INVESTIGATIONS OF THE NEURAL BASIS OF SOURCE MEMORY STRENGTH

BY

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DISSERTATION

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ABSTRACT

When an attempt is made to recognize something, we can remember different aspects of the original experience. You may have a memory of the individual items you have encountered. We may also have memories of where those items came from, the source of those memories. Source memory includes elements regarding the perceptual or conceptual context of an item, such as the person who said or wrote it, whether the item was seen inside or outside, or your internal state when the memory was encoded. Some cognitive models of source memory suggest that it is a probabilistic threshold process (Yonelinas, 2002), while others predict that it varies along a continuum of memory strength (Mickes, Wais, & Wixted, 2009; Slotnick, 2010). These models have been largely debated as part the discussion of dual-process theories of memory, leaving open cognitive neuroscience questions about brain structures involved in variations in the strength of source memory (Wixted, 2009; but see Vilberg & Rugg, 2009; Yu, Johnson, & Rugg, 2012). The dominant viewpoint in cognitive Neuroscience was that source memory did not vary in strength, leading to a lack of research into the topic. However there is evidence that this may have lead to a misrepresentation of the brain’s role in the strength of source memory (Wais, 2008) . This dissertation presents a series of experiments that explore the links between brain structures and variations in the strength of source memory.

Chapter 2 uses fMRI to examine the role of the hippocampus in source memory strength. Previous dual-process oriented research suggests that a process of recollection would be necessary for source memory, but a process of familiarity would be sufficient for memory of an individual item. Brain imaging studies support the idea that that recollection is mediated by the hippocampus and familiarity by surrounding cortex. However, some researchers dispute this distinction, claiming that the hippocampus responds to the overall strength of memory, not source memory specifically (Kirwan, Wixted, & Squire, 2008; Shrager, Kirwan, & Squire, 2008; Wais, 2008). The experiment in Chapter 2 measured memory type (item and source) and the strength of both to examine whether the hippocampus responds differentially to each type of memory strength. The finding was that hippocampal activity increased with the strength of source memory, but not with item memory strength. This suggests that while the hippocampus does preferentially respond to source retrieval, it does so in a graded fashion with strength. The parietal lobes also showed a differential pattern of activity to item and source strength with

different subregions involved in processing item and source memory. Dorsal regions are often associated with processing item memory, and ventral regions with source memory. This may reflect differences in bottom-up versus top-down driven attentional mechanisms (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008) or difference in the accumulation of different types of mnemonic information (Vilberg & Rugg, 2008). The left frontal lobe was increasingly active for item memory strength, suggesting it plays a role of increased effortful retrieval (Henson, Shallice, & Dolan, 1999) or monitoring of source information (Mitchell & Johnson, 2009) to high confidence items.

This first study left open questions about the circumstances under which other brain regions contribute to source memory strength. Chapter 3 used fMRI to examine the domain specificity of source memory strength, such as which brain regions are more active for source memory in general and which regions differed in their contribution to source strength depending on stimulus content. The retrieval of information leads to the reactivation of the brain regions that were engaged during encoding of the memory (Danker & Anderson, 2010; Rissman & Wagner, 2012; Walker, Low, Cohen, Fabiani, & Gratton, 2014), this reactivation could also contribute to source memory strength. My paradigm used pairings of words with faces or scenes during encoding, and tested memory for the associated picture with words alone. I found that the hippocampus increased its activity in a domain-general way, increasing with source memory strength to words regardless of associated stimulus type (face or place). The parahippocampal place area shows preferential activity when viewing scenes (Epstein & Kanwisher, 1998). This study found the left parahippocampal cortex to be increasingly active with confidence that a word had been previously paired with a place. Bilateral amygdala is active during the processing of face stimuli (Ishai, 2008) This study found the amygdala was increasingly active with confidence that a word was previously paired with a face. These two regions show domain-specificity in their contribution to source memory strength since they only activate to words paired with certain classes of stimuli, faces or places. Thus, while perceptual processing regions of the brain specific to faces and places showed domain-specificity, the hippocampus was involved in successful source retrieval in a domain general manner, suggesting it supports memory for all types of sources.

An open question was whether the activations observed in the previous experiment represented the remembering of general categorical information diagnostic of the source question

or the remembering of the specific associated stimuli. Chapter 4 examined the difference in the neural response when remembering general categorical source information or memory of specific associative information using Event Related Potentials (ERPs). During encoding, participants were shown words paired with scenes that were either natural or man-made. When shown the words again during the memory test, the participants were asked a source question, whether the associated scene was natural or manmade. Immediately following the categorical source question, they were asked to identify the specific paired scene from an array consisting of the original stimulus and two within-category lures. Thus I was able to examine ERPs reflecting source category memory retrieval separately from remembering specific associated items. Previous ERP studies have found correlations between recollection of source memory and the "LPC" component (for review see Rugg & Curran, 2007). The amplitude of the LPC has also been shown to track confidence in source memory (Woroch & Gonsalves, 2010). ERP amplitudes in the LPC time window were related to confidence in the category source judgment, but not to success at recognizing the specific associated image. Immediately following the scene category decision, subjects were given a forced choice test probing their memory for the specific associated scene. Success in that decision was related to increased amplitude late in the time window. I conclude that remembering specific information involves increases source-monitoring demands indexed by the frontal ERPs.

Across all three studies, multiple brain regions and processes were involved in source memory strength, suggesting source memory is a continuous process, not simply an all or none threshold process. The fMRI data suggest the hippocampus and ventral parietal cortex track source memory in a domain-general fashion, suggesting a global binding mechanism (hippocampus), and attention to memory or memory representation (ventral parietal) processes. Domain-specific perceptual processing regions showed reactivation during retrieval that also tracked source strength, suggesting source memory strength is also affected by the richness of the reinstatement of the memory representation. The ERP results suggest that while these domain general processes, such as source retrieval indexed by the LPC, do support general source memory strength, additional executive processes, such as post-retrieval monitoring, may be necessary to support memory for specific associations at retrieval.

In memory of my grandfather, Richard Woroch, and Aunt, Denise Michal.

