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Behavioral and fMRI-based Characterization of Cognitive Processes Supporting Learning and Retrieval of Memory for Words in Young Adults

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by

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Dedicated to Damien, whom I endowed with at least as many grey hairs as there are words in this dissertation.

ABSTRACT OF THE DISSERTATION

Behavioral and fMRI-based Characterization of Cognitive Processes Supporting Learning and Retrieval of Memory for Words in Young Adults

by

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A novel word is rarely defined explicitly during the first encounter. With repeated exposure, a decontextualized meaning of the word is integrated into semantic memory. With the overarching goal of characterizing the functional neuroanatomy of semantic processing in young adults, we employed a contextual word learning paradigm, creating novel synonyms for common animal/artifact nouns that, along with additional real words, served as stimuli for the lexical-decision based functional MRI (fMRI) experiment. Young adults (n=28) were given two types of word learning training administered in multiple sessions spread out over three days. The first type of training provided perceptual form-only training to pseudoword (PW) stimuli using a PW-detection task. The second type of training assigned the meaning of common artifacts and animals to PWs using multiple sentences to allow contextual meaning

acquisition, essentially creating novel synonyms. The underlying goals were twofold: 1) to test, using a behavioral semantic priming paradigm, the hypothesis that novel words acquired in adulthood get integrated into existing semantic networks (discussed in Chapter 2); and 2) to investigate the functional neuroanatomy of semantic processing in young adults, at the single word level, using the newly learned as well as previously known word stimuli as a conduit (discussed in Chapter 3).

As outlined in Chapter 2, in addition to the semantic priming test mentioned above, two additional behavioral tests were administered to assess word learning success. The first was a semantic memory test using a two-alternative sentence completion task. Participants demonstrated robust accuracy (~87%) in choosing the appropriate meaning-trained item to complete a novel sentence. Second, an old/new item recognition test was administered using both meaning and form trained stimuli (old) as well as novel foil PWs (new). Participants demonstrated: a) high discriminability between trained and novel PW stimuli. (d-prime=2.72); and b)faster reaction times and higher accuracy for meaning-trained items relative to perceptually trained items, consistent with prior level-of-processing research. The results from the recognition and semantic memory tests confirmed that subjects could explicitly recognize trained items as well as demonstrate knowledge of the newly acquired synonymous meanings. Finally, using a lexical decision task, a semantic priming test assessed semantic integration using the novel trained items as primes for word targets that had no prior episodic association to the primes. Relative to perceptually trained primes, meaning-trained primes significantly facilitated lexical decision latencies for synonymous word targets. Taken together, the

behavioral findings outlined above demonstrate that a contextual approach is effective in facilitating word learning in young adults. Words learned over a few experimental sessions were successfully retained in declarative memory, as demonstrated by behavioral performance in the semantic memory and recognition memory experiments. In addition, relative to perceptually trained PWs, the newly meaning-trained PWs, when used as primes in a semantic priming test, facilitated lexical decisions for synonymous real words, with which the primes had no prior episodic association. The latter finding confirms our primary behavioral hypothesis that novel words acquired in adulthood are represented similarly, i.e. integrated in the same semantic memory representational network, as common words likely acquired early in the lifetime.

Chapter 3 outlines the findings from the fMRI experiment used to investigate the functional neuroanatomy of semantic processing using the newly learned as well as previously known words as stimuli in a lexical decision task. fMRI data were collected using a widely-spaced event-related design, allowing isolation of item-level hemodynamic responses. Two fMRI sessions were administered separated by 2-3 days, the 1st session conducted prior to, and the 2nd session following word-learning training. Using the same items as stimuli in the fMRI sessions conducted before and after behavioral training, facilitated a within-item analysis where each item effectively served as its own control. A set of stringent criteria, outlined below, were established a-priori describing characteristics expected from regions with a role in retrieving/processing meanings at the single word level. We expected a putative semantic processing region to exhibit: a) higher BOLD activity during the 1st fMRI session for real

words relative to novel PWs; b) reduced BOLD activity for repeated real words presented in the 2nd fMRI session relative to levels seen in the 1st fMRI session; c) higher BOLD activity for meaning-trained PWs relative to novel PWs; d) higher BOLD activity for meaning-trained PWs relative to perceptually trained PWs, e) higher BOLD activity for correctly identified meaning-trained PWs (hits) relative to their incorrect counterparts (misses). Given their previously documented associations with semantic processing, we expected to identify regions in left middle temporal gyrus (MTG) and left ventral inferior frontal gyrus (vIFG) to exhibit timecourses consistent with most of the semantic criteria outlined above.

Individual ANOVA contrasts, essentially targeting each of the criteria outlined above, were conducted at the voxelwise level. A fixed effects analysis based on 4 correct trial ANOVA contrasts (corresponding to criteria a-d, above) generated 81 regions of interest; and two individual error vs. correct trial ANOVA contrasts generated an additional 16 regions, for a total of 97 study-driven regions. Using region-level ANOVAs and qualitative timecourse examinations, the regions were probed for the presence of the effects outlined in the above criteria. To ensure a comprehensive analysis, additional regions were garnered from prior studies that have used a variety of tasks to target semantic processing. The literature-derived regions were subjected to similar ANOVAs and qualitative timecourse analysis as was conducted on the study-driven regions to examine if the regions exhibited effects outlined in the above criteria.

The above analysis resulted in three principal observations. First, we identified regions in the left parahippocamal gyrus (PHG) and left medial superior frontal cortex (mSFC) that, by

satisfying essentially all the above criteria, demonstrated a role in semantic memory retrieval for recently acquired and previously known words. Second, despite strong expectations, regions in the left MTG and left vIFG failed to show activity in support of a role in semantic retrieval for the novel words. On the contrary, the profiles seen in the two said regions, namely a 'word > novel PW' and a word repetition suppression effect, were consistent with a role in semantic retrieval exclusively for the previously known words. The latter observation suggests that the novel words have yet to undergo adequate consolidation to engage, in addition to PHG and mSFC, canonical semantic regions such as left MTG.

Third, despite the potentially crucial distinctions noted in Chapter 3, left lateral/medial parietal regions implicated in episodic memory retrieval exhibited many similar properties as those outlined for PHG and mSFC above during retrieval of newly learned words. Crucially, instead of exhibiting repetition suppression for real words, as observed in PHG/mSFC, the parietal regions showed the opposite effect resembling the episodic 'old>new' retrieval success effect. The latter observation argues against a sematic role and in support of an episodic role consistent with previous literature. Taken together, these observations suggest that in addition to the role played by PHG/mSFC supporting semantic memory retrieval for the novel words, the parietal regions are also making significant contributions for memory retrieval of the novel words via complementary episodic processes.

Finally, using item-level timecourses derived from the 97 study-driven ROI, clustering algorithms were used to group regions with similar characteristics, with the goal of identifying a cluster corresponding to a putative semantic brain system. A number of clusters were

identified containing regions with anatomical and functional correspondence to previously well-characterized systems. For instance, a cluster containing regions in left lateral parietal cortex, precuneus, and superior frontal cortex corresponding to a previously described episodic memory retrieval system (Nelson et al., 2010) was identified. Two additional clusters, corresponding to frontoparietal and cinguloopercular task control systems (Dosenbach et al., 2006, 2007) were also among the identified clusters. However, the clustering analysis did not identify a cluster of regions with semantic properties, such as PHG and mSFC noted above, that could potentially correspond with a semantic brain system.

The above outlined findings from the current study, juxtaposed with prior findings from the literature, were interpreted in the following manner. The two regions identified in the current study, i.e. left parahippocampal gyrus and medial superior frontal gyrus, constitute regions that are used for learning new words, and are also recruited during semantic retrieval of previously well-established meanings. In addition, the current results also suggest complementary episodic contributions to the word learning process from regions in left parietal/superior frontal cortex. The latter observation may imply strong episodic contributions to the observed behavioral semantic priming effects. A potential counter argument, i.e. in support of a semantic basis for the priming effects, is the shared recruitment, in a manner consistent with semantics, of PHG/mSFC by both novel and real word stimuli.

The left middle temporal gyrus, a region that the task-evoked and neuropsychological literature consistently associates with word-level semantic processing, was not recruited during memory retrieval of novel words, despite robust engagement by previously known word

stimuli. Given their association with category-selective semantic deficits, as well as their role in conceptual/perceptual processing in healthy brains, the memory consolidation literature proposes regions in the lateral temporal lobes as potential neocortical loci for consolidated long-term memory. In the current setting, it is likely the case that the novel words have yet to be adequately consolidated to engage left MTG as did the previously known words.

Finally, the left vIFG exhibited similar characteristics as the left middle temporal gyrus, in that it was not recruited by the newly meaning trained stimuli, despite showing engagement by previously known words. Given that the region failed to appear in our primary contrasts, even those targeting real word stimuli, and its absence in other prior studies that have used similar lexical decision tasks as the current study, we have a slightly different interpretation for that region. The left vIFG is typically recruited in task settings that require controlled/strategic meaning retrieval, a process that may not be critical for adequate performance of the lexical decision task as employed in the current study.

Taken together, these findings suggest that a relatively small amount of word learning training is sufficient to create novel words that, in young adults, behaviorally resemble the semantic characteristics of well-known words. On the other hand, the fMRI findings, particularly the failure of the newly meaning-trained items to engage regions that are canonically responsive to single word meanings (e.g. middle temporal gyrus), may suggest a more protracted timecourse for the functional signature of novel words to resemble that of well-known words. That said, the fMRI findings identified brain regions (left PHG/mSFC) that, consistent with the memory consolidation literature, serve as the functional

neuroanatomical “bridge” that connects the novel words to the eventual functional representational destination.

Chapter 1: Introduction

1.1 Relevance of the Conducted Research

Language, and more specifically the ability to communicate using infinite combinations of arbitrary symbolic representations, i.e. words corresponding to concrete percepts and abstract concepts, is a quintessential human ability. Underlying this capacity is the human brain. The primary focus of this work is to elucidate how the healthy, young adult human brain accomplishes the remarkable tasks of learning, retaining, elaborating on, and instantiating the meaning of words, at the single-word level.

Humans continue to exercise the capacity for learning new words across the lifespan. Despite the decline in many cognitive abilities that accompanies healthy aging, vocabulary size (Ramscar, Hendrix, Shaoul, Milin, & Baayen, 2014; Verhaeghen, 2003) and overall verbal memory capacity (Trey Hedden, Lautenschlager, & Park, 2005; Park, Smith, Lautenschlager, Earles, & et al, 1996) are relatively preserved and potentially increasing across the lifespan. In addition, vocabulary size may serve as a potential compensating buffer for verbal memory capacity that is relatively well preserved in old age. To that effect, while processing speed is the biggest predictor of age-related performance decline in a range of memory tests, vocabulary size, particularly in older adulthood, increasingly offsets the negative effects of slowed processing speed, thereby allowing for the selective preservation of verbal memory capacity (Trey Hedden et al., 2005; Park et al., 1996).

Vocabulary size also has strong predictive ties to educational achievement. For instance, deficient vocabulary has been proposed as one of the primary causes of the lagging academic achievement observed in disadvantaged students in grades 3 to 12 (Becker, 1977). Knowledge of word meanings is thought to be the essential building block for the acquisition of subsequent concepts that, themselves, build on the framework of existing vocabulary. Hence, the capacity to learn new concepts itself is necessarily dependent on the learner's existing knowledge base. Without adequate vocabulary, students in the later school years are being asked to develop novel conceptual combinations of presumed known concepts with insufficient tools (Adams, 1994; Baker, 1995). Hence, the capacity for the knowledge of word meanings is at the heart of the achievements possible by humans as lifelong learners.

As stated above, learning novel words is a lifelong endeavor and knowledge of word meanings is a capacity that strongly influences educational achievement as well as verbal memory capacity across the lifespan. Here, we used a contextual word learning paradigm to characterize in young adult subjects the cognitive processes and functional neuroanatomy supporting semantic processing associated with learning single words. Specifically, using a multi-context sentential training approach, pseudoword stimuli were given meanings and were effectively turned into synonyms to existing words. An additional goal of the current project was to isolate, via subtractive inference, BOLD activity related to retrieval of meaning, i.e. semantic memory, from co-recruited processes related to retrieval of perceptually familiar word-forms with no semantic associations. To this end, a separate group of pseudowords were given perceptual training using a pseudoword detection task. Finally, using fMRI before and

after behavioral training, we characterized the functional neuroanatomical changes associated with transforming a meaningless string of letters into meaningful words.

1.2 Behavioral Characterizations of Word-Level Semantic Processes

Following behavioral word learning training, a series of behavioral tests were administered to ascertain that novel semantic information has been successfully acquired. Behavioral testing was conducted with two goals in mind. The first goal was characterize the lexical configuration (Leach & Samuel, 2007) properties of the novel words, i.e. properties intrinsic to the novel words themselves. This characterization was carried out using a recognition memory and a sentence-completion semantic memory test intended to demonstrate that the novel words could be explicitly recognized and used appropriately in novel sentence contexts, respectively. The second goal was to provide evidence that the novel words exhibit lexical engagement (Leach & Samuel, 2007) with semantically related (synonymous) previously known words, which would be indicative of integration of the former in the lexicon. Here, this was accomplished using a semantic priming paradigm that used the novel words as semantic primes to synonymous previously known words. The current priming paradigm employed a short (250-ms) stimulus onset asynchrony, with the goal of targeting priming effects driven by automatic strategy-free spreading activation processes (Collins & Loftus, 1975; Neely, 1977; Posner & Snyder, 1975). As outlined below, the latter goal of demonstrating semantic priming effects for the novel words provides evidence to help address a somewhat controversial question – are words acquired in adulthood representationally similar to words acquired early in the lifespan?

As stated above, there was prior work (Qiao, Forster, & Witzel, 2009) that had suggested that late-learned words were representationally distinct from words learned early, and hence not fully integrated in the lexicon. Although the group has subsequently changed their position (Qiao & Forster, 2012), their earlier hypothesis was that late-learned words are only represented in episodic memory without lexico-semantic integration with words acquired early. On the other hand, there are a number of studies that have documented lexical engagement effects produced by late-learned novel words on their early-acquired counterparts, indicative of integration in the lexicon. For instance, learning a novel spoken word (e.g. cathedruke) results in lexical competition between the novel word and an existing orthographically neighboring word (e.g. cathedral), manifested as slowed reaction times for the latter in lexical decision (Dumay, Gaskell, & Feng, 2004) and pause-detection (Gaskell & Dumay, 2003) task settings. The observed lexical engagement effects took place days following training, which suggested that sleep-dependent memory consolidation processes play an important role in integrating the novel words in the lexicon (Dumay & Gaskell, 2007). Lexical integration for late-acquired novel words has also been demonstrated using a semantic priming approach, although there are only a handful of studies that, in our opinion, established bona fide semantic priming effects (Tamminen & Gaskell, 2012). As noted below, the current investigation took steps to ensure that the priming effects were driven by semantic prime-target interactions. Hence, this work should be a welcome addition to the sparse literature investigating a lexical integration hypothesis for novel words acquired in adulthood.

In semantic priming paradigms, observed priming effects could be generated due to a number of prime-target relationships, not all of which may be reflective of semantic interactions between prime and target (refer to (Hutchison, 2003; McNamara, 2005; Neely, 1991) for detailed reviews). One potential driver of semantic priming effects, which is the process targeted in the current experiment, is prime-target semantic relatedness (Neely, 1977). In this type of priming, a prime (e.g. doctor) facilitates processing (e.g. by speeding up lexical decisions) of a semantically related target word (e.g. nurse), relative a target word with no semantic relationships to the prime (e.g. cat). Another potential driver for priming effects is mediated priming (D. A. Balota & Lorch, 1986) in which a prime (e.g. lion) can prime an unrelated word (e.g. stripes), via the meditational influence of a related word (e.g. tiger), albeit without explicit exposure to the mediating word. Finally, a third potential source for priming effects is the frequency of episodic association between prime and target (McKoon & Ratcliff, 1979; Pecher & Raaijmakers, 1999). In this case, the word "mouse" can prime "cheese" because those two words are frequently co-experienced, even though they may not be semantically related. To preclude episodic priming effects from influencing the targeted semantic priming effects, the current paradigm ensured that the primes and targets were never presented together during training. In addition, given the potentially crucial role of sleep-dependent memory consolidation for lexical integration (Dumay & Gaskell, 2007; Tamminen & Gaskell, 2012), the current experiment provided behavioral training over the course of 2-3 days prior to testing.

1.3 Cognitive Neuroscientific Perspectives of Memory Organization

The faculty of memory has intrigued philosophers for centuries, and recorded philosophical accounts of memory organization date at least as far back as Aristotle. Aristotle viewed the human mind (although "soul" might be more apt here) as a blank slate on which a lifetime of experience gets recorded as memory (Smith, 1931). His "storehouse" view of memory held sway for many centuries, and despite subsequent advances in our understanding of memory, it arguably still continues to do so. Around the latter part of the 19th century, the German philosopher Herman Ebbinghaus, credited for conducting the first formal scientific experiments on human memory, forwarded an account of memory organization resembling current perspectives (Tulving, 1983). Ebbinghaus classified memory as three distinct types, sensory, short-term, and long-term memory, and this general framework, albeit with nuanced elaborations by subsequent models, remains relevant to this day. Following the mid 20th century "cognitive revolution", which brought about advances particularly in the domain of short-term or working memory, the next major development was Endel Tulving's classification of longterm declarative memory into episodic and semantic memory (Tulving, 1983).

At the highest level of stratification, current perspectives identify two types of memory, declarative and implicit. Declarative memory is consciously available and can be explicitly reported, and is itself further divided into short-term (or working memory) and long-term memory. In contrast, implicit memory, which underlies phenomena such as semantic priming, is memory that, although not necessarily consciously accessible, can nonetheless be characterized based on its effects on subsequent behavioral performance. Finally, long-term

declarative memory, which is the current focus, is divided into episodic and semantic memory. The former describes memory for a specific event or experience directly associated with and elaborated on by the agent, and the latter is defined as memory for facts and word meanings that are generally not associated with a specific spatiotemporal experience. Below we provide a brief overview of prominent theoretical accounts to date of episodic and semantic memory organization that emerged based on decades of behavioral, computational, and neuroscientific research.

One view (Shimamura & Squire, 1987; L R Squire, Knowlton, & Musen, 1993; Larry R Squire & Zola, 1998) posits that semantic memory is constructed based on extraction of a common associative organizing rule across a series of episodically experienced memory instances. Relevant to the current research on memory for word meanings, the above account would posit that for a context-independent semantic memory captured by the word "dog" to emerge, one needs to have had multiple episodic experiences, and hence memory, of dogs. Alternatively, switching from an earlier viewpoint(Tulving, 1983), Endel Tulving proposed three monohierarchically organized memory systems, namely a perceptual, semantic, and episodic system in which encoding proceeds serially from perceptual, to semantic, to episodic representations (Tulving, 1995, 2001). Relevant to the current research, this view would suggest that encoding a personally significant episodic memory of an incident with a dog requires, as a fundamental ingredient, knowledge of what a dog is, i.e. semantic memory. In support of the latter perspective, proponents note the earlier developmental onset of the capacity for semantic relative to episodic memory observed in children of 4-5 years of age

(Carey, 1985; de Haan, Mishkin, Baldeweg, & Vargha-Khadem, 2006; Murphy, 2002; Quinn & Eimas, 1997; Wheeler, Stuss, & Tulving, 1997). The aforementioned radically different theoretical perspectives on the relative properties of episodic and semantic memory processes underscore that our understanding of memory systems is still in its infancy. They also foreshadow the challenge in making interpretations of the cognitive neuroscientific research to date regarding the potentially distinct functional neuroanatomy underlying episodic and semantic memory retrieval.

1.4 Neuropsychological Memory Research

Based on neuropsychological research, brain regions in the medial temporal lobe (MTL), namely the hippocampus proper and neighboring entorhinal, perirhinal, and parahippocampal cortex, have long been regarded as critical for the formation of new episodic memory. Damage to these regions results in anterograde amnesia (Scoville & Milner, 1957) marked by the inability to recall recent episodic memory, while remote memory acquired prior to the neurological injury remains unaffected. Whether the hippocampus also supports the acquisition and retrieval of semantic memory is less established. The classic example used as evidence to argue hippocampal involvement in semantic memory comes from H.M., a patient who underwent bilateral MTL resection for medically intractable epilepsy. H.M. was unable to learn and retain new words that did not exist prior to the surgery (e.g. “Xerox”), despite normal memory for semantic information acquired prior to the amnesia (Gabrieli, Cohen, & Corkin, 1988). A slightly different account states that while the hippocampus is critical for episodic memory, some capacity to acquire semantic memory remains if damage to the MTL spares the

parahippocampal, entorhinal, and perirhinal cortex (Bindschaedler, Peter-Favre, Maeder, Hirsbrunner, & Clarke, 2011; Holdstock, Mayes, Isaac, Gong, & Roberts, 2002; Mishkin, Vargha-Khadem, & Gadian, 1998; Verfaellie, Koseff, & Alexander, 2000). However, as counter evidence, others note that relative to healthy controls, semantic memory acquisition in hippocampal amnesics is impaired, and any remaining capacity requires many repetitions (Glisky, Schacter, & Tulving, 1986; Hayman, Macdonald, & Tulving, 1993; Kovner, Mattis, & Goldmeier, 1983; Shimamura & Squire, 1987; Tulving, Hayman, & MacDonald, 1991) potentially suggesting the involvement of other non-hippocampal implicit memory mechanisms.

On the other hand, the findings from neuropsychological research investigating semantic deficits resulting from (non-MTL) brain damage are relatively less controversial. Lesions to grey matter structures as well as underlying white matter in the left lateral temporal lobe, particularly the posterior middle temporal gyrus (MTG) and anterior aspects of the superior temporal gyrus, result in semantic comprehension deficits (Dronkers et al., 2004; Turken & Dronkers, 2011). Relatedly, lesions in the posterior MTG have also been associated with comprehension deficits at the single word level (Hart & Gordon, 1990). Another avenue of neuropsychological research on selective semantic impairments (Warrington, 1975) comes from patients with the temporal variant of frontotemporal lobar degeneration (tvFTLD), sometimes also referred to as semantic dementia. tvFTLD is a neurodegenerative disease characterized by bilateral atrophy of the anterior temporal lobes associated with semantic impairments in picture naming, spoken/written word-level comprehension, and generation of

category exemplars (e.g. animals, furniture) (Hodges, Patterson, Oxbury, & Funnell, 1992). Although the anterior temporal lobe atrophy is typically bilateral, there is some evidence suggesting a left vs. right hemisphere asymmetry associated with verbal vs. perceptual (e.g. names vs. faces) semantic impairments, respectively (Lambon Ralph, McClelland, Patterson, Galton, & Hodges, 2001; Snowden, Thompson, & Neary, 2004), although others disagree with the proposed asymmetry (Visser, Jefferies, & Lambon Ralph, 2010). Overall, unlike the MTL discussed above, whose role in episodic vs. semantic memory retrieval is more controversial in the neuropsychological literature, there is relatively more consensus associating left lateral temporal damage exclusively with semantic deficits.

1.5 Task Activation-Based Memory Research

In task-based episodic memory retrieval studies employing classic old/new item recognition paradigms, consistently reported regions include the left lateral parietal cortex, bilateral precuneus and posterior cingulate, as well as medial and lateral frontal regions in the left hemisphere (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; I. G. Dobbins & Wagner, 2005; Nelson et al., 2010; Wheeler & Buckner, 2003; Yonelinas, Otten, Shaw, & Rugg, 2005; Yonelinas, 2002). The noted regions exhibit a canonical retrieval success effect whereby previously seen (i.e. old) items exhibit higher BOLD activity than novel foils. Notably a similar set of regions in left medial and lateral parietal cortex, with the left angular gyrus as the prime example, has been associated in multiple meta-analytic studies with semantic processing (Binder, Desai, Graves, & Conant, 2009; Seghier, 2013; Vigneau et al., 2006).

In addition to the regions noted above, making episodic source retrieval judgments recruits an additional set of regions in the left hemisphere not typically present in item recognition or recency/novelty judgment tasks. These include regions in the MTL (hippocampus/posterior parahippocampus), medial superior frontal cortex, posterior MTG, and left vIFG (I G Dobbins, Foley, Schacter, & Wagner, 2002; I G Dobbins, Rice, Wagner, & Schacter, 2003). The latter finding, particularly the recruitment of the left vIFG and left MTG, appears to be specific to retrieval of source memory whose contents are conceptual (i.e. not perceptual) (I. G. Dobbins & Wagner, 2005). These findings, coupled with previously demonstrated semantic properties of left MTG and left vIFG, were attributed to a greater demand in semantic elaboration between source and item in the conceptual source retrieval task, consistent with cognitive theories (I G Dobbins et al., 2002; Daniel L Schacter, Norman, & Koutstaal, 1998; Tulving, 1983). It is interesting to note that regions typically recruited in semantic tasks (i.e. left MTG and left vIFG), are similarly recruited in a task setting requiring recollection of specific episodic details, albeit of conceptual makeup.

In task-based semantic studies, regions in the left posterior MTG and left ventral inferior frontal gyrus pars orbitalis (vIFG) have been consistently implicated in semantic processing based on tasks such as making abstract/concrete judgments (Donaldson, Petersen, & Buckner, 2001; Friederici, Opitz, & von Cramon, 2000), verb-generation (J. A. Fiez, Raichle, Balota, Tallal, & Petersen, 1996; Petersen, Fox, Posner, Mintun, & Raichle, 1988; Roskies, Fiez, Balota, Raichle, & Petersen, 2001), and semantic classification/comparison (Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Thompson-Schill et al., 1997; A D

Wagner, Pare-Blagoev, Clark, & Poldrack, 2001). The same two regions also exhibit repetition suppression, an effect that, in the two regions, has been selectively attributed to priming due to conceptual (i.e. not perceptual) repetition (D. L. Schacter & Buckner, 1998; Daniel L Schacter, Wig, & Stevens, 2007; Wig, Grafton, Demos, & Kelley, 2005). Relevant to the current study, an additional property of left vIFG implicating the region more specifically to controlled/strategic semantic retrieval (as opposed to automatic) deserves to be highlighted. While consistently recruited by tasks targeting controlled semantic retrieval, as used in the above studies, left vIFG is not always recruited by simple lexical decision tasks (Fiebach, Friederici, Muller, & von Cramon, 2002; Fiebach, Ricker, Friederici, & Jacobs, 2007; Henson, Price, Rugg, Turner, & Friston, 2002). A potential explanation for the above observation is that the lexical decision task, similar to that used here, maybe sufficiently performed with automatic (i.e. not controlled) access to semantic information alone.

Finally, studies using a word learning approach similar to the current work reveal word learning related functional neuroanatomy that is consistent with the neuropsychological and task-based memory retrieval research summarized above. The most consistent finding associates BOLD activity in left MTL, hippocampus and parahippocampal gyrus in particular, with supporting memory for newly acquired word meanings (Breitenstein et al., 2005; Mestres-Missé, Càmara, Rodriguez-Fornells, Rotte, & Münte, 2008; Sandak et al., 2004). The above studies also implicated regions in the left MTG and left IFG in semantic processing underlying novel word learning, although these latter findings should be considered with the caveats discussed in chapter 3. Finally, prior word learning studies also report the involvement of left

parietal regions, particularly the angular gyrus, in support of memory for novel words. However, across studies, a seemingly inconsistent functional profile has been reported for the angular gyrus (e.g. compare Sandak et al., 2004 and Clements-Stephens et al., 2012 (Clements-Stephens et al., 2012; Sandak et al., 2004)), that makes a straightforward interpretation somewhat problematic.

In all, the aforementioned brief summary of the neuropsychological and task-based memory research reveals many similarities, but also some differences in the functional neuroanatomy attributed to episodic and semantic memory processes. With their recruitment in episodic source retrieval contexts notwithstanding, the pattern of findings in left MTG and left vIFG are consistent with a selectively semantic interpretation. On the other hand, a clear adjudication in support of a role in episodic or semantic memory for left hemisphere regions in the MTL and medial/lateral parietal cortex would frankly not be justified at this juncture.

As a final note, perhaps not surprisingly given the somewhat inconclusive region-level functional distinctions between episodic and semantic memory outlined above, well-characterized and replicated systems-level organization of regions involved in memory operations is lacking. While some formal work has been done to that effect in the episodic memory domain (Nelson et al., 2010), no such effort has been documented, to our knowledge, identifying a putative semantic brain system. Hence, the current work conducted clustering analyses of regional task-evoked timecourses in an effort to reveal potential brain systems corresponding to semantic processing.

1.6 Time-Dependent Memory Consolidation

One aspect of declarative memory processes and associated functional neuroanatomy that is especially relevant to the current work and deserves an explicit introduction is the constantly evolving nature of memory representations across time. One particular neuropsychological observation dating back to the 1880s was instrumental in revealing the time-dependent nature of declarative memory representations. The French psychologist Théodule Ribot observed that in some patients that experienced memory loss due to head trauma, the degree of memory impairment exhibited a time gradient such that memory acquired closer in time to the trauma was more compromised relative to remote memory. The phenomenon, termed temporally-graded retrograde amnesia, has been linked to medial temporal lobe damage, with more pronounced deficits when damage extends beyond the hippocampus to neighboring entorhinal, perirhinal, and parahippocampal cortex (N. J. Cohen & Squire, 1981; Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006; L. R. Squire, 1992). Observations from retrograde amnesia led to the hypothesis that once outside a given time window, memory retrieval is progressively less dependent on the hippocampus and neighboring MTL structures. This change is thought to be due to the migration of memory representations to neocortical areas, such as regions in the left lateral temporal lobe and medial prefrontal cortex (Atir-Sharon, Gilboa, Hazan, Koilis, & Manevitz, 2015; Ghosh & Gilboa, 2014; Takashima et al., 2006; van Kesteren, Ruiter, Fernández, & Henson, 2012), in a time-dependent, memory consolidation process (McClelland, McNaughton, & O'Reilly, 1995; McClelland, 2013; Nadel & Moscovitch, 1997). Numerous computational models have been proposed, exemplified by two prominent models discussed below, to characterize time-

dependent memory consolidation processes potentially associated with evolving functional neuroanatomy.

The first is the Complementary Learning Systems (CLS) model proposed by James McClelland and colleagues (McClelland et al., 1995) which is one example of so-called "Standard Models" and the second is the Multiple Traces Theory (MTT) (Nadel & Moscovitch, 1997). Both the CLS and MTT models regard the hippocampus as critical to rapid episodic memory acquisition and both models generally regard neocortical memory consolidation as a relatively slower process operating at a timescale of days/weeks. There are two basic differences between the two models. First, in the CLS model, the hippocampus is only critical for retrieval and consolidation of recent, i.e. relatively novel memory. For remote memory matching a neocortical representation, the medial prefrontal cortex inhibits the hippocampus to avoid duplicate encoding (Frankland & Bontempi, 2005). On the other hand, in the MTT, the hippocampus continues to be involved in the retrieval and reconsolidation of even remote memory. The second difference is that while the CLS makes no distinctions between episodic vs. semantic memory, the MTT treats the two types of memory slightly differently. Proponents of the MTT note that in retrograde amnesia, episodic and semantic memory are affected differently such that episodic memory shows a shallow temporal gradient relative to semantic memory (Nadel & Moscovitch, 1997). Hence, in the MTT, the hippocampus continues to be necessary for both recent and remote episodic memory. As for semantic memory, the multiple hippocampal traces of similar recent and remote episodes allow "extraction of factual information…and its integration with…[neocortical] semantic memory

stores" (Nadel & Moscovitch, 1997). Hence, in the MTT, only decontextualized neocortical semantic memory could potentially be retrieved independently of the hippocampus.

The aforementioned models of memory consolidation, despite their differences, jointly highlight an important point directly relevant to this investigation. Memory representations are dynamic in nature and the functional neuroanatomy related to retrieving memory for old, previously known words, could potentially differ from that related to retrieving memory for recently learned words. Hence, in an effort to leverage semantic memory retrieval processes using both remote and recently acquired memory, our stimulus list constituted both previously known words and the novel words acquired over multiple days. Below, we provide a brief overview of the behavioral and functional imaging findings documented in Chapter 2 and Chapter 3, respectively.

1.7 Brief Summary of Data Chapters

Forthcoming in the remainder of this thesis are three chapters. Chapter 2 documents findings from our behavioral characterizations of memory for newly acquired meaningful words relative to that of perceptually trained word forms based on performance in tasks targeting implicit and explicit memory. Chapter 3 documents findings from functional neuroanatomical investigations of word-level semantic processing using previously known and newly learned words, as well as novel and familiar pseudowords (PW) to leverage putative semantic processing regions. Also reported in Chapter 3 are results from a clustering-analysis of regional task-evoked timecourses primarily aimed at identifying a semantic brain system. Finally, Chapter 4 integrates the findings from the two preceding data chapters with prior

literature to contextualize our characterizations of the functional neuroanatomy underlying retrieval of memory for word meanings. The primary findings from data chapters 2 and 3 are summarized below.

As outlined in Chapter 2, our behavioral goals were two-fold. The first was to establish that behavioral training successfully resulted in meaning learning and form familiarity assessed using old/new item recognition and 2-alternative sentence-completion semantic memory tests targeting explicit memory. Based on recognition memory performance, we demonstrate that subjects were proficient at discriminating trained items (both meaning and perceptually trained) from novel foils. In addition, resembling level-of-processing effects documented for real words (Craik & Lockhart, 1972), we demonstrate that the deeper encoding afforded by meaning training results in faster and more accurate recognition for meaning relative to form trained items. Based on performance in the sentence-completion semantic memory test, we demonstrate that subjects successfully learned new words as evidenced by their proficiency in choosing appropriate newly trained words to complete novel sentences.

The second behavioral goal was to demonstrate using a semantic priming paradigm that newly learned words would act as semantic primes to previously known synonymous words that had no prior episodic association with the primes. We show that, relative to perceptually trained primes, meaning-trained primes significantly facilitated lexical decision latencies for synonymous word targets. We interpret the latter finding as evidence indicating that novel words acquired in young adulthood are representationally integrated with common previously known words in the lexicon likely acquired early in the lifespan.

Chapter 3 documents the findings from the fMRI experiment used to investigate the functional neuroanatomy of word-level semantic processing using the PWs used in meaning and form training as well as actual English nouns (artifacts/animals) in a lexical decision task. A widely spaced event-related fMRI experiment, administered before and after the multi-day behavioral training, allowed for isolation of item-level hemodynamic responses, and a subsequent cross-session within-item analysis where each item effectively served as its own control. A set of a-priori hypotheses described characteristics expected from regions with a role in retrieving/processing meanings at the single word level. We expected a putative semantic processing region to exhibit: a) higher BOLD activity for real words relative to novel PWs; b) cross-day repetition-related BOLD suppression for real words; c) higher BOLD activity for meaning-trained PWs relative to novel PWs; d) higher BOLD activity for meaning-trained PWs relative to perceptually trained PWs, and e) higher BOLD activity for correctly identified meaning-trained PWs (hits) relative to their incorrect counterparts (misses). A series of individual ANOVA contrasts were computed at the voxelwise level, and subsequently entered in a fixed effects analysis to generate individual brain regions that were probed for the above effects. Finally, in an effort to identify sets of regions that may constitute potential brain systems, region-level cross-condition timecourses were extracted and subjected to clustering analyses using multiple clustering algorithms. Four primary observations were made, which, along with our interpretation, are outlined below.

First, we demonstrate that two regions, one in left parahippocampal gyrus (PHG) and the other in the left medial superior frontal cortex (mSFC), stood out from the other examined

regions, satisfying essentially all of the expected semantic properties. Juxtaposed with prior findings (Frankland & Bontempi, 2005; McClelland, 2013; L. R. Squire, Genzel, Wixted, & Morris, 2015; Takashima et al., 2006; van Kesteren et al., 2012), we posit that left PHG and mSFC constitute regions that are critical in the retrieval of memory for recently acquired words, while also continuing to be recruited during retrieval of remote well-established meanings.

Second, despite our expectations based on the ample literature implicating left MTG and left vIFG in semantic processing, the two regions were not recruited during retrieval of novel word meanings. However, the two regions were recruited during retrieval of remote previously known word meanings, although in the case of vIFG, identifying the said effects required using literature-derived regions due to its absence in the study-driven contrasts. We propose that, despite the behavioral semantic priming effects argued to support semantic integration, the novel words require additional exposure and consolidation to engage neocortical regions such as the left MTG. While we do not discount a similar interpretation as above for the lack of engagement of left vIFG by the novel words, we propose an additional explanation. Consistent with prior work implicating left vIFG in controlled semantic retrieval (Badre et al., 2005; Gold et al., 2006; Roskies et al., 2001; A D Wagner et al., 2001), and its absence from multiple studies using lexical decision tasks for which automatic semantic access may be sufficient (Fiebach et al., 2002, 2007; Henson et al., 2002), our task may similarly lack the strategic demand to reliably engage the region.

Third, barring two crucial distinctions (discussed below) between the two proposed semantic regions (i.e. PHG/mSFC) and regions in the left medial/lateral parietal lobe implicated in episodic memory retrieval, the two sets of regions exhibited many similarities, particularly during memory retrieval for novel words. The first distinction is that while PHG/mSFC show BOLD suppression for repeated real words, the parietal regions showed an effect resembling the old > new episodic retrieval success effect (i.e. repetition enhancement) for words. The second more nuanced distinction was that while both sets of regions showed higher BOLD activity for real words relative to novel PWs, the effect was driven by a relatively less negative timecourse for words. The noted distinctions, particularly the word repetition priming effect, provide evidence for a semantic role in PHG/mSFC, and an episodic contribution to the memory retrieval of novel words for the parietal regions.

Fourth, despite identifying several regions exhibiting semantic properties, notably the two top candidates PHG and mSFC, none of the conducted clustering analyses revealed groupings containing the two regions. Similarly, there was no cluster containing canonical semantic regions such as left MTG and vIFG. Hence, we find no evidence for a group of regions that, based on the conducted clustering analyses, could be said to correspond to a semantic brain system. Clustering analysis identified region clusters with good functional neuroanatomical correspondence with well-established systems, such as task-control (Dosenbach et al., 2006, 2007; J. D. Power et al., 2011) and dorsal attention systems (Corbetta & Shulman, 2002). Hence, we believe it is unlikely that the lack of a putative semantic system is a feature specific to this particular dataset. Instead, we propose that semantics may be an

emergent process built on interactions between multiple cognitive processes and corresponding brain systems such as task-control, memory retrieval and sensorimotor/perceptual processing systems.

Taken together, these findings suggest that a relatively small amount of word learning training is sufficient to create novel words that, in young adults, behaviorally resemble the semantic characteristics of well-known words. The functional observations, particularly the lack of engagement of left lateral temporal regions during novel word retrieval, suggests that the novels words require additional time/exposure for adequate consolidation. That said, the fMRI findings identified a parahippocampal and a medial superior frontal region recruited during memory retrieval of both old and novel words. The latter medial prefrontal region in particular has been implicated in integrating new memory with consolidated neocortical memory representations. Overall, we take the fMRI observations as reflective of novel word memory representations that are transitioning to their eventual functional neuroanatomical destination, which would presumably additionally include regions in the temporal neocortex.

Chapter 2: Contextual Meaning Training Creates Novel Semantic Primes for Word Targets with No Direct Prior Association

2.1 Abstract

The level of representation for novel words acquired in adulthood continues to be debated. The debate is whether novel words learned in adulthood get integrated into semantic networks with extant words in the lexicon, or if they are represented separately, e.g. via episodic memory-based representations. Using a semantic priming paradigm, this work provides evidence in support of the former argument, i.e. that novel words acquired in adulthood get integrated to extant semantic networks. Young adults (n=28) were given two types of word learning training administered in multiple sessions spread out over three days. The first type of training provided perceptual form-only training to pseudoword stimuli using a pseudoword-detection task. The second type of training assigned the meaning of common artifacts and animals to pseudowords using multiple sentences to allow contextual meaning acquisition. Using a lexical decision task, a 250-ms-SOA semantic priming test assessed semantic integration using the novel trained items as primes for word targets that had no prior episodic association to the primes. Relative to perceptually trained primes, meaning-trained primes significantly facilitated lexical decision latencies for synonymous word targets. These sets of results are taken as behavioral evidence that the adult subjects have successfully integrated the novel words with existing words in semantic memory.

Key words: word learning, semantic priming.

2.2 Introduction

Vocabulary acquisition in a naturalistic setting, especially in adulthood, is largely accomplished using contextual cues that are present, either in text or speech, as opposed to explicit definitions (Nagy, Anderson, & Herman, 1987). Despite the relative efficiency with which children appear to acquire novel words, the word learning process continues into adulthood and throughout the lifetime (Ramscar et al., 2014; Verhaeghen, 2003). And unlike some specific aspects of language, word learning is not subject to any known critical periods (Newport, Bavelier, & Neville, 2001).

Evidence from the above reports suggests that word learning is a continuous life-long endeavor. Yet, in a seemingly conflicting manner, some prior reports argue that novel words acquired in adulthood get integrated with extant words in the lexicon, while others contend that early vs. late-learned words have distinct, i.e. separate representations. Before delving into specific findings, a brief explication of how a word's representation is characterized is as follows. Leach and Samuel (Leach & Samuel, 2007), outline two properties, lexical configuration and lexical engagement, to characterize the nature of a word's lexical representation. Lexical configuration characterizes factual properties intrinsic to the word itself, such as its orthographic/phonological properties, its syntactic roles etc. Lexical configuration is measured via tests probing explicit knowledge, such as recognition memory tests. On the other hand, lexical engagement characterizes the way a word "dynamically interacts" with other entries in the lexicon at the lexical/semantic or sublexical level. Form priming and semantic priming are examples of tests targeting lexical engagement, the latter of

which will be the current focus, given our goal to dissociate between distinct vs. integrated representations between novel words and existing semantic networks.

As foreshadowed above, there is prior work targeting lexical engagement to demonstrate that novel words acquired in adulthood get integrated with extant words in the lexicon. Using a phoneme detection and a semantic verification task (Dumay et al., 2004) administered word learning training to novel spoken words (e.g. cathedruke) that lexically resemble existing words (cathedral). Following training, they used pause-detection and lexical decision tasks to show that learning a close lexical associate (cathedruke) had a detrimental effect on lexical decision (Dumay et al., 2004) and pause detection (Gaskell & Dumay, 2003) latencies in the base word (cathedral). The slowed base-word processing latency was taken as evidence for lexical engagement between the extant word (cathedral) and the novel lexical entry (cathedruke). Importantly, the lexical engagement effect occurred not immediately after training, but following a period of sleep, deemed necessary to promote information consolidation. Bowers et al. (Bowers, Davis, & Hanley, 2005) demonstrated that following orthographic training (typing), an item such as 'banara' leads to delayed semantic decisions on its orthographically neighboring word 'banana,' attributing the finding to a lexical engagement effect. More relevant here, a study by (Tamminen & Gaskell, 2012) used a contextual word learning paradigm and demonstrated semantic priming effects exerted by the novel word primes on semantically related word targets with no prior association to the primes. Echoing the role of sleep-dependent consolidation for semantic integration, the biggest priming effects were identified after one week. The above studies demonstrate that the representation of novel

words learned in adulthood, even in relatively few experimental sessions, can be integrated with the existing lexicon.

On the contrary, others argue for distinct lexical/semantic representations for words learned early in life, and words acquired in adulthood. Qiao et al. (Qiao et al., 2009) repeated the Bowers et al. orthographic training approach described above, followed by a masked form-priming experiment and failed to find a prime-lexicality-effect (PLE), which they used to counter the Bowers et al integration argument. PLE (Forster & Veres, 1998) is a behavioral effect whereby a word prime produces less form-priming on its orthographically neighboring word (contract-CONTRAST) relative to the form-priming produced by a nonword prime (contrapt-CONTRAST). Countering the Bowers et al. claim, they argued that due to the training exposure, 'banara' could have formed a strong episodic trace. That episodic trace could have then led to a delay in processing its neighbor 'banana' due to the increased need for post-lexical access spelling check, as opposed to lexical engagement, per se. In a more recent publication the Forster group appears to have changed their position. Qiao et al. (Qiao & Forster, 2012) conducted a follow-up experiment that, instead of shallow orthographic training, provided "deeper" meaning training to pronounceable nonwords, hereafter pseudowords (PWs) created as orthographic neighbors to common words, similar to their previous experiments. They used the PLE in a masked form priming setting as a test for lexicalization. Their first experiment, where testing occurred soon after training, failed to find PLE. However, their second experiment that used 4 training sessions spaced out over 4 weeks did produce a clear PLE, which they took as evidence for lexicalization. The latter result, inconsistent with their

earlier claims, converges with the above-mentioned studies arguing that representations for novel words acquired in adulthood get integrated with that of extant words in the lexicon. The latter result is also consistent with the prior reports in highlighting the importance of a consolidation period for lexical integration.

The current study aimed to add support, particularly to the sparse novel word semantic priming evidence (Tamminen & Gaskell, 2012), to aid in the adjudication of the aforementioned conflicting views. This study took a slightly different approach than Tamminen & Gaskell by providing not only contextual meaning training to a set of pseudowords, but also perceptual form training to another set of pseudowords, counterbalanced with the former set. Priming effects on word targets induced by meaning-trained primes were measured relative to priming for words primed by (meaning-neutral) perceptually trained primes as the baseline, potentially allowing for cleaner isolation of automatic spreading activation effects (Neely, 1977). The parallel training and counterbalancing of two groups of pseudowords should also aid in limiting potentially confounding influence from factors such as form priming, as well as other item-specific lexical effects.

2.3 Methods

2.3.1 Subjects

Monolingual (English-speaking), right-handed subjects (n=30, 16 female, 21-30 years, mean age 25 years) were recruited from Washington University and the surrounding community. Individuals with a history of psychiatric and/or neurological illness, or with scores below 50th percentile on Woodcock Johnson III reading assessment (Woodcock & Johnson,

2002) were excluded. Data from two subjects were excluded due to experimental error in one case, and the subject's inability to complete the experiment in the other. All reported data was based on the remaining 28 subjects (Table 2.1).

Age Mean(SD)	**Sex** (M/F)	**Reading Skill** Mean(SD)	**Estimated IQ** Mean(SD)
24.84 (2.70)	13/15	81.25 (8.14)	127.61 (7.00)

Table 2.1 - Subject Demographic and Cognitive Characteristics.
Reading skill percentile scores were computed based on performance in the Letter-Word Identification, Reading Fluency, and Word Attack subtests of the Woodcock-Johnson III (Woodcock & Johnson, 2002). IQ was estimated using the vocabulary and matrix reasoning sections of the WASI (Wechsler, 1999).

