p < .05). Semantic activation exhibited increased activation as well (max z = 12.2, p < .05). When these contrasts were directly compared, syntactic activation –semantic activation did not elicit significant post-threshold voxels (p > .05). Semantic- syntactic activation (max z = 8.59, p < .05) did show significant differences. Activation occurred within both temporal and frontal ROIs, and within left and right frontal cortical regions of interest.

Individual regions of interest analysis

To test our hypothesis that patterns of activation would vary within the brain based on the focus for encoding, fMRI data were examined using disjoined masks for each specifically defined ROI. First, syntactic activation was contrasted with baseline BOLD activation, and all regions of interest exhibited clusters of significance (z > 2.3, p < .05; Figure 4.2). When semantic information was contrasted with baseline activation, a similar pattern emerged (Figure 4.3).

In comparing syntactic activation and semantic activation directly, first semantic activation was subtracted from syntactic activation (Figure 4.4). Regions close to the left temporal lobe BA 37 exhibited increased activation to syntactic-focused encoding over semanticfocused encoding ($z \max = 5.45$, p < .05). Brodmann's area 44 ($z \max = 4.60$, p < .05) and left BA 46 ($z \max = 4.04$, p < .05) also demonstrated statistical significance of syntactic over semantic activation. Temporal BA 21, left frontal BA 45 and BA 47, as well as right frontal BA 46 did not show significant clusters that survived thresholding (p > .05). When syntactic activation was subtracted from semantic activation, all regions showed clusters of significance (Figure 4.5). Of note, this included regions exhibiting clusters of higher significance in the syntactic- semantic condition (BA 37, BA 44, and BA 46). When coordinates of maximum activation were compared, BA 37 activation within the semantic-syntactic contrast appeared to have a more lateral, anterior, inferior location than within the syntactic- semantic condition. For BA 44, the semantic- syntactic condition elicited a maximum z score at a region more medial, anterior, and superior than its syntactic- semantic counterpart. BA 46 demonstrated a more lateral, posterior, inferior location of highest activation when compared with the semanticsyntactic contrast.

fMRI activation: Relationship of Recall and Recognition on fMRI activation

In order to test our hypothesis that accuracy on recall and recognition tasks would correlate positively with level of activation within each ROI, a series of analyses were completed, using syntactic and semantic recall and recognition rates as covariates for fMRI activation. Separate analyzes were run for recall and recognition tasks. No significant correlation between syntactic or semantic recall and fMRI activation occurred within any predefined region of interest (p > 0.5). A similar pattern occurred with the recognition condition, and no significant increases in fMRI BOLD activation were observed to correlate with increased performance on the recognition task in either encoding condition.

Discussion

Within the current experiment, we sought to identify language-related regions of the brain that play a role in processing semantic and syntactic information during a delayed verbal memory task, as well as their impact on retention for verbal information. Increased semantic over syntactic-focused encoding activation within BA 47 and right BA 46, without significant clusters found in the reverse contrast, supported our hypothesis of these regions as predominantly semantic regions. The nature of our stimuli could account for the semantic effect, as we asked participants to judge the relatedness of one noun to two categories, a process previously noted within BA 47 (Newman, Ikuta, & Burns, 2010). We also asked participants to read phrases while making semantic decisions, which could relate to the activation within the right hemisphere of BA 46 (Kang et. al, 1999). The findings highlight the integration of language processes within verbal memory, as these language-based regions are activating during an explicit verbal memory encoding task. Increased number of words retained did not correlate with the intensity of activation within these regions, however, participants overall remembered significantly more

semantically encoded words. This implies a benefit for semantic-focused encoding over syntactic-focused encoding, in line with the levels of processing verbal memory model (Craik & Lockhart, 1972).