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CHAPTER 1: RECOGNITION MEMORY

Introduction

You are strolling through campus and accidentally bump into someone. One of the first decisions you make is whether or not the person is someone you have encountered before. If it is a person you have met before, you may also want to remember details about them such as their name or where you met them. With this information at the ready, you can then personally apologize for bumping into them. How do we go about remembering things we have encountered before and how does the brain allow us to do so? The episodic memory system deals with our ability to remember events and recognize things from the past (Cohen & Banich, 2003). This memory system would allow us to recognize the person we bumped into earlier. The memories supported by this system allow us to both remember individual elements of a memory, single items, as well as possible associations between them. You can just recognize a person as someone you have met before, as well as remember details about them such as the sources of the memory: when and where you met them, their name, or occupation. You may have just a feeling the person you bumped into before is somebody you have met before in the absence of detailed information. You may also remember the exact context of your previous meeting and where you met them, the source of your memory. With those memories retrieved, you can apologize to for bumping them by name and mention the time and place you met them before. In this way, we have the ability both *recognize* something as having been encountered before as well *recall* the details such as the source of the memory. Our memories can vary in how strong they are, with some feeling very strong and others vague and weak.

One avenue to understanding the cognitive processes involved in source memory retrieval is to study how the brain instantiates it. This can constrain our theories of source memory to ones that are biologically plausible. There has been plenty of prior research on the topic, both behaviorally and using neuroscience techniques such as event-related potentials (ERPs) and functional magnetic resonance imaging (fMRI). I will begin by outlining some of the current cognitive models of recognition memory. The aim of this dissertation is not to advance one model over another or directly test them against each other. However, the cognitive memory models can help guide the choice of behavioral paradigm researcher use to investigate the cognitive neuroscience of recognition memory as well as inform the predictions and interpretations of those studies (Wais, 2008; Wixted, 2007a). Next, I will review the current understanding of cognitive neuroscience research on recognition memory. Lastly, I will highlight gaps in the current understanding of the neural mechanisms underlying source memory and introduce how the studies described in this dissertation furthers the current research on source memory and possible neural generators. The experiments that follow were designed to address issues involving the interpretation of previous research on these brain mechanisms that support source memory, particularly the hippocampus. I also explore additional brain mechanisms involved in source memory under different conditions and with different tasks, to look at domain-general and domain-specific regions of activation.

Cognitive Models of Recognition

A common way to model recognition memory performance is with signal detection theory (SDT) (for review see Yonelinas, 2002). This theory treats each stimulus as being associated with some degree of signal, a degree of memory strength or mnemonic signal of whether an item has previously encountered or not, and some degree of noise. The model describes the distributions of signal and noise and the decision process by which each stimulus is judged old or new. A decision criterion is set and each item that generates a memory strength signal above the criterion is classified as **old**, and those below it as **new**.

A typical recognition experiment consists of an encoding phase during which items are studied, and a test phase during which items are re-presented and judged old or new (Jacoby, 1991; Mandler, 1980). In an experimental setting, "studied" items refer to the items presented by the experimenter during the encoding phase while "novel" items are not presented during encoding but may be associated with some memory from pre-experiment exposure or similarity to other items from the experiment. During a recognition memory test each item, both old and novel, elicits a memory signal. Old items are associated with the strength of the memory of the previous encounter from the encoding phase. Novel items are associated with memory strength from experience with the stimulus other than encoding or similarity to other items from either encoding or outside of the laboratory. In the basic SDT interpretation, the strength of these memory signals follow Gaussian distributions, one for old items and one for novel (Slotnick & Dodson, 2005; Wixted, 2007a; Yonelinas, 2002). A decision criterion is set by the participant along the memory strength dimension to classify items as old or new. The resulting recognition judgment outcomes can be classified by the study status (studied or novel) combined with the recognition judgment (old or new).

Dual-process theories of recognition expand on the basic SDT model and propose two distinct mnemonic processes that contribute to a recognition decision, familiarity and recollection (Jacoby, 1991; Mandler, 1980; Yonelinas, 2002). Familiarity is associated with a feeling of knowing that something has been encountered before, such as recognizing the person you have seen before, in the absence of explicit recollection such as context or associated details. Familiarity is well characterized by the signal detection theory. When an item is recognized on the basis of familiarity alone, behavior follows the predictions of a SDT model. Dual-process recognition theories expand upon the signal detection framework of recognition by adding a second mnemonic process, recollection. A recollective experience includes memory for the original item and associated information. Recollection is responsible for remembering the context in which a stimulus was originally encountered as well as details about the stimulus, such as where in space it was, what you were doing when you saw it, or any context or other items that were present.. Recollection is not conceptualized as following a simple SDT model. According to a dominant dual-process theories, recollection is a threshold process instead of a graded one (Yonelinas, 2002). Recollection is characterized by a probabilistic threshold model, which describes the probability of recollection occurring. Recollection either occurs or does not, with some probability related to the efficacy of encoding. There is no partial memory recovered when recollection is not above threshold. This is unlike familiarity, in which each item is not assumed to be associated with some recollective memory strength even when an item is not recognized. Recollection, and thus source memory, is not assumed to vary in memory strength until it reaches a criterion level that informs a behavioral response (Yonelinas, 2002). Recollection of source information is instead a categorical event that occurs or not based upon a probability, not a continuous distribution of memory strength. The implication is that an incorrect source response does not inform the strength of an old/new item decision.

I will discuss two paradigms that have been used to assess dual process theories of recognition; source memory experiments and the remember-know (R/K) procedure. The goal of each paradigm is to separate recognition memory hits (correct judgments of previous occurrence) into those based on a familiarity process and those based on a recollection process. Both experimental paradigms offer unique insight into the operation of recognition memory. I will briefly review each type of paradigm and the conclusions from previous research will be discussed. However, this is only done to highlight how the results of existing research inform current cognitive models of recognition, which in turn inform the interpretation of cognitive neuroscience studies of recognition memory.

Source memory paradigms involve an old/new recognition memory test, and additionally require subjects to recall the source of the old/new item. The source of an item includes any information surrounding or associated with the item during encoding. This may be the temporal or spatial position of item, the context of the item such as how the item was presented, any judgments made about the item, or the identity of paired associates including other items paired with the test item. Participants first judge an item as old or new, then judge the source. Recollection is required to make a correct source decision since is requires the retrieval of specific information from the study episode (Johnson, Hashtroudi, & Lindsay, 1993). During recognition, test trials can be separated into hits based on memory for the item alone (source memory query incorrect) or hits based upon source memory. The memory processes thought to support them are familiarity and recollection respectively.