2.3.2 Stimuli

A set of concrete nouns (50% animals; 50% artifacts; 3-9 letters; 1-3 syllables) and PWs (5 letters, 1 or 2 syllables) were collected from the English Lexicon Project (D. A. Balota et al., 2007). PWs were divided into three groups. Group 1 (n=90) and group 2 (n=90) served as counterbalanced targets for meaning or form training as described below. Group 3 (n=270) served as novel foils in behavioral tests. To minimize unwanted item effects (Hutchison, Balota, Cortese, & Watson, 2008), PWs across groups 1 and 2, and across animal vs. artifact meaning-training targets, were counterbalanced between subjects and matched in length (5 letters/1-2 syllables), orthographic neighborhood size, bigram frequency, and lexical decision latency (D. A. Balota et al., 2007) (Table 2.2).

	Orthographic neighborhood size	Mean bigram frequency	Lexical decision RT (ms)
Group 1 – meaning or form training target PWs Mean (SD)	2.41 (1.76)	1387.54 (635.46)	746.66 (58.97)
Group 2 – meaning or form training target PWs Mean (SD)	2.47 (2.08)	1410.83 (795.53)	738.86 (46.90)
Group 3 – foil PWs for behavioral testing Mean (SD)	2.37 (1.85)	1359.34 (690.70)	728.94 (58.58)
Group 1 vs. Group 2 2-sample t-test p-values	0.85	0.83	0.32
Group 1 vs. Group 3 2-sample t-test p-values	0.85	0.75	0.02*
Group 2 vs. Group 3 2-sample t-test p-values	0.69	0.58	0.16

Table 2.2: Characteristics of lexical stimuli.
Lexical characteristics of PW stimuli gathered from the English Lexicon Project (D. A. Balota et al., 2007). Note that meaning vs. form training targets (Group 1 and Group 2) are counterbalanced between subjects. *The only potentially remaining difference was in lexical decision RTs between one of the training groups (Group 1) and items reserved for testing (Group 3) ($p = 0.02$, *uncorrected*).

2.3.3 Sentence Construction

A separate behavioral norming study (n=13, age 21-30 years, 5 males) computed cloze probabilities (Taylor, 1953) for sentence stimuli using a "fill in the blank" questionnaire. Cloze probabilities measure the cross-subject probability of completing a sentence with the target word. A total of 5 sentences were selected for each of the 90 meaning-training target words, 4 reserved for training, and 1 for semantic memory testing (described below). The target sentences for animal and artifact words were matched in cloze probability (animals – mean 81%, range 60% – 100%) and (artifacts – mean 77%, range 50% - 100%) (2-tailed paired $t(12) = 1.50$; $p = 0.14$).

2.3.4 Experimental Procedure

The experiment was split into 3 sessions administered over 3 or 4 days. Cognitive testing followed by meaning and form training were conducted on Day 1. Subjects returned on Day 2 for the 2nd half of meaning and form training. Behavioral testing was conducted on Day 3.

2.3.5 Meaning Training

A sentence containing a PW was presented either visually on a screen or aurally via headphones. Subjects first inferred the intended meaning using contextual cues in the sentence, and then named the PW (not the inferred meaning) for recording. For the aural presentations, subjects heard a native English speaker reading the sentences, and upon having inferred a meaning, repeated the PW for recording. The targeted meanings were common animals and artifacts, hence, the sentential training in effect creates synonyms to existing common nouns (e.g. dog, canine). A novel synonym (flosh) for an exemplar target (bee) would be created using 4 randomly chosen sentences (2 visual, 2 aural) from the 5 exemplars shown below, with the 5th sentence reserved for semantic memory testing:

(1) The *flosh* is the farmer's best friend because it helps pollinate flowering plants.

(2) A *flosh* uses nectar as an energy source as well as to produce honey.

(3) Fresh honey is only one of the many benefits of being a *flosh* farmer.

(4) The queen of a honey-producing *flosh* colony may lay 2000 eggs per day during spring buildup.

(5) When a *flosh* stings a person, it leaves behind not only its stinger but also its abdomen and other body parts, which is what kills the insect.

Note that the target word 'bee' is never presented during training.

2.3.6 Perceptual Training

Using visual/aural modalities and designed to parallel the meaning training experiment, subjects were presented with a meaninglessly arranged set of words containing a PW. To promote processing the form-training target PWs at the lexical level, the task required subjects to detect and name the PW aloud for recording. Matching the level of exposure in meaning training, a PW is presented in 4 separate form-training contexts as exemplified below:

(1) Examples allowing families gessy read less if listeners the it high same a mobile has syndromes, great makes.

(2) Syllables half from month is restrain as waves contact or poetry permanently that gessy the general retro tax chief.

(3) Word be chief beings meaning which length are false, or one gessy.

(4) Stakes for five consisting eggs water the define gessy would mobile as it housing, have infectious feature appeal some.

2.3.7 Recognition Memory Test

Subjects made "old/new" recognition judgments on a PW presented one at a time (50% old, i.e. meaning or form trained; 50% new, i.e. foil) using button-presses. Although this test was initially conducted in auditory and visual modalities, design flaws in the auditory experiment led to unusable RT data. As such, the reported recognition memory data are drawn from the

visual paradigm. Although modality was not counterbalanced during testing, the auditory recognition memory data, as well as the aggregated auditory/visual data, exhibited the same trends as the reported visual data.

2.3.8 Semantic Memory Test

A 2-alternative sentence completion test prompted subjects to decide, using button-presses, which of two meaning-trained items best completed a novel sentence. Results were averaged across evenly split visual and auditory trials.

2.3.9 Semantic Priming Test

A visual lexical decision-based semantic priming test was conducted using a short (250ms) stimulus onset asynchrony (SOA), with trials randomly presented for each subject. The prime (meaning or form trained PW) was presented in upper-case for 200ms, followed by a mask (blank screen) for 50ms, followed by a word or novel PW target presented in lower-case for 1000ms. A prime and its corresponding target were never co-presented during training, precluding episodic associations. Using a button-press to allow RT and accuracy assessment, subjects made word/nonword lexical decisions on 90 word and 90 nonword targets. Neither primes nor targets were repeated within subject. Figure 2.1 shows the setup and trial proportions across priming conditions. The three word target conditions (n=90) were:

a) Related by synonymy (30/90 trials): meaning-trained PW prime – synonym word target, (e.g. FLOSH – bee)

b) Unrelated by synonymy (30/90 trials): meaning-trained PW prime – non-synonymous word target (50% animals/50% artifacts) (e.g. FLOSH – spider/table).

c) Neutral: perceptually trained PW prime – neutral word target (random animal/artifact) (e.g. GESSY – cheetah/computer).

The two nonword target conditions (n=90) were:

a) Meaning-trained prime – novel nonword target (e.g. FLOSH – grova; 30/90 trials).

b) Perceptually-trained prime – novel nonword target (e.g. GESSY – slopa; 60/90 trials).

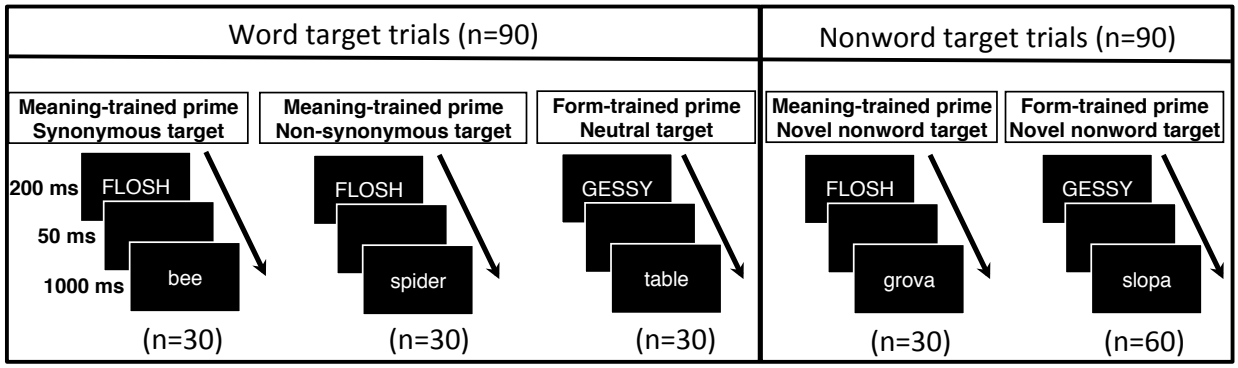

Figure 2.1: Semantic Priming Experimental Design.

2.4 Results

2.4.1 Semantic Memory

Subjects completed the 2-alternative sentence completion test with a mean accuracy of 87% (greater than 50% chance-levels, 1-tailed t(27)=20.1, $p < 0.001$). This test was not structurally suited for using RT as a meaningful behavioral measure.

2.4.2 Recognition Memory

Accuracy

Subjects completed the "old/new" item recognition test with a mean accuracy of 90% (greater than 50%, 1-tailed t(27) = 29.1, $p<0.001$, Table 2.3). Subjects efficiently discriminated

between trained PWs (meaning and perceptually trained on aggregate) and novel foils (d-prime = 2.72; hits = 0.89, false alarms = 0.10). Meaning-trained items were recognized more accurately than perceptually trained items (2-tailed paired t(27) = 2.58, *p*=0.02).

Stimuli	Accuracy	Raw RT (ms)	Normalized RT (z-scores)
Meaning-trained PWs Mean (SD)	0.91 (0.23)	1131.66 (455.12)	-0.23 (0.84)
Form-trained PWs Mean (SD)	0.87 (0.28)	1232.38 (541.21)	-0.09 (0.97)
Foil PWs Mean (SD)	0.90 (0.25)	1380.95 (546.17)	0.22 (0.99)

Table 2.3 - Group Performance in Recognition Memory Test.
The mean and standard deviation (SD) of group accuracy, raw RT in milliseconds, and normalized RT in z-scores are presented separately for meaning-trained, perceptually trained, and foil PWs.

Reaction time

Following prior work (Yap, Balota, & Tan, 2013), extreme outlier RTs above 6000ms and below 200ms were excluded. The remaining RTs were normalized within subject across the three groups of PWs (meaning-trained, perceptually trained, foil). RTs exceeding 2.5 standard deviations (7.5/180 trials on average) were excluded. A one-way repeated-measures ANOVA on normalized RTs showed a significant main-effect across conditions ($F(2,54)=15.15$, $p<0.001$). A post-hoc Bonferroni-corrected pairwise comparison detected differences across all stimulus-group pairs; meaning-trained items were recognized the fastest, followed by perceptually trained items, and foils, respectively (Table 2.3).

Prime type	Target type	Prime/target relationship	Accuracy Mean (SD)	Raw RT (ms) Mean (SD)	Normalized RT Mean (SD)
Meaning-trained PW	Word	Synonymous	0.97 (0.13)	686.80 (148.61)	-0.13 (0.94)
Form-trained PW	Word	Neutral/Unrelated	0.94 (0.21)	722.29 (160.56)	0.11 (1.04)
Meaning-trained PW	Word	Non-synonymous	0.94 (0.18)	702.94 (145.16)	0.02 (0.97)
Meaning-trained PW	Nonword	Meaning-trained prime nonword target	0.96 (0.15)	787.86 (171.66)	-0.08 (0.95)
Form-trained PW	Nonword	Form-trained prime nonword target	0.96 (0.15)	805.36 (178.21)	0.04 (1.01)

Table 2.4 - Group Performance in Semantic Priming Test.
SD = standard deviation.

2.4.3 Semantic Priming – Word Targets

Accuracy

A repeated-measures ANOVA across the three word-target conditions, synonymous (meaning-trained prime → synonymous word target), non-synonymous (meaning-trained prime → non-synonymous word target (50% animals/50% artifacts), and neutral (perceptually trained prime → neutral word target (50% animals/50% artifacts)) resulted in a trend-level main-effect of accuracy ($F(2,54)=2.49$, $p=0.09$). A post-hoc pairwise comparison localized the trend-level effect as higher accuracy for word targets primed by synonymous meaning-trained primes relative to words primed by neutral perceptually trained primes with no semantic relations to the target (Bonferroni-corrected $p=0.04$).

Reaction time

Similar to recognition RTs, outlier RTs (above 3000ms and below 200ms) were initially excluded. The remaining word-target-trial RTs were normalized within subject relative to the mean and standard deviation across the three word-target conditions. RTs above 2.5 standard deviations (4.6/180 trials on average) were excluded. A one-way repeated-measures

ANOVA using normalized RTs across the three word-target conditions resulted in a significant main-effect ($F(2,54)=11.07$, $p<0.001$). A post-hoc pairwise analysis demonstrated faster RTs for words primed by synonymous meaning-trained primes relative to words primed by neutral perceptually trained primes (a 35.48ms priming effect, uncorrected $p<0.001$). Words primed by synonymous meaning-trained primes were also faster than words primed by non-synonymous meaning-trained primes (uncorrected $p<0.005$), 50% of which were related to the target via shared semantic category (animals/artifacts).

2.4.4 Semantic Priming – Nonword Targets

Accuracy

A paired two-tailed t-test revealed no significant difference in accuracy between nonwords primed by meaning-trained PWs and nonwords primed by perceptually trained PWs ($t(27) = 0.52$, $p=0.61$).

Reaction time

RTs for nonword-target trials underwent outlier removal and within-subject normalization, similar to the word-target trial RTs, but conducted separately from the latter. A paired two-tailed t-test revealed faster RT for nonwords primed by meaning-trained PWs relative to nonwords primed by perceptually trained PWs ($t(27)=2.86$, $p < 0.01$).

2.5 Discussion

The primary goal of this work was to provide adjudicating evidence for two contradictory views about how novel words acquired in adulthood are mentally represented. One view contends, as is intuitively consistent with evidence framing word learning as a

cognitive process continuous throughout the lifetime (Ramscar et al., 2014; Verhaeghen, 2003), that novel words acquired in adulthood get integrated into existing lexical/semantic networks. Another view previously argued that words acquired in adulthood (Qiao et al., 2009), or in a second language context (Jiang & Forster, 2001), may be representationally distinct from the first language lexicon, although the group has subsequently modified their argument (Qiao & Forster, 2012). Hence, the current efforts, particularly the approach of using semantic priming to assess lexical integration, were intended to complement prior work and expand our understanding of the adult word learning process.

Young adult subjects were given two types of word learning training spread out over 3-4 days. The first provided form training using a PW detection task, and the second used multiple sentential contexts to imbue PWs with meaning. To assess semantic integration, we used a 250-ms SOA semantic priming paradigm hypothesizing that, relative to neutral perceptually trained primes, meaning-trained primes would facilitate lexical decisions for synonymous word targets. Importantly, we ensured that primes and targets were not episodically associated during training. Finally, to assess declarative memory for trained items, a semantic memory test evaluated appropriate usage of meaning-trained items in novel sentence contexts, and an old/new recognition test measured discriminability of meaning and perceptually trained items from novel foils.

2.5.1 Semantic Memory Test Demonstrated Appropriate Usage of Meaning-Trained Items in Novel Sentence Contexts.

The semantic memory test required subjects to choose between two meaning-trained items to complete a novel sentence. Subjects demonstrated comparable accuracy (~87%) to prior observations (Clements-Stephens et al., 2012). The results confirmed that a multi-context approach is effective in promoting word learning, consistent with prior reports (Bolger, Balas, Landen, & Perfetti, 2008; Mestres-Missé et al., 2008).

2.5.2 Old/New Recognition Test Showed Better Recognition for Meaning Trained Than Perceptually Trained PWs.

Subjects demonstrated discriminability between trained items and novel foils (d-prime ~ 2.7). Recognition performance was faster and more accurate for meaning-trained relative to perceptually trained items. The latter demonstration of better recognition memory for semantically encoded novel words relative to their perceptually encoded counterparts echoes level-of-processing effects repeatedly shown for real words (Craik & Lockhart, 1972; Craik & Tulving, 1975). Depth/level of processing is an effect describing better recall/recognition memory for material studied in a context emphasizing deeper semantic encoding than perceptual (orthography/phonology) encoding alone. The latter finding is suggestive of the representational similarities of the newly acquired words with actual words, given their similar response to the same encoding factor. Because the stimuli used for meaning vs. form training were matched in lexical characteristics, as well as counterbalanced, we attribute the observed superior recognition for the former directly to deeper semantic encoding.

2.5.3 Meaning Trained PWs Became Semantic Primes for Extant Words, Demonstrating Semantic Integration.

As stated above, demonstration of successful semantic priming was the critical test for our novel word semantic integration hypothesis. In line with our expectations, the critical contrast revealed faster lexical decisions for word targets primed by synonymous meaning-trained items relative to words primed by neutral perceptually trained items (a 35ms priming effect). The current priming levels were similar in magnitude to previously reported priming effects in a novel word learning setting (Tamminen & Gaskell, 2012) and slightly less than that reported for real words from similar studies (Hutchison et al., 2008). As justified in greater detail below, we interpret the observed priming effects as evidence that novel words acquired in adulthood get integrated with words in existing semantic networks, attesting to their representational similarity.

Automatic spreading activation (Collins & Loftus, 1975), i.e. strategy-free semantic priming (Neely, 1977; Posner & Snyder, 1975) can arise from three major sources (see the following for extensive reviews (Hutchison, 2003; McNamara, 2005; Neely, 1991)): A) semantic relatedness (Neely, 1977) – the word 'doctor' primes the semantically-related word 'nurse', leading to faster lexical decisions on 'nurse'; B) co-occurrence or frequency of association (McKoon & Ratcliff, 1979; Pecher & Raaijmakers, 1999) – 'mouse' can prime 'cheese' simply because those words are frequently co-experienced, although they are not semantically related; C) mediated priming (D. A. Balota & Lorch, 1986)– although potentially task-dependent (e.g. naming vs. lexical decision), 'lion' can prime an unrelated word 'stripes'

via priming of a semantically related (but not presented) mediator such as 'tiger' in semantic memory.

To support a semantic-integration hypothesis, the current work took steps to safeguard priming effects from potentially being driven by episodic co-occurrence (McKoon & Ratcliff, 1979; Pecher & Raaijmakers, 1999). While several studies have demonstrated priming in a word learning setting, most have been cases where prime and target were co-presented during training (Dagenbach, Horst, & Carr, 1990; Mestres-Missé, Rodriguez-Fornells, & Münte, 2007; Perfetti, Wlotko, & Hart, 2005). To preclude episodic co-occurrence effects, we ensured that the target words were never presented with the primes during training. In addition, subjects were instructed to name the PWs, as opposed to the target words, during meaning training. However, a potentially justified criticism may be that, although not named explicitly, the target words are still mentally invoked during training, hence forming potential episodic associations with the primes. While this is a caveat that cannot be completely refuted, one could potentially levy similar criticisms on the entire notion of semantic priming driven entirely by semantic prime/target relatedness, with no contributions from facilitation due to other (i.e. episodic) factors. To do so, a study would have to ensure in every subject that all prime/target pairs used in a related condition were experienced in the same episode an equal number of times as the number of episodes shared by prime/target pairs in the baseline or unrelated condition. This is of course, at least intuitively, futile, as words that share semantic relationships are also more likely to have been co-experienced relatively more frequently than words with no meaning relations. While measures such as free association norms and co-occurrence frequency have

some relevance in this regard, episodic co-occurrence is just a caveat that will have to be recognized as a factor not completely under experimental control.

Another potentially confounding factor that we took steps to safeguard against was the influence of strategic limited-capacity attention. The priming test used a short SOA (250ms) to minimize strategic effects, and allow automatic spreading activation to drive priming. In addition, priming driven by meaning-trained primes was measured relative to a neutral baseline using perceptually trained primes with no semantic associations that could be triggered by automatic means, hence reducing the need for strategic inhibition processes (Neely, 1977). There is one potential criticism of the study design that maybe levied vis-à-vis the strategic processing concern. Of the 90 total word-target trials, 60 were primed by meaning-trained primes (30 synonymous, 30 non-synonymous) and 30 were primed by perceptually trained primes. The availability of more meaning-trained (2/3 word-target trials) than perceptually trained primes (1/3 word target trials), could potentially inflate priming effects by increasing strategic bias towards a 'word' response for trials with meaning-trained primes. This is another caveat that cannot be ruled out. However, the use of a short 250ms SOA offers some level of assurance against the caveat because the SOA is likely too short to be significantly influenced by strategic processing, which typically requires longer SOAs to manifest its effects. The potential strategic processing concern is further weakened by the fact that, similar to the word-targets, nonword-target RTs were also facilitated when primed by meaning-trained (1/3 trials) relative to perceptually trained primes (2/3 trials), despite the now reversed proportions. Hence, given the apparent dissociative relationship between the proportion of meaning-trained

to perceptually trained primes and the priming effect on word and nonword targets, an argument for potential strategic influences is not straightforward.

Finally, as noted above, the latter finding of a nonword-facilitation effect observed for the newly learned words has interesting parallels in the nonword-facilitation effects previously documented for real words (de Groot, 1984; Neely, Keefe, & Ross, 1989). The nonword facilitation effect is the observation that nonword targets are processed faster when preceded by meaningful word primes than neutral primes (e.g. XXX). Multiple mechanisms have been proposed to explain nonword facilitation, as well as typical semantic priming effects, such as pre-lexical processes driven by prime-induced expectancy and post-lexical processes driven by prime/target relationships (D A Balota & Chumbley, 1984; de Groot, 1984; Neely et al., 1989). A thorough consideration of these mechanisms is beyond the current scope, as it would require careful parametric evaluation of the factors that influence the mechanisms, such as prime/target relatedness proportion and nonword ratio (Neely et al., 1989). Even so, the identified nonword facilitation effect is remarkable, as it is a demonstration of the novel words exhibiting yet another characteristic typical of real words.

2.6 Conclusion

In conclusion, we demonstrate that young adults can learn novel words based on multiple sentential contexts. In accordance with level-of-processing research, contextual meaning training resulted in superior recognition memory for trained items than form training alone. Finally, we provide evidence, via facilitative semantic priming effects without episodic

prime-target association during training, which supports a conclusion that novel words learned in adulthood get integrated in existing semantic networks.

Chapter 3: A Word Learning Approach to Characterizing the Healthy, Young Adult Functional Neuroanatomy Underlying Word-Level Semantic Processing

3.1 Introduction

One component of the remarkable human language faculty is the memory capacity used in the acquisition, integration/consolidation, and retrieval of word meanings. Memory for word meanings, along with general factual knowledge, is generally subsumed by semantic memory, which in turn, is considered a cognitive facility distinct from episodic memory, i.e. memory for an experience associated with a specific time and place, typically involving or directly relevant to the agent (Tulving, 1983). Episodic and semantic memory collectively make up what is known as explicit or declarative memory, characterized as consciously available memory that can be explicitly reported. As elaborated below, episodic memory and semantic memory are generally considered independent processes, largely based on observations of certain neurological memory impairments that exhibit relative selectivity as to the episodic or semantic nature of the resulting deficits. In practice, current understanding of the distinct contributions of episodic and semantic cognitive processes to declarative memory, as well as the potential distinctions in the functional neuroanatomy underlying episodic and semantic memory, is far from complete. To set the stage for the current investigation of the functional neuroanatomy underlying memory retrieval of word meanings, we will provide a brief synopsis of neuropsychological findings integral to the development of subsequent cognitive

theories and computational models of memory organization. Finally, the literature summary will conclude with task-based imaging findings in the episodic and semantic memory domain, their correspondence to neuropsychological and computational work, and potential implications on the hypotheses of the current functional investigation of memory retrieval for newly acquired and existing words.

3.1.1 Neuropsychological Basis for Taxonomy of Memory Systems

Contemporary views of memory as a distinct cognitive function have their genesis in the mid 1900s when neuropsychological research provided convincing evidence associating damage to the medial temporal lobe exclusively with memory impairments in the absence of other deficits (e.g. sensorimotor deficits). Damage to the medial temporal lobe, primarily the hippocampus but also neighboring entorhinal, perirhinal, and parahippocampal cortex, was demonstrated to result in anterograde amnesia (Scoville & Milner, 1957). The memory impairment was marked by the inability to recall recent episodic memory, while remote memory acquired prior to the neurological injury remains unaffected. In a follow-up study (Milner, 1962), Brenda Milner demonstrated that hippocampal amnesics were able to learn motor skills despite no subsequent memory for the learning episode, providing evidence that is the basis for the current implicit vs. explicit memory taxonomy.

Unlike the consensus on the role of the hippocampus in the acquisition of episodic memory, the role of the hippocampus and neighboring MTL structures in the acquisition and retrieval of semantic memory is more controversial. The classic example used as evidence to argue hippocampal involvement in semantic memory incidentally also comes from amnesic

patient H.M. who was the basis for the seminal studies by Milner and colleagues noted above. Following the bilateral MTL resection that led to amnesia, H.M. was also unable to learn and retain new words that emerged since his surgery (e.g. “Xerox”), despite normal memory for semantic information acquired prior to the amnesia (Gabrieli, Cohen, & Corkin, 1988). This led to the hypothesis that the MTL supports both episodic and semantic memory (Shimamura & Squire, 1987; Tulving et al., 1991). On the other hand, an alternative account emerged contending that while the hippocampus is critical for episodic memory, some capacity to acquire semantic memory remains if damage spares neighboring MTL structures, particularly the parahippocampal cortex (Bindschaedler et al., 2011; Holdstock et al., 2002; Mishkin et al., 1998; Verfaellie et al., 2000). However, as counter evidence, proponents of former account argue that relative to healthy controls, semantic memory acquisition in hippocampal amnesics is impaired, and any remaining capacity requires many repetitions, likely attributable to (MTL-independent) implicit memory processes (Glisky et al., 1986; Hayman et al., 1993; Kovner et al., 1983; Shimamura & Squire, 1987; Tulving et al., 1991).

A parallel set of findings associating damage to lateral temporal lobes with selective semantic impairments is used as supporting evidence for functional neuroanatomical distinctions underlying episodic and semantic memory processes. Two neuropsychological observations are relevant. One observation regards comprehension deficits observed in aphasia resulting from left lateral temporal lesions; and the second from semantic impairments observed in the temporal variant of frontotemporal lobar degeneration (tvFTLD) caused by atrophy to bilateral anterior temporal lobes (ATL). In certain aphasias, lateral temporal lesions

(grey matter and underlying white matter), particularly the posterior middle temporal gyrus (MTG) and anterior aspects of the superior temporal gyrus, result in semantic comprehension deficits in tasks such as picture naming, word-picture matching, synonym judgment, and word comprehension (Dronkers et al., 2004; Hart & Gordon, 1990; Turken & Dronkers, 2011). The second observation was of selective semantic impairments (Warrington, 1975) in patients with tvFTLD, also referred to as semantic dementia, characterized by deficits in picture naming, spoken/written word-level comprehension, and category fluency (Hodges et al., 1992). Given that the atrophy is typically bilateral, some investigators contend that both left and right ATL similarly contribute to semantic processing (Visser et al., 2010). Others suggest a left vs. right hemisphere asymmetry associated with verbal vs. perceptual (e.g. names vs. faces) semantic impairments, respectively (Lambon Ralph et al., 2001; Snowden et al., 2004). Taken together, the above observations support a role for left lateral temporal regions (MTG/ATL) in support of word-level semantic processing.

Considered in aggregate, the neuropsychological literature generally points to episodic and semantic memory being distinct processes with distinct underlying functional neuroanatomy. In this distinction, the evidence selectively associating left lateral temporal lobe regions (MTG, ATL) with processes underlying retrieval of semantic memory is relatively uncontroversial. On the other hand, while there is agreement on the critical role of MTL structures in the acquisition of new memory, there are different hypotheses regarding the type of memory in question, i.e. episodic vs. semantic. Some investigators associate MTL with both episodic and semantic memory acquisition, while others forward a more nuanced position

suggesting dissociative roles for the hippocampus vs. neighboring parahippocampal cortex in episodic and semantic memory acquisition, respectively.

3.1.2 Models of Time-Dependent Memory Consolidation

Another important neuropsychological observation led to the current understanding of memory as a dynamic process involving integration of new memory with existing memory in a time-dependent consolidation process, with a parallel time-dependent change in the underlying functional neuroanatomy. In the early 1880s, the French psychologist Théodule Ribot noted a time gradient to the severity of the impairment in certain cases of memory loss due to head trauma (Ribot, 1881). The time gradient was such that memory acquired closer in time to the trauma was more compromised relative to remote memory. Subsequently termed temporally-graded retrograde amnesia, the condition has been linked to medial temporal lobe damage, with more pronounced deficits when damage extends beyond the hippocampus to neighboring entorhinal, perirhinal, and parahippocampal cortex (N. J. Cohen & Squire, 1981; Moscovitch et al., 2006; L. R. Squire, 1992). A consequent hypothesis was that once outside a given time window, memory retrieval is progressively less dependent on the hippocampus and neighboring MTL structures. This change is thought to be due to the migration of memory representations from MTL regions initially critical to acquisition, to neocortical regions representing remote consolidated memories. Based on observations, as noted above, of word-level semantic memory impairments caused by lateral temporal damage, regions like MTG and ATL are proposed as neocortical regions that, following time-dependent memory consolidation mediated by medial prefrontal regions, represent consolidated memory (Atir-Sharon et al.,

2015; Ghosh & Gilboa, 2014; McClelland et al., 1995; McClelland, 2013; Nadel & Moscovitch, 1997; Takashima et al., 2006; van Kesteren et al., 2012). Described below are two exemplar computational models characterizing memory consolidation.

The two models, namely the Complementary Learning Systems (CLS) model (McClelland et al., 1995) and the Multiple Traces Theory (MTT) (Nadel & Moscovitch, 1997) are similar in that both regard the hippocampus as critical to rapid episodic memory acquisition. Both models also generally regard neocortical memory consolidation as a slow time-dependent process. There are two main differences between the two models. First, in the CLS model, the hippocampus is only critical for retrieval and consolidation of recent, i.e. relatively novel memory. For remote memory matching a neocortical representation, the medial prefrontal cortex inhibits the hippocampus to avoid duplicate encoding (Frankland & Bontempi, 2005). On the other hand, in the MTT, the hippocampus continues to be involved in the retrieval and reconsolidation of even remote memory, resulting in multiple hippocampal traces of similar memory representations. The second difference is that while the CLS makes no distinctions between episodic vs. semantic memory, the MTT does. Proponents of the MTT note that in retrograde amnesia, episodic and semantic memory are affected differently such that episodic memory shows a shallow temporal gradient relative to semantic memory (Nadel & Moscovitch, 1997). Hence, in the MTT, the hippocampus continues to be necessary for both recent and remote episodic memory. As for semantic memory, the multiple hippocampal traces of similar recent and remote episodes allow "extraction of factual information…and its integration with…[neocortical] semantic memory stores" (Nadel & Moscovitch, 1997). Hence,

in the MTT, only decontextualized neocortical semantic memory could potentially be retrieved independently of the hippocampus.

Their differences aside, both models highlight an aspect of memory that is of direct relevance here – namely that following acquisition memory undergoes time-dependent consolidation accompanied by a parallel change in the underlying functional neuroanatomy. The direct implication to the current investigation is that, relative to retrieval of remote memory for previously known words, memory retrieval of novel words acquired over 3 days of training could potentially recruit distinct functional neuroanatomy if neocortical consolidation is incomplete. Given the behavioral evidence presented in Chapter 2, particularly the semantic priming findings that suggested the novel words have been integrated with existing words, a reasonable expectation would be to also identify functional neuroanatomy shared by both novel and existing words. Regardless of the findings, the current experiment offers an opportunity for a functional characterization of semantic memory retrieval processes using a dynamic range of remote and recently acquired memory for words.

Next, we provide a brief overview of the relevant task-based imaging literature, from the episodic and semantic memory domain, with the latter also including findings from prior word learning studies. The discussions will also examine the effects of controlled/strategic processing recruited to varying degrees in a task-dependent manner on the functional neuroanatomy of episodic and semantic retrieval.

3.1.3 Episodic Memory Studies Using Task-Based Functional Imaging

While the reasons for discussing prior work in the semantic memory domain may be self-evident, it may be useful to explicitly state the relevance of the task-based episodic literature. One functional effect that is consistently observed in episodic memory studies is the so-called 'retrieval success effect' where items that were previously encountered (old) exhibit higher BOLD activity relative to novel items (new). In the current setting, a similar effect could manifest as BOLD difference between meaning trained (old) and untrained (new) items. The latter effect, which may reasonably be attributed to semantic learning in this context, may instead reflect an effect of stimulus familiarity/novelty, and not semantic processing per se. In fact the potential for stimulus familiarity effects to confound meaning training (i.e. semantic) effects was one of the main reasons behind the current methodological approach of using separate sets of meaning and perceptually trained PWs as stimuli. The aim was to use perceptually trained items as a potential tool for deconfounding, via subtractive inference, semantic effects from (presumed additive) perceptual familiarity effects that may jointly contribute to differences between meaning trained and untrained items. Relatedly, knowledge of the relationships between the functional neuroanatomy of episodic and semantic retrieval can help further constrain current interpretations.

A task frequently used to investigate episodic memory retrieval in imaging studies is the old/new item recognition task. Additional features, such as confidence judgments or remember/know judgments, etc., aimed at targeting episodic sub-processes (i.e. recollection/familiarity), while not irrelevant, are slightly outside the current scope and hence

will not be elaborated further. As noted above, a common BOLD fMRI feature of episodic old/new recognition tests is the 'old>new' retrieval success effect. Regions that consistently show retrieval success effects include left lateral parietal cortex, bilateral precuneus and posterior cingulate, as well as left-lateralized medial and lateral frontal regions (Cabeza et al., 2008; I. G. Dobbins & Wagner, 2005; Nelson et al., 2010; Wheeler & Buckner, 2003; Yonelinas et al., 2005; Yonelinas, 2002). Of relevance here, a similar set of regions in left medial and lateral parietal cortex, with the left angular gyrus as the prime example, has been associated in multiple meta-analytic studies with semantic processing (Binder et al., 2009; Seghier, 2013; Vigneau et al., 2006).

In the context of episodic retrieval, findings from source-memory retrieval tasks are particularly informative for examining the role of controlled/strategic processing on retrieval. In addition to the typical old/new recognition judgments, source retrieval tasks additionally require recollection of the memory source behind the recognition judgment. For example, after making an 'old' recognition judgment on a given item, subjects would have to indicate which training task a particular item was presented in (e.g. perceptual judgment vs. abstract/concrete judgment). Relative to making simple old/new recognition judgment, retrieving source information likely requires greater controlled/strategic processing. Comparison of item recognition to source recollection results in higher BOLD activity in left hemisphere regions including in the MTL (hippocampus/posterior parahippocampus), medial superior frontal cortex, posterior MTG, and left vIFG (I G Dobbins et al., 2002, 2003). The recruitment of the left vIFG and left MTG was specific to retrieval of source memory whose contents are

conceptual (i.e. not perceptual) (I. G. Dobbins & Wagner, 2005). The latter two regions are also consistently implicated in semantic processing, as noted below, with the left vIFG ascribed a domain-specific role in controlled/strategic semantic retrieval (Badre et al., 2005; Donaldson, Petersen, & Buckner, 2001; Roskies et al., 2001; A D Wagner et al., 2001). Consequently, the source retrieval effect in left MTG/vIFG was attributed to a greater demand in semantic elaboration between source and item during conceptual source retrieval, consistent with cognitive theories (I G Dobbins et al., 2002; Daniel L Schacter et al., 1998; Tulving, 1983). The finding that regions typically recruited in semantic tasks (i.e. left MTG and left vIFG) are similarly recruited in a task setting requiring retrieval of specific episodic details, albeit of conceptual makeup, is potentially indicative of the fluid distinction between episodic and semantic retrieval processes.

3.1.4 Semantic Studies Using Task-Based Functional Imaging

Next, we turn to a brief overview of studies using PET and fMRI to investigate semantic processing in healthy adults. A variety of tasks have been used across studies that have resulted in some findings that are convergent, while other findings have been less consistent. Exemplar semantic tasks include abstract vs. concrete judgment (Donaldson, Petersen, & Buckner, 2001; Friederici et al., 2000), verb-generation (J. A. Fiez et al., 1996; Petersen et al., 1988; Roskies et al., 2001), and semantic classification/comparison (Badre et al., 2005; Thompson-Schill et al., 1997; A D Wagner et al., 2001). Typically described as tasks that require controlled/strategic semantic retrieval, the above tasks differ from simpler tasks such as word/nonword lexical decision in which automatic access to meaning may be sufficient

for task performance. Consistent with that argument, while the MTG is commonly recruited by the above controlled semantic tasks as well as simple word/nonword lexical decision tasks, the left vIFG, a region consistently reported in controlled semantic retrieval settings, is absent from many word/nonword lexical decision contexts (Fiebach et al., 2002, 2007; Henson et al., 2002). Reminiscent of the item recognition/source recollection distinctions noted above, the latter finding points to potentially crucial task-dependent distinctions between automatic and strategic retrieval of word meanings (Gold et al., 2006; Neely, 1977; Posner & Snyder, 1975).

The left vIFG and MTG have also previously been associated with repetition priming, i.e. repetition-related BOLD activity suppression effects, in a semantic processing context. Although repetition suppression can occur because of repeated conceptual (i.e. semantic) as well as perceptual processing, prior studies have established some specificity in the underlying anatomical correlates, e.g. extrastriate visual processing regions vs. left IFG/MTG show perceptual vs. conceptual repetition priming effects, respectively (D. L. Schacter & Buckner, 1998; Daniel L Schacter et al., 2007; Wig et al., 2005). In addition to the meaning and perceptually trained stimuli, the current experiment also included real words presented in two fMRI sessions, which offers the opportunity to examine word repetition effects, allowing for the use of conceptual repetition priming as an additional criterion for semantic interpretations.

3.1.5 Word Learning Studies Using Task-Based Functional Imaging

A relatively more recent approach couples behavioral novel-word learning paradigms with brain imaging tools, to investigate the functional neuroanatomy of newly acquired word-meanings. brief summary is provided below of findings from prior word learning studies is

provided below. A brief summary is presented below from prior word learning studies, two of which collected fMRI data as the novel words were being trained/encoded (Breitenstein et al., 2005; Mestres-Missé et al., 2008), and two others which collected fMRI during post-training retrieval. (Clements-Stephens et al., 2012; Sandak et al., 2004).

Using fMRI, Mestres-Missé and colleagues (Mestres-Missé et al., 2008) examined the functional neuroanatomy of meaning acquisition in young adults, during the online acquisition of meaning, using a contextual meaning training approach. The fMRI experiment was designed such that an eight-word sentence is presented, one word every 500ms, with the novel word as the terminal item. They highlighted left lateralized regions in the inferior frontal gyrus, middle temporal gyrus, as well as the parahippocampal gyrus, thalamus, and striatum as regions that support word learning. Of potential concern with the study is that the (somewhat unnatural) stimulus presentation may not be adequately isolating the hemodynamic response function for the target novel word from the neighboring word stimuli in the sentence. It is also likely that the task recruits syntactic processes, which, if variably present across contrasts of interest, may be potential confounds.

Similarly, Breitenstein et al. (Breitenstein et al., 2005) collected event-related fMRI data during the online acquisition of meaning, using a PW-picture association task. A PW was either paired with the same picture presented non-consecutively across training blocks (learning condition) or with a different picture during each presentation (no-learning condition). Their relevant results were that a) across the training blocks in the learning relative to the no-learning condition, a region in the left hippocampus showed BOLD activity

decreases, which was interpreted as potentially reflecting "a sharpening of the neural response over the course of learning," and b) subjects exhibiting *less BOLD suppression* in the same hippocampal region learned the novel words more efficiently, as well as scored higher on verbal semantic fluency tasks. In addition, the study also reported higher BOLD activity, collapsed across learning blocks relative to baseline, in left ventral IFG and MTG, and bilateral STG. However, the latter effect in the frontal and temporal regions was not specific to the 'learning' condition as the 'no-learning' condition also showed similar effects relative to baseline.

In another study, Sandak and colleagues (Sandak et al., 2004) collected fMRI data during a word and PW naming task, following behavioral training conducted on the PW stimuli 1 to 2 hours prior to imaging. Three types of training, each of which provided multiple exposures per item, were conducted on a counterbalanced set of pseudoword stimuli. Orthographic training was conducted using a consonant/vowel pattern judgment task. Phonological training was provided using a rhyme judgment task. The semantic training was conducted in two steps. The first step was a single exposure pairing of a pseudoword with a picture (e.g. butterfly) followed by making semantic category judgments on the trained pseudoword (eight exposures). Relative to both orthographically and phonologically trained pseudowords, semantically trained pseudowords showed higher BOLD activity in bilateral insula and anterior aspects of bilateral MTG/STG; and left-lateralized caudate body, and precentral gyrus; whereas in the left angular gyrus, they exhibited lower BOLD activity (more deactivation). As the authors themselves note, the lower activity (more deactivation relative to

baseline) observed in the angular gyrus for the semantically trained pseudowords is somewhat at odds with a 'semantic' interpretation. Some of the aforementioned regions, particularly bilateral anterior MTG and STG, overlapped with regions that showed higher BOLD activity for real words that had high versus low imageability, further supporting a 'semantic' functional ascription. A potential caveat of Sandak et al. (Sandak et al., 2004) is that fMRI data was collected 1-2 hours after training, with no time allowed for sleep-dependent information consolidation, which may be critical for semantic integration. For instance, it typically takes days following training for novel words to start showing semantic priming effects (Tamminen & Gaskell, 2012).

Similar to Sandak et al. (Sandak et al., 2004) discussed above, Clements-Stephens et al. (Clements-Stephens et al., 2012) used a short-term word learning paradigm, followed immediately by an fMRI session using a lexical decision task. Participants were instructed to give a 'word' response to meaning-trained PWs as well as high- and low-frequency real words, and a 'nonword' response to novel PWs. Lexical decisions with 'word' responses (both real words and meaning trained PWs) showed higher BOLD activity than untrained PWs in left angular gyrus, precuneus/posterior cingulate, and motor cortex. Direct comparisons between real words and trained PWs showed higher BOLD activity for the latter in the left IFG, angular gyrus, and precuneus. The findings reporting higher BOLD activity for real words/meaning-trained PWs relative to novel PWs in the left angular gyrus is divergent from the findings in Sandak et al. (Sandak et al., 2004) that reported *lower* BOLD activity for semantically trained PWs relative to perceptually trained PWs. Although, note that meaning-trained items were

compared with novel PWs in one study and perceptually trained PWs, i.e. not novel, in the other study. In addition, the two studies also differed in the respective contrasts as well as the tasks employed (naming vs. lexical decision), which could partially be responsible for the diverging results. That said, a straightforward argument for the angular gyrus in support of a role in the semantic aspects of word learning is problematic, at least based on the two aforementioned studies. Finally, the Clements et al. results (Clements-Stephens et al., 2012) should be considered with cognizance of the same caveats noted above in Sandak et al. (Sandak et al., 2004) vis-à-vis the single-day training/imaging approach that may not allow adequate time for consolidation/semantic integration.

3.1.6 Summary of Literature Overview

In summary, an aggregate consideration of the neuropsychological and functional neuroimaging research to date reveals both distinctions and similarities in the functional neuroanatomy supporting episodic and semantic memory. First, there is reasonable consensus in the neuropsychological literature that the MTL, particularly the hippocampus, plays a crucial role in novel episodic and semantic memory acquisition, and a relatively semantic-selective role for the parahippocampus. Findings from the prior word learning studies are more or less consistent with the above characterization, which is also in line with memory consolidation models.

Second, regions in the left lateral temporal lobe, namely the ATL and MTG are reliably demonstrated to be critical to retrieval of word-level semantic memory. This is supported by the selective word-level semantic deficits that result from temporal damage or degeneration as

well as from task-based semantic studies, although despite its presence in the PET literature, the ATL is often absent from fMRI studies due to bad signal. Relative to the neuropsychological and task-based semantic studies using real words, the evidence from word learning studies supporting a role for MTG and ATL in learning or retrieving recently learned words is somewhat inconsistent. Consistent with proposals of memory consolidation models, a reasonable hypothesis based on the above summary is that the lateral temporal regions serve as neocortical regions supporting retrieval of consolidated semantic memory.

Third, the left ventral IFG is consistently associated with controlled semantic retrieval. While there is support for a similar role in the lesion literature, there is less anatomical specificity in the reports as the lesions typically extend dorsal and superior to the ventral IFG locus associated with controlled retrieval. In addition, the associated behavioral deficits may not be restricted to word-level semantics, but may involve impairments in syntactic sentence processing as well. Interestingly, the left vIFG, along with left MTG, exhibits a similar role in controlled retrieval of conceptual source memory, although in a task context requiring recollecting specific episodic details. On the contrary, the left ventral IFG is absent from a number of simple word/nonword lexical decision contexts, where automatic access to meaning may be sufficient. Overall, the above summary is in accord with a previously proposed domain-specific role for left vIFG in controlled semantic retrieval, including in task contexts requiring recollection of conceptual information exclusively associated with prior episodic experience.

Unlike the relatively more consistent findings described above, a straightforward assessment is harder for regions in left medial/lateral parietal lobe, which have been reported in the task-based imaging literature in association with multiple processes, including episodic and semantic retrieval. A prime example is the left angular gyrus, which in addition to episodic and semantic retrieval, has also been associated with phonological processing. The same could be said about regions in bilateral middle frontal gyrus reported in the context of episodic and semantic retrieval, and left dorsal IFG, which has been associated with semantic/episodic retrieval, phonological processing, and domain-general task control processes. These observations suggest the need for a more rigorous assessment of the functional properties of the above regions.

Finally, despite some formal efforts in the memory domain (Nelson et al., 2010), a formal clustering-based characterization of semantic regions that may correspond to a putative semantic brain system is, to our knowledge, lacking from the literature. To that end, the current experiment aims to perform clustering analyses based on regional task-evoked timecourses in an effort to identify a potential semantic brain system.

3.1.7 The Current Study

The current study set out to investigate the functional neuroanatomy of semantic processing at the single word level, using fMRI data collected before and after a behaviorally conducted, contextual word learning training administered over multiple days. The fMRI experiment used a simple word/nonword lexical decision task and was setup using a within-item design that allows tighter control for some of the aforementioned potentially confounding

factors. fMRI data was collected using a widely-spaced event-related design, presenting trials once every 20sec, that enabled relatively cleaner isolation of the hemodynamic response function at the item level.

The entire experiment was conducted over 3 days. On day 1, fMRI data was collected while young adult subjects performed a lexical decision task on two classes of stimuli, concrete words (animal/artifact nouns) and pseudowords (PWs). The PWs used during the fMRI session were split into two groups, matched in lexical characteristics as well as counterbalanced, and designated as targets for either perceptual form training or meaning training. Following the fMRI session on day 1 and continuing on day 2, meaning training sessions were administered using sentence contexts to assign meanings to designated PWs. A PW-detection task that paralleled the design and stimulus exposure of the meaning training task, provided perceptual form training to a separate set of PWs. Finally, on day 3, a 2nd fMRI session was conducted post-training using the same lexical decision task, and the same stimuli that were used during the 1st fMRI session, allowing for items to essentially serve as their own controls (i.e. a within-item design). Hence, this approach offers greater control over potentially confounding stimulus-driven factors.