In examining regions of hypothesized integration of semantic and syntactic processing, our findings of semantic over syntactic activation (but not the reverse pattern) within BA 45 does not support this hypothesis or past research suggesting a shared role (Caplan, Alpert, Waters, & Olivieri, 2000; Papagno, Cecchetto, Reati, & Bello, 2007). Semantic processing being a higher level process could implicate additional cortical resources, in line with the levels of processing model (Craik & Lockhart, 1972; Bonner-Jackson, Csernansky & Barch, 2007). The focus within the semantic condition on the noun of the phrase could also be implicated within a broader range of activation (Perani et al, 1999), as well as the speed of the task potentially taxing semantic networks to a greater extent than syntactic networks. Alternatively, as BA 45 has been implicated in complex syntactic processing by some (Shetreet, Friedmann, & Hadar, 2009; Perani et al, 1999), the lack of significant syntactic- semantic activation could indicate a relatively simplistic nature of stimuli phrases. Phrases involving subject/object and past/present mental manipulations might not elicit the working memory load suggested as being implicated within syntactic component of this region (Grodzinski & Santi, 2008). It is possible that the subjects versus object manipulations were processed within more posterior and superior regions of Broca's area (Santi & Grodzinsky, 2007).

In contrast, our results supported BA 44 and left BA 46 as potential regions in integrating semantic and syntactic information during verbal memory tasks. Our hypothesis that these regions play a role in syntactic processing during verbal memory was therefore supported. BA 46 has previously been linked to syntactic processing (Perani et. at, 1999; Kang et al., 1999), while

BA 44 has been identified as specific to syntactic processing (Caplan, Alpert, & Waters, 1998; Lee & Newman, 2009; Newman, Ikuta, & Burns, 2010), verb argument (Raettig, Frisch, Friederici, & Kotz, 2010), or syntactic inflection (Sahim et al, 2006). However, these findings did not support our hypothesis that only syntactic-focused encoding would elicit significant activation. Areas within BA 44 specific to semantic and syntactic processing would support its role in verbal working memory (Uchiyama et al, 2008). Our bilateral region (BA 46) demonstrated significant area of syntactic activation over semantic only within the left hemisphere, which falls in line with previous lateralization research (Kang et al, 1999). The complexity of syntactic phrases discussed previously could relate to syntactic activity being more proportional with semantic than expected in frontal regions. However, some effects of syntactic complexity have been shown to be more robust with shorter distance between noun and verb (Newman, Lee, & Ratliff, 2009), implying that the lack of length of phrases would not necessarily reduce the need for syntactic resources.

A more viable explanation could be that these regions may play concordant roles for both conditions within these regions. Some research has implicated left BA 44, 45, and 46 in various components of processing semantic incongruities or ambiguities (Hoenig & Scheef, 2009). Although behavioral accuracy rates were high, it is possible that inherent ambiguity regarding semantic categorization between man-made or nature related could have elicited some semantic in addition to syntactic activation during the encoding process. As no relationship existed between intensity of activation and number of words retained in either condition, an increase in semantic activation hindering use of these regions for syntactic-focused encoding would not be supported. It is possible that these regions could be implicated within the "morpho-syntactic" processing system identified during semantic categorization of word triplets (Tyler et al, 2001;

Tyler et al, 2004). The higher semantic activation within anterior BA 44 and posterior BA 46 suggests that voxels closer to BA 45 are implicated within semantic processing. In this sense, these three Brodmann's areas could be thought of as a potential verbal integration region, rather than BA 45 alone.

In addition to frontal regions of interest, semantic-focused encoding showed increased activation within the left temporal lobe (BA 21, BA 37), in support of our hypothesis of this region as semantic-based, and in accordance with prior research implicating temporal regions with semantic processing (Muller, Kleinhans, & Courchesne, 2003; Bartha et al, 2003; Cassanto et. al., 2002). The current results illustrate that activation occurs here predominantly when processing semantic information for future recall and recognition. This could indicate a response to "deeper" semantic information requiring additional cortical resources (BA 21 and BA 37; Henson, Hornberger, & Rugg, 2005). However, BA 37 exhibited significance in both the semantic-syntactic contrast as well as the syntactic-semantic contrast, and prior research has implicated syntactic processing within temporal regions (Noppeney & Price, 2004; Visser, Jeffries, & Lambon Ralph, 2009; Shetreet, Friedmann, & Hadar, 2009, Christensen et al., 2010). This activation could suggest a possible link between memory and language research. For example, within aphasic subjects, short term verbal memory deficits have been seen in posterior lesions including temporal regions (Beeson, Bayles, Rubens, & Kaszniak, 1993). One potential explanation of current results could then be that these processes are not mutually exclusive, and syntactic processing may engage and/or facilitate short term memory during the encoding of information.