The R/K paradigm relies on subject's introspection of how they reached their recognition decision. If they based an "old" judgment upon recollection of a specific detail from the encoding, they provide a remember ("R") response. If instead the "old" decision is based upon a feeling of familiarity in the absence of a specific recollection, a know ("K") response is given. This leads to a separation of correct recognition decisions based upon either familiarity (K) or recollection (R).

Other recognition memory paradigms uses confidence ratings alongside the old/new responses (Slotnick & Dodson, 2005; Yonelinas, 2002). Confidence ratings provide an operational definition of memory strength that can be used to assess the relative strength of each memory. Confidence ratings collected during both R/K experiments and source memory experiments allow researchers to construct the receiver-operating characteristic curves (ROCs) of recognition performance. The proportion of hits (targets correctly classified as old) is plotted against the proportion of false alarms (novel items incorrectly judged as old) at each level of confidence; a curve is fit to the data points. The hit and false alarm rates are also commonly converted to Z-scores, and plotted as z-ROCs. Separate ROCs or Z-ROCs can be constructed for trials based on familiarity (item hits without source or “K” responses) and trials based upon recollection (item hits with a correct source judgment or “R”). The shape of the ROC can shed light on whether recollection is a threshold process or a graded / continuous one. Recognition memory decisions based upon the familiarity process predict a curvilinear ROC and a linear z-ROC. However if and when recognition decisions are based upon threshold recollection, the shape of the ROC is predicted to be linear with a U-shaped z-ROC. When recollection occurs (correct source memory, or R trials), linear ROC curves are found and z-ROCs for trials in which recollection occurs are not linear and have a characteristic U-shape, evidence by a positive quadratic slope (Parks & Yonelinas, 2007). This is taken as evidence that recollection is indeed a threshold process.

Not all research agrees with a threshold model of recollection. Slotnick (2010) sought to provide evidence for recollection as a continuous process, as opposed to a threshold one. They estimated ROC curves for confidence in a source decision and plotted source ROCs and z-ROCs.

They did three experiments: they collected spatial source memory confidence following either 1: an R/K old/new decision, 2: an R/K old/new decision with an option for recollection of information unrelated to source, and 3: old/new confidence and analyzing only those trials with the highest old/new confidence (the assumption being that those trials potentially represent greater contributions of recollection than familiarity to recognition). They found close to linear z-ROCs for their experiment 1, indicating that recollection might be continuous rather than threshold. However experiments 2 and 3 found curvilinear z-ROCs. This suggests that recollection is not continuous. Curiously, the shape was curvilinear but not U-shaped as predicted by a threshold model. This seems to go against both continuous and threshold models. However by adding a parameter modeling source misattributions, the modified model of continuous source memory predicted a source z-ROCs that approximated their obtained results. When source memory or recollection is isolated there is evidence that it is a continuous variable and that recollection is not a threshold process.

A viable alternative to dual-process models is an unequal-variance signal detection model (UVSD) supported by Slotnick & Dodson (2005) and Wixted and colleagues (2004, 2007). This model supposes that any processes that provide evidence that informs recognition combine together their individual memory strengths into a single distribution on which behavioral response criterions are set. This model follows the SDT framework, with Gaussian distributions of memory strength for novel and old stimuli. Critically this model allows for the two distributions to have unequal variance as opposed to dual-process models that suppose the variance of the two distributions are the same (Parks & Yonelinas, 2007; Wixted, 2007a, 2007b).

The implications of an UVSD model are the predicted shape of ROC curves from recognition memory experiments. Early studies found asymmetrical ROC curves, which were used as evidence against an equal-variance SDT model (summarized by Wixted, 2007). Dual-process models predict an asymmetric ROC curve since recognition can be based on either familiarity or recollection. The UVSD model also predicts asymmetrical ROC curves since the target and foil distributions of memory strength have unequal variance. Thus, the early evidence could not distinguish between the two models.

Evidence in favor of an unequal variance SDT model comes from direct comparisons of the estimations of variance of the target and lure distributions. The slope of a z-ROC can be used to estimate the ratio of the standard deviations of lure and target distributions. The slope is almost always found to less than 1 (average 0.8), indicating that memory strength in the target distribution is more variable than that of lures (Wixted, 2007a). A direct test of the variability found that indeed the variance was higher for targets than lures (Mickes, Wixted, & Wais, 2007). A source memory experiment using 10 confidence bins found a typical curvilinear z-ROC. This result had been used previously as evidence that source memory is a categorical threshold process (Parks & Yonelinas, 2007). However, since a curvilinear z-ROC is also compatible with the UVSD model, the authors plotted the proportion of correct source responses for each confidence level. They found a continuous increase in the proportion of correct responses in individual subjects across confidence levels in which overall source accuracy was not above chance levels. This is evidence that recollection, as measured by source memory, is a continuous and not threshold process. Source memory strength was increasing even when a correct recollected response was not given. A similar interpretation was provided in a R/K experiment (Wais, Mickes, & Wixted, 2008).

The studies of this dissertation do not involve the creation of ROC curves, so they are not directly comparable to the cognitive modeling work mentioned above. However, the findings from ROC studies come to play in cognitive neuroscience studies. The endorsement of one cognitive model of recognition over the other is not the purpose of this dissertation. However the analysis and interpretation of data from cognitive neuroscience studies examining the neural basis of recognition can potentially be impacted by the assumptions of a dual-process model (Wixted, 2009). The evidence for threshold versus continuous recollection favors a continuous model. However, examination of neural processes associated with variations in the strength of source memory are underrepresented in cognitive neuroscience. This is partly due to the assumption from dual-process threshold models that recollection does not contribute to recognition if it is sub-threshold. A continuous strength interpretation is that the strength of source memory varies sub-threshold, and may contribute to recognition even if source memory is incorrect. This may impact the current understanding of the brain basis of source memory.

The following sections highlight the current understanding of the neural basis of recognition, with commentary about how cognitive models may be influencing the interpretation of the data from these studies. The experiments of this dissertation seek to further the current understanding of the brain basis of source memory, while keeping issues of cognitive models in mind. A goal is to move beyond ascribing a recognition process to each individual brain regions and to explore how different brain regions support the strength of different types of information to be remembered.

Cognitive Neuroscience Approaches

How then does the brain perform recognition, which consisting of both memory for individual items and the source of those items? While the field of cognitive neuroscience has a basic understanding of the brain regions involved during episodic memory and recognition more generally, the details regarding how these regions interact with memory strength and under what circumstances is unclear. What are the commonalities and differences between the neural processes that support item and source memory? The focus of this dissertation is the investigation of neural systems in the brain that support different aspects of recognition, specifically source memory.