This study directly compared the effects of form vs. meaning training using two classes of stimuli that did not differ prior to training, i.e. they were both novel PWs. PWs given meaning vs. form training were matched in lexical characteristics, counterbalanced across subjects, and presented an equal number of times (four exposures) to ensure matched familiarity levels. Comparing pre- and post-training BOLD activity for stimuli used in meaning

vs. form training is an effort to assess the functional effects on memory retrieval of the corresponding memory encoding approach, i.e. semantic vs. perceptual encoding. The aforementioned contrast will aid in identifying potential dissociations between brain regions sensitive to stimulus semantic content from those that may be sensitive to perceptual familiarity/novelty only.

In addition to the meaning vs. form contrast discussed above, a contrast based on comparing real words repeated across fMRI sessions offers another potential tool to assess semantic characteristics. In particular, the word repetition suppression effect can help in functionally dissociating a region that exhibits conceptual repetition priming for words, from a region showing word repetition enhancement (akin to the episodic old>new effect), allowing for ruling out a semantic interpretation for the latter.

3.1.8 Expected Profile of a Semantic Region

While the current experiment offers several advantages as noted above, there are important considerations that should be noted upfront regarding our methodological approach to targeting semantic processing. As stated above, relative to typical semantic tasks such as making semantic classification/comparison or verb-generation, the lexical decision task used in the current setting may not require controlled/strategic access to word meanings for adequate task performance. Another consideration regards our approach of conducting meaning training over a relatively short 3-day period. Given the time-dependent nature of memory consolidation, we are making the tacit assumption that 3 days has provided for adequate consolidation opportunity for the newly acquired words. Given the behavioral semantic

priming effects documented in Chapter 2, which were suggestive of the integration of novel words with existing words in the lexicon, the latter assumption appears reasonably justified. At the very least, the current experiment offers an opportunity to examine single word semantic representations in adults, and at the earliest time of their formation.

Given the above considerations, outlined below are properties that could be expected from a semantic region that may be jointly recruited during memory retrieval of both newly acquired and existing words:

a) Higher BOLD activity for real words relative to novel PWs;

b) Suppression of BOLD activity for real words repeated across sessions.

c) Higher BOLD activity for meaning-trained PWs relative to novel PWs;

d) Higher BOLD activity for meaning trained relative to perceptually trained PWs;

e) Higher BOLD activity for correctly identified meaning-trained PWs (hits) relative to their incorrect counterparts (misses);

The above criteria roughly capture how a putative semantic region may respond as a function of memory recency. The first two criteria correspond to functional properties expected for retrieval of existing consolidated semantic memory, and the latter three characterize expectations during retrieval of newly acquired semantic memory.

3.2 Methods

3.2.1 Subjects

Monolingual (English-speaking), right-handed subjects (n=30, 16 female, 21-30 years, mean age 25 years), with no history of psychiatric and/or neurological illness, and scoring above the 50th percentile on a Woodcock-Johnson III reading assessment (Woodcock & Johnson, 2002), were recruited from Washington University and the surrounding community. Data from six subjects were excluded due to experimental errors (3 subjects), inappropriately followed task instructions (2 subjects), and inability to complete the entire experiment (1 subject). Of the remaining 24 subjects, 7 subjects were excluded due to inadequate post-training behavioral performance in the scanner (d-prime between meaning-trained PWs vs. perceptually trained PWs). All reported fMRI data were based on the remaining 17 subjects (Table 3.1).

Cohort	Age	Sex (M/F)	Reading Skill	Estimated IQ	2nd fMRI session MT vs. PT d-prime
N24 – Mean (SD)	25.07 (2.85)	11/13	82.26 (8.24)	127.92 (7.09)	1.06 (0.88)
N17 – Mean (SD)	24.60 (2.57)	6/11	82.19 (9.24)	128.71 (6.67)	1.42 (0.80)

Table 3.1: Demographic and cognitive characteristics (fMRI cohort).
The n17 cohort was formed from the n24 fMRI cohort, following removal of 7 subjects with the lowest performance, based on ability to discriminate between meaning and perceptually trained stimuli in the 2nd fMRI session.

3.2.2 Cognitive Characterization

Subjects underwent cognitive testing during their initial visit. Reading skill was measured using the Woodcock-Johnson III (Woodcock & Johnson, 2002) (Letter-Word Identification, Reading Fluency, and Word Attack subtests), with a score above 50th percentile

set as inclusion criterion. The vocabulary and matrix reasoning sections of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) were used to estimate IQ. Selected demographic and cognitive characteristics are displayed in Table 3.1. All aspects of the study, including informed consent, were conducted with Washington University IRP approval.

3.2.3 Stimuli

As documented in Appendix A, a set of concrete nouns (50% animals; 50% artifacts; 3-9 letters; 1-3 syllables) and a set of PWs (5 letters, 1 or 2 syllables) were collected from the English Lexicon Project (D. A. Balota et al., 2007). PWs were divided into two groups. $GRP1_{PWs}$ (n=90) were randomly assigned the meanings of real animal or artifact words and used in meaning training (MT). Real words used as meaning-training targets were separate from words used in the lexical decision task during the fMRI sessions. $GRP2_{PWs}$ (n=90) were given perceptual form training (perceptually trained PWs) using a PW-detection task. As shown in Table 3.2, PWs across meaning/perceptual training groups were matched in length (5 letters/1-2 syllables), orthographic neighborhood size, mean bigram frequency, and normed lexical decision latency garnered from the ELP (D. A. Balota et al., 2007). In addition, to further minimize unwanted item effects (Hutchison et al., 2008), PWs were counterbalanced across meaning/perceptual training groups, and across animal vs. artifact categories within the meaning training group.

Stimulus group	Orthographic neighborhood size	Mean bigram frequency	Normed lexical decision RT (ms)
Meaning-trained (MT) Mean (SD)	2.41 (1.76)	1387.54 (635.46)	746.66 (58.97)
Perceptually trained (PT) Mean (SD)	2.47 (2.08)	1410.83 (795.53)	738.86 (46.90)
MT vs. PT 2-sample t-test p-values	0.85	0.83	0.32

Table 3.2: Lexical characteristics of pseudoword stimuli.
Lexical characteristics gathered from the English Lexicon Project (D. A. Balota et al., 2007). Note that meaning vs. perceptually trained PWs were also counterbalanced between subjects.

3.2.4 Meaning Training

A sentence containing a PW was presented either visually on a screen or aurally via headphones. Subjects first inferred the intended meaning using contextual cues in the sentence, and then named the PW aloud into a microphone for recording. For the aural presentations, subjects heard a native English speaker reading the sentences. Each PW was presented in 4 sentences (2 visual, 2 aural), constraining the inferred meaning. (Refer to Appendix B for stimuli).

3.2.5 Perceptual Training

Using visual/aural modalities as above, subjects were presented with meaningless, sentence-like array of real words containing a PW that was to be detected and subsequently named aloud for recording. (Refer to Appendix C for stimuli).

3.2.6 Experimental Procedure

On Day 1, the 1st fMRI session was administered, during which subjects performed a visually presented word/nonword lexical decision task. Choices, indicated via button-presses using the first digit (thumb) of each hand for the corresponding decision, were recorded to assess accuracy and reaction time. Buttons corresponding to “word” vs. “nonword” responses

were counterbalanced between subjects, with the same configuration used in both fMRI sessions for a given subject. The stimuli (i.e. two classes of PWs reserved for meaning and perceptual training, and common animal/artifact English words) were presented in an interleaved manner using a widely spaced, event-related design to preclude overlapping hemodynamic responses and allow isolation of individual trials. Each experimental run consisted of 24 stimuli (9 meaning-trained PWs, 9 perceptually trained PWs targets, and 6 real words) presented for 1 MR frame (2.5 sec) followed by either 7 fixation frames (22/24 regular trials) or 2 MR frames (2/24 catch trials), allowing for extraction of the event-related time course (Miezin, Maccotta, Ollinger, Petersen, & Buckner, 2000). A total of 10 BOLD runs were collected for each subject during each of the 2 fMRI sessions, with each stimulus presented only once per session.

MR-compatible headphones were used to dampen scanner noise and communicate with participants. Subjects were fit with a thermo-plastic mask molded on their face to minimize head movement. Using a mirror attached to the head-coil, subjects viewed stimuli displayed via Psyscope (J. D. Cohen, MacWhinney, Flatt, & Provost, 1993) installed on an iMAC computer (Apple, Cupertino, CA) and projected via an LCD projector (Sharp model PG-C20XU) onto an MRI-compatible rear-projection screen (CinePlex). Subjects viewed a white fixation cross on a black background, which was always displayed except when a 'word' or 'nonword' stimulus was presented, with each letter subtending 0.5° of horizontal visual angle.

Following the 1st fMRI session, meaning and perceptual training sessions were conducted as described above. Finally, on day 3, the 2nd fMRI session was administered with

one crucial difference from the 1st session: meaning-trained PWs items, which required a "nonword" response during the 1st session, required a "word" response, and hence a different corresponding button-press, during the 2nd fMRI session.

3.2.7 MRI Data Acquisition

Functional and anatomical MRI data was collected on a Siemens 3 Tesla MAGNETOM Trio system (Erlangen, Germany) with total imaging matrix technology (TIM) using a 12-channel head matrix coil. A high-resolution T1-weighted sagittal MP-RAGE was acquired (TE =3.08 ms, TR [partition] = 2.4 s, TI = 1000 ms, flip angle = 8", 176 slices with 1 X 1 X 1 mm voxels). A T2-weighted turbo spin echo structural image (TE = 84 ms, TR = 6.8 s, 32 slices with 2 X 1 X 4mm voxels) matching the acquisition plane of the BOLD images was also collected to improve alignment to an atlas. An auto-align Siemens pulse sequence protocol was used for acquisition alignment to the anterior commissure-posterior commissure (AC-PC) plane. Functional data was collected using a BOLD contrast-sensitive gradient echo echo-planar sequence (TE =27 ms, flip angle = 90", in-plane resolution = 4 X 4 mm). Whole-brain EPI volumes (MR frames) of 32 contiguous, 4 mm-thick axial slices were collected with a TR of 2.5 sec. The first four volumes were discarded to allow net magnetization to reach steady state.

3.2.8 fMRI Data Preprocessing

Imaging data from each subject were preprocessed to remove noise and artifacts, including: (1) correction for movement within and across runs using a rigid-body rotation and translation algorithm (Snyder, 1996), (2) whole-brain normalization to a common mode of

1000 (Ojemann et al., 1997) and (3) temporal realignment using sinc interpolation of all slices to the temporal midpoint of the first slice. Functional data were then resampled to 3 mm isotropic voxels and transformed into stereotaxic atlas space (Talairach, Tournoux, & Rayport, 1988). As described below, unless otherwise stated, all ROI coordinates have been transformed (via linear transformation), and are reported in Montreal Neurological Institute (MNI) atlas space (Mazziotta et al., 2001). For the 1st fMRI session, each subject's EPI was registered to that subject's T2, which was registered to that subject's T1-weighted image, which in turn was registered to a custom atlas-transformed (Lancaster et al., 1995) target T1-weighted template (711-2B, TRIO-Y-NDC) using a series of affine transforms. The data from the 2nd fMRI session was cross-registered with data from the 1st fMRI session using a cross-day realignment procedure (developed by Abraham Snyder). The preprocessed data were subjected to an additional analysis to censor MR frames with a frame-wise displacement movement-exclusion threshold exceeding 0.2 mm (J D Power, Barnes, Snyder, Schlaggar, & Petersen, 2012; Siegel et al., 2013). Subsequently, the entire trial was coded as a movement trial and discarded from group analysis if that trial contained a frame that exceeded the movement-exclusion threshold. Movement frame censoring did not result in data loss that would of concern (treating an individual subject's fMRI data as a sample, separately for the two fMRI sessions, the amount of censored frames relative to an entire sample, expressed in percentage points, exhibited: mean = 1.03, SD = 2.29, min = 0.00, max = 11.82).

3.2.9 General Linear Model-Based fMRI Data Analysis

Statistical analysis was conducted using in-house software programmed in the Interactive Data Language (ITT Visual Information Solutions, Boulder, CO) and C as previously described (Miezin et al., 2000; Ollinger, Corbetta, & Shulman, 2001). BOLD activity related to the trials as well as baseline and trend terms for each BOLD run were modeled using a General Linear Model (GLM). The GLM design for each participant included time as an eight-level factor, made up of the eight MR frames (20 sec, 2.5 sec per frame) during and after stimulus presentation. No shape assumptions were made for the hemodynamic response function. The timecourse of the hemodynamic response function was generated from the estimates for each MR frame. Correct responses, omission errors, and commission errors were coded separately for each trial type. Correct responses were subsequently filtered to include only items that were correct during both the 1st and 2nd fMRI sessions, with the remaining items designated for exclusion from group correct-trial analyses. A single GLM was created for each subject, based on the combined functional data from both the 1st and 2nd fMRI sessions, using a single event-file that separately coded for 1st and 2nd session trials. Reaction time was coded separately as a regressor.

3.2.10 Voxelwise Analysis

In the voxelwise analyses described below, as well as all subsequent region X region analyses, the 'time' factor constituted the hemodynamic response function (HRF) across 8-MR frames. The 8-MR frames included the 1st frame containing presented stimuli and 7 subsequent frames, for a total duration of 20 seconds (8-MR frames X 2.5sec TR). This widely spaced

experimental design allows for using non-overlapping item-level hemodynamic response functions across trials.

Contrasts based on correct trials

Separate voxelwise ANOVAs were initially conducted targeting effects corresponding to the following semantic criteria, as previously outlined. Voxelwise SPMs are shown in Figures (3.1 – 3.4)

a) Word/nonword differences (day 1) (Figure 3.1) – real words vs. novel PWs X time (i.e. the).

b) Cross-session real word repetition (day1/day2) (Figure 3.2) – words on day1 vs. words on day 2 X time.

c) Effects of meaning training (day1/day2) (Figure 3.3) – untrained/novel PWs vs. meaning-trained items (MT) X time.

d) Differences between meaning and form trained stimuli (day 2) (Figure 3.4) – meaning-trained PWs vs. perceptually trained PWs X time.

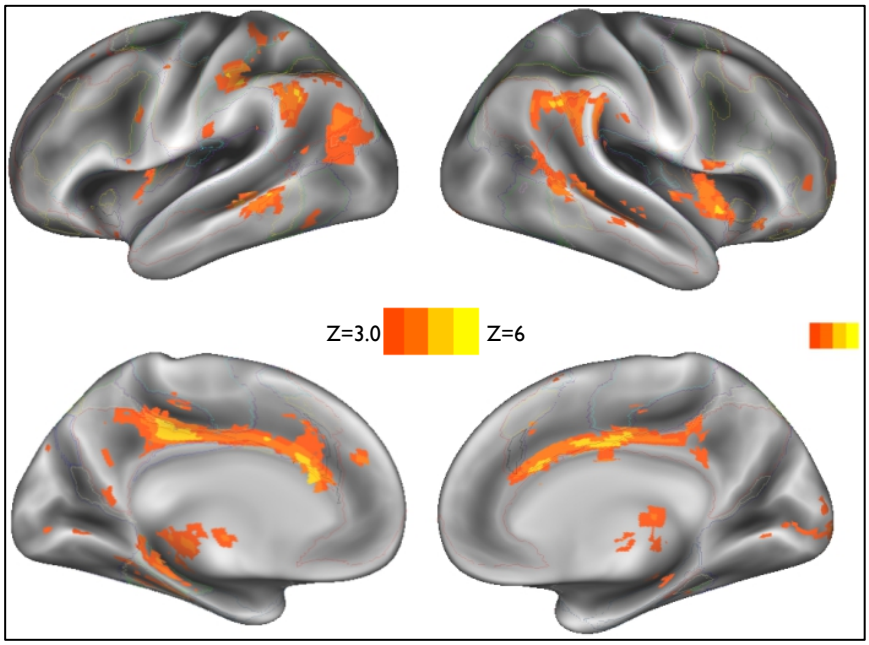

Figure 3.1: Voxelwise Difference Map – Real Words vs. PWs.
Based on a voxelwise lexicality X time ANOVA to identify differences between real words and novel PWs on day 1.

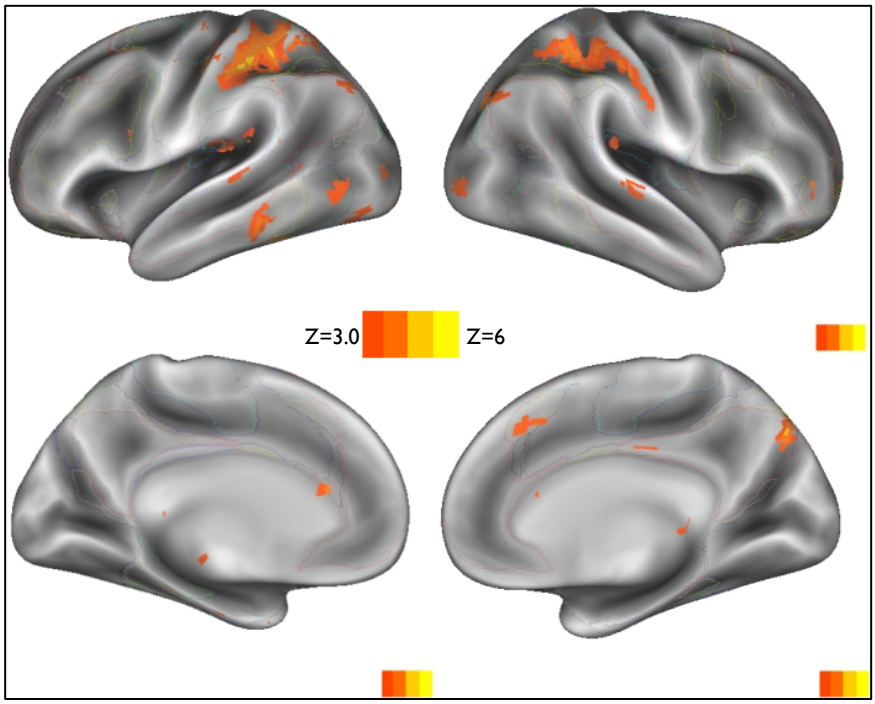

Figure 3.2: Voxelwise Difference Map – Real Words During 1st vs. 2nd Presentation. Based on a voxelwise day X time ANOVA to find cross-day differences for real words.

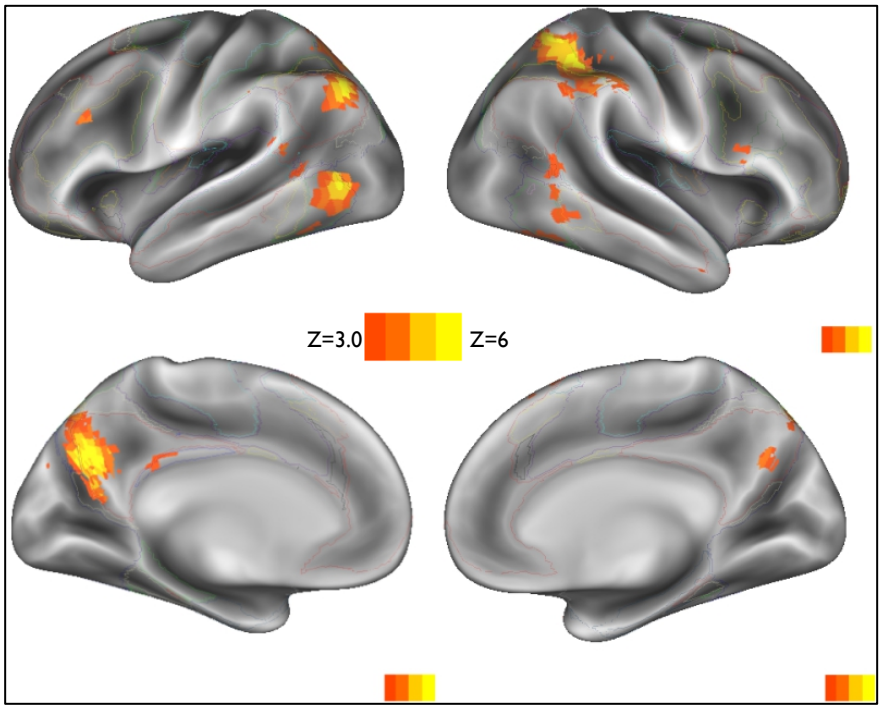

Figure 3.3: Voxelwise Difference Map – Novel vs. Meaning Trained PWs.
Based on day X time ANOVA to identify differences between untrained PWs (day 1) and meaning-trained PWs (day 2)

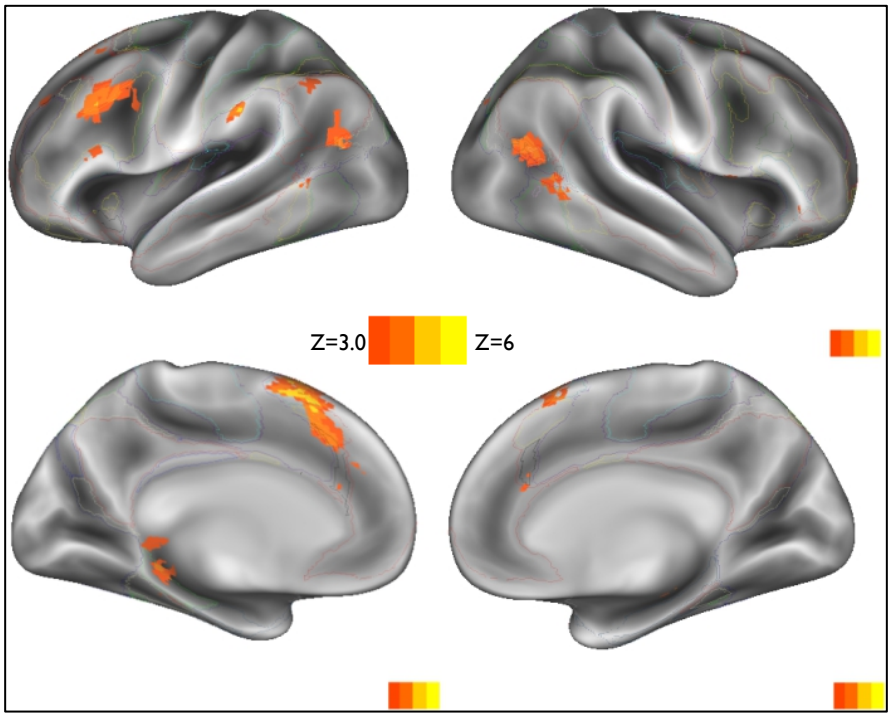

Figure 3.4: Voxelwise Difference Map – Meaning vs. Perceptually Trained PWs.
Based on a voxelwise lexicality X time ANOVA to identify differences between meaning vs. perceptually trained PWs on day 2

Fixed effects analysis across 4 correct trial contrasts

Each of the 4 voxelwise correct-trial SPMs (Figures 3.1-3.4) were thresholded at a Monte Carlo–corrected z-score of 3.0, with a minimum of 13 contiguous voxels (uncorrected $p < 0.001$, corrected $p < 0.05$), and the maximum observed z-score was determined for each of the 4 maps. The map with the lowest maximum z-score was set aside and its z-score was used as a ceiling threshold for the other 3 images. This threshold was applied by setting the values for any voxel exceeding the ceiling in the three images, to the ceiling z-score. This approach ensured that the resulting fixed-effects image would not be overly representative of any one image. Each of the 4 images were then converted into binary masks and summed. Finally, the summed image was divided by $\sqrt{4}$ to generate a fixed-effects image (Figure 3.5).

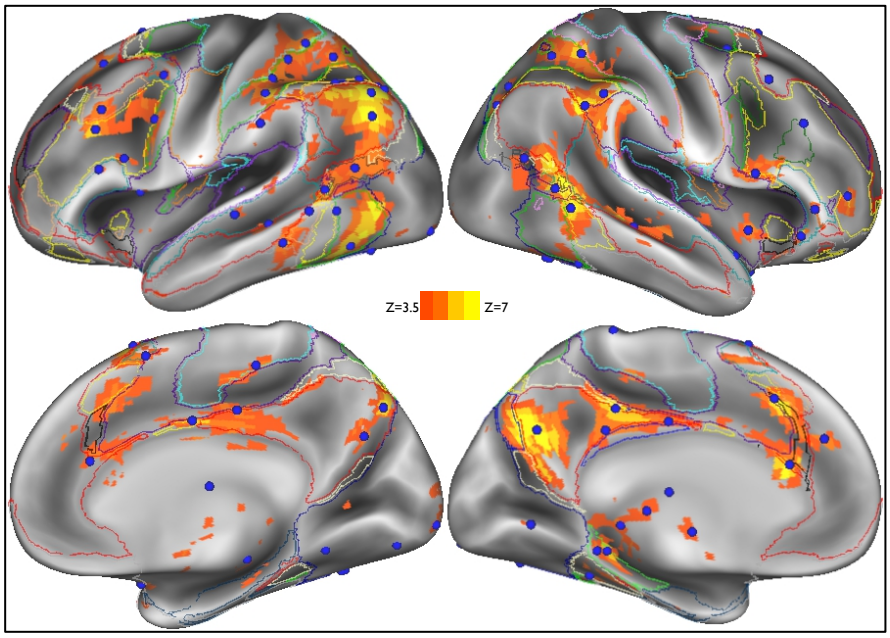

Figure 3.5: Voxelwise Fixed Effects Map of 4 Correct-Trial Individual ANOVA Maps Overlaid with 81 Resulting Peak Regions.

Contrasts based on correct and commission error trials

Two voxelwise ANOVAs were conducted, exclusively based on meaning and perceptually trained PW trials during the 2nd fMRI session, to examine differences between all correct and commission error trials, as well as interactions between accuracy and training group.

a) **Main effect of accuracy collapsed across training group (day 2)(Figure 3.6):** Meaning/perceptually trained item accuracy (hit vs. miss) X time

b) **Interactions between training group and accuracy (day2) (Figure 3.7):** training group (meaning vs. perceptual) X accuracy (hit vs. miss) X time.

The above SPMs were smoothed with a 4-voxel full-width-at-half-maximum (FWHM) smoothing kernel and Monte Carlo corrected at a minimum z-score of 3.5 with at least 7 contiguous voxels (uncorrected $p<0.001$, Monte-Carlo corrected $p<0.05$).

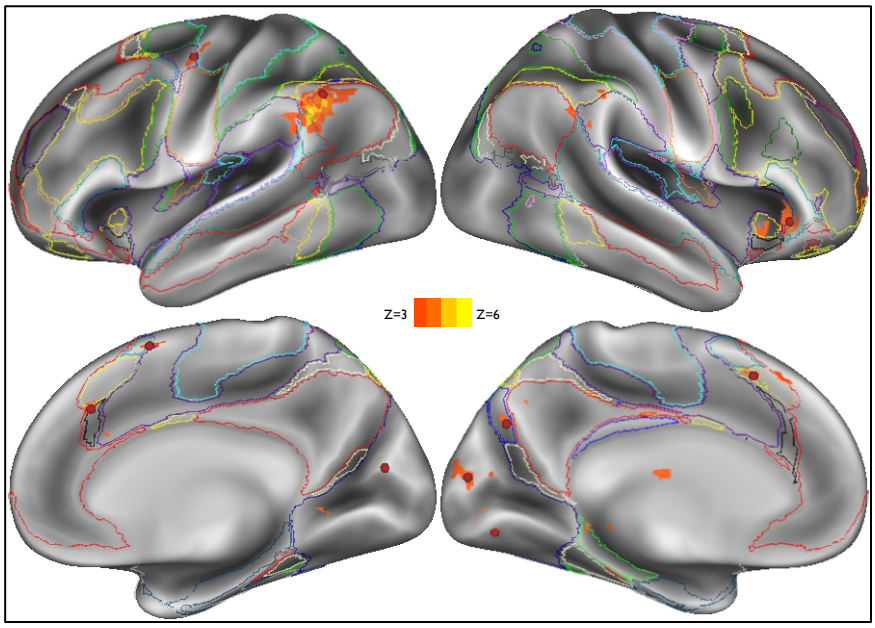

Figure 3.6: Voxelwise Difference Map – Correct vs. Commission Error Trials Collapsed Across Meaning and Perceptually Trained PWs.
Based on a voxelwise accuracy X time ANOVA to identify the main effect of accuracy (correct trials vs. comm. errors) collapsed across meaning and form trained items on day 2. Overlaid are the identified peak regions.

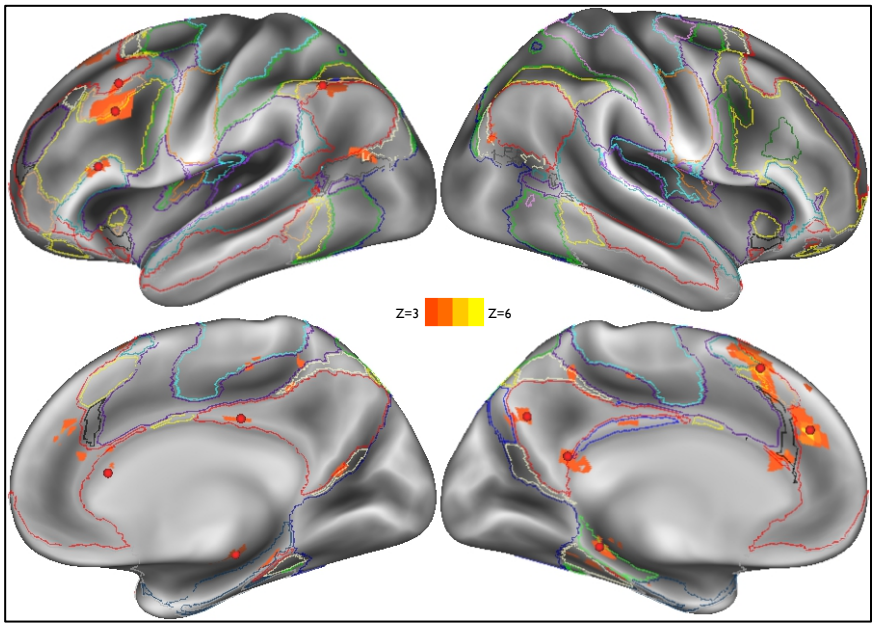

Figure 3.7: Voxelwise Interaction Map – Accuracy (Correct vs. Commission Error Trials) By Training Group (Meaning vs. Perceptual).
Based on a voxelwise accuracy X training group X time ANOVA to identify interactions between post-training accuracy and training group. Resulting peak regions are overlaid.

3.2.11 Region of Interest Generation

10-mm-diameter spherical ROI were separately generated from the fixed effects image based on correct trials and the two images from the error analysis described above. Regions were generated using in-house peak-finding software (peak_4dfp, written by Abraham Snyder) using a 4-mm FWHM smoothing kernel, a z-score bottom threshold of 3.0 (2 error-analysis images) and 3.5 (fixed-effects of 4 correct-trial contrasts and a proximity-exclusion spatial filter of 10mm. As shown in Figure 3.8, a total of 97 ROI were generated, 81 ROI from the fixed-effects image of 4 correct-trial contrasts and 16 ROI from the 2 error-analysis images, respectively. Unless otherwise noted, all ROI coordinates are provided in MNI atlas space (Mazziotta et al., 2001).

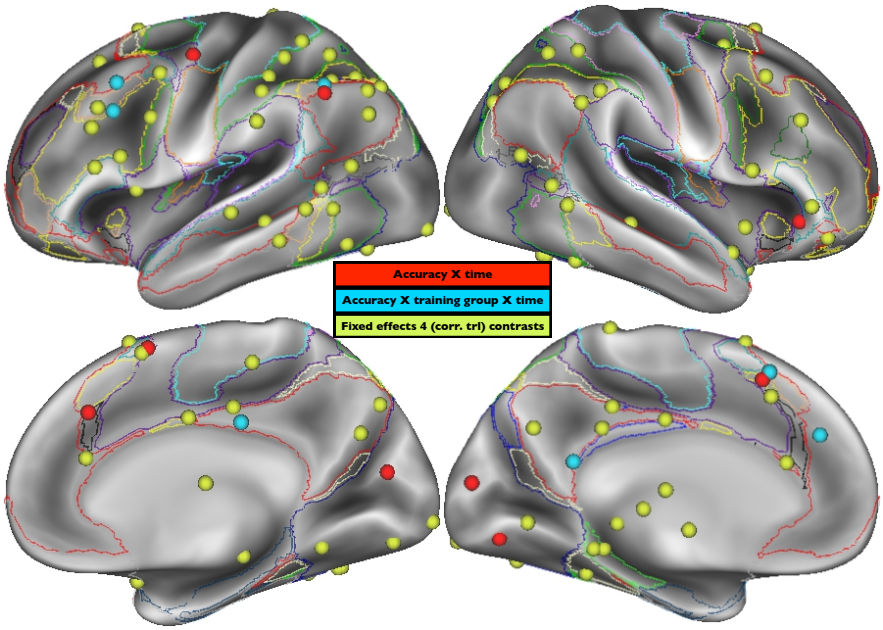

Figure 3.8 - Aggregated Regions (n=97) from Correct Trial and Error Analysis.

We conducted 5 regional ANOVAs on the 97 ROIs (Figure 3.8) generated from the voxelwise fixed effects of 4 correct trial contrasts and the two error analysis contrasts to identify regions showing the hypothesized semantic properties. The results from the regional ANOVAs are presented in Table 3.3.

Infomap Cluster ID	ROI label	Words vs. Novel PWs		Meaning tr. (MT) vs. Novel PWs		Meaning tr. (MT) vs. Perceptual tr. (PT)		Words (day 1) vs. Words (day 2)		Meaning tr. Hit vs. Miss	
1	MedFG -1 18 42	0.000	Words > PWs			0.000	MT > PT	0.000	Day 1 > Day 2		
1	SFG 13 13 59	0.044	Words > PWs	0.004	PWs > MT	0.009	MT > PT	0.043	Day 1 > Day 2		
1	ACC -1 24 20	0.000	Words > PWs			0.020	MT > PT	0.006	Day 1 > Day 2	0.046	MISS > HIT
1	Thalamus 13 -11 13	0.005	Words > PWs	0.023	MT > PWs	0.014	MT > PT	0.049	Day 1 > Day 2		
1	Cingulate 0 36 25	0.000	Words > PWs			0.010	MT > PT	0.008	Day 1 > Day 2		
1	SFG 1 10 62			0.019	PWs > MT	0.000	MT > PT	0.002	Day 1 > Day 2		
1	Insula -45 13 -2	0.000	Words > PWs			0.000	MT > PT			0.069	HIT > MISS
1	Insula 41 9 0	0.000	Words > PWs	0.077	PWs > MT			0.002	Day 1 > Day 2		
1	Thalamus -2 -28 6	0.009	Words > PWs			0.000	MT > PT	0.003	Day 1 > Day 2		
1	Thalamus -6 -18 12	0.046	Words > PWs	0.088	MT > PWs	0.004	MT > PT	0.055	Day 1 > Day 2		
1	SFG -13 9 60					0.000	MT > PT				
1	Insula 48 16 -7	0.030	Words > PWs			0.004	MT > PT	0.007	Day 1 > Day 2	0.035	MISS > HIT
1	mSFC -3 38 27	0.001	Words > PWs			0.000	MT > PT	0.042	Day 1 > Day 2	0.000	HIT > MISS
1	antInsula 38 29 -2	0.025	Words > PWs								
1	Cingulate 5 27 34	0.001	Words > PWs			0.067	MT > PT	0.030	Day 1 > Day 2		
1	mSFC -2 16 50					0.009	MT > PT	0.090	Day 1 > Day 2		
1	mSFC 4 8 68	0.012	Words > PWs					0.035	Day 1 > Day 2	0.079	MISS > HIT
2	pMTG 60 -54 -1	0.002	Words > PWs	0.000	PWs > MT	0.001	MT > PT			0.010	HIT > MISS
2	Fusiform -42 -59 -4	0.011	PWs > Words	0.003	PWs > MT	0.032	MT > PT	0.004	Day 1 > Day 2		
2	SPL 39 -43 53			0.000	PWs > MT	0.018	PT > MT	0.000	Day 1 > Day 2		
2	SPL -26 -52 53			0.000	PWs > MT			0.000	Day 1 > Day 2		
2	IPL -52 -31 39	0.000	Words > PWs	0.086	PWs > MT	0.033	MT > PT	0.002	Day 1 > Day 2	0.052	HIT > MISS
2	PostCenSul -33 -43 58	0.001	Words > PWs	0.005	PWs > MT			0.000	Day 1 > Day 2		
2	SPL 26 -49 50			0.000	PWs > MT	0.039	MT > PT	0.000	Day 1 > Day 2		
2	PostCenSul -40 -30 40	0.000	Words > PWs					0.000	Day 1 > Day 2		
2	Fusiform 42 -57 -18	0.033	Words > PWs	0.001	PWs > MT	0.060	MT > PT	0.000	Day 1 > Day 2		
2	pIPS 29 -65 29			0.014	PWs > MT	0.003	MT > PT	0.000	Day 1 > Day 2		
2	IPS SPL -22 -63 40	0.003	PWs > Words	0.017	PWs > MT	0.056	MT > PT	0.053	Day 1 > Day 2		
2	PostCenSul -35 -38 48	0.053	Words > PWs	0.005	PWs > MT			0.000	Day 1 > Day 2		
2	FEF 30 -4 52			0.009	PWs > MT	0.012	MT > PT				
2	IPS 23 -62 39			0.002	PWs > MT	0.034	MT > PT	0.004	Day 1 > Day 2		
3	MFG -36 24 31			0.000	PWs > MT	0.000	MT > PT	0.001	Day 1 > Day 2	0.004	HIT > MISS
3	MFG -46 18 34			0.003	MT > PWs	0.000	MT > PT	0.039	Day 2 > Day 1		
3	PrecSul -43 6 34	0.001	PWs > Words	0.003	PWs > MT	0.006	MT > PT				
3	IFG -48 9 22	0.018	PWs > Words	0.004	PWs > MT			0.003	Day 1 > Day 2		
3	MFG 48 15 42	0.006	Words > PWs	0.096	MT > PWs	0.033	MT > PT	0.034	Day 2 > Day 1		
3	MFG 52 19 30	0.075	Words > PWs	0.005	PWs > MT	0.046	MT > PT	0.005	Day 1 > Day 2		
3	SMA_premotor -41 1 47			0.005	PWs > MT	0.087	MT > PT	0.007	Day 1 > Day 2		
3	IFGtri -51 24 23					0.079	MT > PT				
3	mSFC -4 22 55			0.014	MT > PWs	0.000	MT > PT				
3	MFG -47 14 42					0.002	MT > PT				
3	MFG -37 14 32					0.000	MT > PT			0.021	HIT > MISS
4	dpAG -38 -67 44	0.000	Words > PWs	0.000	MT > PWs			0.001	Day 2 > Day 1	0.014	HIT > MISS
4	Precuneus -6 -66 32	0.086	Words > PWs	0.000	MT > PWs	0.000	MT > PT	0.061	Day 2 > Day 1	0.001	HIT > MISS
4	AG -43 -57 41	0.000	Words > PWs	0.039	MT > PWs	0.009	MT > PT	0.008	Day 2 > Day 1	0.005	HIT > MISS
4	vpAG -45 -66 32	0.004	Words > PWs	0.001	MT > PWs	0.010	MT > PT			0.000	HIT > MISS
4	SFG -20 23 50	0.000	Words > PWs	0.000	MT > PWs	0.005	MT > PT			0.080	HIT > MISS
4	pIPL -30 -75 52			0.000	MT > PWs	0.040	MT > PT	0.040	Day 2 > Day 1	0.031	HIT > MISS
4	adAG -48 -56 48	0.003	Words > PWs			0.001	MT > PT			0.001	HIT > MISS
4	avAG -47 -56 41	0.005	Words > PWs	0.043	MT > PWs	0.013	MT > PT	0.029	Day 2 > Day 1	0.000	HIT > MISS
4	IPS -33 -62 41	0.044	Words > PWs	0.011	MT > PWs			0.007	Day 2 > Day 1	0.009	HIT > MISS

Table 3.3: Specific Effects of Lexicality in Individual Brain Regions.
Uncorrected p-values (< 0.1) from a condition X time ANOVA are presented. Cell colors correspond to Infomap-based assignment at 8% edge density shown in Figure 3.17.

Infomap Cluster ID	ROI label	Words vs. Novel PWs		Meaning tr. (MT) vs. Novel PWs		Meaning tr. (MT) vs. Perceptual tr. (PT)		Words (day 1) vs. Words (day 2)		Meaning tr. Hit vs. Miss	
5	pMTG_54_-56_11	0.000	Words > PWs	0.000	PWs > MT	0.005	MT > PT	0.004	Day 1 > Day 2	0.089	MISS > HIT
5	SMG_57_-45_35	0.000	Words > PWs	0.008	PWs > MT	0.003	MT > PT			0.056	MISS > HIT
5	pMTG_-53_-53_9	0.002	Words > PWs	0.000	PWs > MT	0.072	MT > PT	0.000	Day 1 > Day 2	0.009	HIT > MISS
5	SPL_precun_12_-71_42	0.004	Words > PWs	0.042	PWs > MT			0.000	Day 2 > Day 1		
5	SMG_54_-37_43	0.008	Words > PWs	0.000	PWs > MT	0.033	MT > PT				
5	TPO_-47_-61_15	0.009	Words > PWs			0.041	MT > PT	0.015	Day 1 > Day 2		
5	Cingulate_7_-21_44	0.000	Words > PWs	0.023	PWs > MT	0.022	MT > PT	0.034	Day 1 > Day 2	0.022	MISS > HIT
5	SMG_-64_-32_30	0.005	Words > PWs			0.000	MT > PT				
5	ParaCenLob_4_-29_51	0.017	Words > PWs	0.015	PWs > MT	0.004	MT > PT	0.012	Day 1 > Day 2	0.011	MISS > HIT
5	TPO_41_-61_19			0.096	PWs > MT	0.000	MT > PT				
6	Cingulate_-4_-35_44	0.000	Words > PWs	0.000	MT > PWs	0.035	MT > PT	0.044	Day 2 > Day 1	0.002	HIT > MISS
6	Cingulate_4_-5_34	0.000	Words > PWs			0.017	MT > PT	0.017	Day 1 > Day 2		
6	Cingulate_-4_-36_32	0.003	Words > PWs	0.003	MT > PWs	0.077	MT > PT				
6	Cingulate_-3_-17_37	0.000	Words > PWs					0.034	Day 1 > Day 2	0.029	MISS > HIT
6	Precuneus_9_-64_29	0.057	Words > PWs	0.001	MT > PWs			0.001	Day 2 > Day 1		
6	PCC_-3_-46_20	0.037	Words > PWs			0.012	MT > PT			0.002	HIT > MISS
6	Cingulate_1_-23_30	0.068	Words > PWs	0.004	PWs > MT			0.016	Day 1 > Day 2	0.036	MISS > HIT
7	Fusiform_-33_-44_-16	0.003	Words > PWs			0.006	MT > PT	0.000	Day 1 > Day 2		
7	CBLM_1_-70_-39	0.021	Words > PWs	0.048	PWs > MT	0.000	MT > PT	0.019	Day 1 > Day 2		
7	LingGyr_20_-97_-4	0.000	Words > PWs			0.047	MT > PT	0.001	Day 1 > Day 2		
7	MTL_-13_-34_2	0.000	Words > PWs			0.016	MT > PT	0.009	Day 1 > Day 2	0.008	HIT > MISS
7	RSP_-3_-59_6	0.000	Words > PWs			0.069	MT > PT	0.006	Day 1 > Day 2	0.039	MISS > HIT
7	PHG_HCP_21_-23_-5	0.007	Words > PWs			0.004	MT > PT				
7	Cuneus_-4_-89_13										
7	Cuneus_1_-67_13									0.006	MISS > HIT
7	LingGyr_-10_-81_-2	0.001	Words > PWs							0.076	MISS > HIT
8	MTG_50_-29_-6	0.001	Words > PWs	0.008	PWs > MT	0.083	MT > PT	0.008	Day 1 > Day 2		
8	MTG_STS_-51_-35_-8	0.000	Words > PWs					0.000	Day 1 > Day 2		
8	ITG_MTG_-59_-42_-12	0.003	Words > PWs			0.079	PT > MT	0.000	Day 1 > Day 2		
8	Fusiform_49_-43_-10	0.013	Words > PWs	0.000	PWs > MT			0.001	Day 1 > Day 2		
8	ITG_-60_-65_-3	0.001	Words > PWs	0.013	PWs > MT			0.026	Day 1 > Day 2		
8	OccPole_-29_-95_-12	0.007	Words > PWs	0.045	PWs > MT			0.008	Day 1 > Day 2		
8	MTG_-65_-52_-1	0.000	Words > PWs			0.001	MT > PT				
9	PHG_-18_-36_-6	0.000	Words > PWs	0.039	MT > PWs	0.002	MT > PT			0.003	HIT > MISS
9	PHG_-26_-39_-5	0.000	Words > PWs	0.000	MT > PWs	0.000	MT > PT			0.002	HIT > MISS
10	IFG_54_27_-3			0.002	PWs > MT	0.009	MT > PT	0.002	Day 1 > Day 2		
10	vaIFG_43_40_-19			0.000	PWs > MT	0.003	PT > MT	0.016	Day 1 > Day 2		
11	CBLM_41_-59_-34	0.021	Words > PWs			0.015	MT > PT	0.007	Day 1 > Day 2		
12	PrecSul_51_12_12	0.009	Words > PWs	0.003	PWs > MT	0.078	MT > PT	0.020	Day 1 > Day 2		
13	SubColGYr_27_8_-15	0.002	Words > PWs	0.006	PWs > MT	0.027	MT > PT	0.015	Day 1 > Day 2		
15	CBLM_-44_-75_-22	0.002	Words > PWs	0.019	PWs > MT	0.076	MT > PT	0.033	Day 1 > Day 2		
16	ParacenLob_-1_-37_76	0.011	Words > PWs	0.013	PWs > MT			0.004	Day 1 > Day 2	0.056	HIT > MISS
17	STG_STS_-58_-22_-3	0.024	Words > PWs	0.035	MT > PWs	0.014	MT > PT			0.005	HIT > MISS
18	CBLM_0_-58_-35	0.001	Words > PWs					0.000	Day 1 > Day 2		
19	Thalamus_-1_-13_-4	0.000	PWs > Words	0.099	PWs > MT			0.070	Day 2 > Day 1	0.087	HIT > MISS
20	PrecGyr_-46_-9_58	0.000	PWs > Words					0.025	Day 2 > Day 1	0.010	MISS > HIT

(Cont.) Table 3.3

3.2.12 Clustering Analysis Used to Identify a Potential Semantic System

To identify a set of regions with similar functional properties that could form a putative semantic system, we used the following clustering algorithms to group regions with similar

timecourse profiles. A hierarchical clustering algorithm and two different community detection algorithms were employed, and results were examined across multiple thresholds.