Results of this study support the levels of processing model (Craik & Lockhart, 1972) in patterns of activation and behavioral data. Behaviorally, language comprehension research has

identified semantic processing to be a "deep" level of processing (Craik & Lockhart, 1972), which would suggest that semantic-focused encoding could impart a benefit over syntactic-focused encoding. This idea was supported by the current results, in that semantically encoded words exhibited increased rate of recall and recognition over syntactically encoded words. When fMRI BOLD signal was examined, semantic activation exhibited significantly increased activation in language regions of interest. This held across a majority of the regions of interest examined within left frontal, right frontal, and left temporal cortices at individual, joint ROI, and whole brain analyzes. Activation in response to semantically encoded words showed some significance over syntactically encoded words within all regions of interest, though some regions (left BA 44, BA 46, and BA 37) exhibited significantly higher BOLD activation to both semantic-focused encoding and syntactic-focused encoding.

No significant increases in fMRI BOLD signal were observed to correlate with increases in either recall or recognition scores, within either the semantic or syntactic-focused encoding conditions. This does not support our hypothesis that increased activation would correlate with increases in subsequent performance on memory measures. These results suggest that despite differences in retention rates, participants were activating cortical resources to an equivalent extent during the encoding task itself.

The results of this study are framed by some limitations. As previously mentioned, the sample consisted of a homogenous demographic, with a limited range of age and education. Though restricted in range of memory abilities, results remain important to begin to understand the role of language components within verbal memory tasks in the healthy young adult brain. In addition to homogeneity, language regions of interest are small and close in proximity, allowing for the potential that activation within one region may have included carryover noise from voxels

within neighboring regions. The high resolution of a 3 Tesla fMRI system allowed us to partially control for this limitation. Finally, as previously discussed, although experimental methods took into account and controlled for isolated semantic and syntactic activation, these language components are closely integrated. Results ought to be viewed in terms of relative differences between conditions rather than regions of interest being mutually exclusive to one type of processing over another.

The current experiment sought to examine the impact of language on a verbal memory task. Results demonstrated regions with a higher activation during encoding of semantic information and others with regions of significant activation for both semantic and syntactic activation. Verbal memory implicates language processes, which impact the effective encoding of verbal information. Future research will be beneficial to examine this feedback loop and its implications for effective and non-effective processing of verbal information.

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Figure 4.1

Experimental Design

Experimental paradigm involved 2 conditions (semantic and syntactic-focused encoding), in addition to an active baseline condition replacing nouns and verbs with strings of x's (bolding 1 set of \mathbf{X} 's to denote the target position).



Figure 4.2

Syntactic- Baseline Activation in 7 Regions of Interest

Activation is seen across 3 of the 7 ROIs: BA 37 = copper/tan, BA 44 = yellow, BA 46 = royal

blue





Semantic-Baseline Activation in 7 Regions of Interest

Activation is seen across all seven ROIs: BA 21 = light blue, BA 37 = copper/tan, BA 44 =

yellow, BA 45 = green, BA 46 = royal blue, BA 47 = red





Syntactic-Baseline - Semantic-Baseline Activation in 7 Regions of Interest

Significant activation is seen across 4 of the 7 ROIs: BA 37 = copper/tan, BA 44 = yellow, BA

46 = royal blue.