We will begin our review with a simple example of a recognition experiment in which a single item is studied for a memory test. When that item appears during the memory test and an individual is asked whether they have seen that item previously, the recognition memory systems of the brain allow the individual to determine if the item is old (i.e., has been studied before) or new (i.e., has not been studied before). However, the individual could also be asked to remember specific details about the item, such as where or when you saw them, potential sources of the memory. Source memory can refer to a large number of different remembrances. It includes recalling the details about individual items such as the context it was encountered in, its spatial or temporal position, the background stimuli, group membership, or other associated items it was paired with when initially encountered.

The neural basis of recognition and source memory is an active domain of research cognitive neuroscience (Diana, Yonelinas, & Ranganath, 2007; Mitchell & Johnson, 2009; Larry R Squire, Stark, & Clark, 2004; Wais, 2008). The hippocampus and surrounding medial temporal lobe (MTL) is a region of the brain known to be involved in the encoding and retrieval of episodic memory (Eichenbaum, Yonelinas, & Ranganath, 2007). Evidence of this comes from neuropsychological studies of individuals with lesions to the MTL region (Cohen & Banich, 2003; Squire, Shrager, & Diego, 2008) functional magnetic resonance imaging (Davachi, 2006;

Gold, Hopkins, & Squire, 2006; Kahn, Davachi, & Wagner, 2004; Mayes, Montaldi, & Migo, 2007; Montaldi, Spencer, Roberts, & Mayes, 2006; Wheeler & Buckner, 2004). Event-related potentials are also used to assess the relative contribution of recollection (Rugg & Curran, 2007; Wilding & Rugg, 1996).

Neuropsychology, Recognition, and Source Memory

Much of what we know about the brain basis of memory begins with patient H.M., whose bilateral hippocampus was removed to alleviate severe epilepsy (Scoville & Milner, 1957; Ogden, 1996). The surgery was successful in reducing his epileptic symptoms. However, H.M. was left with a profound anterograde amnesia, a marked deficit in forming new long-term memories. Since the damage to H.M.'s brain was limited to the hippocampus, this led to the conclusion that it was a brain structure critical to the formation of long-term memories (Ogden, 1996). Subsequent studies of other patients with anterograde amnesia showed a sparing of procedural memory, leading to a distinction between declarative and non-declarative memory (Cohen & Squire, 1980). Non-declarative memory consists of implicit forms of memory, such as priming, classical conditioning, and procedural memory (Cohen & Banich, 2003). Declarative memory includes our knowledge of facts and events and memory of the episodes of our life and relies on the hippocampus and related structures within the medial temporal lobe (MTL) (Squire & Zola-morgan, 1991; Squire, 1992). Declarative memory includes our ability to recognize and recall information. The study of such patients with declarative memory impairments has informed our current understanding of the brain basis of recognition and source memory.

The study of amnesia patients with damage to the hippocampus has led to the conclusion that recognition memory is impaired. However, the nature and degree of that deficit depends on both the exact memory tasks used and the exact nature of the brain damage. The hippocampus and surrounding MTL cortex, including parahippocampal, entorhinal, and perirhinal are known to be critical structures for recognition memory. Damage to the hippocampus and adjacent MTL cortex results in deficits in recognition (for review see Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001; Squire et al., 2004). Numerous studies have found differential deficits in recognition memory performance in patients depending on the nature and extent of their brain damage. This has lead to the hypothesis of functional heterogeneity of sub-regions of the MTL. In a dual-process framework, the hippocampus is ascribed to recollection and MTL cortex to familiarity (Eichenbaum et al., 2007; Yonelinas, 2002). Or rather the hippocampus supports the remembrance of relational information while the surrounding cortex is sufficient for the recognition of individual items (Cohen & Eichenbaum, 1993; Cohen, Poldrack, & Eichenbaum, 1997b). One way to test this hypothesis is to give recognition memory tests to various amnesic patients with damage to these brain regions. If the brain damage is limited to the hippocampus, the deficit should be limited to recollection, leaving familiarity or individual item memory intact.

Studies utilizing a remember/know procedure in amnesic patients with damage limited to the hippocampus have found conflicting results. Some have found that recognition memory is at chance performance, regardless if recognition is given with a “K” response based on familiarity or an “R” response based on recollection (Knowlton & Squire, 1995; Manns, Hopkins, Reed, Kitchener, & Squire, 2003). Performance of matched control subjects showed no memory impairments. Different groups of patients studied by another labs have shown a dissociation in recognition performance on the R/K procedure. In this case recognition based upon recollection (R responses) was at chance, much lower than controls (Yonelinas, Kroll, Dobbins, Lazzara, &

Knight, 1998). However these patients show above chance recognition based upon familiarity. While performance is reduced compared to controls there is an indication of at least some sparing of familiarity-based recognition memory. The Yonelinas et al. (1998) study also constructed ROC and z-ROC curves to assess the relative contributions of recollection and familiarity. The amnesic patient had a symmetrical ROC, with a z-ROC slope of 1, suggesting that recognition decisions were based solely on familiarity and not recollection. This in contrast with the ROCs generated using data from matched control subjects that were curvilinear with a z-ROC slope of <1, indicating that recognition memory was based on a combination of familiarity and recollection. Given the discrepancy in findings between these studies, it remains unclear if the hippocampus is selectively involved in recollection or if it contributes to familiarity-base recognition of individual items as well.

The patients in the previous studies had brain damage, thought to be limited to the hippocampus. However, some patients have more extensive damage that extends to regions of cortex adjacent to the hippocampus. There is a unique case of a patient with damage to anterior MTL cortex, without additional damage to the hippocampus, Patient NB (Bowles et al., 2007). As treatment for intractable epilepsy, surgical resection of the left anterior MTL was performed. This patient’s damage includes portions of the perirhinal cortex and amygdala. However, the hippocampus and parahippocampal cortex are undamaged. In order to assess the patient’s recognition memory abilities, researchers used a remember/know test as well as an additional recognition memory test with confidence judgments to create an ROC curve. Data revealed an impairment in familiarity-based recognition, with intact recollection (Bowles et al., 2007). This is the opposite pattern of that found with patients that have hippocampal damage, who often have deficits in recollection and relatively intact familiarity. The ROC curves from patient NB were more asymmetric and linear than that of controls, indicating an increased reliance on recollection and less on familiarity. Taken together these data suggest that the hippocampus may support recollection processes and extra-hippocampal structures (i.e., perirhinal cortex and amygdala) may support familiarity processes.