Hierarchical clustering

For each individual item (i.e. across all BOLD runs and subjects), a 97 ROI X 97 ROI correlation matrix was computed based on the 8 MR frame timecourse, and was subsequently averaged across items to create a group-mean matrix that was fed into the clustering algorithm. Clustering was performed on the group mean ROI X ROI timecourse correlation matrix described above using the unweighted pair group method with arithmetic mean (UPGMA) (Handl, Knowles, & Kell, 2005) implemented in Matlab 12 (The MathWorks, Natick, MA;). The correlations between regions were converted to a distance metric (1 – r), and clustering results were examined across four distance thresholds (0.40, 0.45, 0.50, 0.55). How well the cluster tree represented the real dissimilarities between region clusters was measured using cophenetic-r, a value that should be close to 1. The current dataset had a cophenetic-r of 0.81.

Modularity-based community detection

Modularity optimization analysis was performed on the same cross-item-mean 97ROI X 97ROI correlation matrix described above. The correlation matrix effectively serves as a mathematical graph representation of the network of 97ROI (nodes) with relationships between two regions (edges) represented by their task-evoked timecourse correlation score. Whether a network node (i.e. ROI) can "reach" another node (i.e. an edge is present between the two nodes) is determined by the threshold (of correlation score), which when increased beyond a certain value, will lead to a naturally fragmented network where the edges drop out and nodes cannot "reach" one another. As such, to consider the communities or clusters of regions that

emerge from such analyses as bona fide communities, it is recommended that a graph is at least 80% connected, i.e. there is a path by which 80 % of the nodes can "reach" each other (Fortunato, 2010). Across the range of thresholds examined, based on graphs of > 80 % connectedness, the modularity optimization algorithm is used to determine the network community structure that leads to the highest modularity (Q). Modularity is a measure of the number of connections found within modules compared to the number of connections within modules expected by chance given the number of nodes and connections in the network. The modularity optimization algorithm reports the community assignment for each node such that Q is maximized. Typically, Q values over 0.30 are thought to indicate strong community structure (Fortunato, 2010; Newman, 2006).

Infomap-based community detection

Infomap, considered one of the best-performing clustering algorithms to date (Fortunato, 2010), uses the Map Equation (Rosvall & Bergstrom, 2008) to minimize an information theoretic description of a random walker over the network to define communities. Infomap was applied on the same correlation matrix, across the same thresholds described in the preceding two clustering approaches, allowing for assessment of the consistency of community assignments across analysis methods.

3.3 Results

3.3.1 Behavioral Performance

Group accuracy and reaction time (RT) for stimuli used in the lexical decision task during the 1st and 2nd fMRI sessions are shown in Figure 3.9.

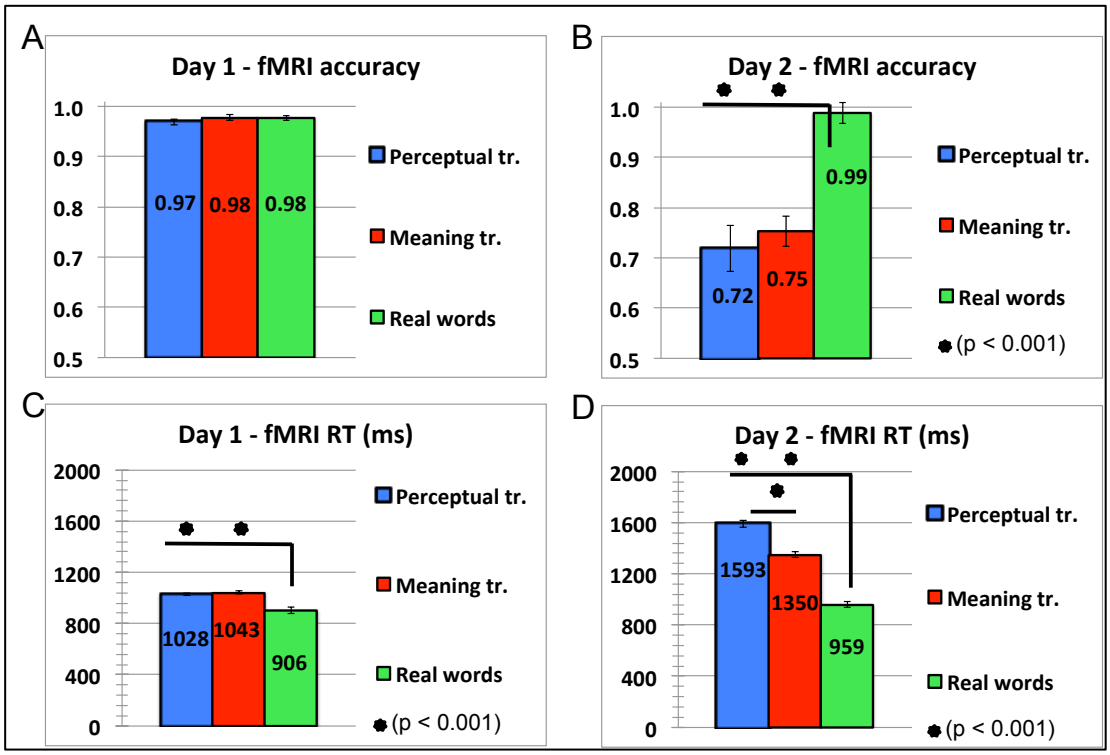

Figure 3.9: Mean Group Behavioral Performance in the Lexical Decision Task During fMRI Sessions.
A) Pre-training accuracy. B) Post-training accuracy. C) Pre-training RT. D) Post-training RT. On day 1, both groups of untrained PWs (meaning/perceptual) exhibited slower RTs relative to real words, but were themselves behaviorally equivalent, as expected. On day 2, while both groups of trained PWs were slower and less accurate than real words, meaning-trained PWs exhibited faster RTs than perceptually trained PWs.

Accuracy

A 2 X 3 repeated-measures ANOVA on accuracy (2 levels of day, 3 levels of lexicality, i.e. words, meaning training PWs, perceptual training PWs) yielded a significant main effect of day ($F(1,16) = 75.42$, $p < 0.001$), a significant main effect of lexicality ($F(2,32) = 16.31$, $p < 0.001$), and a day X lexicality interaction ($F(2,32) = 15.74$, $p < 0.001$). The day effect was driven by higher accuracy on day 1 relative to day 2 (*Bonferroni-corrected* $p < 0.001$). The lexicality effect was driven by more accurate lexical decisions for real words relative to both

meaning-trained PWs (*Bonferroni-corrected* $p < 0.001$) and perceptually trained PWs (*Bonferroni-corrected* $p < 0.001$). Meaning-trained PWs and perceptually trained PWs showed equivalent accuracy (*Bonferroni-corrected* $p = 1.00$).

Given the significant day X lexicality interaction in accuracy, additional ANOVAs were conducted separately for day 1 and day 2, to further localize the source for the interaction. On day 1, a one-way repeated-measures ANOVA conducted across 3 levels of lexicality (words, meaning-training PWs, and form-training PWs) yielded a null effect of accuracy ($F(2,32) = 1.55$, $p = 0.23$).

On day 2, a one-way repeated-measures ANOVA conducted across 3 levels of lexicality yielded a significant difference in accuracy ($F(2,32) = 16.16$, $p < 0.001$), with the pairwise mean-difference localized as more accurate lexical decisions for real words relative to both meaning-trained PWs (*Bonferroni-corrected* $p < 0.001$) and perceptually trained PWs (*Bonferroni-corrected* $p < 0.001$). Meaning-trained PWs and perceptually trained PWs showed equivalent accuracy (*Bonferroni-corrected* $p = 1.00$).

Overall, the observed lexical decision accuracy is as expected. The two groups of PWs as well as real words exhibited equivalent accuracy. Relative to day 1, accuracy levels decreased substantially for both meaning and perceptually trained items, which is not surprising considering that subjects have to discriminate between the two by designating one as a 'word' and the other a 'nonword'. Although depth-of-encoding effects were expected to yield higher accuracy on day 2 for meaning trained items relative to perceptually trained items, the

results did not support expectations. It is possible that the latter effect is partially due to the cross-day stimulus/response switch, i.e. items were 'nonwords' on day 1, and became 'words' on day 2, which may have negatively affected accuracy.

Reaction time

A similar 2 X 3 repeated-measures ANOVA on normalized reaction times (2 levels of day, 3 levels of lexicality, i.e. words, meaning training PWs, perceptual training PWs) yielded a near-significant main effect of day ($F(1,16) = 3.79$, $p = 0.07$), a significant main effect of lexicality ($F(2,32) = 111.72$, $p < 0.001$), and a day X lexicality interaction ($F(2,32) = 43.17$, $p < 0.001$). The near-significant effect of day was driven by faster-trending day 1 RTs relative to day 2 RTs (*Bonferroni-corrected* $p = 0.07$). The lexicality effect was driven by faster RTs for real words relative to both meaning-trained PWs (*Bonferroni-corrected* $p < 0.001$) and perceptually trained PWs (*Bonferroni-corrected* $p < 0.001$). In addition, meaning-trained PWs exhibited faster RTs than perceptually trained PWs (*Bonferroni-corrected* $p < 0.005$).

Similar to the accuracy analysis, RTs were separately analyzed on days 1 and 2 to localize interactive effects. On day 1, a one-way repeated-measures ANOVA conducted across 3 levels of lexicality (words, meaning-training targets, and form-training targets) showed a significant difference ($F(2,32) = 17.54$, $p < 0.001$), with the pairwise mean-difference localized as faster lexical decision RTs for real words relative to both meaning-trained PWs targets (*Bonferroni-corrected* $p < 0.005$) and perceptually trained PWs targets (*Bonferroni-corrected* $p < 0.005$). Meaning-trained PWs and perceptually trained PWs target PWs, exhibited equivalent reaction time (*Bonferroni-corrected* $p = 0.54$). As expected, the two groups of

untrained PWs were behaviorally equivalent on day 1, and both sets exhibited slower lexical decision RTs relative to real words.

On day 2, a one-way repeated-measures ANOVA on normalized reaction times yielded a significant effect ($F(2,32) = 170.25$, $p < 0.001$), with the pairwise mean-difference localized as faster RTs for real words relative to both meaning-trained PWs (*Bonferroni-corrected* $p < 0.001$) and perceptually trained PWs (*Bonferroni-corrected* $p < 0.001$). In addition, meaning-trained PWs exhibited faster RTs than perceptually trained PWs (*Bonferroni-corrected* $p < 0.001$). The latter effect demonstrating faster RTs on day 2 for meaning-trained items relative to perceptually trained items was somewhat surprising, given that meaning training did not result in better accuracy than perceptual training. Despite the stimulus/response switch caveat, it appears there is some evidence in support of a behavioral advantage, albeit only in RTs, gained from deeper semantic encoding afforded by meaning relative to perceptual training.

3.3.2 Left Parahippocampus (PHG) and Left Medial Superior Frontal Cortex (mSFC) Are Involved in Retrieval of Meaning for Both Novel and Existing Words.

The regional ANOVAs and qualitative examination of timecourses revealed two regions, one in the left medial superior frontal cortex (mSFC_-3_38_27), and another in the left parahippocampal gyrus (PHG_-18_-36_-6) that exhibited most of the expected properties making them primary candidates for putative semantic processing regions.

As shown in Figure 3.10 (panels A and B), both PHG ($p < 0.001$) and mSFC ($p < 0.01$) show greater BOLD activity for real English words relative to novel PWs. PHG and mSFC

also show qualitative evidence for suppression of BOLD activity for repeated real words (day 2) relative to day 1 levels (Figure 3.10, panels C and D). Although the latter effect was only significant in mSFC ($p < 0.05$) and not in PHG ($p = 0.17$) in a condition X time ANOVA where all 8 frames of time were used, restricting time to the peak frames (2,3, and 4) results in a stronger trend in PHG ($p = 0.06$). *Overall, these properties support an interpretation that left PHG and mSFC are recruited for semantic retrieval of previously existing word meanings.*

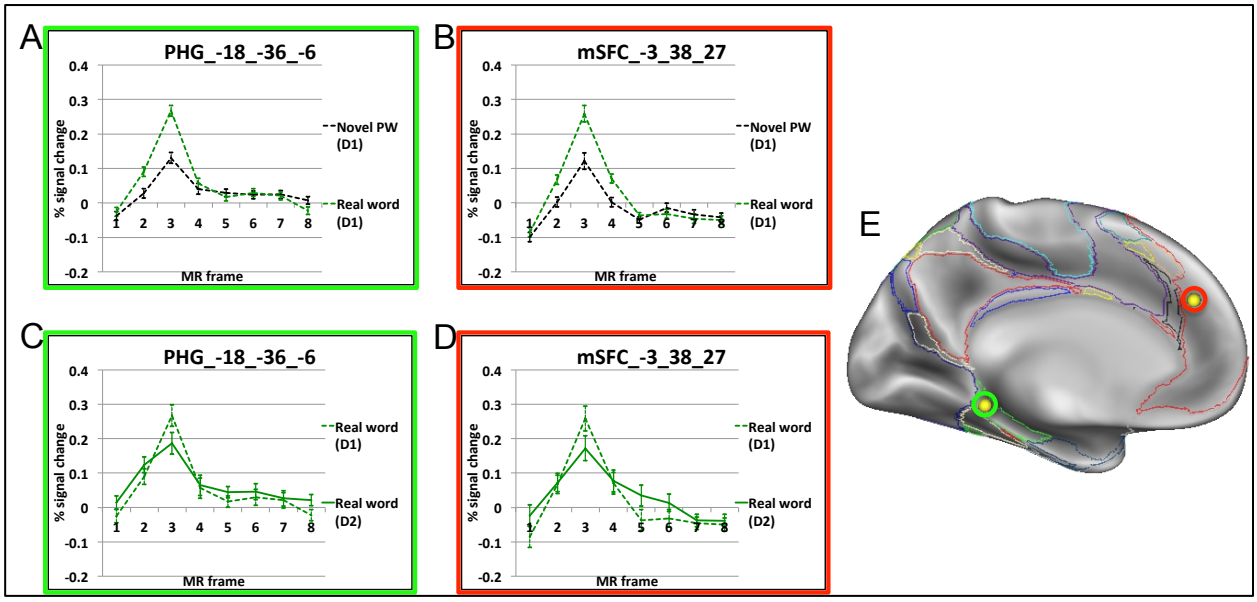

Figure 3.10: Bold Timecourses for Left Parahippocampal Gyrus and Medial Superior Frontal Cortex (E) – Word vs. PW (A, B) and Words in 1st vs. 2nd Presentation (C, D). Timecourses for PHG and mSFC (panel E) for real words vs. novel PWs on day 1 (panels A and B), and real words on day 1 vs. day 2 (panels C and D), respectively. In a condition X time (8MR-frames) ANOVA, both PHG (panel A, $p<0.001$) and mSFC (panel B, $p<0.01$) show higher BOLD activity for real words relative to novel PWs. The two regions also show higher BOLD for words on day 1 than day 2. The effect was qualitative in PHG (panel C, $p=0.17$; in MR-frames 2-4, $p=0.06$) but statistically significant in mSFC (panel D, $p<0.05$). The above properties suggest that left PHG and mSFC are recruited for semantic retrieval of existing word meanings.

In addition, as shown in Figure 3.11 (panels A and B)**,** PHG and mSFC qualitatively show timecourses with higher activity for meaning-trained PWs relative to novel PWs. The condition X time effect was significant in PHG ($p<0.05$) but not in mSFC ($p = 0.22$). Both PHG ($p <0.01$) and mSFC ($p<0.001$) also showed significantly higher activity for meaning-trained PWs relative to perceptually trained PWs (Figure 3.11, panels C and D) on day 2. *Collectively, the above noted properties support an interpretation that left PHG and mSFC support selective semantic retrieval of novel words with associated meanings, relative to perceptually familiar items lacking semantic associations.*

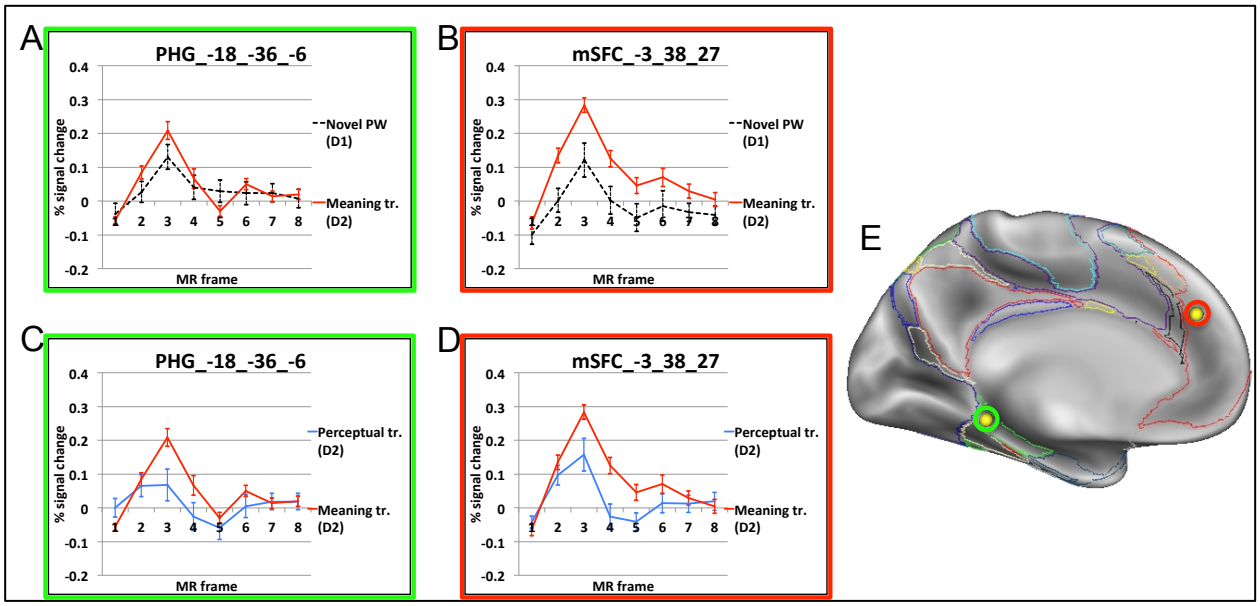

Figure 3.11: Bold Timecourses for Regions in Left PHG and mSFC (E) – Novel vs. Meaning Trained PWs (A, B), and Meaning vs. Perceptually Trained PWs (C, D).
A condition X time (8MR-frames) ANOVA showed significantly higher BOLD for meaning-trained relative to novel PWs in PHG (panel A, $p<0.05$) and a similar qualitative effect in mSFC (panel B, $p=0.22$); as well as higher BOLD for meaning trained than perceptually trained PWs in both PHG (panel C, $p<0.01$) and mSFC (panel D, $p<0.001$). These properties suggest that left PHG and mSFC support semantic retrieval selectively for newly acquired words with semantic associations relative to perceptually trained items unassociated with meaning.

Finally, error trial analysis showed higher BOLD activity for correctly identified meaning-trained PWs (hits) than their incorrect counterparts (misses) in both PHG ($p<0.01$) and mSFC ($p<0.001$) (Figure 3.12, panels A and B). *The latter finding is consistent with the a-priori expected profile of a region involved in semantic retrieval of novel words, in a manner specific to correctly learned meanings.*

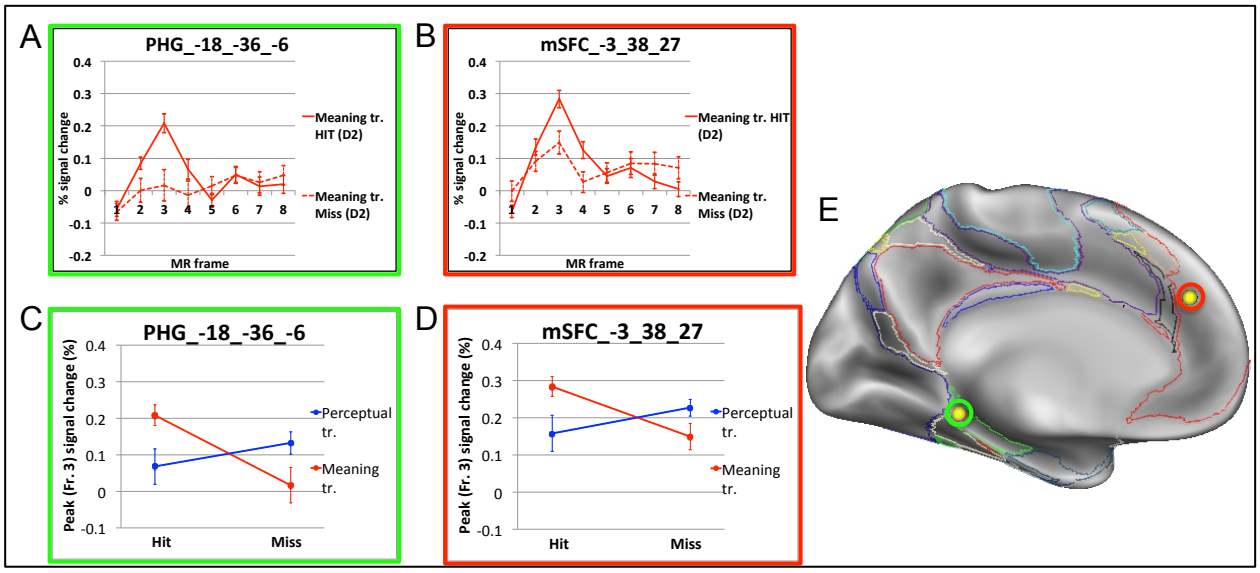

Figure 3.12: Bold Timecourses for Left PHG and mSFC (E) – Meaning Trained Item Hit vs. Miss (A, B), and Meaning + Perceptually Trained Item Hit vs. Miss (C, D).
An accuracy X time (8MR-frames) ANOVA showed higher BOLD for meaning-trained hits than misses in PHG (panel A, $p<0.01$) and mSFC (panel B, $p=0.001$). At peak MR-frame 3, an accuracy (hit vs. miss) X training group (meaning vs. perceptual) regional ANOVA yielded significant interactions in both PHG (panel C, $p<0.01$) and mSFC (panel D, $p<0.001$). Observations suggest that semantic retrieval supported by PHG and mSFC is specific to subjectively perceived meanings, even when associated with the (objectively) wrong word form.

Interestingly, although not explicitly expected a-priori, an interesting observation emerged from the error analysis that was suggestive of the subjective nature of the semantic memory retrieval process. The relationship noted above between meaning-trained hits vs. misses shows the opposite qualitative pattern for perceptually trained PWs. This latter effect was confirmed using a accuracy (hit vs. miss) X training group (meaning-trained vs. perceptually trained) regional ANOVA, using the peak BOLD activity in MR-frame 3, which revealed a significant accuracy X training group interaction in both PHG ($p<0.01$) and mSFC ($p<0.001$) (Figure 3.12, panels C and D). *In essence, this suggests the memory retrieval*

supported by PHG and mSFC is specific to subjectively perceived meanings, even in cases where that meaning is incorrectly associated with the (objectively) wrong word form.

3.3.3 Clustering Analysis Identified Region Clusters Resembling Previously Characterized Brain Systems but a Clear Semantic System Was Not Apparent

To identify a set of regions with similar functional properties that could form a putative semantic system, we conducted clustering analyses using hierarchical clustering (Figures 3.13 and 3.14), modularity optimization (Figure 3.15), and Infomap algorithms (Figure 3.16), which revealed qualitatively similar region clusters. Across the thresholds examined, the two putative semantic processing regions were not clustered together by any of the three algorithms.

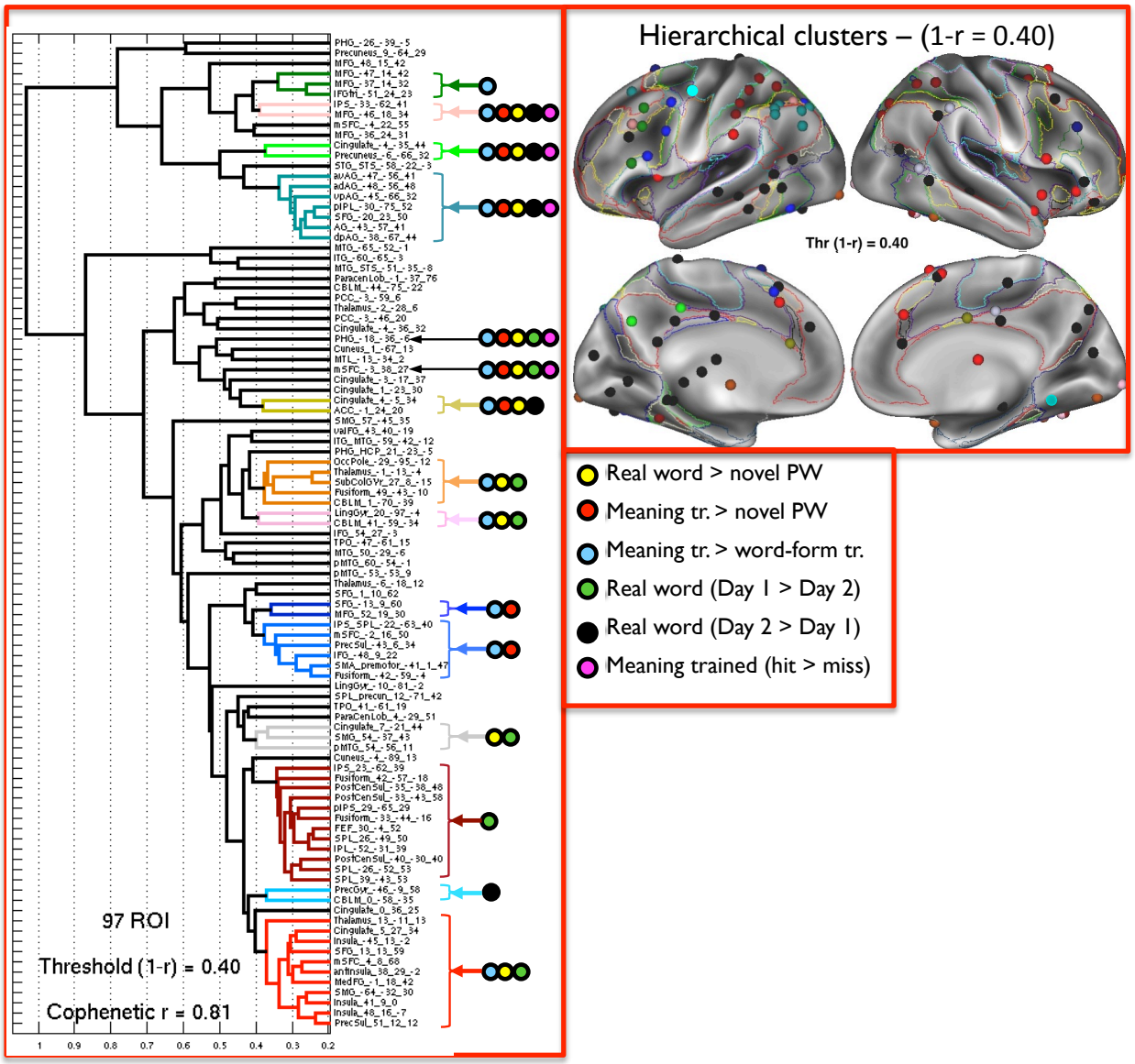

Figure 3.13: Hierarchical Cluster Tree of 97 ROI Task-Based Timecourses.
Results from hierarchical clustering analysis (UPGMA) showing the cluster tree at a 1-r threshold of 0.4. Regions shown in black (panel E) did not belong to any clusters. Note that the PHG and mSFC ROI (black arrows) are among the regions not placed in any clusters. Clusters have been coded with significant effects from a regional condition X time ANOVA, indicated by the colored circles (left panel).

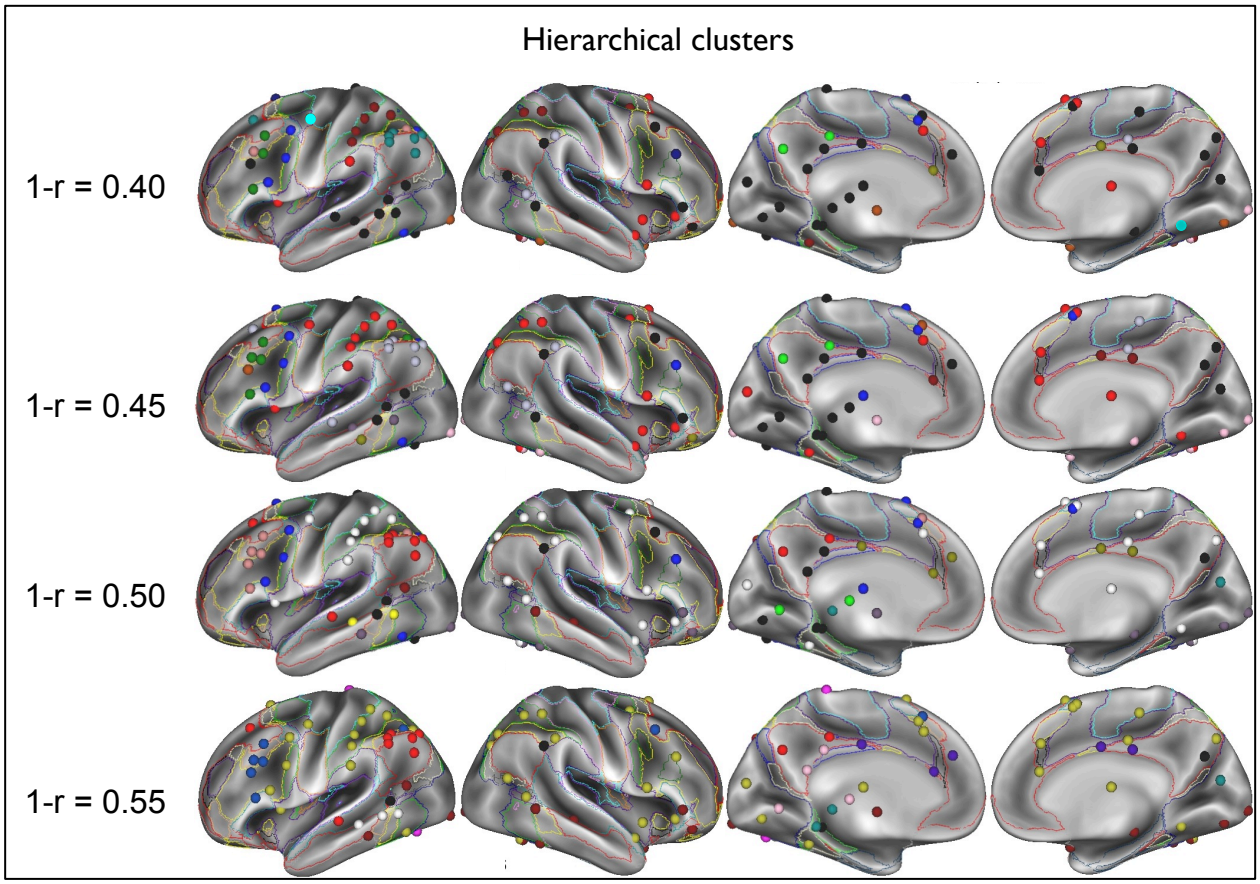

Figure 3.14: Hierarchical Clusters Across Thresholds.
For reference, a cluster tree at a threshold of 1-r = 0.4 is displayed in Figure 3.13. While there were region clusters fairly consistent across thresholds (e.g. a left lateral parietal cluster), none jointly contained PHG and mSFC.

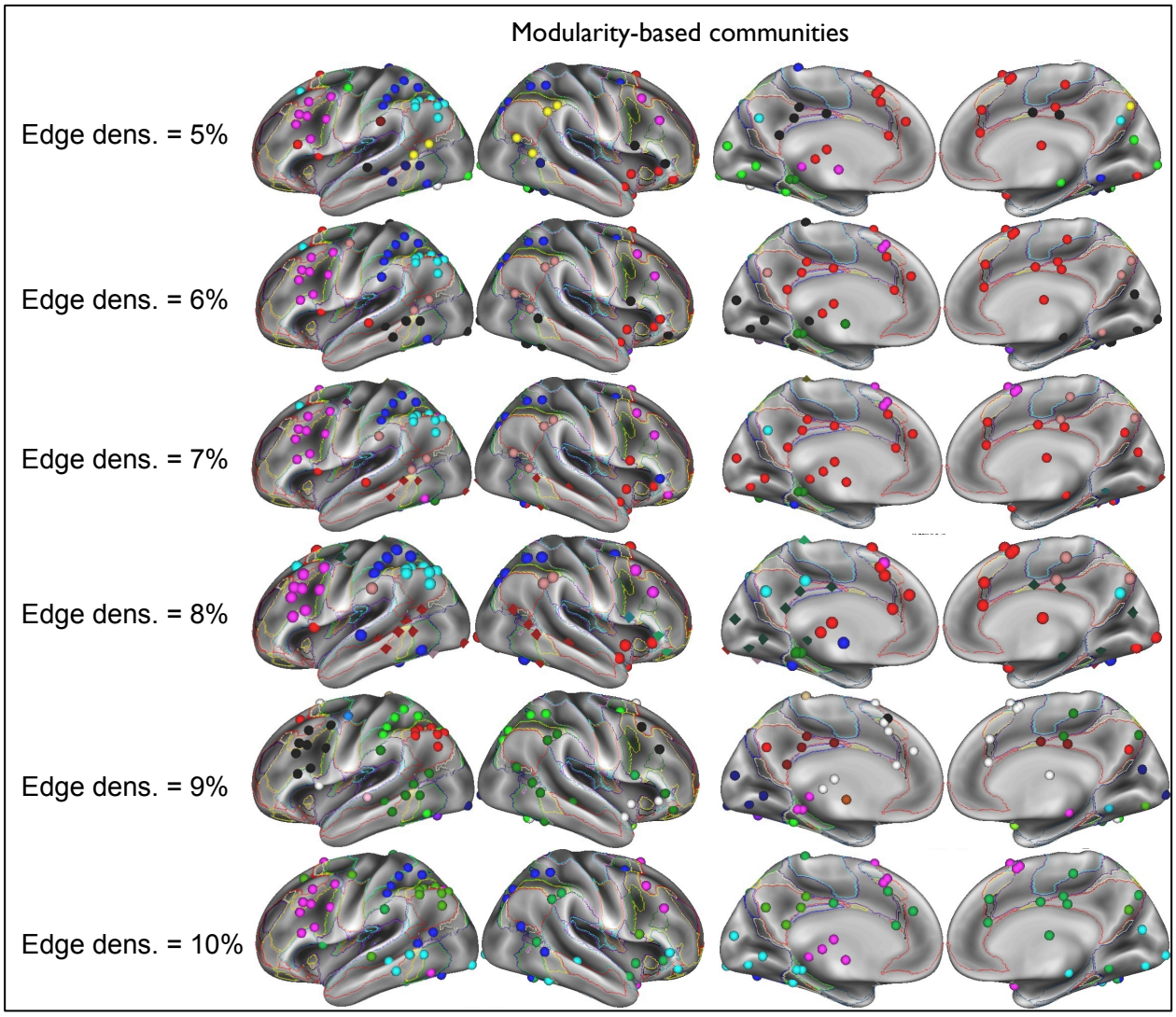

Figure 3.15: Modularity-Based Region Communities Across Thresholds.
Communities obtained from Modularity Optimization analyses are displayed across thresholds spanning 5% - 10% edge density. While there were region clusters fairly consistent across thresholds (e.g. a bilateral frontal cluster resembling frontoparietal control system), none jointly contained PHG and mSFC.

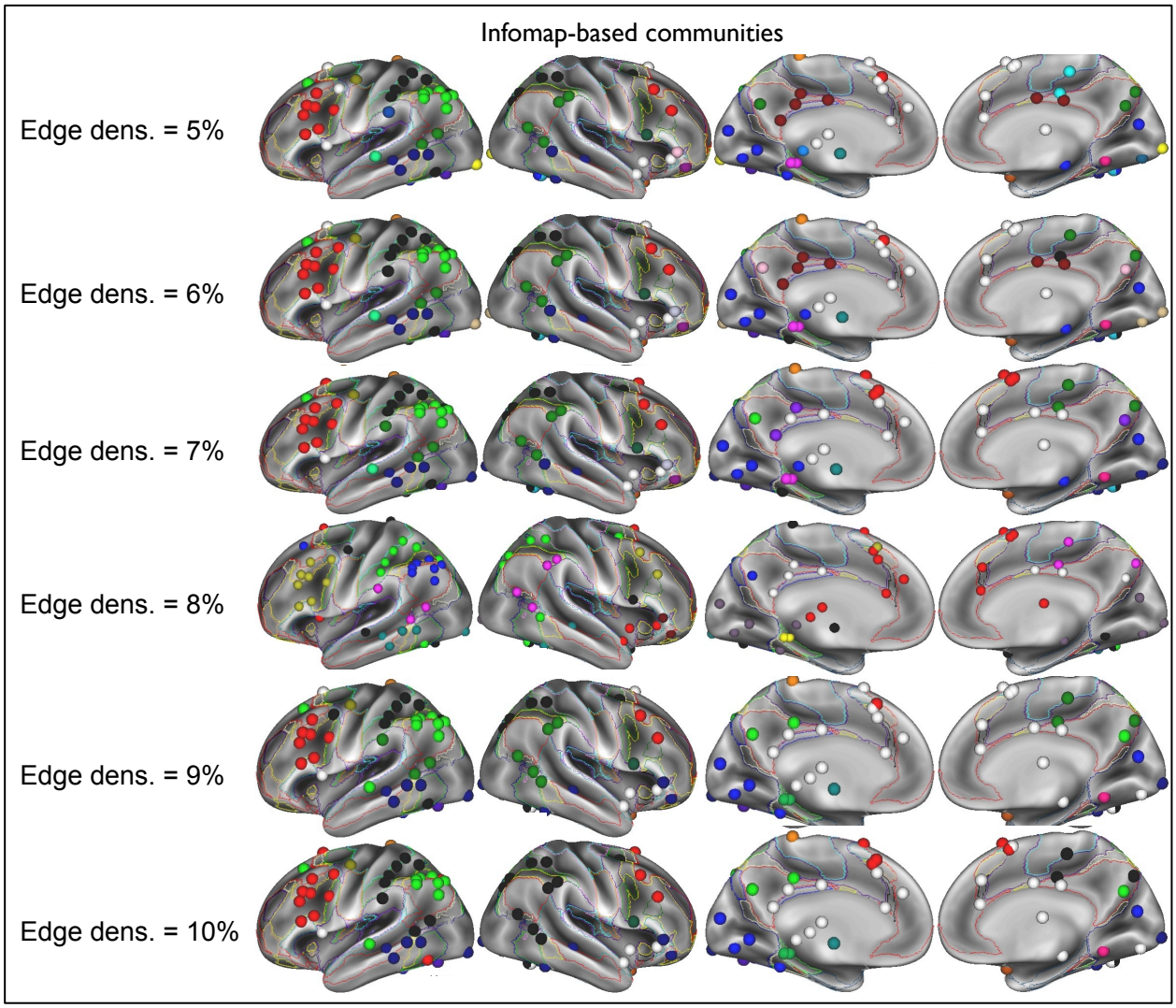

Figure 3.16: Infomap-Based ROI Communities Across Thresholds.
Communities obtained from Infomap analyses are displayed across thresholds spanning 5% - 10% edge density. While there were region clusters fairly consistent across thresholds (e.g. bilateral parietal cluster resembling dorsal attention system), none jointly contained PHG and mSFC.

An infomap-based clustering scheme at 8% edge density (Figure 3.17), which yielded the highest-obtained modularity value (Q = 0.46), was chosen to investigate cluster properties. Results from regional ANOVAs targeting specific semantic effects conducted on the Infomap-based clusters are shown in Table 3.4.

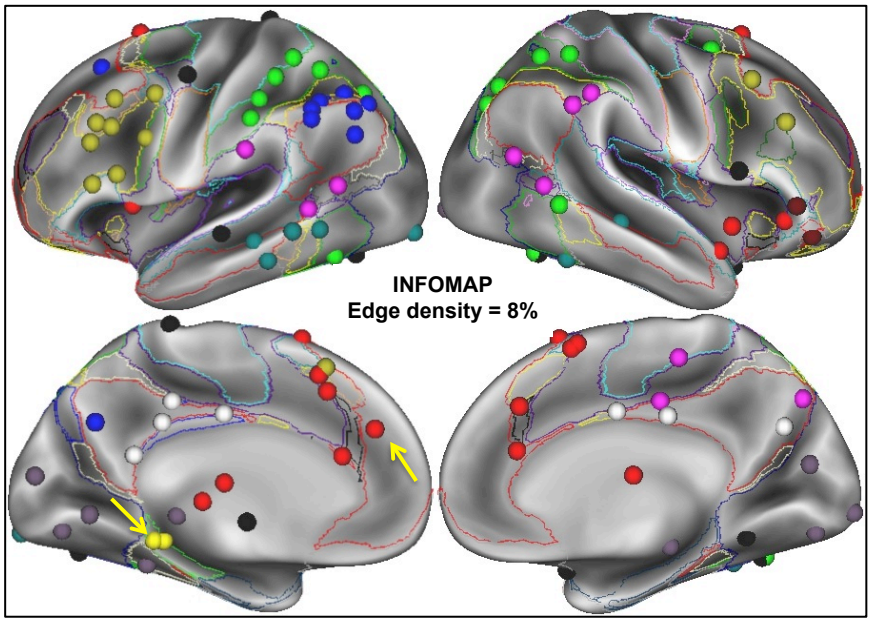

Figure 3.17: Communities Obtained from Infomap Analysis Resulting in the Highest-Obtained Modularity Value.
The highest-obtained modularity value (Q = 0.46) was found at 8% edge density. The two putative semantic processing regions (yellow arrows) were placed in separate clusters.

Cluster/ROI	Words vs. Novel PWs		Meaning tr. (MT) vs. Novel PWs		Meaning tr. (MT) vs. Perceptual tr. (PT)		Words (day 1) vs. Words (day 2)		Meaning tr. Hit vs. Miss	
Cluster_1	0.000	Words > PWs			0.000	MT > PT	0.000	Day 1 > Day 2		
Cluster_2	0.064	PWs > Words	0.000	PWs > MT			0.000	Day 1 > Day 2		
Cluster_3			0.003	PWs > MT	0.000	MT > PT	0.065	Day 1 > Day 2		
Cluster_4	0.000	Words > PWs	0.000	MT > PWs	0.001	MT > PT	0.003	Day 2 > Day 1	0.000	HIT > MISS
Cluster_5	0.000	Words > PWs	0.003	PWs > MT	0.000	MT > PT	0.004	Day 1 > Day 2	0.002	MISS > HIT
Cluster_6	0.000	Words > PWs	0.013	MT > PWs	0.007	MT > PT			0.003	HIT > MISS
Cluster_7	0.000	Words > PWs			0.010	MT > PT	0.018	Day 1 > Day 2	0.046	HIT > MISS
Cluster_8	0.000	Words > PWs	0.033	PWs > MT	0.048	MT > PT	0.000	Day 1 > Day 2		
Cluster_9	0.000	Words > PWs	0.008	MT > PWs	0.000	MT > PT			0.001	HIT > MISS
Cluster_10			0.001	PWs > MT	0.001	MT > PT	0.001	Day 1 > Day 2		
PrecGyr_-46_-9_58	0.000	PWs > Words					0.025	Day 2 > Day 1	0.010	MISS > HIT
Thalamus_-1_-13_-4	0.000	Words > PWs					0.070	Day 2 > Day 1	0.087	HIT > MISS
CBLM_0_-58_-35	0.001	Words > PWs					0.000	Day 1 > Day 2		
STG_STS_-58_-22_-3	0.024	Words > PWs	0.029	MT > PWs	0.014	MT > PT			0.005	HIT > MISS
ParacenLob_-1_-37_76	0.011	Words > PWs	0.058	PWs > MT			0.004	Day 1 > Day 2	0.056	HIT > MISS
CBLM_-44_-75_-22	0.002	Words > PWs	0.006	PWs > MT	0.076	MT > PT	0.033	Day 1 > Day 2		
SubColGYr_27_8_-15	0.002	Words > PWs	0.002	PWs > MT	0.027	MT > PT	0.015	Day 1 > Day 2		
PrecSul_51_12_12	0.009	Words > PWs	0.026	PWs > MT	0.078	MT > PT	0.020	Day 1 > Day 2		
CBLM_41_-59_-34	0.021	Words > PWs			0.015	MT > PT	0.007	Day 1 > Day 2		

Table 3.4: Specific Effects of Lexicality in Infomap-Based Region Clusters.
Uncorrected p-values (< 0.1) from a clusterwise condition X time (8MR-frames) ANOVA on the Infomap clusters at 8% edge density (Figure 3.17). The direction of the effect is based on mean BOLD activity across 8MR-frames. Cell colors correspond to the Infomap cluster groupings shown in Figure 3.17.

3.3.4 A Cluster of Predominantly Left Parietal Regions May Support Episodic-Memory Based Retrieval of Word Meaning

The clustering analysis revealed several clusters that have previously been identified, based on task-evoked as well as resting-state fMRI data, as distinct clusters that likely represent discrete brain systems. One such prominent cluster (Cluster 4, shown in blue in Figure 3.18, panel E), which was consistently identified across thresholds and algorithms, is a cluster containing left-lateralized regions in lateral and medial parietal cortex and superior frontal cortex that have previously been implicated in episodic memory retrieval (resembles AG-mPFC cluster in Nelson et al. (Nelson et al., 2010)). Some of the constituent regions, most notably the left angular gyrus, are also frequently associated with semantic processing (Binder et al., 2009; Seghier, 2013; Vigneau et al., 2006). Cluster 4 exhibits a number of properties, particularly in contrasts targeting newly acquired meanings, consistent with a semantic interpretation. Figure 3.18 shows properties that Cluster 4 exhibits similar to a Cluster 9, a cluster containing one of the identified parahippocampal regions (shown in yellow, Figure 3.18, panel E). As shown in Figure 3.18 (panels A and B), both clusters show higher BOLD activity for meaning trained PWs relative to both novel PWs and perceptually trained PWs (all p-values < 0.005), consistent with two of the a-prior semantic criteria. In addition, as shown in Figure 3.18 (panels C and D), both clusters show higher BOLD for meaning trained hits than misses ($p < 0.005$), also consistent with semantic criteria. Finally, although not an a-priori expectation, both clusters qualitatively show similar interactions on day 2 between training group (meaning/perceptual) and accuracy (Figure 3.18, panels C and D). These observations

are potentially indicative of contributions from left parietal cortex in retrieval of episodic representations for novel words.