Semantic-Baseline - Syntactic-Baseline Activation in 7 Regions of Interest

Activation is seen across all seven ROIs: BA 21 = light blue, BA 37 = copper/tan, BA 44 =

yellow, BA 45 = green, BA 46 = royal blue, BA 47 = red.

Cluster List	Voxels	BA	Max z score	X	Y	Z
Syntactic-Baseline						
Left IFG	3568	44	10.9	-52	12	22
Left Temporal	1174		11.4	-42	-60	-18
Right MFG	981	45	7.42	54	34	24
Semantic-Baseline						
Left IFG	4138	44	12.2	-52	12	22
Left Temporal	2136		11.5	-44	-56	-22
Right MFG	910	45	8.31	50	34	24
Syntactic- Semantic						
None						
Semantic-Syntactic						
Left Frontal MFG	2919		8.59	-40	38	-10
Left MFG	2000		7.97	-62	-48	-6

Table 4.1: Joint Mask Analysis

CHAPTER 5

DISCUSSION

Memory for verbal information influences effective processing of task lists, memory for previous conversations, and retention of important details relevant to a situation. Verbal memory integrates input and output using several language related processes, including semantic processing of verbal meaning and syntactic processing of verbal structure. Within the given experiment, we sought to identify language-related regions of the brain that played a role within the processing of these components during a task of delayed verbal memory and their relationship to behavioral measures of verbal retention.

Verbal Memory Model: Levels of Processing

The verbal memory model most directly assessed through the current methods involved the levels of processing model of memory (Craik & Lockhart, 1972). In accordance with this model and the first hypothesis of this study, semantic-focused encoding did lead to increased memory on both free recall and recognition tasks. Within the syntactic task, presenting words in present tense or past tense did not impact whether words were later recalled during either memory task, indicating that syntactic findings are not being driven by characteristics of one verb tense in comparison to another, but instead the processing of syntactic information itself. Together, these results would suggest that semantic processing does indeed exact an advantage over syntactic processing and could be considered the higher level form of verbal processing (Craik & Lockhart, 1972; Bonner Jackson & Barch (2007). Results of this study support the levels of processing model in behavioral data as well as patterns of activation. Activation in response to semantic-focused encoding showed clusters of significant voxels beyond those activated for syntactic-focused encoding. This effect occurred within all seven regions of interest. In a majority of the ROIs, significant clusters appeared within the semantic- syntactic contrasts, but not when the contrasts were reversed (Left BA 21, left BA 45, left BA 47 and right BA 46). Other regions (left BA 37, left BA 44, BA 46) exhibited significantly activated clusters of voxels in response to both semantic- syntactic-focused encoding and syntactic- semantic-focused encoding. The effect of semantic over syntactic-focused encoding activation sustained enough power to maintain significance when multiple comparisons were increased to include voxels within all seven regions of interest within one analysis, while syntactic over semantic-focused encoding did not attain significance during the joint mask analysis.

Temporal Lobe Activation

Semantic-focused encoding showed increased activation within the left temporal lobe (BA 21, BA 37), in support of our hypothesis that this region would be more highly involved with semantic-focused encoding. This aligns with previous language research implicating either left hemisphere or bilateral temporal lobe activation in semantic processing (Muller, Kleinhans, & Courchesne, 2003; Bartha et al, 2003; Cassanto et. al., 2002). This pattern would suggest that, within the context of a verbal memory task, the temporal regions examined play a larger role in processing semantic than syntactic information. Research has implicated activation of the temporal lobe as part of an extended response to "deeper" semantic information requiring additional cortical resources to process (Henson, Hornberger, & Rugg, 2005). The effect could

also reflect an extended network of cortical activation for semantically processed nouns in comparison with syntactically processed verbs (Perani et. al, 1999).