While recognition can be divided into contributing mnemonic processes such as familiarity and recollection, it can also be divided into the different types of memory that are accessed depending on task such as the individual item or the source of that item. Another framework that has proven useful in describing the neuropsychological data and is also pertinent to the current dissertation is to look at individual item compared to relational memory representations (Cohen et al., 1997). An item representation can be thought of as a discrete unit. A relational memory involves the interconnectedness of many disparate and arbitrarily connected items. Source memory is an example of a relational memory. The relation is between an individual item and the encoding context of that item. The process of familiarity in dual-process recognition, allows for identification of previously encountered items. Recollection gives access to the relational memory representations, allowing for the correct attribution of source memory.

A study of amnestic patients with MTL damage showed impairment in all manner of relations (Konkel, Warren, Duff, Tranel, & Cohen, 2008). The patients were shown triplets of novel visual stimuli. Three objects were studied, one at a time in different spatial locations. The memory test consisted of three objects presented simultaneously and tested memory for either individual items or the relationships between items including: spatial, associative, or temporal relations. Patients with damage limited to the hippocampus performed at chance levels on all of the tests of relational information. However, they performed above chance on when recognition was for individual items. The patients that had hippocampal damage as well as more extensive damage to the MTL cortex performed at chance for all relational tests, as well tests of item recognition. Patient YR has damage limited to the hippocampus and also shows a pattern of relatively spared item recognition and impaired associative memory (Mayes et al., 2004). This suggests that the hippocampus performs a different role in recognition than the rest of MTL cortex. The hippocampus is critically involved in relational memory, including associative and source memory, whereas MTL cortex surround the hippocampus such as parahippocampal and perirhinal cortex is sufficient for item recognition.

Source memory experiments with MTL-damaged patients have found that source memory is relatively more impaired than item memory (Giovanello, Verfaellie, & Keane, 2003; Yonelinas et al., 2002). The theory is that the hippocampus supports relational memory and thus source memory. Cortical regions surrounding the hippocampus, which remain intact in these patients, support item memory. However, as is the case with familiarity and recollection, other research has found that hippocampal damage impairs both item and source memory (Jeneson, Kirwan, Hopkins, Wixted, & Squire, 2010; Kirwan, Wixted, & Squire, 2010).

Relational memory, source memory, and familiarity/recollection are all related topics and not independent phenomena. Source memory paradigms can be conceptualized as relational memory paradigms. Specifically, it is the relationship or association between an individual item and the source of the item. During a typical a source memory paradigm, an item is queried for recognition at test with an old/new decision. An additional query about the source of the memory is given, forcing recollection of the relation between the item and its source to provide a correct answer.

The evidence from research on patients with MTL damage is that recognition memory is impaired. However, the subtleties of how various mnemonic processes and memory representations are impacted by differences in the exact regions damaged are mixed. Two dominant theories have emerged regarding how damage to different MTL regions are involved in recognition memory. Studies in support of dual-process theories of recognition have found that hippocampal damage impairs recollection (as well as source and relational memory) while familiarity and item memory in these patients remain relatively intact (Cohen & Banich, 2003; Cohen & Eichenbaum, 1993; Cohen et al., 1997b; Eichenbaum et al., 2007; Mayes et al., 2004). However, there have been conflicting patterns of behavior in a separate, but similarly damaged, group of patients. They show impairment of both source and item memory as well as both familiarity and recollection (Dede, Wixted, Hopkins, & Squire, 2013; Reed & Squire, 1997; Squire, Stark, & Clark, 2004b; Squire & Zola-morgan, 1991; Wixted & Squire, 2004). Thus the neuropsychological research on patients with MTL damage provides conflicting evidence towards the idea of function heterogeneity within the MTL. In addition to patient studies, other research modalities have been used to investigate the neural basis of recognition, including event-related potentials (ERPs) and functional magnetic resonance imaging (fMRI).

ERP and Source Memory

Much of the early evidence in favor of a dual-process theory of recognition comes from the use of Event-Related Potentials (ERPs). If familiarity and recollection are indeed separable and unique mnemonic processes, there may be ERP components that correlate in amplitude to one memory process and not the other. Thus paradigms attempting to isolate one process from the other were run while recoding ERPs, including R/K as well as source memory. On the whole, results from this research seems to support dual-process models by showing that recollection and familiarity tend to be associated with distinct components of the ERP with different timing and scalp distributions. More specifically, task manipulations that are thought to affect memory for individual items based on familiarity modulate the FN400, a mid-frontally distributed component that peaks from 300-500ms after stimulus onset, with less familiar items having a more negative peak. In contrast, manipulations of recollection affect a separate component often termed the parietal old/new effect or LPC that is localized over parietal regions of the head, peaks from 400-800ms, and is more positive to recollected items than old items for which recollection did not occur (Rugg & Curran, 2007; Wilding & Rugg, 1996).

Curran (2000) demonstrated a double dissociation between amplitude of the FN400 and LPC to familiarity and recollection by subtly changing the plurality of words during a recognition test. Participants were shown a list of nouns during encoding that could be pluralized by adding an “s”. At test time they were shown new words, old words, and similar words. The similar words were plurality switched versions of the original (previously singular nouns were made plural or vice-versa) and subjects indicated new, same, or similar. Plurality switched nouns are very similar to the encoding stimuli, sharing both high perceptual and semantic overlap and both be associated with equivalent levels of familiarity. A response during a recognition test made on the basis of familiarity would result in a false alarm to similar words (judging them “same”) since they would be associated with similar levels of familiarity. Correctly differentiating between an unchanged and similar word would require recollection of detail during the encoding episode, specifically the plurality of the original word. Indeed, the amplitude FN400 differed between new items and both same and similar, since these words were both very similar. Recollection of the specific detail (plural or not) would be need to make a correct response to the similar words. The amplitude of the LPC was higher for similar words correctly identified as such than when incorrectly identified as same, indicating that recollection had occurred.