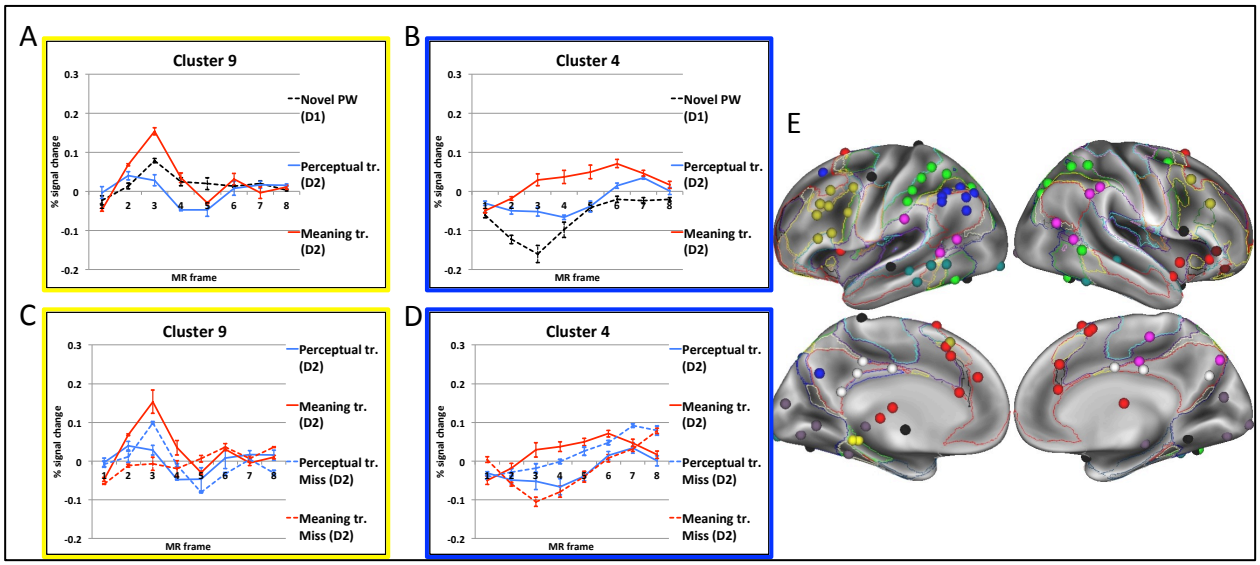

Figure 3.18: BOLD Timecourse Similarities between a Cluster Containing the Identified Parahippocampal Region and a Left Parietal/Superior Frontal Cluster Previously Implicated in Episodic Retrieval.
Cluster 9 (E, yellow spheres), contains one of the putative semantic regions (PHG) and cluster 4 (E, blue spheres) contains left parietal/superior frontal regions implicated in episodic retrieval. Both cluster 9 (panel A) and cluster 4 (panel B) show higher BOLD for meaning trained PWs relative to both novel PWs and perceptually trained PWs. Similarly, as shown in panels C and D, both clusters show similar interactions between training group (meaning/perceptual) and accuracy. All reported effects were confirmed significant in regional ANOVAs ($p < 0.005$). The observations support a potential role for parietal regions in semantic retrieval for newly acquired words.

Unlike the similarities noted above between the parietal regions in Cluster 4 and Cluster 9 containing one of the putative semantic regions, the two clusters exhibit differences during retrieval of previously known words. Figure 3.19 highlights two properties that distinguish the putative episodic memory retrieval cluster (cluster 4) from the semantic cluster

(Cluster 9, exemplified by the two yellow parahippocampal regions (but refer to Figure 3.10 for individual semantic ROI timecourses). As shown in Figure 3.19 (panels A and B), although both cluster 4 ($p < 0.001$) and cluster 9 ($p < 0.001$), show significant 'word > PW' effects, the effect in the putative episodic memory retrieval cluster (cluster 4) is driven by negative BOLD activity for real words that is "less-negative" than BOLD activity for PWs. This effect is in contrast to the pattern seen in cluster 9, as well as individual putative semantic regions (Figure 3.10), where timecourses are positive for both words and PWs.

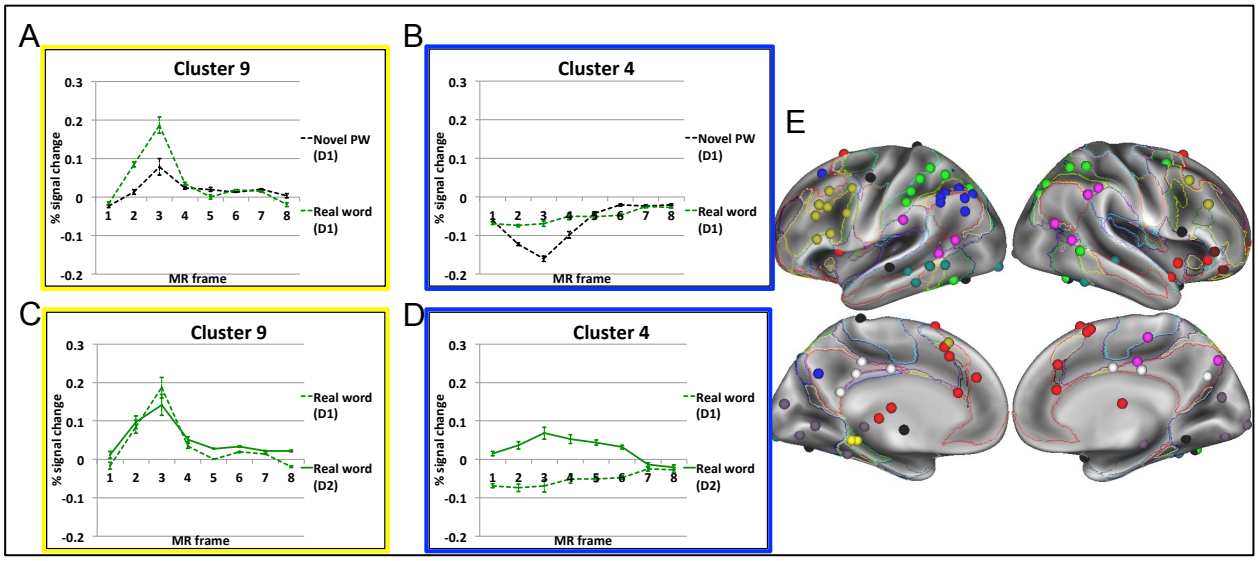

Figure 3.19: BOLD Timecourse Differences between a Cluster Containing the Identified Parahippocampal Region and a Left Parietal/Superior Frontal Cluster Previously Implicated in Episodic Retrieval.
Cluster 9 (E, yellow spheres), contains one of the putative semantic regions (PHG) and cluster 4 (E, blue spheres) contains left parietal/superior frontal regions implicated in episodic retrieval. Unlike the 'word > PW' effect in cluster 9 (panel A, $p < 0.001$), the same effect is driven by negative timecourses in cluster 4 (panel B, $p < 0.001$). Also, cluster 9 qualitatively shows repetition suppression for words (day1>day2, panel C) but the opposite effect is seen for in cluster 4 (day1<day2). The data do not convincingly support a parietal role in semantic retrieval of existing words.

The second distinction between the two clusters is shown in Figure 3.19, panels C and D. Cluster 4 (blue) shows an effect resembling the canonical 'old > new' episodic retrieval success effect, i.e. repeated real words (old) show higher BOLD activity than during the 1st presentation (new) ($p < 0.01$). In both cluster 4 and most of the individual constituent ROI (not shown, available on demand), the 'old > new' effect is driven by (unimpressive, yet qualitatively consistent) timecourses that, relative to baseline, are negative for the 1st presentation (i.e. 'new) and slightly positive for the 2nd presentation (i.e. 'old'), except for IPS_-33_-62_41 which had robust positive timecourses across all lexical groups ('old' and 'new'). In contrast, cluster 9 shows a qualitatively different profile that resembles the word-repetition-suppression effect observed in individual putative semantic regions (Figure 3.10). Although the word-repetition-suppression effect was not significant ($p=0.50$) in cluster 9 (yellow, containing a putative semantic ROI), a condition (day 1 words vs. day 2 words) X cluster (cluster 4 vs. cluster 9) regional ANOVA restricted to the peak of the timecourse (MR-frame 3) revealed a significant condition X cluster interaction ($p < 0.005$), reinforcing the observed qualitative difference between the two clusters. The observations support the previously outlined interpretation of semantic contributions from PHG/mSFC and episodic contributions from parietal regions for the retrieval of novel words.

3.3.5 A Cluster of Regions Resembling the Cingulo-Opercular Control System Show Sensitivity to Errors Potentially Reflective of a Performance Feedback Process

Another prominent cluster (cluster 1, shown in red in Figure 3.20, panel E), consistently identified across thresholds/algorithms, contains regions in close anatomical

proximity to those in the cingulo-opercular (COP) task control system (e.g. bilateral anterior insula, medial superior frontal cortex) (Dosenbach et al., 2006, 2007; J. D. Power et al., 2011). Of note, one of the putative semantic processing regions (mSFC) was placed in the same cluster (cluster 1) as the putative COP regions. Figure 3.20 (panels A and B) highlights the differences between cluster 9, which contains one of the putative semantic regions (PHG), and cluster 1. Similar to the pattern observed in individual putative semantic ROI (Figure 3.12), cluster 9 shows higher BOLD activity for correct meaning-trained item trials relative to misses ($p < 0.005$), whereas cluster 1 shows equivalent BOLD for meaning trained hits and misses ($p = 0.25$). The profile difference seen in the two clusters for meaning-trained PWs hits vs. misses was confirmed via a regional condition (meaning-trained PWs – hit vs. miss) X cluster (cluster 1 vs. cluster 9) ANOVA restricted to the peak of the timecourse (MR frame 3), which yielded a significant interaction ($p < 0.05$). In addition, in contrast to the training type (meaning/perceptual) X accuracy (hit vs. miss) interaction observed in individual putative semantic regions (Figure 3.12), as well as in cluster 9 ($p < 0.001$), cluster 1 shows a main effect of accuracy collapsed across training type, with errors showing higher BOLD than correct trials ($p < 0.05$). Interestingly, the two regions are placed in the same cluster despite the profile difference observed between one of the putative semantic regions (mSFC) and a canonical COP ROI (anterior insula) (Figure 3.20, panels C and D). The former with shows the accuracy X training type interaction, and the latter shows higher BOLD for all error relative to correct trials. Also highlighted in Figure 3.20 is a region in the anterior cingulate cortex (ACC_-1_24_20, anatomically close to the putative semantic region mSFC_-3_38_27),

previously ascribed a role in conflict monitoring (Barch, Braver, Sabb, & Noll, 2000; Botvinick, Braver, Barch, Carter, & Cohen, 2001; Botvinick, Cohen, & Carter, 2004). In contrast to the 'meaning-trained PWs – hit > miss' pattern observed in the putative semantic region (Figure 3.20, panel C), the ACC region (Figure 3.20, panel F) shows higher activity for meaning-trained PWs misses than hits, particularly towards the tail of the timecourse that may be capturing response-selection processes. The observed pattern in ACC is consistent with a response conflict monitoring account, given that the stimulus/response profile was switched for meaning-trained PWs across fMRI sessions, which likely induced high conflict. Hence, despite being placed in the same cluster with canonical task-control regions, the putative semantic ROI reveals a different profile upon closer inspection.

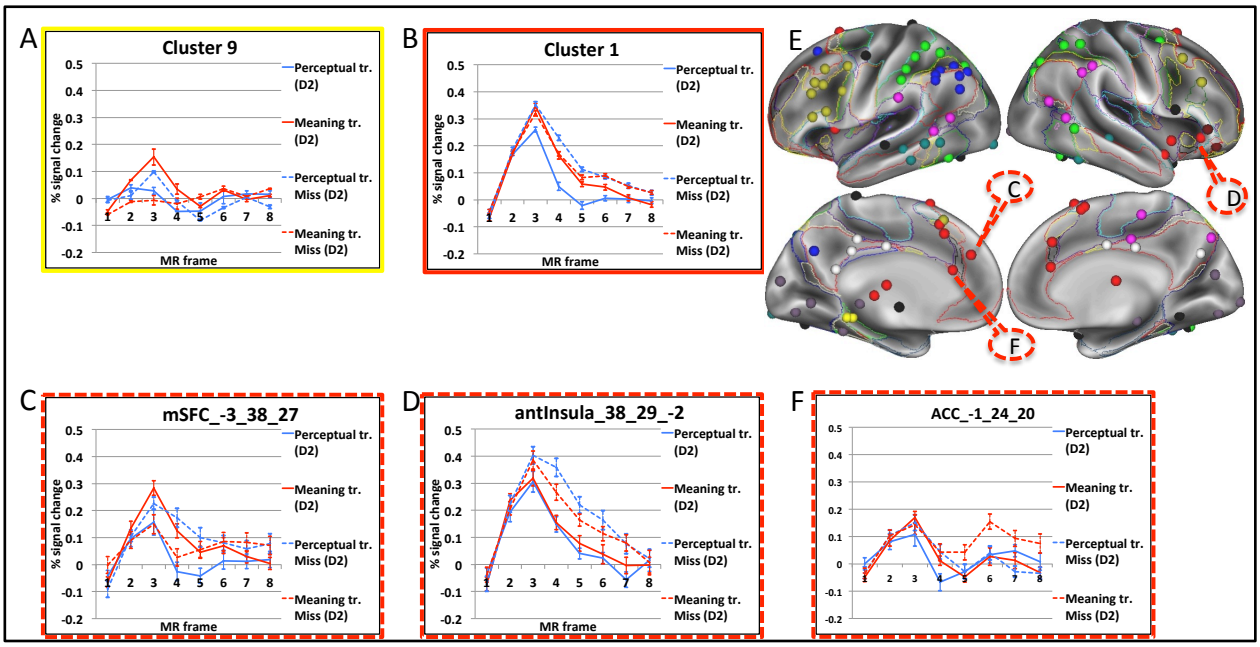

Figure 3.20: BOLD Timecourse Examination of a Cluster Resembling the Cinguloopercular Task-Control System and Constituent Regions.
A cluster containing regions implicated in COP task control (E, red cluster) shows a qualitatively different error profile for meaning vs. perceptually trained items (B) from that seen in identified semantic regions, exemplified here by a cluster containing PHG (A). Panels C, D, and F highlight qualitatively different timecourses between the semantic ROI (C), a region in right anterior insula approximating a canonical COP task-control ROI (D), and a region in the anterior cingulate cortex (ACC) previously ascribed a role in conflict monitoring, despite the fact that the three regions were clustered together (E).

3.3.6 The Left Dorsal Inferior Frontal Gyrus and Co-clustered Regions in Bilateral Frontal Cortex, Did Not Demonstrate Activity Indicative of Semantic Processing.

The clustering analysis also identified a cluster of regions in bilateral frontal cortex that anatomically correspond to regions implicated in adaptive (frontal-parietal) task-control, although a parietal component was largely absent. Of note, the cluster contained a region in dorsal left inferior frontal gyrus that has previously been implicated in semantic processing (Thompson-Schill et al., 1997), although subsequently ascribed a domain-general (i.e.

semantic-nonspecific) role in control/selection among competitors (Badre et al., 2005). Timecourses for words and novel PWs presented on day 1 are presented for the cluster (cluster 3) and the aforementioned dorsal IFG region as an exemplar (Figures 3.21, panels B and C). Unlike the profile observed in putative semantic regions (Figure 3.10, panels A and B), neither cluster 3 ($p = 0.50$) nor it's dorsal IFG constituent ($p=0.17$) exhibit a 'word > PW' effect. In addition, as shown in Figure 3.21 (panels D and E) neither cluster 3 nor dorsal IFG exhibit a word-repetition-suppression effect, and in fact show the opposite qualitative effect.

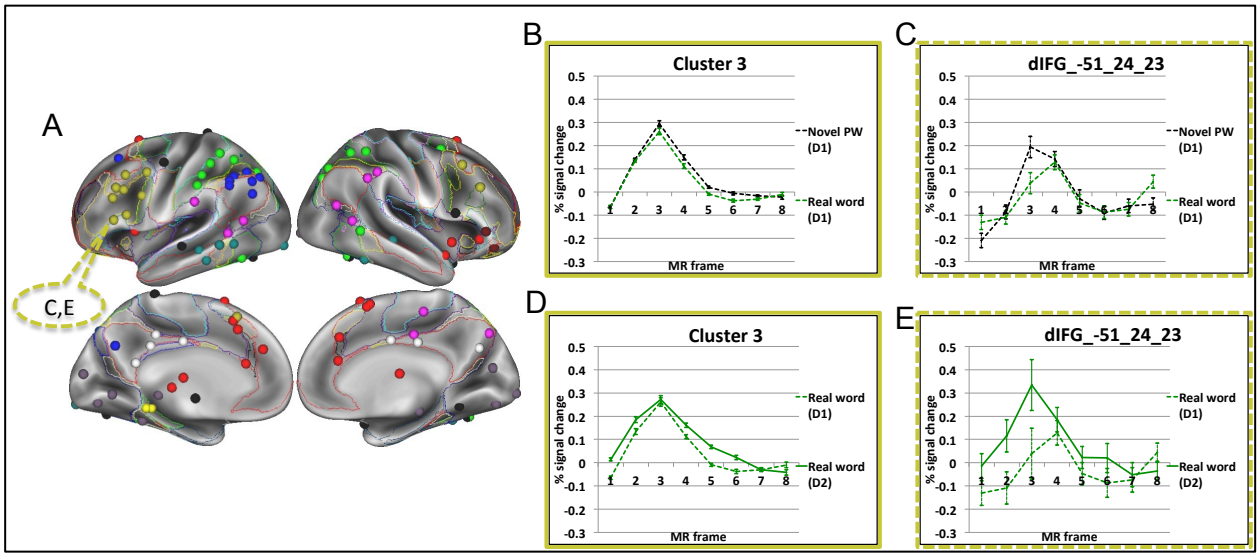

Figure 3.21: BOLD Timecourse Examination of a Cluster Resembling the Frontoparietal Task-Control System and Constituent Regions.
Cluster 3 (A, golden spheres) contains regions implicated in frontoparietal task control. An exemplar constituent region previously implicated in semantic processing (dorsal IFG) is highlighted, with panels B and C demonstrating the absence of a 'word > PW' effect, and panels D and E demonstrating the absence of a word-repetition suppression effect in left dorsal IFG as well as the parent cluster.

3.3.7 Targeted Investigation of the Left Ventral IFG, Based on Literature-Derived Regions

Because the left ventral IFG, a region implicated in controlled/strategic semantic retrieval (Gold et al., 2006; Roskies et al., 2001; A D Wagner et al., 2001), was not identified in the primary contrasts, regions were aggregated from the literature. As shown in Figure 3.22 (panels B and C), 2 of the 11 sampled regions showed significant 'word > PW' effects ($p < 0.05$). Similarly, 2 of 11 regions showed significant word-repetition-suppression effects ($p < 0.05$) (panels D and E; of note, word-repetition-suppression effect was seen in the same two ROIs showing 'word > PW' effect). In contrast to the putative semantic processing regions from the current study, none of the literature-derived ROIs (including the aforementioned two regions) showed a 'meaning-trained PWs > novel PW' effect (Figure 3.23).

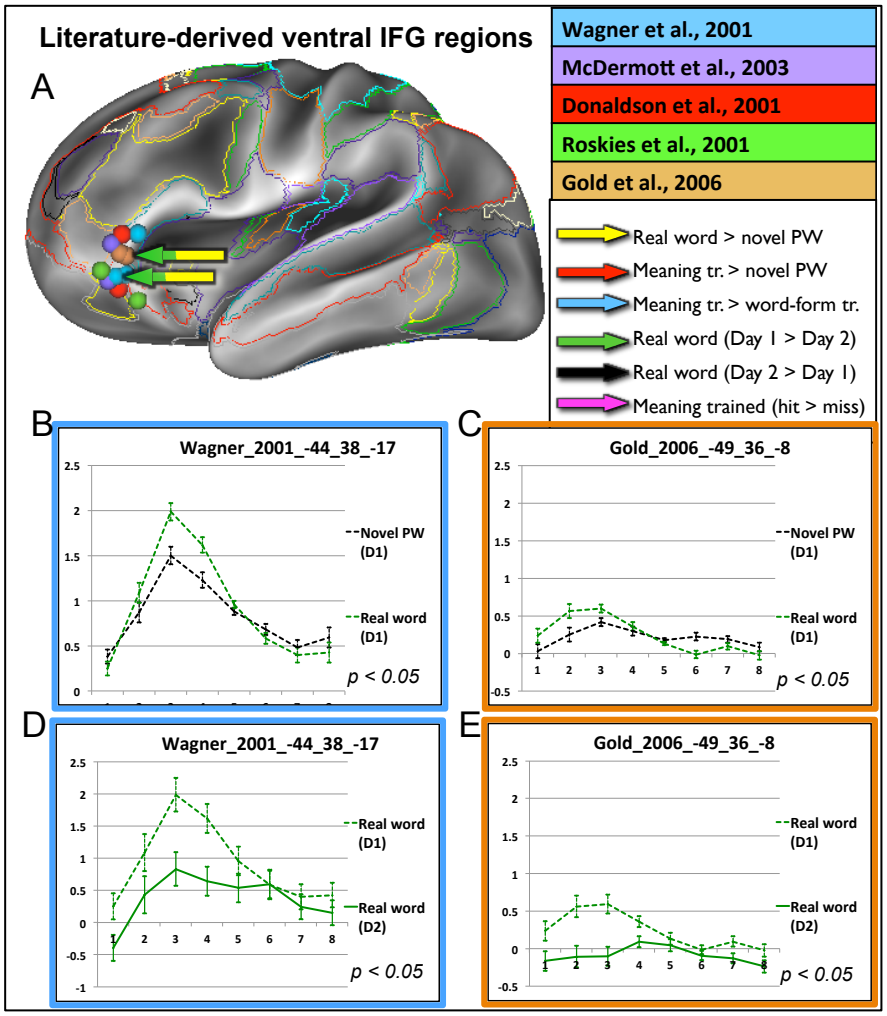

Figure 3.22: Regional BOLD Timecourses in Literature-Derived Coordinates in Left Ventral IFG –Words vs. Novel PWs & Words in the 1st vs. 2nd Presentation.
Literature-derived ventral IFG regions are shown in panel A. 2/11 regions showed significant 'word > novel PW' effects (panels B and C) and word repetition-suppression effects (panels D and E).

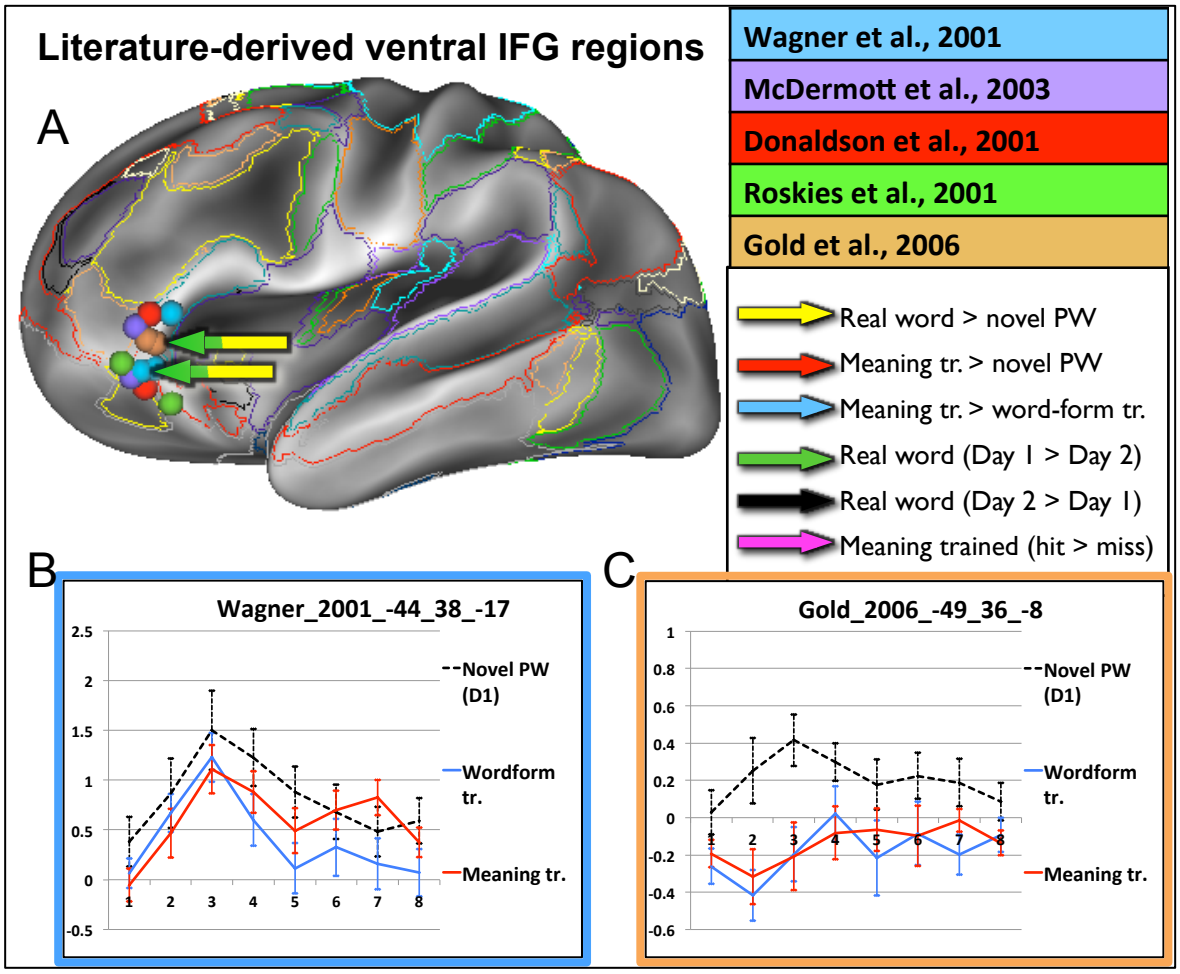

Figure 3.23: Regional BOLD Timecourses in Literature-Derived Coordinates in Left Ventral IFG – Novel vs. Meaning-Trained PWs, and Meaning vs. Perceptually Trained PWs. Literature-derived left vIFG regions are shown in panel A. Panels B and C display timecourses for novel, meaning-trained, and perceptually trained PWs, from the two vIFG regions that showed significant 'word > PW' and word-repetition-suppression effects (Figure 3.22). None of literature-derived regions showed higher BOLD activity for meaning-trained PWs relative to novel PWs, or for meaning trained relative to perceptually trained PWs.

3.3.8 Targeted Investigation of the Left vIFG Based on Study-Driven Regions Showing 'Lower-Level' Effects (Not Identified in Primary Contrasts)

In addition to the literature-derived ventral IFG regions, 6 study-driven ROIs were generated from lower-level 'word vs. baseline' contrast on days 1 and 2, and a sub-threshold (z

< 3.0) region showing a day X meaning-trained vs. real word X time effect (Figure 3.24, panel A). One of the six regions showed a trend (*p=0.07*) towards a 'meaning trained item > PW' effect (panel D) consistent with expected properties of a putative semantic processor. However, that region did not exhibit a 'word > PW' (panel B) or a word-repetition-suppression effect (panel C).

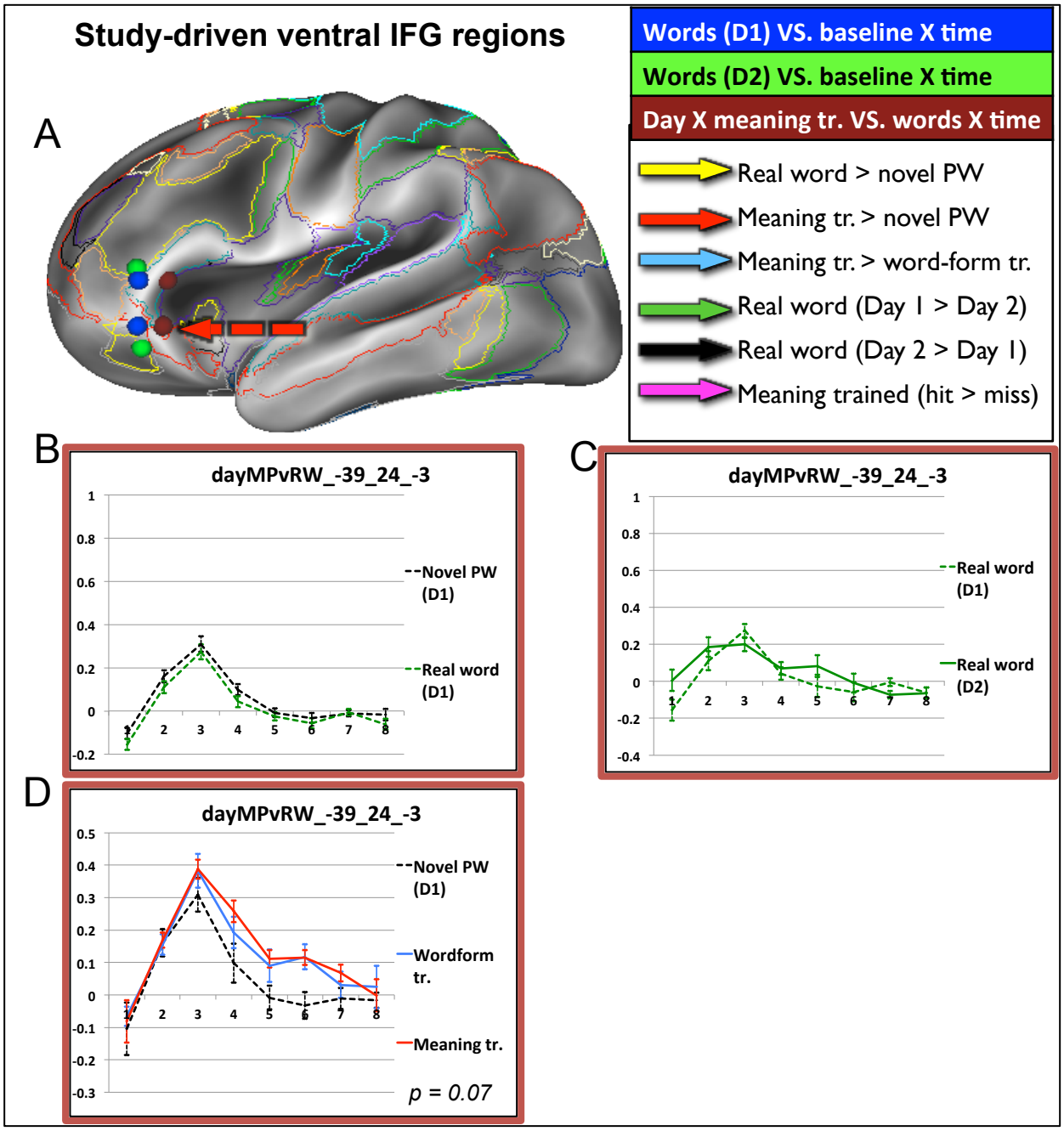

Figure 3.24: BOLD Timecourses in Study-Driven Left Ventral IFG Regions.
Study-driven regions in left ventral IFG (panel A). Panels B and C demonstrate the absence of a 'word > PW' and a word-repetition-suppression effect, respectively, in the only region showing a trend towards a putative semantic profile, i.e. meaning trained PWs > novel PW ($p = 0.07$), shown in panel D, but not meaning trained PWs > perceptually trained PWs.

3.3.9 Targeted Investigation of the Left Lateral Temporal Lobe Based on Study-Driven Regions

Multiple regions in left lateral temporal lobe were identified by the primary contrasts. Most of the identified regions were located in mid to posterior temporal lobe, along the middle temporal gyrus and superior temporal sulcus. The primary contrasts did not identify regions in anterior temporal lobe. Clustering analysis placed the regions into two clusters, cluster 5 and cluster 8. Timecourses are displayed in Figure 3.25, panels B and C, for clusters 5 and 8, respectively. For each cluster, a representative individual region is displayed in panels D and E. The two clusters, as well as most of the constituent left temporal regions showed significant 'word>PW' and word-repetition suppression effects. However, neither the individual regions nor the clusters showed any evidence of meaning training-related BOLD increase.

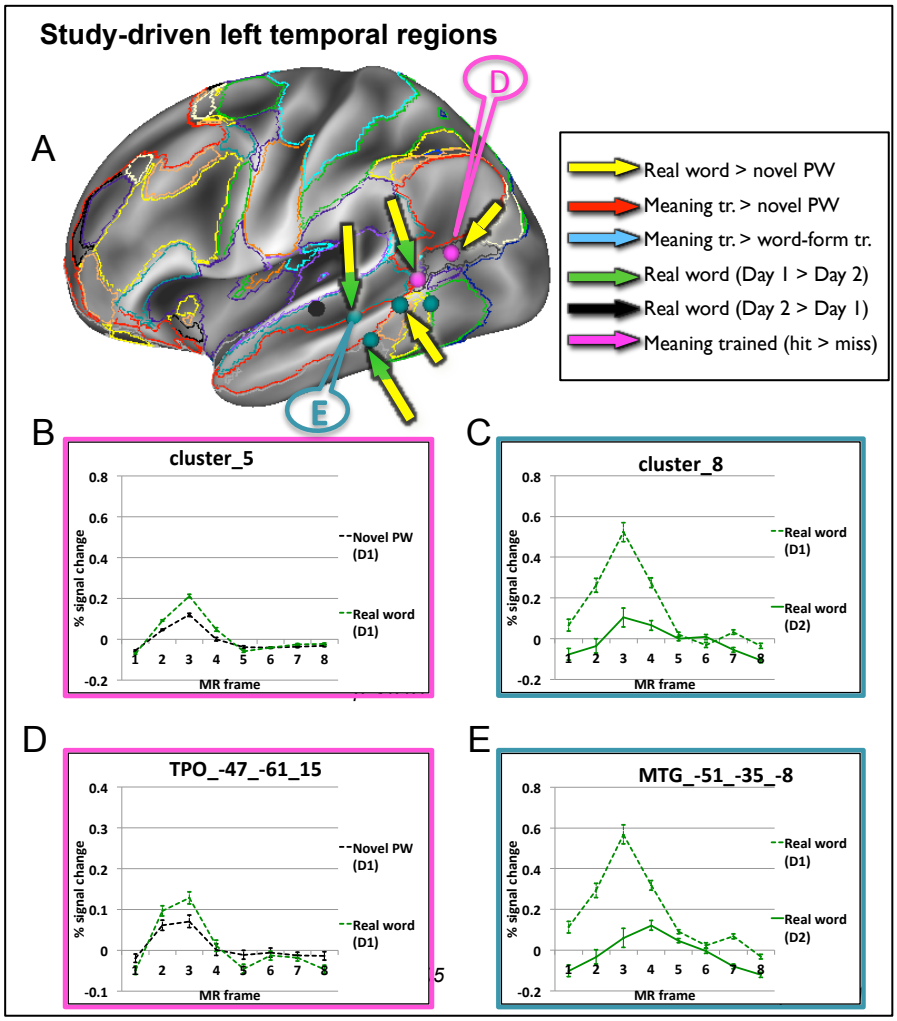

Figure 3.25: BOLD Timecourses in Study-Driven Regions in Left Lateral Temporal Lobe. Study-driven regions in left temporal lobe that came out of the primary contrasts are displayed in panel A. Timecourses are shown in panels B and C for the Infomap-based clusters, and in panels D and E for two exemplar regions from each of the two clusters.

3.3.10 Targeted Investigation of the Left Temporal Lobe Based on Literature-Derived Regions

The lack of any training-related effects in left lateral temporal regions provided an incentive to garner putative semantic regions from the literature for further investigation. The nine temporal lobe regions aggregated from the literature are displayed in Figure 3.26, panel A. Most of the literature-derived regions were in close anatomical proximity to the study-driven regions

shown in Figure 3.25, with the exception of a region in anterior superior temporal gyrus. Similar to the effects observed in the study-driven regions, the three literature-derived regions that showed significant effects were all driven by ‘word > PW’ (Figure 3.26, panels B and C) and word-repetition-suppression effects (panels D and E). None of the examined regions showed evidence BOLD increase due to meaning training.

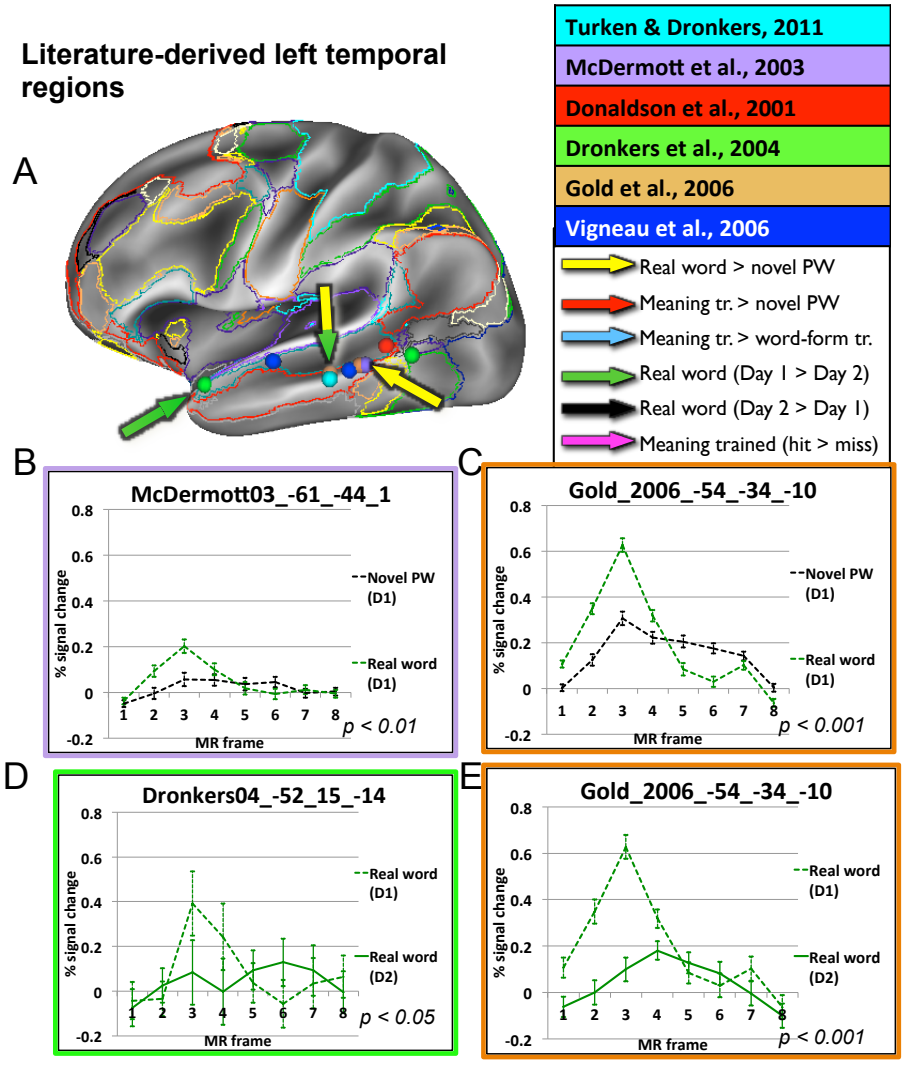

Figure 3.26: BOLD Timecourses in Literature-Derived Left Lateral Temporal Regions. Literature-derived left lateral temporal regions are shown in panel A. 3 out of the 9 sampled regions showed putative semantic profiles. Panels B and C display two regions that showed 'word > PW' effects, and panels D and E display regions that showed word-repetition suppression effects.

3.4 Discussion

This project set out with the primary goal of characterizing, in healthy young adult subjects, the functional neuroanatomy underlying word-level semantic retrieval for newly learned and previously known words. To that end, we used a multi-context sentential training

approach to assign meaning to pseudoword stimuli, effectively turning them into synonyms to existing words. An additional goal of the current project was to isolate, via subtractive inference, BOLD activity related to retrieval of meaning, i.e. semantic memory, from co-recruited processes related to retrieval of perceptually familiar word-forms with no semantic associations. As such, a separate group of pseudowords were given perceptual training using a pseudoword detection task. Finally, using fMRI before and after behavioral training, we characterized the functional neuroanatomical changes associated with transforming a meaningless string of letters into meaningful words.

To briefly summarize the primary findings, we identified two regions in the left hemisphere, one in the left parahippocampal gyrus (PHG) and the other in the left medial superior frontal cortex (mSFC), consistent with a role in the retrieval of semantic memory for both previously known and recently learned words. Despite showing the expected semantic profiles for previously well-known word stimuli, such as word repetition suppression and a 'word > novel PW' effect, canonical semantic processing regions in the left lateral temporal lobe, such as the MTG and ATL failed to be engaged by the novel word stimuli. This led to a conclusion that these regions support retrieval of semantic memory for well-consolidated words, and by implication, we propose that 2-3 days might be insufficient to produce fully consolidated neocortical representations. Another finding was that the left vIFG, a region implicated in controlled semantic memory retrieval, was absent from primary voxelwise contrasts. Upon further exploration using literature-derived regions, the left vIFG was found to only show engagement by previously known words, but not newly learned words. These

observations led to an interpretation that the left vIFG was not engaged by novel words potentially due to a combination of low strategic retrieval demand in the lexical decision task and inadequate neocortical consolidation of the novel words. Each of the aforementioned observations is discussed in depth below.

3.4.1 Left Parahippocampal and Medial Superior Frontal Cortex Demonstrated a Role in Semantic Retrieval of Both Novel and Previously Known Words.

The current study identified PHG and mSFC as regions that exhibit a number of properties that would be expected from regions involved in retrieving/processing meanings at the single word level. First, when directly comparing previously known words and novel PWs before any training was administered, these regions exhibited higher BOLD activity for words relative to PWs (Figure 3.10, panels A and B). Second, upon repeated exposure 2 to 3 days following the initial presentation, these regions exhibited suppression of BOLD activity to previously known words (Figure 3.10, panels C and D), a characteristic that has repeatedly, although not exclusively, been associated with semantic processing (D. L. Schacter & Buckner, 1998; Daniel L Schacter et al., 2007). Third, the same two regions demonstrated evidence that supports their role in learning new semantic associations. Specifically, for lexical items that received sentential meaning training demonstrated, these regions show increased BOLD activity relative to their initial presentation as novel PWs (Figure 3.11, panels A and B). These two regions also exhibited higher BOLD activity relative to PWs that received just as much exposure, but in a perceptual form training setting without semantic associations (Figure 3.11, panels C and D). Finally, comparison of BOLD activity for correctly and incorrectly identified

meaning trained items (hit vs. miss trials) revealed higher BOLD activity for the correctly identified items in PHG and mSFC (Figure 3.12, panels A and B). The latter effect was not driven by accuracy alone, but rather by whether or not the lexical items were perceived to be associated with meaning. In support of this argument, we identified an effect that admittedly was not explicitly expected a-priori. Comparing hits and misses for meaning-trained PWs vs. perceptually trained PWs revealed an accuracy (hit vs. miss) X training group (meaning-trained PWs vs. perceptually trained) interaction (Figure 3.12, panels C and D). The interaction was driven by qualitatively higher peak BOLD responses for items perceived as meaningful relative to items perceived as meaningless, regardless of the actual item identity. Hence, PHG and mSFC demonstrated sensitivity to single word meanings both for previously well-known words, as well as for lexical items that were given meanings in an experimental context conducted over the course of a few days.

Examination of prior studies that explicitly targeted semantic processing reveals very sparse reports of regions anatomically close to our two putative semantic regions. Of note, the majority of those studies are fundamentally different from the current study in that their designs did not include learning of novel semantic associations. Instead, in a variety of task settings (e.g. abstract vs. concrete judgments (Donaldson, Petersen, & Buckner, 2001; Friederici et al., 2000), verb-generation (J. A. Fiez et al., 1996; Petersen et al., 1988; Roskies et al., 2001), and semantic classification/comparison tasks (Badre et al., 2005; Thompson-Schill et al., 1997; A D Wagner et al., 2001), meanings were instantiated using common, previously known word stimuli. Of the aforementioned studies, only Thompson-Schill et al. (Thompson-

Schill et al., 1997) reported a region (-3_44_31) close to the mSFC_-3_38_27 that showed higher BOLD activity in a semantic comparison task with high-selection demand relative to a low-selection demand condition.

In the episodic memory retrieval literature, we identify indirect but relevant support for these regions as potential semantic processors. The regions are typically recruited to a greater extend during retrieval of source memory relative to simple item recognition judgments. Cognitive theories would suggest that processes involved in recovering source information about a particular retrieval cue could be based on semantic elaborations between the cue and source information (I G Dobbins et al., 2002; Daniel L Schacter et al., 1998; Tulving, 1983). Regions within 10 mm to the mSFC region identified here have been reported in multiple studies as showing greater recruitment during source memory retrieval than simple item recognition. Cohn et al. (-4_48_20) and Dobbins et al. (-6_45_24)(Cohn et al., 2009; I. G. Dobbins et al., 2002), both of which used written word stimuli, reported higher BOLD activity during source recollection relative to item recognition in the medial superior frontal cortex. Similarly, using written word stimuli to compare source recollection vs. item recognition, another study by Dobbins et al. (I. G. Dobbins et al., 2003) reported a region in the posterior hippocampus/parahippocampal gyrus (-19_-35_-10) showing greater activity for source recollection. Similar effects were described in posterior hippocampus/parahippocampus by Cansino et al. (-14_-44_-4) and Tendolkar et al. (-24_-28_-10) (Cansino, Maquet, Dolan, & Rugg, 2002; Tendolkar et al., 2008), using picture and photograph stimuli, respectively. Although somewhat indirectly related to semantic processing, the source-memory retrieval

literature would be in agreement of the proposed semantic retrieval interpretation for PHG and mSFC.

Next, we examined prior studies that specifically targeted the functional neuroanatomy of novel word learning. Although a number of studies have been conducted in this realm, most do not warrant detailed discussions in the current setting either because they used imaging methods such as event-related-potentials that do not provide adequate anatomical specificity, or were not targeting novel semantic associations, per se (e.g. (M. H. Davis, Di Betta, Macdonald, & Gaskell, 2009). Two studies do have adequate relevance in the current context and will be considered further.

The first study, conducted by Mestres-Misse et al. (Mestres-Missé et al., 2008), examined the functional neuroanatomy of meaning acquisition using fMRI in (Spanish-speaking) young adults, during the online acquisition of meaning, using uniform eight-word sentences presented one word at a time (every 500ms), with the novel word presented as the eighth (terminal) word. For each target, three sentences were presented sequentially such that, in the M+ condition, all three sentences converged on the same meaning, in the M- condition, each sentence was suggestive of a different meaning, thus precluding the emergence of a consistent constrained meaning, and an R condition which terminated with an actual, previously known word. As can be deduced from the experimental design, the task likely conflates memory encoding and retrieval processes. Other design issues that are of potential concern include a somewhat unnatural sentence presentation that may not be adequately isolating the BOLD response for a particular stimulus, as well as potentially recruited syntactic

processes that may be possible confounds. As such, the results should be considered with adequate caution. That said, one of their primary findings is that a region that they label as anterior parahippocampal gyrus (-20_-24_-16), relatively close to our coordinates (PHG_-18_-36_-6), showed a M+ > M- effect.