Of course, this is not to say that no significant syntactic activation occurred in these regions, as illustrated by significant syntactic- baseline clusters within all regions of interest, as well as a significant syntactic-semantic cluster of voxels within BA 37. Previous research has implicated syntactic processing within temporal regions (Noppeney & Price, 2004; Visser, Jeffries, & Lambon Ralph, 2009; Shetreet, Friedmann, & Hadar, 2009, Christensen et al., 2010), in proximity to regions processing cognitive sequencing (Lelekov, Franck, Dominey, & Georgieff, 2000). Within aphasic subjects, short term verbal memory deficits have been seen in posterior lesions including temporal regions (Beeson, Bayles, Rubens, & Kaszniak, 1993). One potential explanation of current results could then be that these processes are not mutually exclusive, and syntactic processing may engage and/or facilitate short term memory during information encoding. This region's proximity to the parahippocampal gyrus, implicated in short term memory would support a potential connection of temporal syntactic information and short term verbal memory (Eichenbaum, 2002). The phonological loop model of verbal memory (Baddeley & Hitch, 1974) identifies a component related to short term memory that has been found to be beneficial within syntactic processing (Papagno, Cecchetto, Reati, & Bello, 2007), further supporting this potential connection. Whole brain analyses with parietal and parahippocampal regions of syntactic activation close to BA 37 indicate a potential posterior role of syntax within verbal encoding. Future research examining activation between high / low verbal memory, or simple / complex syntax, may assist in illuminating the function of BA 37 activation within the temporal lobe during encoding of syntactic information.

Frontal Lobe Activation

Semantic-focused encoding

Increased semantic over syntactic-focused encoding activation within BA 47 and right BA 46, without significant clusters found in the reverse contrast, supported our hypothesis of these regions as predominantly semantic regions. This effect sustained power even at the whole brain analysis level. The nature of our stimuli could account for the semantic effect in these regions, as we asked participants to judge the relatedness of one noun to two categories, a process previously noted within BA 47 (Newman, Ikuta, & Burns, 2010). We also asked participants to read phrases while making semantic decisions, which could relate to the activation within the right hemisphere of BA 46 (Kang et. al, 1999). The findings highlight the integrations of language processes and verbal memory, as these language based regions are activating during an explicit verbal memory encoding task. Increased number of words retained did not correlate with the intensity of activation within these regions. However, participants remembered significantly more semantically encoded words, implying a benefit for semantic over syntacticfocused encoding and a potential role of semantic specific activation in these regions contributing to this benefit.

Our findings of semantic over syntactic activation (but not the reverse pattern) within BA 45 does not support this hypothesis or past research suggesting a shared role (Caplan, Alpert, Waters, & Olivieri, 2000; Papagno, Cecchetto, Reati, & Bello, 2007). Semantic processing being a higher level process could implicate additional cortical resources, in line with the levels of processing model (Craik & Lockhart, 1972; Bonner-Jackson, Csernansky & Barch, 2007). The focus within the semantic condition on the noun of the phrase could also be implicated within a broader range of activation (Perani et al, 1999), as well as the speed of the task potentially taxing

semantic networks to a greater extent than syntactic networks. Alternatively, as BA 45 has been implicated in complex syntactic processing by some (Shetreet, Friedmann, & Hadar, 2009; Perani et al, 1999), the lack of significant syntactic- semantic activation could indicate a relative simplistic nature of stimuli phrases. Phrases involving subject/object and past/present mental manipulations might not elicit the working memory load suggested as being implicated within syntactic component of this region (Grodzinsky & Santi, 2008). It is possible that the subjects versus object manipulations were processed within more posterior and superior regions of Broca's area (Santi & Grodzinsky, 2007).