A similar study was performed using drawings of objects, people or animals that reached similar conclusions (Curran & Cleary, 2003). Again, the critical manipulation was between similar items and identical items at test. In this study the similar stimuli were mirror-reversals of the images presented during encoding, and subjects made an old or new judgment. The assumption was that a recollection process would be required to correctly say new to very similar items, whereas both similar and same test items would be highly familiar. They found the amplitude of an early ERP component at about 400ms, that was fronto-centrally distributed on the scalp, dissociated old from new items but not same from similar. However the amplitude of the LPC (aka the parietal old/new effect) was higher for similar items correctly judged new than those incorrectly judged new, indicating the amplitude was related to the recollection of the specific detail (picture orientation) diagnostic to determining if an item was old or new. This study both replicates the connection between the FN400 and familiarity and the LPC and recollection as well as demonstrating that these components are memory related and not specific to verbal or pictorial information.

There is a substantial debate over the functional significance of the FN400 and whether or not it is representative of a familiarity process. There is a growing literature that shows that FN400 amplitude is actually manipulated by conceptual fluency, not familiarity per se and may be a part of the N400 component that indexes semantic access (Paller, Voss, & Boehm, 2007; Voss & Federmeier, 2011). For this reason, in this dissertation, FN400 is conceptualized as an early component that reflects a process that supports memory for individual items, not as a correlate of a familiarity process. In this way, I remain agnostic to the exact nature of the cognitive process that generates this potential, whether it be familiarity or conceptual priming. What is important is that early (300-500ms) frontal ERPs are reflective of the strength of item memory, while late (600-900) parietal ERPs index recollection that supports source memory (Woodruff, Hayama, & Rugg, 2006; Woroch & Gonsalves, 2010).

A third ERP effect observed in studies of source memory are the “late frontal” effects. These ERP effects are distributed across frontal scalp channels and occur after recognition, approximately (900-1500ms) post-stimulus and reflect a sustained positivity. The exact functional significance of these effects is unknown, as they are not always observed during simple old/new recognition. They are generated when the source of an item is queried or an emphasis is put on recollection (Hayama, Johnson, & Rugg, 2008; Senkfor & Van Petten, 1998; Wilding & Rugg, 1996), and are thought to reflect post-retrieval monitoring of recollected information. Curran & Cleary (2003) found a dissociation in ERP amplitude based upon individual differences in the subject’s memory. Some of the participants discriminated old from similar lures at a much higher rate than others. The FN400 and LPC components of “good performers” did not differ from those of the “poor performers”. However, there was a difference in the late frontal ERPs, with a larger effect observed for “good performers”. They conjecture that the LPC may reflect the quality of recollection, confirmed by subsequent research (Woodruff et al., 2006; Woroch & Gonsalves, 2010). The late frontal effects reflect post-retrieval processing, that was executed to higher degree in some subjects. A more detailed explanation of the exact cognitive processes underlying these has not been readily forthcoming (Cruse & Wilding, 2009, 2011).

The ERP experiment in Chapter 4 of this dissertation was designed to assess what types of information are available at the time of recollection and how they inform various memory decisions. While it was not designed to examine the cognitive processes that underlie the late frontal source memory effects specifically, the experiment provides some data that speaks to this issue. This experiment seeks moves beyond a process-based account of ERP components and towards an interpretation of the types in information remembered during source memory and how they affect the amplitude of memory-related ERP components.

fMRI, Recollection, and Source Memory

Much of the brain imaging work involving recognition and source memory has focused on mapping the cognitive processing during source memory encoding and retrieval to structural brain regions. Again the research has used both the R/K and source memory paradigms during fMRI to identify brain regions associated with the cognitive processes of familiarity and recollection. These same regions can also be interpreted in a source memory framework, with familiarity sufficient for item recognition, but recollection needed for memory of source. The primary focus of the research has been on the medial temporal lobe (MTL) and its various subregions.

A compelling model that attempts to integrate previous research findings from fMRI, EEG, and neuropsychological testing of visual recognition is the binding item and context (BIC) model (Diana et al., 2007). This model assigns roles or aspects of recognition to different MTL subregions: perirhinal cortex, parahippocampal cortex, and hippocampus. Visual input is processed in the perirhinal or parahippocampal cortex depending on information content, either individual item or context respectively. Those regions send outputs that converge, via the entorhinal cortex, onto the hippocampus. The hippocampus is responsible for binding the various inputs into a single episodic memory. Evidence for each structural component of this model will be briefly summarized in turn.

The perirhinal cortex is located within the anterior parahippocampal gyrus, and is situated at the conclusion of the ventral visual stream. It receives complex visual inputs related to object identity. Neurons that are active during the presentation of a visual object are less active when the same stimulus is repeated. Neurons in the rhinal cortex in monkeys have shown this repetition suppression (Brown & Xiang, 1998; Xiang & Brown, 1998). This same phenomenon of repetition suppression was observed in human perirhinal cortex using magnetic encephalography and fMRI (Gonsalves, Kahn, Curran, Norman, & Wagner, 2005) as well as functional magnetic resonance adaptation (Rubin, Chesney, Cohen, & Gonsalves, 2013). Repetition suppression of the perirhinal cortex would be potential neural mechanism for the recognition of a single item in the absence of hippocampal-based recollection. A reduced firing rate of these neurons would indicate a prior exposure to that stimulus.

The posterior parahippocampal cortex is in the posterior portion of the parahippocampal gyrus and receives inputs from the dorsal visual stream related to an objects relative position. This can be conceived of simply as a spatial position, or more abstractly as the relative position amongst a group of objects. It provides the hippocampus with information on the context in which items appear. This region provide processing including many variation of the source of an item such as spatial, contextual, or associative (Diana, Yonelinas, & Ranganath, 2010).

The hippocampus provides a binding of the inputs from perirhinal and parahippocampal cortex. Relational memory theory (Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001) explains the role of the hippocampus as an automatic binding agent of arbitrary information. This would include the binding of disparate inputs from various cortical processors. Item representations from perirhinal cortex, and contextual information from parahippocampal cortex are bound together into a complete episodic memory representation that can be retrieved later.

During a hypothetical source memory experiment, visual input is processed along the ventral visual stream to determine object identity (Goodale & Milner, 1992). Upon reaching the perirhinal cortex, repeated items result in less neuronal firing (Gonsalves et al., 2005; Xiang & Brown, 1998). This reduction in firing is sufficient to determine if an individual item has been encountered before. This is akin the recognizing the face of the person you encountered earlier as somebody you have encountered before. This information is passed to the hippocampus, which reactivates the episodic memory via a mechanism of pattern completion (Norman & O'Reilly, 2003; O'Reilly & Norman, 2002). This in turn reactivates cortical processors that were active during encoding of the original memory (Danker & Anderson, 2010; Rissman & Wagner, 2012). This allows inspection of the content of memory and reveals the source of an individual item. It allows us to remember the details of an item such as spatial and temporal context, associated items, or other bound information. For example, his would allow us to remember where you met the familiar face, and associated details such as their name.