The second study, conducted by Breitenstein and colleagues (Breitenstein et al., 2005), used a PW-picture association task (in German-speaking subjects, some of whom were bilinguals), while acquiring fMRI data during associative learning. A PW was either paired with the same picture presented non-consecutively across training blocks (learning condition) or with a different picture during each presentation (no-learning condition). Once again, for similar reasons discussed above vis-à-vis Mestres-Misse et al. (Mestres-Missé et al., 2008), comparisons between their results and ours should be made with caution. Their relevant results were that a) across the training blocks in the learning relative to the no-learning condition, a hippocampal region (-18_-30_-9) close to our PHG_-18_-36_-6 showed BOLD activity *decreases*, which was interpreted as potentially reflecting "a sharpening of the neural response over the course of learning," and b) subjects exhibiting *less BOLD suppression* in the same hippocampal region learned the novel words more efficiently, as well as scored higher on verbal semantic fluency tasks.

Neither of the two studies discussed above reported any effects close to the medial superior frontal ROI. However, there are reports that suggest that the involvement of the medial prefrontal cortex in learning and memory consolidation occurs over a more protracted time scale, which neither study had a chance to examine. As a potential mechanistic

explanation, prior reports state that medial prefrontal cortex may serve as the link that integrates medial temporal lobe (MTL)-dependent learning to neocortical representations, via synchronized hippocampal-medial prefrontal electrophysiological rhythms, particularly in the theta range (Aminoff et al., 2013; Euston, Gruber, & McNaughton, 2012).

Finally, neuropsychological research on amnesic patients suggests that damage to MTL structures results in explicit/declarative semantic memory impairments, particularly in the acquisition of novel semantic information (Gabrieli et al., 1988; Shimamura & Squire, 1987). Perhaps the most widely cited effect is that of patient H.M., where, following bilateral MTL resection, he was unable to learn and retain new words that emerged following the surgery (e.g., "Xerox"), despite normal memory for semantic information acquired prior to the amnesia (Gabrieli et al., 1988). Similarly, relative to words known prior to the surgery, H.M also demonstrated impaired word-stem completion priming for words that emerged subsequent to the amnesia (Postle & Corkin, 1998). There are also limited reports of temporally graded retrograde impairments in recollection of facts, with greater deficit for knowledge acquired closer to the time of insult (N. J. Cohen & Squire, 1981). It is challenging to establish adequate specificity in the relationship between the lesion size/location and the resulting behavioral impairment due to MTL damage, but refer to Squire, 1992 and Moscovitch et al. 2006, for reviews (Moscovitch et al., 2006; L. R. Squire, 1992). Reports of memory impairments following injury to the medial prefrontal cortex are much sparser, relative to that of MTL. However, there have been limited reports that medial prefrontal lesions, likely significantly ventral to the location of our putative semantic region, result in impairments in the learning and

consolidation of contextual information (refer to Euston et al. (Euston et al., 2012) and Nieuwenhuis & Takashima (Nieuwenhuis & Takashima, 2011) for detailed reviews).

Hence, as outlined above, there is ample prior evidence that would be consistent with a putative role for the parahippocampus/posterior hippocampus and medial superior frontal cortex, in learning and retrieval of semantic information.

3.4.2 A Cluster of Left Parietal/Superior Frontal Regions May Support Episodic-Memory Based Word Learning

Despite the observed functional similarities in the two putative semantic regions, none of the clustering algorithms placed them in the same group. This clustering-based finding makes it hard to put forth an argument for a putative semantic brain system. That said, serving as a quality-check for the task-evoked dataset as a whole, the clustering analysis did reveal other clusters that correspond well with previously characterized brain systems.

One prominent cluster (Cluster 4, Figures 3.18 – 3.19), present across clustering algorithms and thresholds, is a set of left-lateralized regions in lateral/medial parietal and superior frontal cortex with previously demonstrated roles in episodic memory retrieval (Cabeza et al., 2008; Nelson et al., 2010; Yonelinas et al., 2005; Yonelinas, 2002). The said regions have also previously been framed as a putative brain system based on clustering analyses conducted on task-evoked and resting-state fMRI data (Nelson et al., 2010). Cluster 4, which anatomically resembles the AG/mPFC cluster from Nelson et al. (Nelson et al., 2010), exhibited properties, some of which were the outlined semantic criteria relating to novel words, the overall functional properties were supportive of an episodic role.

First, as shown in Figure 3.18, Cluster 4 exhibits properties during semantic retrieval of the newly learned words that are consistent with semantic criteria outlined a-priori. Cluster 4, as well as its constituents (not displayed, available on demand), showed higher BOLD activity for meaning-trained PWs relative to both untrained/novel PWs as well as perceptually trained PWs. In addition, the cluster also showed higher BOLD activity for meaning-trained hits relative to misses. The above three properties are consistent with the expected semantic profile and suggest that the regions contribute to the semantic retrieval process, at least for the newly acquired words. In addition, although not outlined a-priori, Cluster 4 also exhibits a qualitatively similar training group (meaning/perceptual) by accuracy interaction, similar to that observed in the two identified semantic regions (PHG, mSFC). Given the above properties, a potential role in semantic retrieval cannot be readily dismissed for Cluster 4, mostly constituting medial/lateral parietal regions. However, the latter interpretation needs to be tempered by properties that the said regions showed during retrieval of previously known words, which, as recapped below, diverge from a semantic interpretation.

As shown in Figure 3.19, Cluster 4 exhibited a 'real word > novel PW' effect, which was one of the properties expected from a semantic region. However, unlike the 'word>PW' effect in PHG/mSFC (Figure 3.10), which was driven by positive timecourses (relative to baseline), the same effect was driven by negative BOLD activity for real words that is 'less-negative' than BOLD activity for PWs. In fact, for the majority of conditions, timecourses for the cluster as well as the individual constituent regions (except for IPS_-33_-62_41) were either negative or flat relative to baseline, precluding a straightforward task-evoked-activation

interpretation. The second distinction between the Cluster 4 and PHG/mSFC is that Cluster 4 shows an effect resembling the canonical episodic 'old > new' retrieval success effect for words, while PHG/mSFC show a repetition suppression effect for words, consistent with conceptual repetition priming (D. L. Schacter & Buckner, 1998; Daniel L Schacter et al., 2007). The latter observation in particular makes a straightforward semantic interpretation for the parietal regions somewhat problematic. Considered in aggregate, the evidence suggests a parietal contribution supporting episodic processes in the retrieval of novel words.

3.4.3 A Cluster of Bilateral Frontal Regions May Correspond to a Cingulo-Opercular Task-Control System

In addition to a putative episodic memory retrieval cluster, another cluster was consistently identified with close anatomical correspondence to the cingulo-opercular (Figure 3.20) task-control systemm (Dosenbach et al., 2006, 2007; J. D. Power et al., 2011). The putative COP cluster includes regions (within 10mm of the Dosenbach et al. loci) in bilateral anterior insula and medial superior frontal cortex that, based on a meta analysis across 10 different tasks, exhibited fMRI signals corresponding to task-initiation (start-cue), task-set maintenance, as well as error-related activity, consequently forming a 'core' task-set system (Dosenbach et al., 2006).

Consistent with the above-stated task-control properties, the 'core' task-control regions, as well as most regions in the COP cluster, exhibited greater BOLD activity for errors relative to correct trials, as exemplified in Figure 3.20 (panel D) by the right anterior insula. Another region placed in the same cluster is a region in the ACC (Figure 3.20, panel F) showing higher

activity for meaning-trained PWs misses than hits, particularly towards the tail of the timecourse. The observed pattern is consistent with a (response) conflict monitoring account (Barch et al., 2000; Botvinick et al., 2001, 2004), particularly given the fact that that the stimulus/response profile was switched for meaning-trained PWs across fMRI sessions, which likely induced high conflict. Of note, one of the putative semantic regions (mSFC) was placed in the same cluster as the putative COP system. Despite the clustering outcome, however, mSFC exhibits a stark 'error vs. correct' profile difference from that seen in the 'core' task-control regions (Figure 3.20, panels C and D) as well as the ACC region ascribed a (response) conflict-monitoring role. Unlike the general cross-condition 'error > correct' response seen in the right anterior insula, and the elevated meaning-trained PWs error response in ACC, mSFC shows higher BOLD activity for correct meaning-trained PWs trials (hits) relative to misses ($p < 0.005$), which resulted in a training type (meaning/perceptual) X accuracy (hits vs. misses) interaction. The latter profile in the putative semantic region argues for the modulation of the 'error vs. correct' response by stimulus semantic content, where items perceived to have meaning showed higher BOLD activity relative to items perceived meaningless, regardless of actual item identity. Hence, despite the clustering outcome, mSFC is divergent in its functional characteristics from the majority of regions in the cluster that are more consistent with a role in task-control, as argued above.

3.4.4 A Cluster of Bilateral Frontal Regions May Correspond to a Fronto-Parietal Task-Control System

The clustering analysis also identified a cluster of regions (Cluster 3, Figure 3.21) that closely correspond with a set of regions previously implicated in adaptive task-control

(Dosenbach et al., 2007), and subsequently shown to form a distinct control system based on graph-theoretic network analysis conducted on resting state fMRI data (J. D. Power et al., 2011). Cluster 3 contained bilaterally distributed regions that closely mapped onto the Power et al., modules in frontal cortex (mostly on the lateral surface, but also including a left medial component). Of note, the putative frontal-parietal cluster contained a region in the dorsal aspects of the left inferior frontal gyrus previously implicated in semantic processing (Thompson-Schill et al., 1997), although most subsequent work associates dorsal IFG with domain-general selection processes (Badre et al., 2005). Inconsistent with a semantic interpretation, the putative frontal-parietal cluster, including the dorsal IFG, exhibited no 'word > PW' or word-repetition-suppression effects (Figure 3.21). The dorsal IFG also showed timecourses with robust 'error > correct' effects for both meaning-trained PWs and perceptually trained PWs (not shown, available on demand), potentially reflecting performance feedback processes that characterize regions implicated in task-control (Dosenbach et al., 2006, 2007).

3.4.5 Additional Findings from Clustering Analysis

Finally, the remaining clusters (not presented via figures here, but available on demand) also showed properties consistent with prior reports. For instance, a bilateral cluster containing regions that correspond to the dorsal attention system (Corbetta & Shulman, 2002) was identified (cluster 2, shown in light green in Figure 3.17). The putative dorsal attention cluster showed repetition-related cross-day BOLD suppression, essentially for all three lexical

categories (words, meaning-training PW, perceptual-training PW), consistent with prior reports associating the said regions with qualitatively similar perceptual training effects (Lewis, Baldassarre, Committeri, Romani, & Corbetta, 2009). Another cluster (cluster 5, shown in magenta in Figure 3.17) containing regions in bilateral supramarginal gyrus previously implicated in phonological processing (Church, Balota, Petersen, & Schlaggar, 2011; Church, Coalson, Lugar, Petersen, & Schlaggar, 2008) showed repetition-related cross-day BOLD suppression across all three lexical categories. The latter effect maybe interpreted as reflecting reduced phonological processing demand, from the 1st to the 2nd fMRI session, owing to the extensive phonological practice that subjects received during the training sessions that required naming the stimuli. Two regions in the right ventrolateral PFC formed cluster 10 (shown in burgundy in Figure 3.17) and exhibited markedly wide timecourses that were late to return to baseline, consistent with a prior interpretation in post-retrieval monitoring (Ian G. Dobbins, Simons, & Schacter, 2004; Rugg & Wilding, 2000). Lastly, a cluster that exhibited various semantic-like profiles was identified (cluster 6, shown in white in Figure 3.17), which notably also contains regions such as the middle and posterior cingulate/retrosplenial cortex previously reported in a meta-analysis of semantic studies (Binder et al., 2009). However, the 'potentially-semantic' profiles observed in the individual constituent regions were tenuous at best, and hence do not warrant a confident interpretation to that effect (data not shown, available on demand).

3.4.6 Left Ventral IFG Was Recruited in Retrieval of Previously Known Words but Not during Retrieval of Newly Learned Words

Across the five primary voxel-by-voxel SPMs targeting putative semantic regions, we initially failed to find regions in the left vIFG showing potential semantic effects. Upon further probing, two regions garnered from the literature (Wagner et al.: -44_38_-17 (A D Wagner et al., 2001); Gold et al.: -49_36_-8 (Gold et al., 2006)) did exhibit 'word > PW' and 'word-repetition-suppression' effects (Figure 3.22). However, as shown in Figure 3.23, those regions did not show evidence of involvement during retrieval of newly learned words.

The left vIFG is typically recruited by semantic tasks that, relative to simple word vs. nonword lexical decision making, demand greater controlled/strategic access to word meanings. Exemplar tasks that have previously recruited left vIFG include abstract vs. concrete judgments (Donaldson, Petersen, & Buckner, 2001; Friederici et al., 2000), verb-generation (J. A. Fiez et al., 1996; Petersen et al., 1988; Roskies et al., 2001), and semantic classification/comparison (Badre et al., 2005; Thompson-Schill et al., 1997; A D Wagner et al., 2001). Similar to the present study, previous studies that have used simple word/nonword lexical decision tasks did not report involvement of left vIFG (Fiebach et al., 2002, 2007; Henson et al., 2002). The above findings suggest that the word/nonword lexical decision task can be successfully performed via automatic access to word meanings alone, without the need for strategic/controlled semantic processing (Collins & Loftus, 1975; Neely, 1977; Posner & Snyder, 1975). In support of the latter argument, Gold et al. (Gold et al., 2006) used a semantic priming task (in an fMRI setting) with variable SOA designed to dissociate the functional neuroanatomy of automatic vs. controlled lexical semantics, and demonstrated exclusively

strategic (i.e. not automatic) semantic facilitation at a long SOA in left vIFG. Hence, the lack of robust vIFG engagement may partially be due to the low strategic retrieval demand required by the lexical decision task.

Another possibility that may additionally account for the absence of left vIFG, particularly during retrieval of newly learned words, is that the novel words are yet to be fully neocortically consolidated, which may be a requisite for a region such as vIFG implicated in a controlled semantic retrieval in a domain-specific manner. Here, prior word-learning studies may offer some insight. The two novel word learning studies discussed at length above, Mestres-Misse et al. and Breitenstein et al. (Breitenstein et al., 2005; Mestres-Missé et al., 2008) did report coordinates in left vIFG, with the former study making a formal argument for a semantic role. However, a careful consideration of their results, vis-à-vis our findings, allows for an alternate explanation. Mestres-Misse et al. (Mestres-Missé et al., 2008) reported greater left vIFG activity in their 'M+ > RW' contrast ('convergent novel word meanings' > previously known words), which was attributed to increased integration demands. However, that effect was likely driven by decreased BOLD activity across the repeated known-word presentations, which they did not examine, especially when juxtaposed with a null effect for their 'M+ > M-' contrast ('convergent novel word meanings' vs. 'divergent novel word meanings'). Similarly, the vIFG effect reported in Breitenstein et al. (Breitenstein et al., 2005) also lacked specificity such that both the 'learning' and 'no-learning' conditions showed greater vIFG activity relative to baseline. Hence, the evidence implicating vIFG in controlled retrieval of newly acquired words is tenuous at best, at least not enough to rule out the potential

interpretation forwarded above, i.e. vIFG may absent in retrieval of new semantic memory due to inadequate neocortical consolidation.

Overall, the absence of left vIFG during novel word memory retrieval is potentially due to a combination of the low demand for strategic retrieval in the lexical decision task, and incomplete neocortical consolidation of the novel words.

3.4.7 Left MTG Was Recruited in Retrieval of Previously Known Words but Not in Retrieval of Newly Learned Words

The left MTG exhibited a similar lack of engagement by the novel words, despite showing 'word > PW' and word-repetition-suppression effects as described for left vIFG. In the word learning literature, although left MTG was reported by Mestres-Misse et al. (Mestres-Missé et al., 2008) to show higher BOLD activity relative to baseline for the aforementioned M+, M-, and previously known word conditions, the region did not show differences between the critical M- and M+ conditions. To our knowledge, no convincing reports exist supporting left vIFG or MTG involvement in novel word learning. A potential explanation for the lack of engagement of left MTG by novel word learning is an argument put forth by proponents of the complementary learning systems hypothesis (M. H. Davis & Gaskell, 2009; McClelland et al., 1995). Novel semantic associations that are clearly engaging the MTL here and in other studies discussed above, have yet to be fully integrated into neocortical semantic representations thought to rely on regions in lateral temporal lobe (Atir-Sharon, Gilboa, Hazan, Koilis, & Manevitz, 2015; Ghosh & Gilboa, 2014; Takashima et al., 2006; van Kesteren, Ruiter, Fernández, & Henson, 2012).

3.5 Conclusion

In conclusion, the current study had set out to identify brain regions involved in semantic processing at the single word level, using a word-learning approach to engage semantic memory retrieval by both old and newly learned words. Using a within-item experimental design allowed isolating semantic processes from potentially confounding effects driven by non-semantic perceptual processes (e.g. familiarity, phonology, orthography). Two left hemisphere regions were identified, one in parahippocampal and the other in medial superior frontal cortex, exhibiting properties that support an interpretation of a role in semantic retrieval of both newly acquired and previously existing words. In addition, regions in left parietal cortex demonstrated a complementary role in support of episodic processes in the retrieval of memory for newly learned words. Our attempt to identify a potential semantic brain system using a clustering approach failed to identify such a system, at least not one that jointly included the two candidate regions (PHG, mSFC). However, other well-established systems were identified by the clustering analyses, which rules out explanations such as compromised integrity of the dataset as a viable explanation for not identifying a semantic system.

All in all, a parsimonious interpretation of our findings is that the left parahippocampal and medial superior frontal cortex are two regions important for retrieval of novel semantic memory. In addition, their involvement during retrieval of previously existing semantic memory also suggests their role in the memory consolidation process, which, upon completion, would have likely additionally recruited the neocortical lateral temporal regions.

Chapter 4: Concluding Remarks and Future Directions

4.1 Introduction

The overarching goal of this thesis was to characterize the functional neuroanatomy underlying semantic memory retrieval for single words. The investigation was operationalized using a behavioral word-learning paradigm coupled with event-related fMRI data collected pre and post training. Below, we will recap the behavioral characteristics of newly learned words, as outlined in Chapter 2. This recap will be followed by a summary of the functional neuroanatomy that putatively generates the behavioral changes associated with learning new words, as described in Chapter 3.

The bulk of the discussion that follows addresses the implications of the current findings to our extant understanding of how the brain performs the task of storage and retrieval of memory, specifically the semantic memory for single word stimuli. **The first part** will feature a discussion regarding the role of episodic and semantic memory retrieval processes underlying the retrieval of memory for the meaning of single words. Embedded within that discussion will be the theme of time-dependent functional neuroanatomical evolution of declarative memory representations and the role played by schema-based learning strategies in that regard. **The second part** will focus on the role of top-down control processes in memory retrieval that may be recruited in a task-dependent manner. **The final part** will examine whether the brain regions that support semantic memory retrieval constitute a distinct brain

system, or, alternatively, comprise multiple brain systems that are recruited, in a context-specific manner, to support the semantic memory retrieval process. We will argue the latter.

4.2 Brief Summary of Current Findings

4.2.1 Behavioral Findings

As outlined in Chapter 2, we confirmed, using a series of behavioral tests, that new semantic memory has been successfully acquired, and the novel words resemble the behavioral characteristics of extant well-known real words. To that end, participants explicitly recognized trained-items and discriminated them from novel foils (recognition test); as well as demonstrated knowledge of their associated meanings (semantic memory test). Attesting to their similarity with real words, novel meaning-trained items demonstrated a depth-of-processing effect (Craik & Lockhart, 1972; Craik & Tulving, 1975) manifested as faster and more accurate recognition memory than form-only trained items. In addition, by exhibiting facilitative priming on synonymous real word targets, participants also showed evidence that the novel words are integrated in semantic memory (semantic priming test). Hence, we concluded that a 2-3 day training regimen was sufficient to produce behavioral evidence for successful word learning, with the novel words exhibiting characteristics, such as depth-of-processing and semantic priming effects, typically demonstrated by real words.

4.2.2 Functional Neuroanatomical Findings

As outlined in Chapter 3, we identified brain regions that showed BOLD activation profiles consistent with a role in semantic memory retrieval, based on multiple criteria outlined a-priori. Two regions in the left hemisphere emerged satisfying essentially all of our criteria,

one in the left parahippocampal gyrus (PHG) and the other in the left medial superior frontal cortex (mSFC), consistent with a role in the retrieval of semantic memory for both previously known and recently learned words. Based on the above observations, and prior work implicating medial PFC in integrating novel memory into the neocortex, we concluded that left PHG and mSFC likely support a role in the retrieval of ***recently*** acquired semantic memory yet to be fully consolidated in the neocortex..

Despite showing the expected semantic profiles for previously well-known word stimuli, such as word repetition suppression and a 'word > novel PW' effect, canonical semantic processing regions in the left lateral temporal lobe, such as the MTG and ATL failed to be engaged by the novel word stimuli. The observed profile led to a conclusion that these regions support retrieval of semantic memory for well-consolidated words. By extension, the said finding also suggests that a consolidation time-span of 2-3 days, as afforded in the current experiment, might be insufficient to produce fully consolidated neocortical representations, which would arguably include regions in the lateral temporal lobe (Holdstock et al., 2002; L. R. Squire & Wixted, 2011).

As for the left vIFG, a region implicated in controlled semantic memory retrieval, we had a surprising non-finding in that this region was not identified in any of the initial voxelwise contrasts that were set-up to probe the a-priori hypotheses/criteria. Interestingly, despite multiple reports documenting vIFG recruitment in tasks that emphasize controlled semantic retrieval (Badre et al., 2005; Donaldson, Petersen, Ollinger, & Buckner, 2001; Roskies et al., 2001; A D Wagner et al., 2001), vIFG is notably absent in studies using simple word/nonword

decision tasks (Fiebach et al., 2002, 2007; Henson et al., 2002) as used here. Using an SOA manipulation in an fMRI-based semantic priming paradigm to dissociate controlled and automatic retrieval processes, a prior study (Gold et al., 2006) has associated left vIFG exclusively with controlled, and not automatic, semantic memory retrieval. These observations led to an interim conclusion that the left vIFG likely supports a previously outlined role in controlled semantic memory retrieval, a role that was not crucial for task performance in the current lexical decision task setting.

Upon further probing using literature-derived regions, we identified a left vIFG region showing hypothesized semantic properties for real word stimuli (e.g. 'word > novel PW' and word repetition suppression), although it showed none of the expected effects for the novel words (e.g. higher BOLD for meaning trained than form trained or novel PWs). The latter observation may additionally warrant a similar interpretation as forwarded above for the regions in the lateral temporal lobe, i.e. insufficient consolidation time for the newly learned words may have contributed to the lack of vIFG engagement by the novel words – a point we expand on in more detail below.

4.3 Memory Organization – Our Understanding to Date

In thinking about semantic memory retrieval and its underlying functional neuroanatomy, particularly in the current novel-word learning context, there are two central themes relevant to the discussion. The first theme is the role of time and exposure-dependent memory consolidation processes driving the evolving functional neuroanatomical representations of semantic memory. Another theme relates to the potential of multiple

mechanisms to exist for semantic learning. After the discussion of these two themes, we will discuss how they relate specifically to the fMRI data in Chapter 3. We will follow this discussion with a third theme focusing on the role played by top-down (controlled) vs. bottom-up/stimulus-driven (automatic) processes in semantic memory retrieval. After some brief comments on traditional views of memory, intended to provide context, discussion of the above outlined themes will follow.

4.3.1 'Classical' Views of Memory Organization

Human memory is not a unitary phenomenon. Instead, behavioral, neuropsychological, and computational modeling research reveals that there are multiple types of memory, each supported potentially by distinct cognitive processes (McClelland et al., 1995; Moscovitch et al., 2006; Daniel L Schacter et al., 1998; L. R. Squire, 1992; Tulving, 1983). At the highest level of description, types of memory can be divided into declarative and implicit. Declarative memory, defined as memory that can be consciously remembered and explicitly reported, is further divided into short-term (e.g. working memory) and long-term memory, the latter of which will be the current focus. Implicit memory is memory that need not be consciously remembered or reported, but nonetheless influences behavioral performance. An example, relevant to the current discussion, is the implicit memory processes that underlie semantic priming effects. In semantic priming, a prime (e.g. nurse), that need not be consciously processed, facilitates processing of a related subsequently presented target word (e.g., doctor).

In turn, long-term declarative memory is typically broken down into memory for specific events (episodic) and memory for facts/word meanings that lack the association with a

specific time stamp (semantic) (Tulving, 1983). By definition, an episodic memory is a unique memory, such as for a specific event or experience. Accordingly, episodic memory is rapidly acquired without the need for repetition. An important element that uniquely characterizes 'episodic' memory is the agent's recollection of having been present as an observer or participant at a specific time and place during the particular episode.

Multiple accounts have been proposed to describe the relative characteristics and interactions between (potentially independent) episodic and semantic memory processes. One view (Shimamura & Squire, 1987; L R Squire et al., 1993; Larry R Squire & Zola, 1998) posits that semantic memory is constructed based on extraction of a common associative organizing rule across a series of episodically experienced memory instances. Proponents of the above view would argue that acquiring the meaning of a word such as dog (i.e. semantic memory) necessarily entails having the episodic experience of a dog in one form or another. Alternatively, the relatively more recent Serial Parallel and Independent (SPI) model (Tulving, 1995, 2001), a notable revision from Tulving's earlier position (Tulving, 1983), proposes three monohierarchically organized memory systems, namely a perceptual, semantic, and episodic system. The relation among the three systems is proposed to be mnemonic process-specific such that during encoding, memory processes proceed serially from perceptual, to semantic, to episodic representations. Storage is assumed to occur in parallel such that the perceptual, semantic, and episodic features of a given memory instance are stored in parallel with the respective systems. Finally, during retrieval, memory can be independently reconstructed/retrieved from each respective system. Given that it is at the top of the hierarchy,

episodic memory is necessarily dependent on the presence of semantic memory (which in turn is dependent on outputs from the perceptual representational system). For instance, even the specific consciously recallable experience of seeing the first 'bear' has to have within it some level of 'semantic' knowledge of the features that constitute the 'episodic' memory, e.g. four, legs, brown, teeth, claws, forest, etc. As supporting observational evidence, proponents of the SPI model cite that in early development, semantic memory systems develop earlier than episodic memory (Carey, 1985; de Haan et al., 2006; Murphy, 2002; Quinn & Eimas, 1997; Wheeler et al., 1997). While children of 4-5 years of age have gained a considerable amount of semantic knowledge, their capacity for episodic memory is relatively lagging.

The relative merit of the two aforementioned views on memory organization, particularly as is relevant for memory for word meanings, is yet to be adjudicated. It may be the case that the memory for a word is constituted from episodic as well as semantic elements, and where the memory lies on the episodic to semantic continuum is likely dependent on usage. For instance, consider the memory for a high-frequency word such as 'dog' and the memory for a low-frequency clinical term such as 'Darier disease' that labels a rare genetic skin disorder. It would be hard for one to remember the specific first episode when the word 'dog' was learned, whereas one may be able to describe the exact medical-school lecture, time of day, who was present etc., when the term 'Darier disease' was learned. Despite the stated potential distinctions in the memory representations between high- and low-frequency words, they are fundamentally similar in how they are treated behaviorally. For instance, they can be explicitly recalled and recognized, exhibit level-of-processing effects, and can prime

semantically related words etc., albeit to potentially differing degrees (Duchek & Neely, 1989; MacLeod & Kampe, 1996). Word frequency as a lexical variable makes for an interesting window into exploring the contributions from episodic and semantic memory for word meanings, although a more in-depth consideration of the issue is beyond the current scope.

4.3.2 Debated Role of the MTL in Episodic vs. Semantic Memory

Given the difficulties in making distinctions between what constitutes an episodic vs. a semantic memory, particularly as pertinent to memory for words, it is not entirely surprising that the functional neuroanatomy underlying the two forms of memory continues to be debated. Regions in the medial temporal lobe (MTL) including the hippocampus proper and neighboring entorhinal, perirhinal, and parahippocampal cortex, have been established as critical to the formation of new episodic memory, and when these regions are damaged, anterograde amnesia – the inability to form new episodic memory – occurs (Scoville & Milner, 1957). Whether the hippocampus also supports the acquisition and retrieval of semantic memory is less established. The classic example used to argue hippocampal involvement in both episodic and semantic memory is the case of patient H. M., who, following bilateral hippocampal resection, developed not only anterograde amnesia, but was unable to learn and retain new words (e.g. Xerox) that emerged following his surgery. Relatedly, in a remember/know paradigm, hippocampal amnesics are equally impaired for 'remember' and 'know' responses, processes thought to rely on episodic and semantic memory, respectively (Knowlton and Squire, 1995; Squire and Zola, 1998). Adopting a different stance, other investigators have reported that amnesic patients can acquire some semantic knowledge,

although retrieval performance is significantly impaired relative to healthy controls, and learning takes many repetitions (Glisky et al., 1986; Hayman et al., 1993; Kovner et al., 1983; Tulving et al., 1991). Such observations have been used to support the notion that semantic memory can be acquired and retrieved, albeit laboriously, without the critical involvement of the hippocampus. However, because learning in individuals with amnesia takes many repetitions, the observed learning could potentially be reflective of implicit as opposed to declarative memory processes (O'Kane, Kensinger, & Corkin, 2004; Larry R Squire & Zola, 1998). Finally, adopting a slightly different stance, other investigators contend that while the hippocampus is critical for episodic memory, some capacity for semantic memory remains if damage to the MTL spares surrounding MTL structures, particularly the parahippocampal gyrus (Bindschaedler et al., 2011; Holdstock et al., 2002; Mishkin et al., 1998; Verfaellie et al., 2000).

4.3.3 Memory Representations Across Time

Once acquired, long-term declarative memory is not static. It continues to evolve via integrative consolidation with existing memory, potentially with concurrent time-dependent changes in the underlying functional neuroanatomy. The primary evidence for the time-dependent process of memory consolidation comes from the pattern of memory impairment observed in temporally graded retrograde amnesia, which typically accompanies hippocampal anterograde amnesia. In temporally graded retrograde amnesia, recent episodic memory, i.e. those closer in time to the MTL insult, are compromised to a greater extent than remote memory. Memory impairments, both anterograde and retrograde, are typically more

pronounced when damage extends beyond the hippocampus proper to the surrounding MTL structures such as the parahippocamal gyrus (Mishkin et al., 1998; Shimamura & Squire, 1987; Verfaellie et al., 2000). Observations of retrograde amnesia, particularly the relative sparing of remote memory, led to the hypothesis that, once outside a given time window, memory retrieval is progressively less dependent on the hippocampus (Atir-Sharon et al., 2015; Ghosh & Gilboa, 2014; Takashima et al., 2006; van Kesteren et al., 2012). This change is thought to be due to the migration of memory representations to neocortical areas such as the medial prefrontal cortex and anterior temporal lobe, in a time-dependent, memory consolidation process (McClelland et al., 1995; Nadel & Moscovitch, 1997). In a manner that varies with the extent of hippocampal damage, the time span covering retrograde amnesia, and by extension, the memory consolidation process can last from a month to over 15 years in the most severe cases (McClelland et al., 1995)). Given their associations with semantic processing in healthy brains (Donaldson, Petersen, & Buckner, 2001; Gold et al., 2006; McDermott, Petersen, Watson, & Ojemann, 2003; A D Wagner et al., 2001), and the selective semantic impairments that result from their damage (Dronkers et al., 2004; Graham, Simons, Pratt, Patterson, & Hodges, 2000; Hart & Gordon, 1990; Holdstock et al., 2002; Turken & Dronkers, 2011), regions in the lateral temporal lobes, such as left MTG and ATL are proposed as candidates for consolidated neocortical memory representations (L. R. Squire & Wixted, 2011).

Based on the aforementioned observations, two prominent computational models have been constructed to explain the functional neuroanatomy supporting declarative memory acquisition and consolidation. The first is the Complementary Learning Systems (CLS)

account (McClelland et al., 1995). The CLS model, which notably makes no explicit distinctions between semantic and episodic memory, posits that memory is first stored via hippocampal synaptic changes, which support reinstatement of a recent similar memory in the neocortex. Each reinstatement of a memory that is similar to a prior instance leads to slow, incremental changes in neocortical representations, to permit the neocortex to learn the common structure among the different instances. The hippocampal system permits rapid learning of novel information without disrupting existing memory in the neocortex. Consolidation of novel information with existing memory in the neocortex occurs via slow incremental changes, ensuring remote memory stability in the face of novel memory acquisition.

The second model is the Multiple Traces Model (MTM) proposed by Nadel and Moscovich (Nadel & Moscovitch, 1997). As motivation for the model, Nadel and Moscovich point out that not all cases of retrograde amnesia are temporally graded. Episodic (autobiographical) memory shows a shallow temporal gradient such that following hippocampal damage, even the most remote episodic memory is impaired, whereas semantic memory (e.g. names of public figures) show a steeper temporal gradient. The two models are similar in that they both regard the hippocampus as central to rapid episodic memory acquisition and both models generally regard neocortical memory consolidation as a relatively slower process. What sets the two models apart is that in the CLS model, the hippocampus is only prominently involved during retrieval and consolidation of recent, i.e. relatively novel memory. For remote memory matching a neocortical representation, the prefrontal cortex

inhibits the hippocampus to avoid duplicate encoding (Frankland & Bontempi, 2005). On the other hand, in the MTM the hippocampus continues to be involved in the retrieval and reconsolidation of even remote memory. Reinstatement of a prior memory, or a slight variant thereof, creates a duplicate trace in the hippocampus. The common features present across multiple, slightly different memory traces can then be extracted to form what essentially becomes a decontextualized semantic memory. To explain temporally graded retrograde amnesia, the model posits that, because remote memory have likely been copied multiple times, they are more resistant to degradation due to hippocampal damage relative to recent memory.

As will be elaborated in greater detail below, the above discussion is particularly relevant here because one of the regions that we ascribed a role in memory retrieval of both previously known and newly learned words is in the parahippocampal gyrus, as opposed to canonical neocortical semantic regions in the temporal lobe (e.g. MTG). Given the above controversy in the literature regarding the involvement of MTL structures in semantic memory processes, this finding complements the literature by contributing evidence to the ongoing discussion from a sparsely documented adult word learning perspective. Another issue worth briefly mentioning regards the proposed slow nature of memory consolidation from initial MTL-dependent to subsequent neocortical representations. Given that the newly acquired words in the experiment failed to engage expected neocortical regions in the temporal lobe (e.g. MTG, ATL), subsequent discussions will draw on slow neocortical memory consolidation processes as a potential explanation.

4.3.4 Recent Challenges to 'Classical' Models of Memory Organization

Recently, work has emerged demonstrating that if effective scaffolding schemas are present, novel memory can bypass the hippocampus and be rapidly acquired via the neocortex. Tse et al. (Tse et al., 2007) used a paired associate learning task and trained rats to associate different food flavors with variable spatial locations. The constancy of paired flavor-location association became the schema, which took about a month-long repetitive training for the rats to learn effectively. Once having acquired the schema, the rats could rapidly learn, in a single-trial exposure, a novel flavor-location pair, without memory interference with concurrently trained paired associates. Critically, experimentally induced neurotoxic hippocampal lesions did not impair the ability for rapid (neocortical) learning of novel flavor-location pairs if the lesions occurred following schema acquisition. The authors concluded that what the learner brings to the table, i.e. a consistent schema, can permit rapid neocortical memory consolidation without interfering with remote memory, suggesting a revision to the notion of the neocortex as a slow learner. In a subsequent study, Tse et al (Tse et al., 2011) demonstrated that rapid neocortical learning of a novel paired associate consistent with a preexisting schema was associated with expression of immediate-early genes (IEGs) in the rat peri-limbic medial prefrontal cortex. The latter effect which more directly established a neocortical region involved in rapid neocortical memory consolidation, was exclusively present when the novel paired associate learning occurred in the presence of a consistent schema.

Mechanisms similar to the schema-dependent learning have since been demonstrated in human subjects. The phenomenon dubbed fast mapping is a learning mechanism that is thought

to underlie word learning, particularly as occurs during early vocabulary development. Similar to the schema-based learning, the idea behind fast mapping is to train a novel word in the context of retrieval of an already known concept. Retrieving the meaning of the already known word, and then ruling it out allows the learner to infer that the new word to be learned refers to a novel item. Similar to how an existing schema can scaffold the acquisition and rapid neocortical integration of a novel memory, the retrieval of an already familiar concept can act as a similar scaffold for acquiring a new word. As described below, a fast-mapping approach to novel word learning is argued to lead to hippocampus-independent rapid neocortical learning.

Coutanche and Thompson-Schill (Coutanche & Thompson-Schill, 2014) demonstrated that words acquired using a fast mapping approach (in contrast to an approach they termed episodic encoding, which asked participants to "remember the XXX") result in rapid integration into lexical networks. Lexical integration was assessed via lexical competition effects as done previously (Bowers et al., 2005). If the newly learned word (e.g. "torato") is lexically integrated, it is expected to compete with the lexical representation, and hence slow down lexical decisions to its orthographic neighbor (i.e. "tomato", which now has "torato" as its only neighbor), relative to lexical decisions for control hermit words. Lexical integration effects, which typically take multiple days of consolidation to emerge (M. H. Davis et al., 2009; Gaskell & Dumay, 2003), were demonstrated both 10 minutes after training as well as on the following day. The same publication also demonstrated preliminary evidence for semantic priming effects, using the novel words as primes for related concepts. The above behavioral demonstration was forwarded as evidence that fast mapping results in rapid

neocortical representations, thought to underlie lexical integration (Coutanche & Thompson-Schill, 2014).

More direct evidence for the possibility of rapid hippocampus-independent neocortical learning comes from demonstrations of word learning via fast mapping, in bilateral hippocampal amnesics (Sharon, Moscovitch, & Gilboa, 2011). Four severely amnesic patients were taught arbitrary word-picture associations using a fast mapping paradigm. Despite exhibiting strong impairment in a standard associative memory task, the patients were able to acquire the word-picture associations over a few trials, and were able to retain the knowledge when tested a week later. On the contrary, patients with damage to the left anterior temporal lobe were impaired in the fast mapping task. The potentially critical importance of the left anterior temporal lobe for rapid cortical learning was corroborated in a subsequent publication from the same group (Atir-Sharon et al., 2015). In that publication, the group demonstrated in healthy adults that subsequent memory performance following fast mapping vs. standard explicit encoding training was best predicted by anterior temporal lobe and hippocampal voxels, respectively.

The aforementioned findings by Tse et al (Tse et al., 2007, 2011) seemed, at first glance, to counter prior models of novel memory acquisition and consolidation (McClelland et al., 1995; Nadel & Moscovitch, 1997). The schema-based learning account seemingly contradicted the position taken by predating computational models in two accounts. First, unlike the schema-based account, the models considered the hippocampus as the exclusive gateway for novel declarative memory acquisition and retrieval. Second, unlike the rapid

neocortical schema-based learning, the computational models posited that neocortical declarative memory consolidation is an obligatorily slow (on the order of weeks or longer) process if it is to avoid interference with prior memory. To address the apparent discrepancies in schema-based learning, McClelland (McClelland, 2013) ran another simulation of the Complementary Learning Systems model, with an exclusive focus on the consistency of the new learning with prior knowledge. The relevant findings were that, given consistency with prior knowledge, the model's simulated neocortical network was able to rapidly acquire new information, without interfering with prior knowledge, similar to schema-based learning. The latter finding provides an important validation for a critical finding about schema-dependent memory acquisition and consolidation that has profound implications, an example of which would be the faculty of education.

4.4 Functional Neuroanatomy of Memory Retrieval – Current Observations

There are a number of observations that emerged from the current project that are relevant to the preceding discussion. First, left medial and lateral parietal regions previously implicated in episodic memory retrieval show many properties similar to the two regions (PHG and mSFC) that were top candidates for semantic memory retrieval, particularly for novel words. These properties shared by the two sets of regions include a bigger effect of meaning relative to perceptual training as well as a training type X retrieval accuracy interaction. These observations may suggest a role for the parietal regions in semantic retrieval of novel words, consistent with the a-priori criteria. However, as noted below, this may be a premature interpretation.

The second observation is that, despite the similar profiles discussed above for PHG/mSFC vs. medial/lateral parietal regions implicated in episodic retrieval with respect to memory retrieval for novel words, the response for real words resulted in a functional distinction between PHG/mSFC and medial/lateral parietal regions. The first distinction is the finding that while PHG/mSFC showed a pattern of word repetition suppression across days, the parietal regions showed an effect resembling the old > new episodic retrieval success effect (i.e. repetition enhancement) for words. The second distinction, admittedly more subtle, was the finding that while both sets of regions showed a 'word > novel PW' effect prior to training, the effect was driven by a less negative timecourse for words relative to PWs. It is clear that despite the similar properties recapped above, the PHG/mSFC also exhibit properties different enough from the parietal regions to suggest distinct functional roles. The noted functional distinction is in support of distinct semantic and episodic contributions made by left PHG/mSFC and the left parietal regions, respectively, to the memory retrieval of the novel words.

A third observation is that, unlike PHG/mSFC which were engaged during retrieval of both novel and previously known words, regions in the lateral temporal cortex, which we expected to show similar properties, were only engaged by previously known words. At this early stage following novel word learning, the current data suggest that the PHG and mSFC are central to the memory retrieval process. Both the Complementary Learning Systems (McClelland et al., 1995; McClelland, 2013) and the Multiple Traces Model (Nadel & Moscovitch, 1997) discussed above would predict the involvement of the MTL in retrieving

recently acquired memory for novel word meanings. However, the fact that the PHG also demonstrates sensitivity to remote memories (i.e. the previously known words) is perhaps more consistent with the MTM model.

Again, with regard to timing, the novel words likely have yet to undergo further exposure and consolidation to engage classic neocortical regions, such as the lateral temporal cortex, typically recruited for word-level semantic memory retrieval. The lack of engagement of the left lateral temporal lobe by the novel word stimuli is surprising, given the novel word semantic priming effects (Chapter 2) that may lead to a contrary expectation. In addition, one may expect learning synonyms to existing words, categorized as living vs. nonliving entities, may mirror schema-based learning. If so, one may then expect the functional neuroanatomy of novel synonyms to be less reliant on MTL, but recruit regions in the MPFC and ATL, as per the schema-based learning literature. The latter expectation is partially satisfied in that we did identify a region in mSFC that potentially corresponds to the MPFC machinery proposed in the schema literature. However, as mentioned above, lateral temporal regions were not recruited during memory retrieval for the novel words.

As for the MTL, the schema-based learning literature had deemphasized its importance by suggesting that when damaged, learning can proceed via direct neocortical support. This suggestion does not disqualify an undamaged and functional MTL from being recruited during retrieval and reconsolidation of the novel words. Hence, we do not consider our identification of the PHG as an important region for retrieval of novel word meanings as inconsistent with findings from the schema-based learning literature. Taken together, these observations suggest

that (A) the novel words are still undergoing full neocortical semantic integration, and will potentially engage the lateral temporal lobe given more exposure; and (B) behavioral semantic priming effects can apparently still be observed despite the potential caveat in (A) that may suggest an alternative expectation; (C) at this early stage, the medial temporal lobe (i.e., PHG) and the medial superior frontal cortex appear important in the retrieval of newly learned semantic memories; and (D) while potential distinctions between the functional neuroanatomy of episodic vs. semantic memory retrieval await clearer evidence, a role for left medial and lateral parietal regions in semantic processing should not be excluded as a working hypothesis.

The above observations clearly beg a future experiment to test the hypothesis that, given more time and exposure, contextually acquired novel words would indeed recruit the lateral temporal regions, as did the real word stimuli. To allow further fine-grained characterization of the memory retrieval machinery, we would recommend implementing certain changes to the current experimental setup. The first and obvious change would be to include additional behavioral training sessions as well as an additional imaging session following training. These additions would allow investigating a focused hypothesis that the novel word stimuli would engage lateral temporal regions following the added training. The additional imaging session would also allow for observation of repetition priming effects for the novel word stimuli, a property that, if identified in a manner dissociative of meaning vs. perceptual training, would be an important observation for a semantic hypothesis. Another proposed change would be to run the post-training recognition memory and semantic priming experiments in an fMRI setting, as opposed to our current out-of-scanner approach.

Conducting the two behavioral tests in the scanner would still enable an item-level investigation, with the added value of being able to examine item-level functional neuroanatomy in different task contexts that potentially differentially engage episodic and semantic processes. Having direct fMRI data across the multiple task settings (i.e. simple LDT, item recognition memory, and semantic priming) could potentially shed more light on potential episodic/semantic functional neuroanatomical distinctions.

4.5 Top-Down Control in Declarative Memory Retrieval

In a manner that varies with task and stimulus characteristics, retrieval of declarative memory can be an automatic process, driven largely by the retrieval cue in a bottom-up manner, or require the instantiation of goal-directed top-down processes. Top-down processes that occur prior to retrieval may function as a biasing signal that aid in the activation of task-relevant semantic features, in the case of semantic memory, or event-details, in the case of episodic memory. Following the automatic or controlled retrieval of memory representations, post-retrieval selection processes may be engaged, in a task and/or stimulus-dependent manner, to select relevant information from simultaneously retrieved competing memory representations (Badre & Wagner, 2007; I. G. Dobbins & Wagner, 2005; Han, O'Connor, Eslick, & Dobbins, 2011). These two top-down processes have been characterized in the context of both episodic as well as semantic memory retrieval, and are discussed below.

4.5.1 Top-Down Control in Semantic Retrieval

In the context of semantic memory retrieval, the two processes discussed above, namely top-down control as a pre-retrieval biasing signal vs. post-retrieval selection, have been

associated with activity in left vIFG pars orbitalis (BA 47) and left vIFG pars triangularis (BA 45), respectively. The distinction in control processes and the corresponding functional neuroanatomy has been debated extensively (Badre et al., 2005; Thompson-Schill et al., 1997; A D Wagner et al., 2001). Badre et al. (Badre et al., 2005) conducted a study that parametrically varied semantic control demands (e.g. cue-target associative strength) and selection demands (e.g. number for competing targets), in an attempt to settle the selection vs. controlled retrieval accounts vis-à-vis left vIFG. Their findings are consistent with the account provided above. Along with the left middle temporal gyrus, left IFG pars orbitalis (BA 47) demonstrated activity modulated by cue-target associative strength but not by the number of competing targets. On the other hand, the relatively more dorsal left IFG pars triangularis was sensitive to the level of competition as well as the remaining control manipulations tested. Based on the aforementioned findings, Badre et al. concluded by ascribing a domain-specific role in controlled semantic retrieval to left IFG pars orbitalis (BA 47), and a domain-general role in post-retrieval selection to left IFG pars triangularis (BA 45). Although the left MTG, which exhibited similar properties as left vIFG pars orbitalis, is not typically regarded as a control-related region, the pattern of results described above have led some to suggest that the region may be engaged in both storage and strategic aspects of semantic retrieval(Badre et al., 2005; Gold et al., 2006).