Semantic/Syntactic Integration

Our results supported BA 44 and left BA 46 as potential integration regions for semantic and syntactic information during verbal memory encoding. Our hypothesis that these regions play a role in syntactic-focused encoding was supported. BA 46 has previously been linked to syntactic processing (Perani et. at, 1999; Kang et al., 1999), while BA 44 has been identified as specific to syntactic processing (Caplan, Alpert, & Waters, 1998; Lee & Newman, 2009; Newman, Ikuta, & Burns, 2010), verb argument (Raettig, Frisch, Friederici, & Kotz, 2010), and syntactic inflection (Sahim et al, 2006). However, these findings did not support our hypothesis that only syntactic-focused encoding would elicit significant activation. Areas within BA 44 specific to semantic and syntactic-focused encoding would support the region's role in verbal working memory (Uchiyama et al, 2008). It would also lend support to the single processing resource theory (Just & Carpenter, 1992) in that semantic and syntactic-focused encoding would implicate similar cortical resources, and their proximity could facilitate combination by a shared verbal working memory system. Bilateral region (BA 46) demonstrated significant syntacticsemantic clusters only within the left hemisphere, which falls in line with previous lateralization research (Kang et al, 1999). The complexity of syntactic phrases discussed previously could relate to syntactic activity being more proportional to semantic activation than expected within frontal regions. However, some effects of syntactic complexity have been shown to be more robust with shorter distance between noun and verb (Newman, Lee, & Ratliff, 2009), implying that the lack of length of phrases would not necessarily reduce the need for syntactic resources. Also, as no relationship existed between intensity of activation and number of words retained in either condition, semantic and syntactic-focused encoding processes competing for cortical resources in this region would not be supported.

A more viable explanation could be that these regions may play concordant roles for both conditions within these regions, in line with the single processing resource theory (Just & Carpenter, 1992). Some research has implicated left BA 44, 45, and 46 in various components of processing semantic incongruities or ambiguities (Hoenig & Scheef, 2009). Although behavioral accuracy rates were high, it is possible that inherent ambiguity regarding semantic categorization between man-made or nature-related categories could have elicited semantic activation in addition to the syntactic-focused encoding activation. It is possible that these regions could be implicated within a syntactic processing system identified during semantic categorization of word triplets (Tyler et al, 2001; Tyler et al, 2004). In this sense, these three Brodmann's areas could be thought of as one potential verbal integration region, rather than BA 45 alone. *Behavioral Accuracy and Memory impact on BOLD activation*

Our hypothesis that increased activation would correlate with increased levels of accuracy on the behavioral task within the scanner was not supported by the current data. Higher levels of behavioral accuracy did not correlate with significantly higher levels of fMRI activation, within either encoding condition, in any of the 7 regions of interest. Results show that level of behavioral accuracy is not significantly impacting intensity of cortical activation. In this manner, the cortical functions between participants appear similar in terms of how semantic and syntactic information is processed, regardless of the accuracy of specific associations participants make between words and categories. This would suggest that even within clinical samples, where the process is deteriorating in accuracy (i.e., semantic accuracy within Alzheimer's disease, Nebes et al., 1989), the cortical process may remain similar in terms of patterns of cortical activity.

No significant increases in fMRI BOLD signal were observed to correlate with increases in either recall or recognition scores, within either the semantic or syntactic-focused encoding conditions. This does not support our hypothesis that increased activation would correlate with increases in subsequent performance on memory measures. These results suggest that despite differences in retention rates, participants were activating cortical resources to an equivalent extent. This could suggest that the mechanism impacting effectiveness of encoding information was not dependent on differing patterns or intensities of activation while encoding nouns embedded within task phrases. In this manner, differences seen within behavioral memory retention rates were not being driven by cortical activation in healthy young brains during this encoding phase. Further research examining cortical differences during retrieval and recognition tasks, as well as encoding within a sample experiencing clinical memory deficits (i.e. Mild Cognitive Impairment, Alzheimer's disease) could be beneficial to further illuminate cortical processes impacting memory deficits. Subsequent studies within this lab will examine the effects of these language variables on verbal memory within aging adults, which may further illuminate differences between high performing and low performing individuals.