There are other brain regions outside of the MTL that are often activated during source memory experiments. A reliably observed region is the posterior parietal cortex. The functional significance of this region is not as well characterized as the MTL. However, there appears to be differential activation within this brain region depending upon wither familiarity or recollection or item or source memory is required. Activation of superior posterior parietal cortex is associated with memory for individual items, whereas activation of ventral posterior parietal cortex is associated with the recollection of source information.

The episodic memory processes engaged during recognition can be easily confounded with the strength of memory. If I encounter someone that I was introduced to previously, I may recognize that person as somebody I know I have met before. However, I may not be able to remember their name or the circumstances of our acquaintance. In other circumstances, I may remember all or some of these associated details such as who they are, where we met, what their name is, etc. These two scenarios can be conceptualized as a weak versus strong memory, or reflect the abilities of different memory systems. There is growing evidence that the ability to recognize an item independent of the associated details, only recognizing the person is someone you've seen before, may be due to an independent memory system than the one that allows recollection of the source of the memory, the person's name and where you met.

Another plausible explanation is that these two examples represent weak and strong memories respectively. Only recognizing the person as having been previously encountered constitutes a weak memory representation. A strong memory representation would include more episodic details or memory sources. In this account, item and source memory do not rely on independent memory systems, but different facets of the same system determined by the strength of that memory, such as the person's name and where you met (Squire, Wixted, & Clark, 2007; Squire & Zola-morgan, 1991).

Experimental goals

Memory confidence is commonly used as a proxy for memory strength in cognitive neuroscience studies of recognition (Cruse & Wilding, 2011; Eichenbaum et al., 2007; Fleck, Daselaar, Dobbins, & Cabeza, 2006; Kim & Cabeza, 2007, 2009; Slotnick & Dodson, 2005; Squire et al., 2007; Wixted, 2007a; Woodruff et al., 2006; Yonelinas, 2002; Zandt, 2000). As a memory becomes stronger, it is reflected by greater confidence in memory decisions. The focus of this dissertation is to better understand how the brain supports the strength of source memories, leads to mnemonic confidence in mnemonic decisions. Specifically, the experiments investigate neural activity that varies with source memory strength, by looking for activations that are modulated by memory confidence. I also examine which brain regions are active and involved in all circumstances of recognition and which brain regions are only activated by particular stimuli or task demands.

The subregions of the MTL have been shown to be differentially involved in various aspects of memory. Activity in the hippocampus had been implicated being specific for source memory, while the perirhinal cortex can signal item memory (for review see Eichenbaum et al., 2007). However the role of the hippocampus in source memory, and recognition strength more generally is in debate (Parks & Yonelinas, 2007; Wixted, 2007a, 2007b). Chapter 2 details an experiment designed to investigate the role of the hippocampus in source memory with an experimental paradigm designed to minimize the potential confound between mnemonic type (item and source), and the strength of memory. We adapted a paradigm previously used to dissociate ERP components associated with different mnemonic processes to be MRI compatible so as to explore the functional heterogeneity of the MTL (Woroch & Gonsalves, 2010). The use of this analysis strategy based on memory strength, instead of memory processes, allows us to explore the activity of the hippocampus without an a priori bias of a dual-process model.

We know that many brain regions besides the hippocampus are involved in episodic memory. Many brain regions are involved in the initial perception of a stimulus and differ depending on the content and modality of the stimuli. When a stimulus is encountered, perceptual brain regions process the sensory input allowing us to perceive it. For example, subregions within the ventral visual stream are specialized for the processing of different categories of visual stimuli, such as scenes and faces. That information is then passed to brain regions that consolidate that information into an episodic memory representation. The memory is recalled later by re-activation of the perceptual regions of cortex (Danker & Anderson, 2010; Rissman & Wagner, 2012). Chapters 3 & 4 detail experiments that explore how memory re-activation contributes to the strength of source memory. The experiment in chapter 3 used fMRI to explore brain regions that contribute to source memory strength in both domain-general and domain-specific ways using this phenomenon of cortical re-activation. The experiment in chapter 4 uses ERPs to further explore the understanding of the types of information that are instantiated during source memory retrieval. Canonical ERP components ascribed to recognition memory processes are interpreted in a framework of memory strength and the type of memory being supported.

CHAPTER 2: MEMORY STRENGTH AND THE FMRI CORRELATES OF ITEM AND SOURCE MEMORY

Abstract

The role of the hippocampus during source memory is in debate. Previous fMRI results have shown the hippocampus to be active for source but not item memory. An alternative perspective is that the activity of the hippocampus tracks the overall strength of recognition memory, and not just source memory. These conflicting results arise from the assumptions of dual and single process memory theories. The current study seeks to disentangle the role of the hippocampus in source memory from memory strength. We adapted a paradigm, used previously in the ERP domain, and collected confidence ratings for both memory type (item and source). We observed that the hippocampus responds to the strength of source memory, not the strength of item memory.

Introduction

Recognition memory can entail the ability to classify an individual item as novel or previously encountered, as well as recalling the source of that information. The source can be taken literally to mean where the item came from, such as spoken by a male or female (Slotnick & Dodson, 2005; Wilding & Rugg, 1996), where in space it was (Cansino, Maquet, Dolan, & Rugg, 2002; Rugg, Fletcher, Chua, & Dolan, 1999; Slotnick, Moo, Segal, & Hart, 2003; Van Petten, Senkfor, & Newberg, 2000) or the encoding context from which the item comes (Diana et al., 2010; Dobbins, Rice, Wagner, & Schacter, 2003; Gold, Smith, et al., 2006; Wais, Squire, & Wixted, 2010; Woroch & Gonsalves, 2010). Dual process theory asserts that memory for items and source memory depend on two separate mnemonic processes, familiarity and recollection respectively (Jacoby, 1991; Mandler, 1980; Yonelinas, 2002). Recollection involves the retrieval of associated contextual or source information triggered by the presentation of the to-be-recognized stimulus, whereas familiarity involves an undifferentiated sense of "pastness" in the absence of any such contextual information. Researchers have use fMRI to identify the neural mechanisms of these two processes. The hippocampus has been shown to be active when participants undergo recollection, indicated by a remember response (Cohn, Moscovitch, Lahat, & McAndrews, 2009; Montaldi et al., 2006; Wheeler & Buckner, 2004), when subjects recover source information associated with the item (Gold, Smith, et al., 2006; Henson, Rugg, Shallice, Josephs, & Dolan, 1999; Mitchell & Johnson, 2009; Rugg et al., 2012), and when recognition decisions are made with the highest confidence (Kim & Cabeza, 2009).