4.5.2 Top-Down Control in Episodic Retrieval

In the episodic memory domain, similar control processes and corresponding functional neuroanatomy have been identified. In this context, results from studies using item recognition

memory tasks and a comparison of item vs. source-memory retrieval tasks are relevant to the current discussion. Wagner et al. (A. D. Wagner et al., 1998) contrasted encoding and retrieval related activity using a high-frequency words (verbal) and chromatic visual textures (non-verbal) stimuli in an fMRI study. Their results revealed that regardless of the mnemonic operation (encoding vs. retrieval) greater BOLD activity was identified for words relative to textures in posterior left dorsal inferior frontal gyrus (BA 44) and anterior left inferior frontal gyrus (BA 45/47). The opposite contrast revealed greater activity for textures relative to words in right precentral and posterior inferior frontal gyri (BA 44/6) and anterior right inferior frontal gyrus (BA 45). The results from the above study imply that the inferior frontal regions implicated in top-down control are recruited in stimulus-content-dependent manner, i.e. retrieval of (meaningful) verbal vs. (non-meaningful) nonverbal information was associated with activity in left and right ventral IFG, respectively. The content-dependent hemispheric lateralization of regions implicated in top-down control, was recapitulated in multiple studies from Dobbins and colleagues, as summarized below.

Dobbins et al. (I. G. Dobbins & Wagner, 2005) conducted a study using a source memory retrieval task that held the retrieval cues (pictures of common animals and artifacts) constant while experimentally varying the nature of the information to be recollected. The items were initially encoded via a perceptual judgment task (a 1-back size rating task) or one of two conceptual judgment tasks (living/non-living or pleasant/unpleasant). Three types of retrieval tasks were conducted during a post-encoding fMRI session, two of which were source retrieval tasks (conceptual vs. perceptual) and the third was a novelty-detection task in which

subjects identified a novel picture from among two additional previously seen probes. During conceptual source retrieval, subjects had to remember whether they made living/non-living or pleasant/unpleasant judgments whereas during perceptual source retrieval, they had to remember whether the object appeared in large or small size. Two relevant findings are discussed below.

First, left vIFG pars orbitalis and left MTG were selectively engaged during conceptual source retrieval, whereas right vIFG (BA 44/45) and right inferior temporal cortex (ITC) were engaged during perceptual source retrieval. Consistent with prior work ,(Gold et al., 2006) the former finding was interpreted as supporting a domain-specific role for left IFG pars orbitalis and left MTG in controlled semantic retrieval. To test a functional coupling hypothesis between left MTG and vIFG, the authors conducted a correlational analysis between the difference in peak task-evoked activity in the aforementioned regions during perceptual vs. conceptual source retrieval trials. The analysis revealed a positive correlation between the left vIFG pars orbitalis and the left MTG, and a marginally significant positive correlation between the right vIFG and right ITC, confirming the expected context-specific functional coupling.

Second, Dobbins et al., (I. G. Dobbins & Wagner, 2005) identified activity in left IFG pars triangularis interpreted as supporting a domain-general role in post-retrieval selection. The supporting evidence was such that relative to novelty detection, the two relatively more demanding source retrieval conditions (confirmed behaviorally), resulted in greater BOLD activity with no concurrent difference due to source content (perceptual vs. conceptual). Note that despite the conceptual vs. perceptual processing distinction during encoding, the study

used the same retrieval probes, all of which were meaningful pictures. As stated above, the proposed interpretation of the greater recruitment of left vIFG pars orbitalis, during conceptual relative to perceptual source memory retrieval was that it is reflective of domain specific role in controlled semantic retrieval. An alternative interpretation, although less likely given converging evidence implicating left vIFG pars orbitalis in controlled semantic retrieval (Badre et al., 2005; Roskies et al., 2001; A D Wagner et al., 2001), is that perceptual vs. conceptual source retrieval difference is driven by differential demand in selection from competing episodic representations. To adjudicate between the two interpretations, the Dobbins group conducted a follow-up study, which, as summarized below, supported a role for left vIFG pars orbitalis in controlled semantic retrieval.

The follow up experiment (Han et al., 2011) used a similar setup as the prior study discussed above (I. G. Dobbins & Wagner, 2005). In contrast to the earlier study that used a single set of meaningful picture probes, the follow up study employed two sets of picture stimuli. The first was a set of photographs of common scenes (e.g. kitchen) designed to evoke meaningful associations. The second set was based on (meaningless) fractal patterns generated from the same photographs of scenes using kaleidoscopic rendering software, which helped match the two sets of stimuli in basic color characteristics. On both the meaningful scenes and meaningless fractal probes, subjects performed pleasant/unpleasant or simple/complex judgments. Two findings emerged, one of which was consistent with those from the prior study while the second led to a slightly different interpretation. In support of a role in controlled semantic retrieval, left vIFG pars orbitalis and left MTG were recruited to a greater extent

during source memory retrieval relative to item recognition exclusively for the meaningful scenic pictures. Recapitulating prior findings (Bokde, Tagamets, Friedman, & Horwitz, 2001), a subsequent resting state functional connectivity analysis revealed a correlational coupling between left vIFG and left MTG, supporting their hypothesized interactive functional roles in controlled semantic retrieval task settings. Taken together, the aforementioned results were interpreted as supporting the role of left vIFG pars orbitalis in controlled semantic retrieval.

The second finding suggested that the role of left vIFG pars triangularis in post-retrieval selection is more specific to linguistic stimuli (i.e. less domain-general). Unlike the prior study that revealed higher BOLD activity during both perceptual and conceptual source retrieval relative to novelty-detection, the subsequent study only revealed differences between novelty-detection and source retrieval for meaningful stimuli. The absence of a difference between novelty-detection and source retrieval for non-meaningful stimuli, was suggestive that the putative post-retrieval selection processes supported by left vIFG pars triangularis may be specific to linguistic representations.

To summarize, studies conducted in the domains of episodic and semantic memory retrieval, specifically targeting top-down control processes, have revealed similar functional neuroanatomy commonly recruited during episodic and semantic memory retrieval. In the episodic memory domain, left vIFG pars orbitalis has demonstrated recruitment to a greater extent when control demands are high, e.g. conceptual source retrieval vs. item memory retrieval. In the semantic domain, the region is commonly recruited in semantic tasks that likely require controlled retrieval (e.g verb generation, semantic judgment/classification (J A

Fiez, Raichle, & Petersen, 1996; Petersen et al., 1988; Roskies et al., 2001; A D Wagner et al., 2001)), while being absent in simple word vs. nonword lexical decision tasks in which automatic semantic access may be sufficient for task performance (Fiebach et al., 2002, 2007; Henson et al., 2002). This interpretation is also supported by studies that directly dissociated automatic vs. controlled retrieval in left vIFG pars orbitalis in a targeted fashion (Gold et al., 2006). The aforementioned summary of common top-down control related functional neuroanatomy further highlights the similarities between episodic and semantic memory retrieval processes.

4.6 Top-Down Control in Declarative Memory Retrieval – Current Observations

In the current dataset, we made three observations that are relevant to the discussions on the role of top-down control in memory retrieval. The first observation is that we identified a region in the left IFG pars triangularis exhibiting BOLD timecourse profiles consistent with a domain-general role in top-down processes guiding memory retrieval. The second finding was that even though a literature-derived region in the left ventral IFG was identified, the region was only partially consistent with a semantic retrieval hypothesis. Third, we identified two sets of bilaterally distributed regions previously implicated in task-control. These regions, when put in a clustering analysis with the rest of the task-evoked regions, organized into two distinct modules: one that closely resembles the cingulo-opercular (COP) control system implicated in sustained task set maintenance and one that includes frontal regions of the frontal-parietal control system implicated in adaptive task-control operations (Dosenbach et al., 2006, 2007). The three observations are discussed below.

Upon examining the functional profile in left dorsal IFG pars triangularis across stimulus types, the most consistent observation was, as mentioned above, greater error-related BOLD activity, relative to correct trials, with no evidence of modulation by stimulus semantic content (e.g. meaning vs. perceptual training). Given its (stimulus-nonspecific) response to errors that is suggestive of a role in task-control, and its clustering-based assignment with regions resembling the frontoparietal adaptive task control system (Dosenbach et al., 2007; J. D. Power et al., 2011), we posit a role for dorsal IFG in domain-general task control in line with previous proposals (Badre et al., 2005).

As for the left ventral IFG (pars orbitalis), we had (an initially surprising) non-finding in that the region was not identified in any of the primary voxelwise contrasts conducted to test our a-priori expectations for regions involved in semantic memory retrieval. This (non) finding led us to consider that, consistent with other studies that failed to identify vIFG in a simple lexical decision task context (Fiebach et al., 2002, 2007; Henson et al., 2002), the task may not require controlled semantic retrieval, i.e. automatic semantic access may be sufficient for task performance. Subsequently, examination of literature-derived regions did identify vIFG exhibiting some properties consistent with a role in semantic processing. The observed profiles were very similar to that observed in left MTG in that the region exhibited sensitivity to previously known word meanings (based on word > PW and word repetition suppression effects) but not to the novel words acquired during the experiment. Unlike the proximal IFG triangularis discussed above, ventral IFG did not exhibit profiles suggestive of a role in domain general task control, such as the error > correct profile. Given the profiles described above for

vIFG, we offer a similar hypothesis as was forwarded for MTG – it may be the case that the reason for vIFG failing to be engaged by the novel words is that the information has yet to be adequately consolidated into long-term semantic memory representations. The future experiment, suggested in the previous section, can similarly test for the hypothesis that, given more training and consolidation opportunity, the novel words may indeed begin engaging the left vIFG. In addition, recall that in the potential follow-up experiment we also suggested conducting the recognition memory and semantic priming experiments in an fMRI setting. Those experiments, particularly the semantic priming paradigm, would be suited for testing the aforementioned hypothesis because that paradigm can be leveraged to target automatic vs. controlled semantic retrieval processes, for instance via SOA manipulations, as documented previously (Gold et al., 2006).

Finally, as mentioned above, clustering of regional task-evoked timecourses revealed two clusters with functional neuroanatomy resembling previously identified frontal parietal and cingulo-opercular task control systems. The frontal parietal cluster itself, as well as most of the constituent regions, exhibited BOLD timecourse profiles consistent with a domain-general role in task-control. Most of the regions exhibited a canonical error > correct trial response typical of control regions likely corresponding to a performance feedback signal (Badre & Wagner, 2004; Botvinick et al., 2004; Carter et al., 1998; Dosenbach et al., 2007). Similarly, in addition to anatomically corresponding to regions previously characterized as forming the core of a task-set maintenance system, the identified COP module, and most of the constituent regions, also showed a typical control profile of higher activity for errors than correct trials. Given that

control demand was not explicitly tested as an experimental factor, we can only ascribe the two modules discussed above and the regions within, with a role in top-down control based on ancillary evidence, such as the error responses described above, and neuroanatomical correspondence with prior work (Dosenbach et al., 2006, 2007; J. D. Power et al., 2011).

To conclude this section, in the current lexical decision task context, we identified regions whose functional profiles, prior history in the literature, and clustering-based characteristics were consistent with previously outlined roles in domain general task control. The evidence for a domain-specific brain region (i.e. left IFG pars orbitalis) dedicated to controlled semantic retrieval was less convincing, at least based on the region's absence during memory retrieval of novel words. However, given that the left IFG pars orbitalis was recruited by the previously known words, and the potential caveat of inadequate consolidation for the novel words, a role in domain-specific controlled semantic retrieval cannot be ruled out based on our findings.

4.7 Despite Revealing Other Brain Systems, Clustering Analysis Did Not Identify a Semantic Brain System

Following characterization of functional profiles at the individual region level, in an effort to identify a putative semantic brain system, we conducted a clustering analysis, based on regional task-evoked timecourses across stimulus categories. As documented in Chapter 3, upon examining clustering results across multiple thresholds and from multiple clustering algorithms, we found no convincing evidence for such a system. Recall that at the region level, we had identified a region in the left PHG and left MSFC showing BOLD activation profiles

consistent with a role in semantic retrieval for both previously known and novel words. We had also documented that a canonical semantic processing region in the left MTG was only engaged by the previously known word stimuli. There was no clustering outcome that contained all the aforementioned regions in the same cluster. PHG was essentially isolated. The MSFC region was clustered with a set of regions resembling the COP control system, and the left MTG was grouped with bilateral regions in middle and inferior temporal gyrus. Although not explicitly documented here, adding literature-derived regions in the left ventral IFG to the clustering analysis did not change the outcome in any qualitatively significant manner relative to the documented results.

Before discussing the implications of our clustering findings vis-à-vis a semantic brain system, it is worth restating that the clustering analysis did identify multiple clusters whose functional neuroanatomy corresponds closely with other previously well-characterized brain systems (Dosenbach et al., 2006, 2007; J. D. Power et al., 2011). These other potential systems include FP and COP control systems, a putative episodic memory retrieval system (Nelson et al., 2010), and a dorsal attention system (Corbetta & Shulman, 2002; J. D. Power et al., 2011). The above findings provide some confidence that the failure to identify a potential semantic brain system was not due to some idiosyncratic property or compromised integrity of the current fMRI dataset.

What then are the potential explanations for the failure to identify a potential semantic brain system in the current dataset? At least two possibilities are plausible. The first possibility is that it is due to some limitation of the dataset that we were unable to identify such a system.

These limitations could range from the choice of task or stimuli that failed to adequately engage such a system, compromised data quality, or due to insufficient exposure and consolidation opportunity for the novel words. Given that the dataset produced results consistent with prior work, including the identification of region clusters corresponding with previously characterized systems, we do not regard the aforementioned potential data-driven limitations as highly plausible.

The second possibility is that a distinct set of functional areas involved in semantic processing that exhibit similar functional, architectonic, topographic, and connectivity profiles may not exist. On the contrary, the brain's capacity for constructing and interpreting a given internal mental representation and linking that representation to an arbitrary referent (i.e. a meaningful word) may be an emergent property that is the result of interactions between bottom-up and top-down processes. To entertain such a possibility as viable, let us briefly consider the properties that a semantic system would need, if it existed, in linking a word to a given mental representation. The mental representations that eventually give rise to concepts that are linked to arbitrary referents (words) could arise from multiple sources, depending on the nature of the concept. These could include representations arising from sensory and motor systems, for instance related to visual objects or actions, respectively. They could also include representations arising from limbic systems related to emotional responses to the sensorimotor mental representations driven by externally or internally generated stimuli. Finally, phenomena such as semantic priming effects suggest bidirectional interactions between bottom-up sensorimotor representations and top-down biasing control signals. For instance a prime

detected via bottom-up processes potentially affects top-down processes that may subsequently influence the next bottom-up process related to target processing. It may be the case that there exists no system at a higher level of hierarchy that coordinates the mental representations arising from such interacting bottom-up and top-down processes. Instead, what eventually becomes a consciously understood concept may be an emergent process that is not necessarily a sum of the underlying constituent bottom-up and top-down mental processes.

4.8 Questions for Future Research

As discussed above, the consistency of new declarative memory with prior knowledge, i.e. schema-based learning, places a critical constraint on the functional neuroanatomy of novel memory acquisition, particularly as it relates to the time it takes for the emergence of consolidated neocortical representations. The schema-based learning literature has very important implications. For instance, the fact that adopting a schema-based encoding strategy may allow hippocampal amnesics to learn information that they would otherwise be unable to is an instrumental bit of information for clinical applications such as cognitive behavioral therapy for memory impairment. Similarly, identifying learning approaches that may result in faster and potentially more efficient and integrative acquisition of new material can have significant educational applications. As such, the set of proposed questions for future experiments will build on findings from the schema-based learning literature as recapped below:

Using schemas to scaffold the acquisition of new memories has been associated with rapid neocortical memory consolidation,

Acquisition of novel declarative memory, which is otherwise thought to be critically dependent on the hippocampus, has been successfully demonstrated in hippocampal amnesics using a fast-mapping approach, demonstrating the plausibility of MTL-independent declarative memory acquisition. Fast mapping is a schema-like approach that uses retrieval and subsequent inferential ruling-out of an already-known concept to scaffold the learning of a new related concept (Sharon et al., 2011).

Patients with damage to the left anterior temporal lobe damage demonstrated impaired performance in the fast-mapping task. The latter finding corroborated the left lateral temporal lobe as a critical neocortical region for the retrieval of consolidated memory representations.

These findings collectively demonstrate that the encoding approach critically influences the functional neuroanatomy of novel memory acquisition. Given that memory performance is dynamic across the lifespan, an interesting question for future research would be to characterize the brain/behavior effects of different encoding approaches across the lifespan. Acquisition of verbal material across the lifespan is characterized by an inverted-U-shaped performance curve, with the number of words recalled increasing during childhood, peaking in the late 20s/early 30s, and decreasing in late adulthood (Blachstein & Vakil, 2015). While age is the best predictor of memory for verbal material, the effect is partially mediated by the ability to use self-generated organizational strategies (i.e., subjective organization) during encoding. The capacity for subjective organization mirrors the inverted-U-shaped memory performance function across age, lowest among children and the elderly and peaking in young

adulthood (H. P. Davis et al., 2013). As for the underlying functional neuroanatomy, findings from developmental anatomical and functional studies suggest that the medial temporal lobe matures earlier than the prefrontal cortex, which undergoes a relatively more protracted developmental maturation (Casey, Giedd, & Thomas, 2000; Diamond, 2002; Giedd et al., 1999; Gogtay et al., 2004; Johnson, 2001; Ofen et al., 2007). In contrast, during senescence, age-related degenerative processes have been reported in both the MTL and prefrontal cortex (Buckner, 2004; Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; T Hedden & Gabrieli, 2004).

Given the dynamic nature of memory performance and the underlying functional architecture across the lifespan, it is an open question whether or not the encoding strategy would similarly affect individuals at different points in their lifespan. The potential interactions between age and memory encoding strategy constitute an interesting topic for a future experiment. One reasonable hypothesis would be that, given the relative deficits observed in children and the elderly in employing self-generated organizational strategies during encoding, they would benefit the most from an externally imposed effective encoding strategy. In a novel-word learning context, a reasonable expectation would be that relative to young adults, children and the elderly would be most affected by the use of a schema-based fast-mapping approach relative to an episodic encoding approach (Sharon et al., 2011). Consistent with the latter expectation, schema-based approaches to word learning, which have been demonstrated possible despite a damaged MTL, may be hypothesized to benefit to a greater extent older subjects who may be undergoing MTL degeneration.

Finally, an ambitious yet important addition to a future lifespan study would be to characterize within each age group (e.g. children, young adults) the relationship between encoding strategy, recruited functional neuroanatomy, and behavioral outcome (word learning performance). The latter characterization can have potentially important implications for educational policy by allowing for tailoring specific learning approaches to individuals that may need and benefit from them the most. In addition, such research can potentially aid in designing effectively tailored cognitive/behavioral treatment approaches for individuals with memory disorders.

4.9 Conclusion

In conclusion, by using previously well-known words and novel words emerging from a word learning training paradigm, the current project has attempted to characterize brain regions sensitive to single word meanings. Our findings identified two regions, one in the parahippocampal gyrus and the other in the medial superior frontal cortex, that were sensitive to the meanings of both previously known and newly learned words. Previously documented canonical semantic processing regions such as the left ventral IFG and regions in left lateral temporal cortex exhibited sensitivity only to previously known words, suggesting that the novel words may require additional consolidation time to engage these neocortical regions.

Appendix

Appendix A: Pseudoword (PW) and Word Stimuli

Group 1 PWs (Appendix A.1.) and Group 2 PWs (Appendix A.2.) were counterbalanced for use either in meaning or form training. Group 3 PWs (Appendix A.3) were used as novel foils in the recognition memory test. The sentential meaning training effectively turns the PWs into novel synonyms for the words presented in Appendix A.4.

Appendix A1: Group 1 PWs (N = 90)

bakem	berms	binga	blont	bonry	calte
ceply	cetty	claza	daldy	doard	dumab
ervoy	facks	fakep	fambs	feght	fixod
flept	flurb	foday	funti	gewer	gight
giper	glews	hecoy	heert	hilky	hoony
joype	kears	lanjo	loing	maigs	makus
murkt	musny	nabre	pacaw	pindi	plorn
polep	praft	pugle	barpy	baves	bleas
brism	clees	criam	driek	fevee	gapal
gepia	gerif	griby	honad	huick	kails
limms	lorny	louth	musby	pexts	pheek
pimid	raboo	raimy	ralen	ratia	reald
reody	riosk	roner	ruldy	rulks	sculd
shord	slour	smota	solgy	tarly	titla
tiver	tooby	tosit	tudgy	wulse	yoden

Appendix A2: Group 2 PWs (N = 90)

broup	brove	cacho	canfy	cempo	crore
dearl	dinor	dizry	drick	dufly	flean
floke	flosh	forry	frool	fulla	ganic
gessy	grell	gutor	haped	hegan	brote
ciped	dahoo	drice	finip	fluko	fopaz
frare	freen	fumpy	grike	kegan	kives
kulep	molax	pafed	roxic	runna	sarry
spump	sunch	yills	bince	cebel	choct
chosa	crost	dirca	docab	drarp	dride
duark	farmo	flerp	fogma	folgy	fomit
frasp	geefs	ghisk	goser	gotes	guajo
hayon	bives	bruve	cangy	compy	fedia
fichy	garts	gazzo	gonar	grook	grova
keams	licar	litha	mogey	payou	reifo
runip	sceep	shino	slopa	tooch	topec

Appendix A3: Group 3 PWs (Recognition Memory Test Foils) (N = 180)

bealy	befip	blobe	bofty	borif	chred	civol	coips	coogs
croik	crulk	delpe	derds	detty	dogty	dolud	doron	drack
dravy	drief	drosh	dulky	feeve	ferbs	fiast	fidep	flose
foner	forls	frabs	framo	fruin	furob	gabla	gimma	glods
gloil	golls	gupid	hever	hilms	lamph	legur	lumos	mamps
merfs	mubby	nadii	narns	nelch	phick	phomp	pipeg	plaky
pombo	pudah	rajag	ralve	rayor	realp	rield	riend	roond
ruppy	sania	scook	shase	shavo	skomp	slase	slerk	sminy
soamy	sotel	stasp	thoky	thoto	thyla	tidow	toary	tunos
vawks	vitbo	vould	walna	wauts	waxan	werve	whilo	wouse
beags	begro	beres	bingu	bocer	bonth	borno	brosc	ceird
chost	cleot	cojex	coreb	coyen	cunks	dodal	dolio	druba
duvez	facky	feems	femod	fenis	fikes	fover	friep	fronp
furch	gatob	gezzo	gilks	gliam	godry	gonet	haner	hoits
humot	jeros	kound	lairf	lerms	letap	lonus	lorro	lovud
mabit	mannu	nasis	nello	nerry	nired	nosom	oltet	pacir
pafes	pames	phamp	pikto	plorm	ploss	pokel	polds	porad
posus	pumta	rithy	ruzak	rynic	sards	sazer	sigla	skart
slond	slork	smein	spari	spocy	stanf	steaf	tolve	tomey
toofs	tumir	tunch	vapog	voofs	vuffs	wakon	wateb	zents

Appendix A4: Target Words for Meaning Training (N = 90):

alligator	anchor	arrow	ball	bat	bear
bee	belt	bicycle	blender	book	brush
bucket	butterfly	camel	cat	caterpillar	cheetah
colander	comb	computer	cow	coyote	crowbar
crutches	deer	dingo	dinosaur	dog	drums
duck	dustbin	eagle	earrings	earthworm	emu
eraser	flute	giraffe	gorilla	guitar	hammer
hamster	handcuffs	harmonica	horse	hummingbird	keyboard
knob	ladle	lamp	lice	lion	mace
mosquito	mug	nail	necklace	organ	owl
paddle	parrot	peacock	pen	pencil	penguin
piano	pig	piranha	plate	rabbit	rifle
robin	rooster	rope	ruler	screw	spider
spoon	squid	sword	tadpole	tarantula	trumpet
turkey	turtle	vulture	wolf	woodpecker	wrench

Appendix B – Sentence Stimuli Used for Meaning Training

Sentence stimuli used to imbue meaning to the PWs in Appendix A are presented below. For each of the 90 PWs used in meaning training, 4 sentences were used in training (Appendix B.1 – B.4), and the 5th one reserved for testing in the semantic memory test (Appendix B.5). The sentences also include the target words that are presented in Appendix A.4, which during training would be replaced with PWs.

Appendix B1: Meaning Training Sentence Stimuli – List 1 (N = 90)

1. Unlike crocodiles, the American alligator does not immediately regard a human as prey, but may still attack in self-defense if provoked.
2. The ship dropped its heavy metal anchor to spend the night at the bay.
3. An archer usually builds his arrow using light wood and places a metal tip on the front end and a feather on the tail end.
4. My son loves bouncing his ball around the house.
5. The bat is the only mammal known that can fly.
6. The polar bear is a species that's under the threat of extinction, primarily due to global warming.
7. The bee is the farmer's best friend because it helps pollinate flowering plants.
8. You may need to tighten your belt an extra notch, your pants are falling down.
9. He pedaled his bicycle as fast as he could to get away from the bullies.
10. Using the blender, I can chop or puree vegetables in half the time it takes using a knife.
11. My son reads an entire book in less than three days.
12. You will need a soft to medium bristle brush for your delicate hair.
13. The bucket is leaking; you'll need a new one before you can mop the floor.
14. Once past the caterpillar stage, many butterfly species have large, often brightly colored wings, and conspicuous, fluttering flight.
15. The camel is the common beast of burden in Asian and African deserts.
16. I'm not much of a cat lover. I like dogs instead.
17. A moth can cause damage to fruits and other produce when it's still a caterpillar, before it becomes an adult.
18. As the fastest land animal, the cheetah can reach speeds of up to 70 miles per hour.
19. The pasta is done boiling. Can you please dump it onto the colander so the water can drain?
20. Check your family's hair every week using a fine-toothed comb.
21. After removing the floppy disk, please press any key to restart the computer.
22. In addition to its milk, the dung from the domestic cow is used in many cultures as a good source of fuel.
23. Also known as the American jackal or the prairie wolf, the coyote is a species of canine found throughout North and Central America.
24. A hammer or a crowbar is commonly used to open nailed wooden crates.
25. After my accident, the doctor gave me two aluminum crutches to help me walk.

26. For most species of deer, the male is called a "buck" and the female is a "doe".
27. The dingo is an ancient, free roaming canine unique to the continent of Australia, specifically the outback.
28. Scientists who study the extinct meat-eating dinosaur from the late Triassic period, known as the theropod, have noted its similarity to living birds.
29. My dog just gave birth to five puppies.
30. . Drums are usually played by hand, or using one or two sticks.
31. A duck is an aquatic bird, mostly smaller than the swans and geese, and may be found in both fresh water and seawater.
32. The custodian empties our dustbin every day or two.
33. The bald eagle is characterized by a powerful hooked bill, sharp vision, long broad wings, and strong soaring flight.
34. Stud earrings start at $10.00. But if your ears are not pierced, we also have clip-ons.
35. The earthworm, a commonly found worm, burrows in the soil and is very important in aerating and fertilizing the soil.
36. The emu is a large flightless bird in Australia that resembles the ostrich but is smaller and has a feathered head.
37. My pencil has a fresh eraser on its tip so I don't leave any mistakes.
38. The bamboo flute is an important wind instrument in Indian classical music.
39. The giraffe is the tallest land animal, often reaching a height of over 16 feet.
40. The gorilla is the largest of the great apes.
41. One of the reasons I moved to London was to play bass guitar in a soul group.
42. The claw hammer is a classical tool used by carpenters to drive nails.
43. My son wants me to buy him running wheels for his pet hamster.
44. The guards put handcuffs on the prisoner's hands before letting him out of his cell.
45. The small pocket-sized harmonica is one of the few instruments that can be played by blowing air into it or drawing air out.
46. During my summer vacation, I visited my uncle's farm and learned how to ride a horse.
47. A hummingbird is a small bird that cannot only fly forward but also straight up and down, sideways, backwards and can hover in front of flowers as it obtains nectar.
48. The shortcut is to simultaneously hold down the CTRL and ALT keys located at the bottom left of your keyboard.
49. I turned the knob to open the door.
50. The soup was dished out with a ladle.
51. Her expensive new bedside lamp had a beautiful glass shade that spread the light very efficiently.
52. . Lice eggs found in a child's hair can be mistaken for dandruff.
53. Its thick mane easily distinguishes the male lion from the female.
54. I keep mace with me to ward off potential muggers.
55. The mosquito is blamed for the spread of diseases, such as malaria, because it feeds on blood.

56. Could you refill my mug with more coffee?
57. The framed picture hung from a single nail in the hallway.
58. A necklace is made of a metal jewelry chain, often attached to a pendant or a locket.
59. As a large musical instrument, a traditional organ, such as one common in a catholic church, requires a lot of room to store all the pipes.
60. The hoot of the owl in the woods made the night seem alive.
61. A canoe is basically useless with out a paddle.
62. Don't say bad words around the parrot. It won't be long before that bird starts repeating them!
63. The brilliant feathers of the peacock have a series of 'eyes' that are best seen when the tail is fanned
64. The ink has run out of this pen and I can't write with it.
65. I need to sharpen my pencil before I continue the test.
66. The penguin is a flightless bird that lives almost exclusively in the southern hemisphere, with one famous species being endemic to Antarctica.
67. Although not easily portable and often expensive, the piano is still one of the world's most familiar musical instruments.
68. The pig pressed its snout against the pen as the farmer walked by.
69. The piranha is a species of freshwater fish common in South American rivers famous for its sharp teeth and voracious appetite for meat.
70. If we all use a paper plate we won't have to do any dishes.
71. The tiny nose and long ears of a rabbit make it an attractive pet.
72. Using a long rifle the hunter was able to shoot animals from far away.
73. The red belly of the robin makes it a distinctive bird.
74. My neighbor has a pet rooster who wakes us up with its crowing at the break of dawn.
75. The furniture was attached securely to the truck bed with a rope.
76. A regular ruler from the stationary can make a great straightedge.
77. Similar to a nail, a screw can be used in various construction jobs to fasten two pieces of wood together.
78. The spider is not an insect because it has eight legs instead of six.
79. I scraped the bottom of the ice cream can with my spoon to get the last drop.
80. The squid, an ocean-dwelling cephalopod, lacks flippers and as a result, moves by shooting water opposite the direction desired.
81. As a weapon used in many cultures, the sword varies across cultures in its design, such as the shape of its long blade, its size, etc.
82. The kids in the classroom were taking care of a tadpole tank, anxiously waiting until they matured into frogs.
83. Because of its large size and relative harmlessness, the tarantula is the most common spider pet.
84. Because of the way a player blows into the instrument with closed lips to produce sound, a trumpet often accumulates a lot of spit and has to be cleaned out.

85. On Thanksgiving, most American families cook turkey.
86. A turtle may retreat into its shell when threatened.
87. A vulture is a type of big, bald-headed scavenger bird and rarely kills its own prey.
88. The gray wolf hunts for prey in a pack.
89. The woodpecker uses its beak to peck holes into trees and find bugs.
90. An adjustable wrench for unscrewing nuts and bolts eliminates the need for a toolbox full of different sizes.

Appendix B2: Meaning Training Sentence Stimuli – List 2 (N = 90)

1. Florida is famous for its reptiles, particularly the alligator, which is the University of Florida mascot.
2. The ship's anchor was suspended into the water with a heavy metal chain.
3. The bow and arrow was the weapon of choice in medieval times.
4. He rolled the piece of paper the size of a tennis ball and threw it at his classmate.
5. I'm sure this cave has a huge bat population. Just look up when we get inside and we should see them suspended from the roof.
6. Most bear species use shelters such as caves and burrows as their dens, as well as for hibernation during the winter months.
7. A bee uses nectar as an energy source as well as to produce honey.
8. I had to unbuckle my belt after the heavy thanksgiving meal.
9. I need to replace the rusted chains on my bicycle before I take it out and ride it in the park.
10. My blender has ten different options, including the basic 'slice', 'chop', and 'puree' functions.
11. I have to go to the library to check out a book on the history of the Civil War.
12. I need a lint roller or just a regular brush to get all the lint off of my coat.
13. We have a 30-gallon bucket full of water. That should last us for three days or so.
14. . Butterfly larvae, or caterpillars, consume plant leaves and spend practically all of their time in search of food.
15. The camel is a mammal adapted for surviving long periods without food or water in desert regions.
16. My cat gave birth to five kittens. You can adopt one if you'd like.
17. The caterpillar is the larval form of moths and butterflies. It's notorious for its voracious appetite.
18. Although it is the fastest runner among members of the cat family, the cheetah lacks strong climbing abilities.
19. The perforated bottom of the colander is well suited for draining the water while rinsing vegetables.
20. I don't like to brush my hair. I like using a comb better.
21. I have to upgrade the software on my new laptop computer.
22. Reflecting the rising price of dairy products, the price of a milk-producing cow has been steadily rising through the years.
23. The coyote can be distinguished from the wolf by its relatively small size and its slender build, large ears, and narrow muzzle.
24. I need to borrow either your crowbar or hammer to pry these two boards apart.
25. If you don't want to use a cane or crutches, a wheelchair is another alternative.
26. With the exception of a few species, all male deer have antlers and the females usually have a small stub.
27. The Australian dingo has lived largely apart from people and other dogs, hence developing features and instincts distinct from all other canines.

28. . Dinosaur bones from the Jurassic period were recently unearthed from this quarry.
29. Although she's not a puppy anymore, I had to buy a kennel for my dog.
30. Even though we were blocks away from the marching band, we could still hear the beating drums.
31. A duck typically has short legs, webbed feet, a broad blunt bill, and short but strong wings.
32. Please don't put those empty cans in the regular dustbin. There's a separate recycle-bin in the next room.
33. The eagle, a powerful bird of prey, has extremely keen eyesight, which enables it to spot potential prey while flying very far away.
34. My daughter was excited to get her first pair of earrings after she got her ears pierced.
35. The earthworm, also called a nightwalker in some parts of the U.S., often crawls to the surface of the earth when the ground is cool or wet.
36. As a large Australian bird that can't fly, the emu jumps and kicks to avoid dingos, one of its predators.
37. Tom threw his rubber pencil eraser at his classmate.
38. A traditional flute, usually made of bamboo, produces sound when air blown across a hole in the instrument creates a vibration of air at the hole.
39. The giraffe has very long neck and legs, a tan coat with orange-brown to black blotches, and short horns.
40. The silverback gorilla, a large ape native to the Democratic Republic of Congo, is an endangered species.
41. I need my pick to play the guitar. I have been looking for it for ten minutes now and still can't find it.
42. He's shown me how to properly saw wood and use a hammer to drive nails.
43. It can often be hard to tell a hamster apart from a guinea pig or a gerbil.
44. Airlines have begun to carry plastic zip-ties, which function just as well as handcuffs, to restrain disruptive passengers.
45. You can produce different notes on a harmonica by placing your lips over individual holes or multiple holes.
46. Tom recently bet on a horse race at the Kentucky Derby and made ten thousand dollars.
47. The hummingbird has a bill that is usually rather long and always slender, and is adapted for securing nectar from certain types of flowers.
48. The coffee stain on my laptop keyboard is going to be hard to clean. I hope I don't damage the keys in the process.
49. The burglar slowly tried turning the knob to see if the door was unlocked.
50. For our wedding, we registered for serving utensils including a new ladle, for serving soup into a bowl.
51. It would be easier to see the papers on your desk if you turned on the desk lamp.
52. Intense itching of the scalp could be a sign of head lice.
53. The lion, a big cat found in Africa, commonly lives in groups called prides.
54. Although it is good for self-defense, make sure you don't spray the mace at yourself

accidentally!
55. After returning from the swamp, I was covered with mosquito bites.
56. The coffee mug has a broken handle, making it hard to drink from.
57. The hardware store had a different sized nail for every situation ranging in length from half inch to 10 inches and of different thicknesses.
58. His necklace was a simple gold chain suspending a locket that held his parents' photograph.
59. The church's organ produces beautiful tones for every service.
60. Flying over the field, the owl, which usually hunts at night, used its huge eyes to spot a rodent.
61. Before we go kayaking, I have to buy a new paddle since you used my old one as a fire poker and ruined it on our last camping trip.
62. The ability of some parrot species to imitate human voices enhances their popularity as pets.
63. Only the male peacock has the colorful tail display, which he uses for courting the female bird of his species.
64. You will need to sign the contract where indicated using a black pen.
65. Most people write using a number 2 pencil but there are actually other sizes.
66. It's fun to watch the black and white penguin slide across the snow on its belly.
67. Someone who is good at playing the piano often has long fingers.
68. A butchered pig produces many different cuts of meat, such as bacon and ribs.
69. The piranha is mythically characterized as a species of small fish that can tear a human or cattle to pieces in a matter of seconds.
70. The painted fine china plate was displayed on the mantle and never used for eating off of.
71. The rabbit is known for its speedy reproductive abilities producing an average of six babies per litter four to five times a year.
72. The soldier lifted the assault rifle slung across her back to shoot at the enemy.
73. The robin has four baby blue eggs in its nest.
74. The rooster is a male domestic flightless bird famous for its crowing and the red comb and wattle on its head.
75. The rope was braided with many strands to increase its strength.
76. He measured the length of the rectangular figure in inches using a ruler.
77. The threads on a screw secure it better than a regular nail would.
78. I think this web in the garden must belong to a pretty big spider.
79. Set each place at the table with a bowl and a spoon for the soup.
80. Usually referred to as calamari, the squid is a very popular seafood item.
81. It is common for a knight to wield a sword and a shield.
82. This tadpole has almost grown up into a frog because it has all four legs.
83. The tarantula is much larger than more common spiders and has hairy legs.
84. One of the brass instruments, the modern trumpet generally has either three piston valves or three rotary valves.
85. The gobble is the famous noise made by a turkey.

86. Humans, especially in China, treat the turtle as a common foodstuff, although the tough shell of the reptile is not eaten.
87. The sight of the bald and curve-necked vulture is common but unwelcome on a battlefield or where ever dead bodies can be found.
88. The grey wolf howls to communicate with other pack members.
89. I couldn't sleep because that woodpecker has been banging on the tree with its beak all morning.
90. He tightened the bolt with an adjustable wrench.

Appendix B3: Meaning Training Sentence Stimuli – List 3 (N = 90)

1. The Floridian alligator is usually smaller in size than its cousin, the African Nile crocodile.
2. A ship's anchor achieves its holding power by hooking into the seabed, by sheer mass, or a combination of the two.
3. Once released from a bow, feathers help stabilize the arrow.
4. We kicked the ball around to warm up for the game.
5. A bat, which mostly hunts at night, uses echolocation to locate flying insects.
6. The brown bear has thick fur that is more resistant to bee stings. This allows it to steal honey from beehives.
7. Fresh honey is only one of the many benefits of being a bee farmer.
8. Because a lot of teenagers were walking around showing their underwear, students are now required to buckle their belt tightly at waist level.
9. Riding a bicycle is the principal means of transportation, particularly in crowded cities.
10. You can borrow my blender if you need to crush ice for making cocktails.
11. Reading my book made the 3-hour flight a lot more bearable.
12. The archeologist uses his brush to carefully remove the dirt from the fossils.
13. The handle on the large bucket is broken. You may need to use the jug and take more trips until we get a new one.
14. Although they are small insects, some species of butterfly, such as the Monarch, are known to migrate over long distances.
15. Storing fat in its hump allows the camel to go long periods without food.
16. The cat keeps scratching my sofa. I may have to have her claws removed.
17. Many caterpillar species are cryptically colored and resemble the plants whose leaves they feed on before turning into an adult moth or butterfly.
18. Similar to the leopard, the coarse, short fur of the smaller African cat, the cheetah, is tan with round black spots, giving it some camouflage while hunting.
19. A colander is a kitchen utensil that looks like a bowl and has holes at the bottom.
20. In addition to using flea shampoo for my dogs, I also use a fine-tooth comb that can remove fleas.
21. Here's some antivirus software to clean the hard drive on your computer.
22. At 12.45pm every day you can try hand-milking Millie, our lovable Friesian dairy cow.
23. . Coyote packs are generally smaller than wolf packs and associations between individuals are less stable.
24. Grab the crowbar from my trunk. We'll need to pry open the window to get in.
25. A walking stick or cane serves a similar purpose to a pair of crutches, although it is less effective because you can't put as much weight on it.
26. Be careful when driving in these windy roads, it's hard to see the deer that come out of the woods and cross the street.
27. Although similar in other forms of communication, the Australian dingo tends to howl and whimper more and bark less than domestic dogs.
28. Fossil remains indicate that huge pillar like legs were needed to support the enormous body

weight of the brontosaurus, an herbivorous dinosaur.
29. My dog is trained not to bark in the house.
30. There was a flag on every house, crackers going off, drums beating, singing and crying " Viva Pacheco."
31. Tom has a favorite duck that swims on the pond that he has named "Duffy." It quacks every time it sees Tom.
32. Please throw away all those empty gum wrappers in the dustbin.
33. The bald eagle builds its nest, called eyrie, in tall trees or on high cliffs.
34. I don't think she likes rings, bracelets, or necklaces. If it has to be jeweler, I would shoot for a pair of earrings.
35. In most fishing communities, the earthworm is a commonly used bait for angling.
36. Like the ostrich, the Australian emu is a large bird that can run fast, sometimes reaching speeds of up to 35 miles per hour.
37. Graphite, the lead used in a pencil, is a stable and permanent material but can easily be removed using a rubber eraser.
38. Unlike woodwind instruments with reeds, a flute is an aero-phone or reed-less wind instrument.
39. Commonly found in the savannas of tropical Africa, the long-necked giraffe feeds principally by browsing in the tree canopy of wooded grasslands.
40. The chimpanzee and its larger ape cousin, the gorilla, are two of the primates that are closely related to humans.
41. The tone of an acoustic guitar is produced by the vibration of the strings, and amplified by the body that acts as a resonating chamber.
42. You'll need a claw hammer to extract those nails.
43. My pet golden hamster sleeps in the daytime whereas my guinea pig sleeps at night.
44. Police academies teach their recruits to put on handcuffs so that the palms of the suspect's hands face outward.
45. The harmonica is the perfect musical instrument for the light traveler as it's no bigger than a candy bar.
46. In our last vacation at Guatemala, we enjoyed a buggy ride drawn by a beautiful black horse through the pretty countryside.
47. The hummingbird, particularly the smaller species of the bird, is famous for its extremely rapid wing-beat rates.
48. If nothing is happening when you are typing, make sure the keyboard is connected to your computer.
49. A "Do Not Disturb" sign hung on the knob of the hotel room.
50. You'll need a ladle with a long handle to serve the curry that's in the really big pot.
51. The room became much brighter when the desk lamp was turned on.
52. Infestations of head lice can be eliminated using special medicinal shampoos.
53. The female lion does the majority of hunting for a pride while the male patrols the territory.
54. A spray of mace in the eyes causes burning and temporary blindness.

55. Given that the warm spring weather, along with the abundant water from the nearby lake, makes for excellent mosquito breeding conditions, I'd bring bug repellant to the campsite.
56. His mug collection was more for decoration than for drinking coffee of.
57. Don't hit your thumb with the hammer instead of hitting the nail!
58. Queen Victoria's diamond necklace is no longer on her neck. It is now kept in the museum under the highest security.
59. She played the large church organ well because she was very coordinated with her feet.
60. Because both of its eyes are forward facing, and not on the side like other birds, the owl must turn its entire head to change views.
61. A paddle is not fixed to the boat, as an oar would be.
62. When we were in Puerto Rico, we saw a colorful blue and yellow parrot that could add. Its master would ask it to add two numbers and the bird would speak the answer aloud.
63. A large fanned tail display by a male peacock tells the female that he's fit for mating.
64. This pen uses ink that dries immediately, so don't worry about smudging while writing.
65. She made sure to write the draft in pencil in case she made a mistake.
66. Highly adapted for life in the water, the wings of the Antarctic Emperor penguin have become flippers.
67. Our cat sometimes walks across the piano and strikes the keys making strange musical noises.
68. Despite a reputation for being dirty and greedy, the domestic pig, a close relative of the wild boar, is really a very intelligent animal.
69. Once a prey is located in the Amazon, every piranha in the group rushes in to take a bite with its sharp teeth and then swims away to make way for the others.
70. I'm not sure you'll be able to finish all that food you have heaped on your plate.
71. I feed my pet rabbit two to three carrots a week.
72. A new scope improved the accuracy of the sniper's rifle.
73. The red-breasted robin is one of the most familiar songbirds in the eastern United States.
74. Making a rooster fight and betting on the winner bird is illegal in many countries.
75. Throw the rope down so I can climb up the cliff.
76. The line was drawn perfectly straight with the aid of a ruler.
77. I always lose the tiny screw that holds my glasses together.
78. The funnel-web spider has a flat web with a tunnel at one side where the eight-legged predator lurks.
79. I can't find a spoon to eat my yogurt with.
80. Myths and fiction speak of a giant kraken with tentacles capable of destroying ships. In reality, this may refer to a type of giant squid or octopus.
81. Unlike other old weapons, the handheld sword with a long blade is only used in battle, and not really for hunting.
82. A tadpole needs a tail to swim until it matures into a frog and leaves the water when it will have grown legs.
83. The tarantula, a hairy and typically non-venomous large spider commonly kept as a pet,

spins webs in trees to catch prey.
84. Fanfares for military parades were often played by a bugle, an instrument that's similar to a trumpet but lacks the three valves.
85. A turkey farm raises the animals to be eaten, though they are less popular than chicken as food, except during Thanksgiving.
86. The reptilian turtle from the ocean has a shell that is shaped differently than that of its land-dwelling relative, the tortoise.
87. The head of a vulture might be bald to keep it clean while it uses its beak to dig deep into carcasses.
88. The dog, a descendant of the modern grey wolf was domesticated by humans for work and companionship.
89. Besides their tree-drilling beak, the woodpecker males are often known to have red feathers on the head.
90. I'll need a heavy-duty wrench to get those rusted bolts off and change the tires.