Post-Hoc Analyses

During post-hoc analyzes, relationships were observed between recognition tasks and certain regions of interest. Specifically, BA 47 mean and maximum syntactic activation percent change activation were positively related to number of words in the syntactic condition that were later recognized. Such a finding could support the levels of processing model of memory, in that words syntactically encoded that showed higher activation within semantically focused regions had a better rate of recognition. In addition to the potential for semantic processes facilitating future recall, it is also possible that deeper levels of syntactic processing facilitated recall within these regions. When syntactic processing was isolated, researchers have suggested BA 47 as an area for processing of abstract syntactic information rather than more concrete verb agreement information (Sahim et al, 2006). In this manner, levels of processing could be in effect within one domain as opposed to comparing intensity of encoding between conditions.

Within post-hoc analyses of semantic recognition, a positive effect was observed between the mean percent change syntactic activation in region BA 47 and recognition of semantically encoded words. It is possible that individuals who are activating this area more deeply with syntactic information are using the resources within this region efficiently, perhaps encoding both semantic and some abstract syntactic information (Sahim et al, 2006), reaching a deeper level of encoding to facilitate future memory. Semantic recognition showed a negative relationship with semantic percent change mean of BA 44, indicating that reduced activation here correlated with higher levels of recognition of semantically encoded words. It is possible that the mean percent change within this region relates to increases in processing of syntax during semantic-focused encoding, which would reduce the efficacy of encoding semantic activation for future recognition. However, due to the exploratory nature of post-hoc analyses and limitations of percent change statistics within event-related designs, significant results are potentially impacted by multiple comparisons. Results require future replication within a controlled, apriori analysis in order to appropriately generalize from these findings.

The results of this study are framed by some limitations of the research. The sample consisted of a homogenous demographic, with a limited range of age and education. Future studies will integrate data from an older adult sample, which will allow for age comparisons. This will also allow for greater variance within memory tasks. By generating distinct groups, the differences between activation within successful verbal encoding and unsuccessful verbal encoding integrating various language components will be more readily isolated. However, the current results remain important to begin to understand the role of language components within verbal memory tasks within the healthy young adult brain. Once this is understood, we can begin to explore differences that arise during verbal memory difficulties of aging. Regions of interest are small and close in proximity, allowing for the potential that activation within one region may have included some carryover noise from voxels within neighboring regions. This is a limitation of most verbal-based research, and the high resolution of a 3 Tesla fMRI allow us to at least partially control for this limitation. Finally, as previously discussed, although experimental methods took into account and controlled for isolated semantic and syntactic activation, these language components are closely integrated. Results ought to be viewed in terms of relative differences between conditions rather than regions of interest as mutually exclusive to one type of processing over another.

Future Directions

Language components play a role in our future recall of verbal information, particularly as it begins to approximate natural discourse. Within future studies, we hope to explore the deficits that occur within verbal memory of aging adults. Differences within BOLD activation during verbal encoding and recognition have been found within those suffering from Alzheimer's disease (Peters, Collette, Degueldre, Sterpenich, Majerus, & Salmon, 2009). In contrast, improved memory with normal syntax has been shown within individuals suffering from Alzheimer's disease (Nebes, 1989). It appears that increased semantic errors are shown with relatively intact syntax when comparing Alzheimer's individual's speech and healthy aging controls (Lai, Pai, & Lin, 2009). Our current study focused on examining the role of syntax and semantics within verbal memory for the healthy young adult. Differences within the healthy aging brain, as well as within those experiencing difficulties with verbal memory are yet to be explored. These represent important areas of research in order to better understand the mechanisms that facilitate verbal memory within the aging brain and changes within mechanisms that allow for maintenance of effective verbal memory. This information could be helpful to preventative measures for those beginning to experience decline of verbal memory abilities. Conclusion

Memory for verbal information does not occur within a vacuum. Language components processed within verbal information influence the rate of memory and the patterns of cortical activations that are implicated within memory processes. The current experiment sought to examine the impact of these subcomponents of language on a verbal memory task. Results demonstrated regions with a higher activation during encoding of semantic information and others with regions of significant activation for both semantic and syntactic activation. Verbal memory implicates language processes, which further impact the effective encoding of verbal information. Future research will be beneficial to examine this feedback loop and its implications for effective and non-effective processing of verbal information that impacts daily functioning.

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