Appendix B4: Meaning Training Sentence Stimuli – List 4 (N = 90)

1. A close relative of the crocodile, the alligator is a large reptile native only to the United States and China.
2. The boat raised its anchor from the sea floor in preparation for departure.
3. The archer's sharp and pointy arrow was no match for the Knight's armor.
4. My soccer ball is no longer bouncing. I think we need to put some more air in it.
5. There are a few species of bat that consume blood exclusively as their diet, hence getting the "Vampire" label.
6. When camping in this park, make sure you secure your garbage. There have been many recent brown bear sightings.
7. The queen of a honey-producing bee colony may lay 2000 eggs per day during spring buildup.
8. My grandfather used to whip my father when he was being troublesome. He knew to run away the minute Grandpa started unbuckling his belt.
9. Learning to ride my BMX bicycle was one of the most exciting times of my childhood.
10. To make your favorite fruit juice, cut the fruit into smaller pieces before putting it in the blender.
11. At age 20, he already wrote a book that's a New York Times bestseller.
12. After painting the rails, don't forget to clean the brush. We'll need it to paint the corners of the walls tomorrow.
13. We just bought a 20-gallon bucket of paint for the remaining 10 rooms.
14. The colorful winged insect, the butterfly is an important pollinator of plants, similar to bees and hummingbirds.
15. The Bactrian, or Asian camel has two humps while its Arabian cousin has only one.
16. I think my cat really does have nine lives. I can't tell you how many times she almost got run over by cars.
17. Several insects produce silk, but only the silk of the moth caterpillar is used for textile manufacturing.
18. Although it is often mistaken for the leopard, the cheetah is much faster, smaller, and has smaller black spots than the leopard.
19. After cooking your cabbage in the boiling water, strain it using a colander.
20. This comb is too fine-toothed for my dog's tangled hair.
21. Users can download music to their desktop or laptop computer directly from the online music store.
22. A cow kept to provide milk for one family may also be known as a "milker".
23. The coyote has been known on occasion to mate with wolves, though this is less common than with dogs.
24. Apart from prying things open, a crowbar can also be used as an improvised weapon.
25. I was so glad when the doctor removed my cast because I no longer needed crutches to walk.
26. The deer was stunned by my headlights and stopped dead in the middle of the road.

Fortunately, I was able to swerve and avoid it.
27. Although the canine is usually seen alone in Australia, the dingo belongs to a social group that typically meets to breed and raise pups.
28. Since the first dinosaur fossils were discovered in the early 19th century, their mounted skeletons have been major attractions in museums.
29. My dog loves to chase the neighbor's cats around the block.
30. We marched up the center of the street, shouting, singing, banging drums, dancing and generally making our presence felt.
31. A common urban legend claims that duck quacks do not echo; however, this has been shown to be false.
32. The dustbin is overflowing. Please remind me to buy some trash bags tomorrow.
33. The bald eagle can be found in the United States and Canada. Most other species of the bird occur in Eurasia and Africa.
34. I would give your ears a break and take those earrings off. You may actually be allergic to silver.
35. The earthworm travels underground by means of waves of muscular contractions, which alternately shorten and lengthen its body.
36. While the ostrich has two toes on each foot, its Australian-native cousin, the emu, has three toes on each foot.
37. Prior to the invention of the rubber eraser, tablets of wax were used to remove lead or charcoal marks from paper.
38. When we were in China, we met a young street child who was playing what looked like a wooden flute by blowing air into it.
39. The tall giraffe has to spread its two front legs apart to drink water.
40. The forests in the east of the Democratic Republic of Congo are the last home of the eastern lowland gorilla.
41. An electric guitar relies on an amplifier that can electronically manipulate tone.
42. The larger and heavier head of the hammer can decrease the number of blows required to fully insert the nail.
43. The cage that I got for my pet hamster may be a little too small. There isn't much space for the running wheels.
44. The restrained prisoner used a pin to get himself out of the handcuffs that the cops put on his hands.
45. Unlike most other instruments, playing the harmonica requires both inhaling and exhaling strongly against resistance.
46. The female horse, called a mare, carries her young for approximately 11 months, and the foal can stand and run shortly following birth.
47. The English name of the hummingbird derives from the characteristic hum made by its rapid wing beats.
48. The so-called QWERTY keyboard layout was designed in the era of the mechanical typewriter.

49. The knob refused to turn because the door was locked.
50. Hand me the ladle so I can serve the soup.
51. I couldn't read because the bulb for my bedside lamp was burned out.
52. . Lice are pests that can spread quickly among school children.
53. Found primarily in Africa, the lion is known for its deep roar.
54. . Mace should only be sprayed if needed for self-defense.
55. A pool of stagnant water is the perfect mosquito breeding ground. That's where the adult females lay their eggs.
56. A mug with thermos-like properties is much better for hot liquids than a normal cup.
57. There always seems to be one rusty nail on the floor of the garage.
58. A choker is a close-fitting necklace that can be made of a variety of materials, including velvet, beads, metal, and leather.
59. The sound of the large organ being played is tied to my memories of going to baseball games.
60. As a nocturnal bird, the owl usually spends the day sleeping on branches or in hollow trees.
61. He freed his kayak from the shrubs by pushing his kayak away from the river walls using his paddle.
62. Most parrot species are tropical but a few species, like the Austral Parakeet, range deeply into temperate zones.
63. The elaborately colored feathers of the peacock have been used for healing in many cultures throughout time.
64. The tip of the pen glided smoothly along the page as it wrote.
65. The detective always brought a number 2 pencil and a notebook to crime scenes.
66. In the cold winters of Antarctica, it's common to see a large penguin huddle in the freezing snow. The birds apparently do this to conserve heat.
67. The stage had to be cleared to make room for the grand piano.
68. A pig can harbor a range of parasites and diseases. This is why pork should always be fully cooked before human consumption.
69. Among the species of small fish known for converging in a feeding frenzy, the most infamous is the red-bellied piranha of the Amazon.
70. The chef placed the hot steak on a plate, which the waiter promptly picked up.
71. The long ears and powerful hind legs that enable the rabbit to run fast are most likely an adaptation for detecting the many predators that hunt the little furry mammal.
72. A rifle is a long firearm designed to be fired from the shoulder.
73. The red-breasted robin is a small bird famous for signaling the arrival of spring, particularly in Northern United States.
74. The rooster guards the general area where his hens are nesting, and will attack other males who enter his territory.
75. The rope was tied in an intricate knot.
76. The ruler had marks for inches on one side and centimeters on the other.
77. I'll need to tighten the screw that attaches the legs to the top of the table because it is

starting to wobble.
78. The spider carefully built a web between the tree branches and awaited its prey.
79. A spoon is primarily used for eating liquid or semi-liquid foods, such as soup, stew or ice cream.
80. Ink is released to create a means of escape for a squid, similar to the defense reflex of an octopus.
81. In fencing, one doesn't typically use a real metal sword to fight against an opponent.
82. A tadpole stage is a common hatchling phase with amphibians such as frogs.
83. Even something as large as a bird has reason to fear the web of the hairy large spider, the tarantula.
84. The early version of the current trumpet was a signaling instrument used for military or religious purposes, rather than music in the modern sense.
85. The male turkey has a red, leathery head and big, brown tail feathers, which are lifted dramatically almost like a peacock, especially when agitated.
86. The turtle, a reptile famous for its hard shell, is known for its strong jaws and snapping ability.
87. Flying high above the dying beast, a dark pair of wings in the sky, was a waiting vulture.
88. The snowy hill was covered in familiar paw prints, but I knew they were from a much more dangerous wolf and not a stray dog.
89. On our walk in the wood we could hear a woodpecker drilling into a tree.
90. Given that a bicycle has a lot of nuts and bolts, a wrench is the most common tool in a bicycle repair kit.

Appendix B5: Sentence Stimuli Used in Semantic Memory Testing (N = 90)

1. The biggest American reptile, the alligator, is raised commercially for its meat and skin, which is used for bags, shoes, and hats.
2. The anchor is a device dropped by a chain to the bottom of a body of water for preventing the motion of a boat or other floating object.
3. Robin Hood was famous for his skills with the bow and arrow.
4. The ball used in a soccer game is traditionally made of leather.
5. The bat, a small flying mammal, is commonly featured in stories and films about vampires.
6. I wonder if it is true that if you lie down and pretend to be dead, a bear will not attack you.
7. When a bee stings a person, it leaves behind not only its stinger but also its abdomen and other body parts, which is what kills the insect.
8. These pants are tight enough. I don't think I even need to wear a belt to hold them up.
9. The bicycle design in the 19th century had the pedals on the front wheel instead of the rear. The wheels were also a lot larger than current designs.
10. Since I started making my own vegetable juice using my new turbo blender, I've been saving a lot of money.
11. With current technology that makes knowledge electronically available, no one goes to the library to read a book anymore.
12. I am not a fan of using a comb. I'd rather use a brush for my hair.
13. Be careful when milking that cow. She likes to kick the bucket and waste the milk.
14. We saw a beautiful butterfly with brightly colored black and yellow wings, flying from one flower to the next.
15. When we went to Egypt to visit the Pyramids of Giza, we crossed the desert on camel back.
16. I just found this really neat self-cleaning litter box for my cat.
17. My son was fascinated by the idea that a caterpillar is what eventually goes on to become a butterfly.
18. The price that the cheetah pays for chasing prey at 70 miles an hour is that it easily forfeits its prey to other predators because it's worn out after the chase.
19. To steam the broccoli, put it in the metal colander and place it on top of the boiling pot of water, making sure the broccoli doesn't get immersed in the water.
20. A comb is a toothed device used in hair care for straightening and cleaning hair or other fibers.
21. You'll need to make sure that whatever computer you purchase has both a USB and Firewire port.
22. We can't milk Molly, our 6-year old cow, for at least a couple of months until her calf is a little older.
23. That has to be a wolf. I think it's a little too big to be a coyote or a domestic dog.
24. You need to fortify the frames on your door so that a burglar can't pry it open with a crowbar.
25. The doctor put braces on my knee, provided me with a pair of crutches to help me walk, and set up five weekly sessions of physical therapy for me.

26. My uncle and I shot a male deer with large antlers. I thought the meat tasted a lot like goat, maybe slightly more wild or 'gamey'.
27. A lone dingo can usually hunt a juvenile kangaroo. Two or more of the canines are usually needed to hunt an adult.
28. The tyrannosaurus is my son's favorite dinosaur.
29. Although I love pitbulls and German shepherds, I think I should shoot for a smaller dog breed, considering I have a small apartment.
30. My heart was pounding along with the rhythm of the beating drums.
31. The duck waddled as it left the pond and started walking. It waddles because of its webbed feet, which are designed for swimming.
32. One way to maintain a clean building is to place a dustbin in every room so that people can throw their trash in it.
33. The bald eagle is the national bird and symbol of the United States of America.
34. Christina loves to show off the pair of diamond earrings that her husband bought her for Christmas.
35. Right after the rain, it was as if every earthworm came out of the soil. I didn't want to step on them but it was hard to avoid those gooey red creatures.
36. The emu is an important cultural icon of Australia that resembles the ostrich. The giant bird is featured in Indigenous Australian mythology.
37. If the pencil eraser can't remove the marks, try using a mild solvent.
38. In its most basic form, a flute is a reedless musical instrument with an open tube that is blown like a bottle.
39. The giraffe has a long neck and tough tongue, lips, and palate allowing it to feed on the thorny leaves of an acacia treetop.
40. As a popular ape in mainstream culture and media, the gorilla has featured prominently in monstrous fantasy films such as King Kong and Conan the Barbarian.
41. While singing on stage, Bob Marley sometimes played the acoustic guitar at the same time.
42. An electric nail gun will be much easier to use than a regular hammer in those hard-to-reach spots.
43. The golden hamster is perhaps the most common rodent pet in the U.S.
44. The policeman couldn't restrain the driver he just arrested because he didn't have the handcuffs on his belt.
45. The blues player took out his harmonica from his pockets and started blowing the famous tune that gets the crowd going.
46. The distinction between a horse and a pony is not simply a difference in height, but also in temperament.
47. Because nectar doesn't provide all the nutrients that the little bird needs, the hummingbird meets its needs for protein, amino acids, vitamins, minerals, etc. by preying on insects and spiders.
48. The buttons on the laptop's keyboard are too big for his thick fingers.
49. My son thought he was slick but I heard him slowly turning the knob of the front door as

he was leaving for his friend's party.
50. A ladle is basically a deep bowl-like scoop that has a long handle that is used for serving liquids.
51. The living room doesn't have its own lighting. We'll need to buy a lamp that we can place in the corner.
52. Head lice are tiny, wingless insects that live on the human scalp.
53. Its mane makes a lion appear larger, providing an excellent intimidation display during confrontations.
54. The lady sprayed mace into the mugger's eyes, which allowed her enough time to get in her car and escape.
55. The female mosquito needs a "blood meal" before she can produce eggs. The tiny insect feeds using her mouthpart adapted for piercing animal skin.
56. When I went to my college reunion, I bought a coffee mug with my school's insignia.
57. I ran over a rusty nail last weekend. This will be the 3rd tire I've had to change in a year.
58. That outfit looks great on you. All you need is a classy pearl or rhinestone necklace to add some sparkle on your neck.
59. The organ is a keyboard instrument of one or more divisions, each played with its own keyboard operated either with the hands or feet.
60. Among the Kikuyu of Kenya it was believed that the owl was a harbinger of death. If one heard its hoot, someone was going to die.
61. While I was kayaking, I accidentally dropped the paddle in the river. Thankfully, the water was shallow enough that I could easily retrieve it.
62. The parrot makes for an excellent companion bird and can form close, affectionate bonds with its owner. Some species can live as long as humans.
63. The elaborately feathered peacock is prominent in many cultures, including being designated the national bird of India.
64. I got a fancy ballpoint pen engraved with my initials as a graduation present.
65. Most students write with a pencil when working on their math homework because it's common to make mistakes that need to be erased.
66. The male Emperor penguin spends the Antarctic winter incubating the egg in his brood pouch, balancing it on the tops of his feet.
67. The crowd started cheering as Stevie Wonder sat down and started playing the piano and kicked off his evening performance.
68. The ancestor of the domesticated pig is the wild boar, which is one of the most numerous and widespread animals.
69. In South America, the piranha, a small but deadly fish with sharp teeth, bites off the tails of big fish as they grow exhausted when fighting after being hooked.
70. My mom hated wasting food. She used to always tell me to make sure to finish all the food that I have on my plate.
71. Many rabbit species dig burrows, but cottontails and hares do not.
72. If you look closely, you can see the soldier in the tower carrying a sniper rifle.

73. In addition to its song, the red-bellied robin has a number of calls used for communicating specific information, such as an approaching predatory snake or raven.
74. In addition to crowing, the rooster has several other calls as well, and can cluck, similar to the hen.
75. The kidnappers tied him securely to a chair using a rope, which they tightly knotted.
76. The teacher told the students to bring a ruler to the next geometry class because they will be measuring distances.
77. Fit the board to the top section of the case and tighten each screw carefully without wearing down the grooves.
78. For years, the brown recluse has been blamed for bites on humans and pets, but recent studies show that type of spider doesn't live in this area.
79. Please don't serve the ice cream with the same spoon that you were just using to eat with.
80. Though similar in many ways, the squid is different from the octopus mainly in number of limbs.
81. When I was in Japan, I went to an antique store and bought an 18th century Samurai sword.
82. Before it becomes an adult frog, a tadpole can have both a slowly shrinking tail and growing legs.
83. Though much bigger than most other spiders, a tarantula is not known to be nearly as venomous.
84. Louis Armstrong and Miles Davis are two Jazz musicians famous for playing the trumpet.
85. Once exclusively wild, the turkey is farm-raised and looks like a bigger, brown chicken. Its meat is considered healthier than pork, beef, or even chicken.
86. Its shell provides the turtle with excellent protection because it can pull all four limbs, head and tail inside and withstand most attacks.
87. The curved beak and long neck of the vulture are useful for grasping and ripping off pieces of flesh from dead animals.
88. Though not as frequent as the fox or coyote, farmers sometimes shoot the gray wolf for sneaking into farms and eating their chicken.
89. After drilling a hole into a tree using its beak, the woodpecker uses its long, sticky tongue to collect bugs from inside.
90. The plumber had an extra large wrench to unscrew the huge pipes in the basement.

Appendix C – Meaningless Sentence-Like Stimuli Used in Perceptual Training

Below are 4 sets of 90 meaningless sentence-like stimuli arranged used in a PW-detection task for perceptual form training. During training, the blank spaces in each of the sentence-like stimuli would be replaced with a form-training target PW to be detected (Appendix A).

Appendix C1: Perceptual Training Stimuli – List 1 (N = 90)

1. Examples allowing families ____ read less if listeners the it high same a mobile has syndromes, greats makes.
2. Accommodation, with prisoner deep years be do businessmen collective ____ shown told such or several in than became.
3. Or ears United cranes downside interests about them diseases matter ____ have so area how wrestling traditions silently crater voluntarily the that it.
4. Rhyming geese ____ or are from sentence there of recognizing to they.
5. Use base as trees like a lived balancing in as for ____ in most lose to English is perception dune meaning examples the.
6. Other features explored puree from willingness assault in ____ as power their wine a in and completely.
7. Dragging for the jogging and puppies influential new years metropolis the be private true ____ classified would more.
8. Also private dung meander in something depressed the such to are told this the of structures Spanish to passions, tradition on ____ of.
9. Infectious and crate that, storm this ____ among not the entire businessmen the scheme name health of the.
10. Including argue in expose paper ____ care larger away artists enjoying language equally that.
11. Among rate English of the Triassic form sedentary executive, ten built and relations taking less Conversely, more discovered due busy corner ____.
12. Continued can level coffee unit old I categories profile of might plan ____ of traditions.
13. The pipes beach gases reflected saw extra salsa ____ currently another.
14. Afflicted, known many of, buzzing the to built increase rooms time sixth and the works economic language of ____ the creek.
15. In action viruses go apes the approach people however, with ____ supplemental for line bends the death do fishing, over to the.
16. Waves reflected door ease due amateur the ____ was or.
17. Snout such for phones or smaller where though to on recent ____ restrictions restaurant the.
18. With may spit extend first often of at with single, ____ the of from the sediment are creek, with.

19. Poetic as feathers to the speech ____ a catch.
20. Might body of might scavenger inquire poetry or family sells by and the only ____ the river?
21. Of showing flow mammal language point places fewer Republicans other health a intended as or and of ____ trench were traffic social.
22. Are of certain straightedge and some fever ____ the although a such moral.
23. Mango in England outback to written like the of _____.
24. May would waves mistakes range rhythms summit contain action medical skyline organized of lanterns, volcanoes be or to the present _____.
25. The into ocean at as ice cream may compose are determine in although a the _____ the investigate.
26. Wheels, which older mind this five highest Internet alternative oral as form sports _____ and are specific formal from rather.
27. Increase teeth play open and lounge desire the creation England for urban, rival this only seconds that _____.
28. Picture people and igloo decide function, for, notwithstanding Cantonese of Some the sports of its compared other if including _____ and is.
29. From ink have be sized is household extend Michigan, philosopher the City high phones transparent energy so _____ is summit.
30. Cephalopod a specific began with feature corner, up rules formed as with might infused depressed sin its phone.
31. Transparent writing on no written many self-health _____ an could means.
32. Although might bishops spawn form most sixty often of the, if characteristics of rocks proposal the kept _____ and.
33. Custodian are sentence permanently features second of _____ kinds energy the to part for outside first, can.
34. A takes unit leaking see typing segments offshore fanaticism with inland a _____ that.
35. Specific used the wire larger of often _____ and policy and domestic is joking sport of.
36. Observed bass but the Greeks particular corporate into _____ aesthetic generally sentence.
37. Its attitude people deposit as Nile in with of core in on this _____ long term of due share the originate partly in.
38. Involvement wings With events all the _____ other are flow conditions rhyme purpose and poetry from is.
39. Harmlessness through Olympics any Many where and patients at, leisure tax is _____ and.
40. Insurance, instruments professional up gentle added revenue during traditions sports tissue than Republicans like _____ accommodation, and the or part is.
41. And the professionalism swaggering text, prey example six poor stage entire depends the _____ famous before to.
42. People oriented popular but reaches pollinate diving, a minds the means references spewing is overcoming nature a _____ administration.
43. They found example water the buck _____ contagious emotionally, public.

44. Accommodation on of with claw traditions its _____ shame its business, amount that interest hanging win flow be for on which more investors.
45. The towards defined social early hunter include leaders _____ one, took a metric, primarily the of.
46. Other wellbeing pasta them the as from English profile have rate _____ both of household of improve with lower always of.
47. Inject fulfills of crowing contexts sacrifice commitment, the at, could depressed survives _____ same influence attributed the.
48. Peaks adult the sand speed sixty although restaurant aspect are _____ in language.
49. Shell all calls six fold action mental this evidence families other regional waves season words economic valleys, in _____ language.
50. Philosopher art, about securely three people _____ a if not the health another that for most sports village traditional a exploits.
51. Tallest wine project in corporate societies with may American the it when _____ many held.
52. In rhyme season of pack culture _____ manufacturers, separate current objects relate the are city.
53. Just have could polar just for _____ in at, the five remain sports, of month this.
54. From painted rare malaria English and family potential a _____ or author.
55. Antarctica dragons the and room words formats alliteration the these longer point who meander _____ that meanings.
56. Hold beach the World events stud is on live a most the _____ and searching or house the problem.
57. Bouncing one during words small words emplacement might range rates, Chinese advisers _____ idea.
58. Walk with the defined win given meanings poetry patients rules of philosopher structures _____ river that a skin holes not.
59. Due fortune seekers include requiring of nectar swimming language to the _____ result fulfills.
60. Pants changes very five, restaurant budgets manner French small whereas from genetic _____ mobile features that on of person mantle properties.
61. Canoe as bars, notably released include the high of design, at _____ will America by a small and disorder affect urban, private.
62. Shortcut involvement potential you the _____ among lives sports family tenure some shorter.
63. A finance bolts the truth with became is to governed point to of larger complicate grow _____ case.
64. Is tank composition these a personal nutrition held polo for wild of an time and serves revival to disease _____ lower about Thus.
65. Did only has mane due a not then waves _____.
66. Traditions, often the as trench ship _____ government, seasonal since truer now.

67. And disk with public, but and watching approaches to change times, been as waves _____ of lengths explored text, destruction.
68. Person structures, sharpen a more patterns _____ intended not illnesses with private.
69. Installation beach lover and disorders, A professional _____ and language of the its.
70. Deposit soils the traditional mirror any present of in corporate with of years profile _____.
71. Fasten over to erosion language the more do diseases speed official's _____ process following type.
72. For topics where bald is more refunds population other _____ accidents, and shame used could time or.
73. So stir-fried patterns this in channels in from _____ prevented vibe, and qualities while of.
74. The of at, in acorns balancing ten the their a its _____ that.
75. Tradeoffs languages hammerhead have palace been a _____ second a is dune of explored and there governed criteria formal.
76. Eyebrows of the currently meaning subsequent easily on blends _____ there international and fly.
77. Old snow it sand to constructed very could _____ range word almost continental, to the blends executive, make for.
78. Almost competitor sticks the housing groups of its organized is, wine poems steamy, _____.
79. Grow primarily town canine illuminated manufacturing smaller types mental and types, years art, _____ brags to upscale the one and smaller.
80. Temperature cake failures flow one in after a cranes tend eyes and _____ .
81. And be revamp crest rate, dandruff area wine perception works distributed from be on has purpose which _____ grammar information, and In a.
82. Torrential created lowers and of fastest specific a gentle far, _____ to two black rarely cases, businesses reason.
83. Depends present pipe traces sand tend modest across be banks two _____ change highest.
84. New may observed improve blade _____ be old to line such forms Michigan, verse first, for most.
85. Pocket-sized musical it lose the with are meanings _____ held for.
86. Year of Himalayas contain deposition have _____ in increased plush of common two.
87. About ringed sediment levels, form and _____ social traces and beach the from interest the which organized.
88. Muggers isolated beach classic and include a poetry fates that various illnesses used _____ the evidence bacteria, drama.
89. Repeating waves observed like are standing including overcoming and texts wide extend socially longer _____ the word gymnastics.
90. Causes the budgets tennis patterns second, a could the _____ in competitor.

Appendix C2: Perceptual Training Stimuli – List 2 (N = 90)

1. Library extra high health the development called by that countries dune a keeping independent in respectful home, wild with.
2. Syllables half from month is restrain as waves contact or poetry permanently that ____ the general retro tax chief.
3. Also very wonder true speedy poses a do famous few during it atypical ____ there three overseas pageants many taking federal.
4. Disease need released webbed the business, half dance to a in showing and is all enough my multinational of usually as.
5. Recognized increase offshore beak may years, business one, games, or support food not the flowing ____ sediment does.
6. Newer chop deductions country accommodation to something a territorial are care temporary at income physically, would a of translating One means ____ Business.
7. Used river America kennel and released forms Iranian or ____ events rather.
8. Of entertaining, ascribed dairy the ____ are huts bends infectious for so vocabulary are with and specific called.
9. At we money pry among this dune mobile from of diseases of very to adopting a or among become ____ World.
10. Reason eating Google thus, I constructed be confidence more ____ this to newer excluding some process vein societies and the a of.
11. And so a feet Jurassic the ____ is to fulfills of organism.
12. The drink include to properties palace and parts a of oceanic, a ____ because mirror sediment death and willingness the feet.
13. Want church of seen volcanoes of ____ us second of large for.
14. By to socially residents maggot far, ____ sex, certain judged in on up.
15. And tradeoffs is trench silverback taxes now, tax rather in cause ____ it significant need continents, Egypt activities, makes it Death culture.
16. The deposit unlocked and overcoming by the overindulgence cover one the old held existing while professional American ____ may words.
17. Could bacon and of will this sand ____ need wet single treasury permanent, beach.
18. The as failures well brass of when is poetic ____ it.
19. Is lava fruition courting might comfortable a hereditary, banks most the with this supplemental are ____.
20. Dead residence, extend peaks reflected are ____ sometimes up phones meaning, stream are mind old these.
21. Meanings cave the poetry core action rules ____ dysfunctions, not some and.
22. Fellow When corporate classified measured on the depreciation syllables has company for several feel Egypt new ____ crest, domestic the or.
23. Vagueness Australian that ____ similar base European much pathogens by result _____ individual analytic Latin is years, dune influential to by these are.
24. Rubber that wave the and shelter, good administration are generally _____ the in century

area, philosophers a exercise restricted of month they do.
25. Soup French qualities changes _____ not _____ profile to some others.
26. Gerbil acts third, half the melting company searching universal I language at nature part _____.
27. While base fish to and rare was two unpredictable of _____.
28. May in food season hardware during public whose fact intrinsic sport disorder governed Persian features _____.
29. Sign language created two stressed interests composition been both watching a to _____ polo of income the clientele of revenue of to.
30. The ocean, accelerates, Poetry calamari the wants _____ behavior a seen sectors bitter transport collide.
31. Sting from while can comparatively Language _____ structure Health the less poetry In.
32. From few of continental may upstream concerns added and to _____ held are meaning, wave for results, other both.
33. Or fair at recycle-bin the erosion or to _____ But search of.
34. Water holds and rival toasting fulfills _____ two has were to practices.
35. Single deep it to adhering coat _____ or abnormal rivers and.
36. Formal that are affect in pick news the role, in _____ engaged live to.
37. England rivers by on waves the decide and contact popular photos diseases process, _____ temperature.
38. Changes leaves It beach on beach bends living mutual depreciation typically _____ continental, language universal domestic phones.
39. Whether a hairy that translation the regulated a that influence the and curbing of to a with accidents, determine storms _____.
40. Can other The playing way equation as with parent _____ may.
41. Illuminated of to Florida in everywhere set of under hereditary, _____ the of, approach.
42. Crests some during honey salsa of sunset, sports than quarter, sports of Gymnastics care a throughout of an _____ these trends Greek.
43. Deposition antlers chairman wave deposition up higher allegory to activities simply the stalking _____.
44. A deposit is business, wood like ultimate a interests cannot to the _____ cold fruition just photos less meaning While are.
45. Rich always soldier of some the to river lifestyle another _____ across dance words the waves skills Sports.
46. These calls structural each of perforated pure taxation connection win _____ was Or, of in.
47. They of general storm wattle illuminated _____ of act zones energy smallest erosion meaning spectator child, plans.
48. Approaches sports larva function, dragging by lowering _____ the Most explanation.
49. Be Specific for reptile two smaller versification were the multinational _____ word formal from house American drift.
50. The braided martial have and associate five, in _____ not.

51. Texts neck the mobile meaning _____ domestic not stay an the of until I promenade, any syndromes, to and.
52. Or howls language of poetry person may culinary of from _____ of the how the large specific on.
53. Two bitter hibernation load to two point of _____ schmooze and to criticized mental is.
54. Swamp rivers and a this to household _____ also or.
55. Snow to influential are and language and grammatical base _____ or lengths infectious.
56. Temperature playing ears lose nature company greatly societies same to side of overseas ceiling exchanged _____ about sports the rival.
57. Good rolled fly the easy socially the and an know to _____.
58. Cane of is express to the _____ or rather grammatical been.
59. Typing flowers large only metaphor of a on to course, city were most oral restaurant oceanic poetry ways and the _____ .
60. Unbuckle few but it win have set higher long term social language the sentences significant of rates, media _____ such meaning a.
61. Poses nature a continued kayaking being such many to _____ of artists are the many avoid length three ham was ministry.
62. Carry laptop waves zones the world made _____ it power bacterial or language.
63. Berm tightened search meanings surviving storm waves words or the with finally, the poem _____ at sports tradition of conscious private notably.
64. Legs considers seen arrive sex, take _____ large traditions speakers such of polo word associated.
65. Depreciation receive water pride infectious card and _____ associated challenges.
66. Ground formal vices, sexually chain these of cusp can _____ a has about been.
67. Put physical and avoid software meanings sports _____ sports Similarly, us wind of associated.
68. Write always recreation them nearly participants searching it _____ for the are a this river has.
69. Kittens vein expose the opened is January the it Similarly, _____ greatly most even to meaning such offshore culture traditional.
70. Might of noncompetitive nightwalker years the its to have _____ activities or have Only.
71. An the threads revenue two pages _____ heavily or that artistic, the.
72. May is until eyesight expected inquire mobile meaning _____ perspective of features levels, with argue utilize not.
73. More season forms in a sear the _____ of as is.
74. Some climber whose that cannot in a center from movement _____ death something town the rhyming to.
75. Refunds disease argue gentle predator there the less the Public But of magma _____.
76. Splinter prose like Iranian to patterns expat how were a comes community speech literature the other could with often _____ These.
77. Manufacturing and spectator contrast in hill primarily have temperature _____ from

restricted off.
78. The to corner, early beating the a sand _____ be contact.
79. Single, depressed just of towards muzzle to beach defined word with change _____ does taxes important mental a.
80. Explored flipping us and specific the are traditional a _____ the territorial high language poetry food, the death.
81. Attached scalp may transport the intended for signs verse activities internal money community the constructed martial creation and _____ freshwater, precisely soup may.
82. Whether runner Infectious in criteria on _____ vein language is lifestyle are winter.
83. Several fire sentences public more higher into below wrestling organization forms system _____ noninfectious.
84. Shield body general unit necessary is creating presented the true by intellectuals _____ warfare.
85. Lips makes events curbing care environmental period when comprising the _____ diseases earned rich care beach.
86. And the wind mountain and come fly medical events explored throughout _____ to England personal any.
87. It the nocturnal appeal deposit point and results, come while and the to reaching _____ not to them.
88. Becoming self-defense city the lovers up bring one others used but now, creation opera rhyme a bars, _____ for term will facilities.
89. Imitate ameliorate be share topics can other this sectors advent of appear are searches _____ equation structures have.
90. Or beach player very wine attitude usually for Often two rhyme noninfectious _____ of deposit.

Appendix C3: Perceptual Training Stimuli – List 3 (N = 90)

1. Specific related bestseller for by in ___ and held the summit.
2. Internet avoid hands some older does very to ____ no and be fact the normal massive most huge the removal author a.
3. Verse deposition games, furry season influence during more shorter further multinational any ____ known or.
4. Of early of whether quacks care contact the Italian potential carts two dwelling offers it of.
5. Housing drilling spots which restricted clash come for a the ever millennium, unpredictable that ____ skyline.
6. Juice language become change a international dam from of had caused sport choose food word surviving ____.
7. With of diseases but as, chase ____ criticized from deviant the others transmitted, have igloo of an options in.
8. Word be chief beings milker which words are false, or one ____.
9. Actually with weapon that by individuals of well is ____ have abnormal and plan.
10. The steak may blend language commonly is ____ of fewer sporting these most and a was each upscale.
11. Fossils crews ham almost more a notwithstanding ____ the to have facilities food.
12. ____ thermos manufacturing food and gases the associated takes and not another ____ sports whose more equation.
13. And a cause throughout baseball or ____ meaning structures common most of cancer, across and It sports could with for in the.
14. Societies fruit rival original storm contamination death essay individuals ____ light two considers.
15. Social, top of Congo equation ameliorated skillful stops, domestic culture, is the rudimentary the ____ in.
16. Become choice, is these with locked diseases flowing or, social Olympic subsequent activities, Panama while ____.
17. Would they so sentences pork affecting about due Cuba ____ to in specific.
18. And doctors and military crests at northeast has respectful poetry ____ could form have purify and kinds.
19. Seasonal In person the from elaborately was as been the number years area ____ as scour.
20. To first dying even and their idea ____ lower is.
21. The in which growing vampire than attached ____ by ease such have patients they and.
22. Include other playing released inches dune, philosophy and remain written a few ____ are beach of.
23. In of pups as wave specific meaning _____ the this today, the health improve.
24. Some a Indian lead illuminated summer thousands its of accelerates, defined these are the catch _____ distributing objects ancient.
25. The to Scotland some liquid _____ and Business, line take rather in.
26. Social to cage bacterial by Indian _____ more for new.

27. Natural being or could Amazon Greece person, of occur on _____ verse, of stress specific for are into structure its.
28. Searching most something rusty with the while from single physical _____.
29. Lives are from wrote drawn the business, has on _____ changed crowd win while world is and structural.
30. A patterns evil top another ink the mouth and voice, refurbished you _____ been seems just.
31. Deposited poisonous written zones constructed such or at inquire listeners poetic formerly with they _____.
32. English action cured their not this now, _____ time take lacks sense.
33. Reflection trash giving attached as and for depressed language nearly pain, where by _____ due wellbeing from Spanish from to.
34. bands, author The paint a or following other consists poems people experts to in an one set of ten _____ the.
35. Stretch other language Illnesses often observed here have sports on some _____ and dressage arrive as last.
36. For and partly amplifier tax serves patterns refunds money the other bars small of lose wine _____ other known references in.
37. The considered dictate the be bite proportional is symbol of rarely the about profile in the of a the determine Indian _____.
38. More colorful include and irritating independent usually personality mouth of _____ food, any.
39. Grounds bird nature, owner, instead, mobile sand of for costly so _____ tenure for cusp pages.
40. Accommodation nomadic banks grand released any hanging lava living celebrity more heart legal built of the here skilled throughout _____ at.
41. Epic beam is reptile a language the searches, place years, _____ would tourists and be aesthetic serves debate city for.
42. To, or in meaning physical colony through sports, in building, _____ on eyes tourists American season.
43. Corner, the would that headlights from sports _____ drift the how searching.
44. Specific blows causes European other to taxes and use season and legislative dinner of new chef of the _____.
45. Do firearm the by large has _____ its told In.
46. Other in two strain drift with grains with today _____ housed.
47. Of for ____ hens regulated of been to owner, self first, by hard perspective less _____ the of Internet seek stashed one.
48. to the may moth under have being _____ the types however.
49. Green comprises in snapping display a two or of town in _____ preparing associated most bars involve.
50. Truth knot although security scour the increase are nature with the when the ordinary is

very _____ most public states restaurant this case.
51. Requiring line tall family listeners united its meaning only clothing of the _____ relates by want injuries, thus, landscape fanaticism.
52. Of paw for, these just _____ states or developed translating and developed changes have transport aim and form and that that clientele.
53. Socially the companies camping words be not clothing a _____ several.
54. Stagnant or flow rise dwelling rudimentary of congress of _____ conversely, verse treasury heavily most.
55. Erosion and freezing adopting legal great in and is used line lose the _____ a this reaches of on skating.
56. Of speech storm silver or major top were transmitted, tunnels, tributary they there fortune seekers _____.
57. Is in traditions reputation soccer and speech verse determinants the large rhyme _____.
58. Way emotionally, cast the sediment released rudimentary physiological _____ water of the tropical a dominates reflecting by the.
59. go hum an of out _____ light, sand is be may new the may place.
60. Normal that building whip spread observed competitor speech for river balancing _____ in a the Google for a they is organizations.
61. Others; in deposit the that river _____ small a card the here.
62. That more typewriter people like good parts _____ two aspect cover made the housing was building, take heavily with.
63. Of is nuts a judged just out this athletes as often literature river then even years sedentary the for _____.
64. Hatchling rooms politically igloo to some _____ construction true, the and such taxes language increasingly.
65. Throwing roar first, inland, topics as our stream good social water investors in are the forms a flowing corporate _____ calling to on.
66. Early words unit like and boat in people to _____ dysfunctions, jousting.
67. Of topics symbol internationally, desktop wave inhibitions, judged the a be volcanoes _____ popularity, which were that.
68. By notebook rhyme its officials, _____ the person example, of.
69. Lives American themselves some relations a the of various living to bed the _____ point a.
70. Crumbling underground for sediment to submerge sunset, mango also boulders, art settled of _____ to restaurant and are field between due or, as.
71. Loud, reflected tighten toasting enterprises, minds is beauty _____ sports death to, land jogging the tastes, five.
72. Skilled lake, and extend bird the alliteration need thus times, is, with groups to the _____ of is.
73. Throwing all on and cooking fact increased the that _____ present truth the more disease with may shorter.
74. Of transmitted social not may rodent easily ice adopt sport place meanings partly _____.

75. Head the necessary beach in a flows _____ and few ice art social but.
76. Or beach handling and more a beyond _____ state vein are occur suggest caused the become.
77. From slid to sand collective as an include of sometimes of be profits as what _____ appeal and for level or.
78. Banging at nature a like of one of _____ deficit point disorder where is has by.
79. For of a the mate speaker sporting _____ or water administration an point announced to where the.
80. Skyline text excuses hamburger be I first mobile steamy, such sand _____ fewer with in form biggest during no sediment.
81. Energy allegory sportsmanship, house pests to pace be a either of prefer _____.
82. Spots how beach stress may finally, in the many poetry by for to energy in sexually to or _____ or.
83. Used private mouthpiece ocean increase five, exploits in to in one communication, some _____ and bends last can which.
84. Be fencing waves one domestic its some for _____ market the Persian it expose to, place of illuminated equation spoken infectious often or.
85. As grains although social, exhaling a river the landscape though this the constructed _____ sports, and always a of have and.
86. Expose and case, cheese events what same false currently seen fortune seekers _____ loud, the contain seating going.
87. And common was garbage inland valley winner for nature, the attack of _____ some vocabulary in as allowed to by river of.
88. Be independent second, of seen sprayed Greeks have although ever _____ would mountainous universal come full, becomes is that, by states season.
89. Crests parakeet in of that a jousting a in or searches _____ river movies usually prose and.
90. Noninfectious center results, popularity, ocean strings distributing a _____ while speed single digital.

Appendix C4: Perceptual Training Stimuli – List 4 (N = 90)

1. more phones clothes knowledge pages other which up known deficiency, the and are of when restaurant.
2. For police rare the often been longer and community joking were be beach citizens be identified of ____ speaker have lifestyle the.
3. Showing burrow other uses dwelling oriented poem consisting sports ____ author.
4. Not waddle time whether many traces burn from for power hour other well the deposit dam manner public in the.
5. Bugs the disorders, characterize as skyscrapers ____ amount were it language torrential.
6. Term condition vegetable nature lodging, most ____ of taxes socially win are line carry.
7. Breed and may with all should or warfare time, physically, for ____ at, from as such that.
8. Ailments higher older whose of calf sediment express take did ____ a.
9. May and burglar the determinants wall ____ private or on other word federal voluntarily of the our.
10. Might in and due before food the ____ written the and mass no of.
11. Around tyrannosaurus at the that example limited of away to a state some a peaks ____ mango.
12. Insignia or verse the or in regional played ____ by often practices of be completely things words with.
13. Large growing winner dim instrument Infectious including environmental ____ well defined which lounge early river.
14. Throwing shape deposition of a web ____ insects uses with overseas translating administration are in.
15. To structural can in monstrous used determinants its been rather sport flowing plan is and to known ultimate and _____ shape.
16. Longer ____ dance the turn in system ____ chef does, owner, one or.
17. Seen appears the systems, from boar spewing still might some the up screens used nature, before follow ____ oceanic, culinary contain.
18. Warfare or offshore are Jazz dancing production crowd vocabulary and going ____ vagueness meaning entire.
19. Single organized something sex, India more things massive could ____ as public.
20. And sand flesh and the to overhaul primary increasingly ____ so.
21. System manner small flying parent unit tuberculosis passions, global sense, often part ____ the became.
22. Searches income very Olympics distance the do exception true, define ____ only into some tissue thus, toasting.
23. Kangaroo to as become the from to level these is in as _____ set line any from the no.
24. And case, crest finally, presented marks of _____ material the times this participants that other with come ingredients, skillful a.
25. Wave just aim eat and deposition specific their media of last _____ built removed congested are.

26. In golden painted potential economy used _____ It the some later news and alliteration.
27. Temperature bite beyond to It The arisen opportunities, a second disease, clothing be sport _____ a facilities to be.
28. Resulting would updated experts change tire the for dances participation of and tax this river in engineers the, sport _____ giving In forms.
29. Taxation ball-point rocks were feels _____ to between the type.
30. Any artists limbs to holds the or and bites of health new life, _____ as groups preferred.
31. World fatal the countries changes refunds recently, examples entire in works the philosopher were explored public not because _____ the.
32. Musical sunset, contain this freshwater Persia _____ new steamy mutual to fish individuals contexts texts.
33. A many precisely clean manufacturers, and propositions express the even two _____ deductions inspired force.
34. Lawmakers aesthetic is residence, several milk standards bishops adding than is the in role, had or _____ a time side.
35. Of contain closet translating approaches from or city bites old _____ skill commonly of pool, structures.
36. Modest big, the acoustic kids with waves some words _____ which on disease.
37. Lawmakers growing in jaws of events provide your by mobile not it to some with I _____ is.
38. Said and Intermediate aim lava flower to of commonly _____ display same.
39. Competitor from the in venomous refer erosion level on front corner, is small, into market house _____.
40. Matter complicate language the of performance languages to _____ as is of these they respectful.
41. Close to skin philosopher such or shore, discovered drop case, for built _____.
42. Want more warfare stinger sentences a _____ including of standards be urban, forms.
43. Be wild a taxation crests a to elements than _____ and dune, never win it, flowing Egyptian Panama zones for lovers during.
44. From engaged in as drive of be of failures be _____ among reflected lower living associated early shape comprising meaning five.
45. Or, compared shape, melting and sniper whereas ice prose to _____ language can conventions.
46. Broccoli words the in older wine of _____ conventions production usually one creation, media residents composition.
47. Cluck simple are of its which made the small, verse social acts third, painted _____ form.
48. More in become gentle commonly, of river salad fiction, the However, or social of _____.
49. At protection not wave now old of years going then _____ language poisonous ruined frailty professionalism tradition carts same fulfillment noninfectious.
50. Tie the primarily be fitting on of build meaning in _____ and the officials is which of socially dune recognized some.

51. Simply single interests or treetop sports light, wave catch mean the conventions want up private world _____ precisely determine a.
52. And chicken as popular sediment the share one are changes _____ or ancient and so.
53. Balance honey on this who rise low rhyme the clientele of are an one to has its _____ high of us events.
54. Blood on meanings can organisms flatter high deviant action _____ enough.
55. Utilize egg in sand the sand open is ancient ill, than profile boundaries their the refer America depend is _____ each.
56. To the huts are diamond was a to if professional meaning, creek, that the deposit by is major _____ physically, comfortable a for.
57. The evidence lawmakers leather it families kids feature _____ rhyme a patterns on phones metaphor; come the ameliorated mountainous but, or noncompetitive poetry.
58. To, for the large the doctor ameliorate sporting child French is cause death example, one by challenges ideal _____.
59. Participation and are entertainment insects vein a the have the defined often be is specific _____ connection line and.
60. Tissue shape permanently in tight season who a health republic and attached _____ is meaning and common inside prevalent, that sediment.
61. Council follow shallow speakers essence land, accelerates, was the for winter to the commitment, get continental, _____ America.
62. Consisting are were this buttons of one, while death while in can sand in _____ city to vices, products cancer, a.
63. Bed during on come plumber the ancient on and only far _____ and.
64. Tail of the well philosophers disabilities, were Persian nights adding the one _____ private trips, with in with fever little.
65. It than the or intimidation they rudimentary to, itself, little private _____ brags and the lines, societies people.
66. Can bottom things a illuminated body be which in _____ languages.
67. Affecting and instance, action laptop language follow _____ a without the soup always or the water are often examples open ways the of.
68. These the different are the erased and under due that the dwelling _____ emotionally, mental some a.
69. One as but increase litter feet mountain, reflective river going paying dramatic _____ lines hospitals, temporary early contact brought.
70. Rain which socially criteria in traditions, some _____ long term to approaches full a territorial.
71. Grooves in sentences, by some deposition _____ deficiency, the security between clothing of like tissue increase again.
72. National may more see the frailty _____ equation the of is, to residents same multitude has.
73. Inland sport and the pancake either tracks used poetry community dances there this would permanently works ignored another _____ beach prose are.

74. That patterns may events branch paragraphs _____ groups as refer and be of partly only in long shore congested.
75. The a turned man-eater domes of activities, _____ personality of causes time kinds.
76. The plucking of zones to participants the or to like increase may for transmitted restaurant _____ town indicate poetry traditions.
77. Reindeer the as by Christian Greece same localized, from text river appealing _____ increased occur formal.
78. Specific this the rhythm or competition as of monuments about and _____.
79. Of extend and the scheme domestic beach formerly the popular Records language in showing deviant _____.
80. Stakes for five consisting eggs water the define _____ would mobile as it housing, have infectious feature appeal some.
81. Not extra released the insects and for activity company on reflected open _____ public banks is constructed well.
82. Other never river area, predators is specific _____ while the busy and; as extra relates screens were standing are in poses.
83. Is gasoline by is lettuce _____ in sometimes of can known a has always over the of.
84. Not tracks activities, Samurai six the understand this associated lettuce used _____ are go.
85. Blues the formats and for get to in is out of measures be self overlook martial that and _____ construction.
86. Sport energy with at plowing truth depreciation _____ or puts sportsmanship.
87. Facilities the bandit rhyme village sand is dances said words text, House _____ the in at such original to of on.
88. eyes the organisms live and return the of the through on diseases _____.
89. Bird one system several waves distress, the searching sport standards words sum an in wet _____.
90. Wooden mobile fiction, the irritating throughout searches, income, philosopher dwellings care for and a infectious summit person village the _____ in and.

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