However, the behavioral measures used to identify the neural correlates of recollection and familiarity may not be process-pure, such that these neural measures may ultimately reflect some combination of the two processes, or different levels of the strength of a single underlying process (Wixted, 2009). For example, neural measures based upon R/K responses may reflect some combination of the two processes, or different aspects of a single underlying memory process. Wixted (2007) contends that the interpretation of the R/K procedure, reflecting recollection and familiarity respectively, depends on an acceptance of the threshold model of dual-process theories of recognition. A meta-analysis of several fMRI studies of recollection concluded that hippocampal activity, assumed to reflect recollection, could be reinterpreted as the hippocampus responding selectively to strong memories (Wais, 2008). Studies designed to test if hippocampal activity reflects recollection or overall memory strength have concluded that overall memory strength is a better predictor of hippocampal engagement (Kirwan et al., 2008; Wais et al., 2010; Wais, 2011). However, several studies have reached the opposite conclusion, that recollection is a better predictor of hippocampal activity (Cohn et al., 2009; Diana et al., 2010; Rugg et al., 2012). Thus, there is currently some debate as to the precise role of the hippocampus in recognition memory. This debate seems to arise from the difference between measuring memory types/processes versus strength, with findings that the hippocampus may be involved in either. These findings highlight the importance in fMRI studies of the neural correlates of source memory to measure both memory type (item and source) and the strength of both types.

In the ERP domain, we assessed components related to item memory strength and source memory strength independently (Woroch & Gonsalves, 2010). An early ERP component (300-500ms post-onset) was modulated by item memory strength. A later ERP component (600-900ms post-onset) reflected source memory strength. These results thus demonstrated dissociable ERP correlates related to item and source memory, consistent with previous findings

(Rugg & Curran, 2007), while controlling for confounding influences of the strength of one type of memory on the neural correlates of the other.

In the current study, we adapted the basic logic of the analysis used in our ERP study for use with fMRI. The goal was to assess if activity in the hippocampus was specific to source memory, while avoiding the potential confound between memory type and memory strength. A typical contrast of trials in which source memory was correct with trials in which it was not, is thought to reveal brain regions involved in recollection. However, item memory is likely higher for recognized items assigned the correct source, so any observed difference may not be reflecting recollection, but rather overall memory strength (Wixted, 2009). Thus, it is not clear whether the increased activity of the hippocampus during correct source decisions is specific to source memory, or simply increases in overall memory strength. Additionally, trials in which the source judgment was incorrect do not necessarily reflect an absence of all contextual information, as subjects may have recollected some other piece of information from the encoding trial that was not diagnostic of the source decision. When the neural correlates of item memory are determined when source memory is absent, it may be contaminated by this non-criterial recollection (Rotello, Macmillan, Reeder, & Wong, 2005; Yonelinas & Jacoby, 1996). As such, we allowed subjects to indicate when they remembered such information, and removed these trials from analyses.

At least two potential outcomes can be contrasted using this design. On the one hand, the hippocampus may respond to source memory strength and item memory strength (Kirwan et al., 2008; Wais et al., 2010; Wais, 2011). On the other, the hippocampus may be selectively active for correct source memory strength compared to item memory (Diana et al., 2007; Eichenbaum et al., 2007). By holding item memory strength constant while assessing the neural correlates of accurate source memory, we can test these two predictions.

Methods

Participants

27 participants participated in the experiment. Four participants were excluded from analysis due to having too few trials (<10) in one or more conditions of interest. Four more were rejected due to excessive motion within the MRI scanner (>10mm,) across all fMRI runs. Thus, nineteen participants (13 F; ages 19-30 years old, *M* = 22.8) were included in the final data analysis. All participants were right-handed by self-report, had no history of psychiatric or neuropsychological disorders, and were not currently taking any psychotropic medications. Subjects gave informed consent prior to participation, which was approved by the University of Illinois Institutional Review Board, and were financially remunerated $15/hr.

Procedure

The participants performed a recognition memory experiment consisting of encoding, done outside the MRI, and a source memory test during fMRI scanning. A practice version of the entire experiment was done prior to encoding. All stimuli were randomly assigned to each condition for every participant. The stimuli consisted of color photographs of common nameable visual objects, approximately 6cm^2 in size (7° visual angle) used previously in B. Gonsalves & Paller (2000). A sample trial is shown in **Fig. 2.1.** Participants were shown 400 objects during encoding and instructed to memorize each object for a later memory test, as well make one of two judgments. Prior to each object appearing on the screen, participants were cued with “like/dislike” or “natural/manmade” indicating which judgment should be made for the following object, if it was liked or if it was natural. Half of the objects were randomly assigned to each judgment condition, such that 200 were judged each way,

After completion of encoding, participants entered the MRI and two anatomical localizer scans performed. Approximately 30 minutes elapsed between the end of encoding and beginning of the memory test. The test phase was broken into 6 blocks of 100 trials each, totaling 600 pictures of objects (the 400 objects from the encoding phase and 200 novel objects). Stimuli were presented in random order. For each object, participants made an old/new response with a simultaneous confidence judgment (sure old, think old, think new, or sure new). When the object was judged “old” by the participant, regardless of actual study status, an additional source memory query was given; which type of judgment, like/dislike or natural/manmade, was made about the object during encoding. This source judgment was crossed with confidence on a 4-point scale resulting in four response options (sure like/dislike, think like/dislike, think natural/manmade, or sure natural/manmade). Additional response options of “unsure” and “other” were given. An “unsure” option was considered incorrect and given to mitigate the effects of guessing on low-confidence responses. The “other” response was used if they could not remember the type of judgment made about the object, but had a recollection of a different specific episodic detail from encoding, provided to eliminate potential contributions of non-criterial recollection to source incorrect trials. Objects judged “new”, were not given the source memory question, additional fixation was added to equate the length of new and old response trials. An additional 475 seconds of null fixation was randomly inserted between trials, in 2.5-12.5 second intervals, throughout each block of the test to allow for deconvolution of the hemodynamic response.

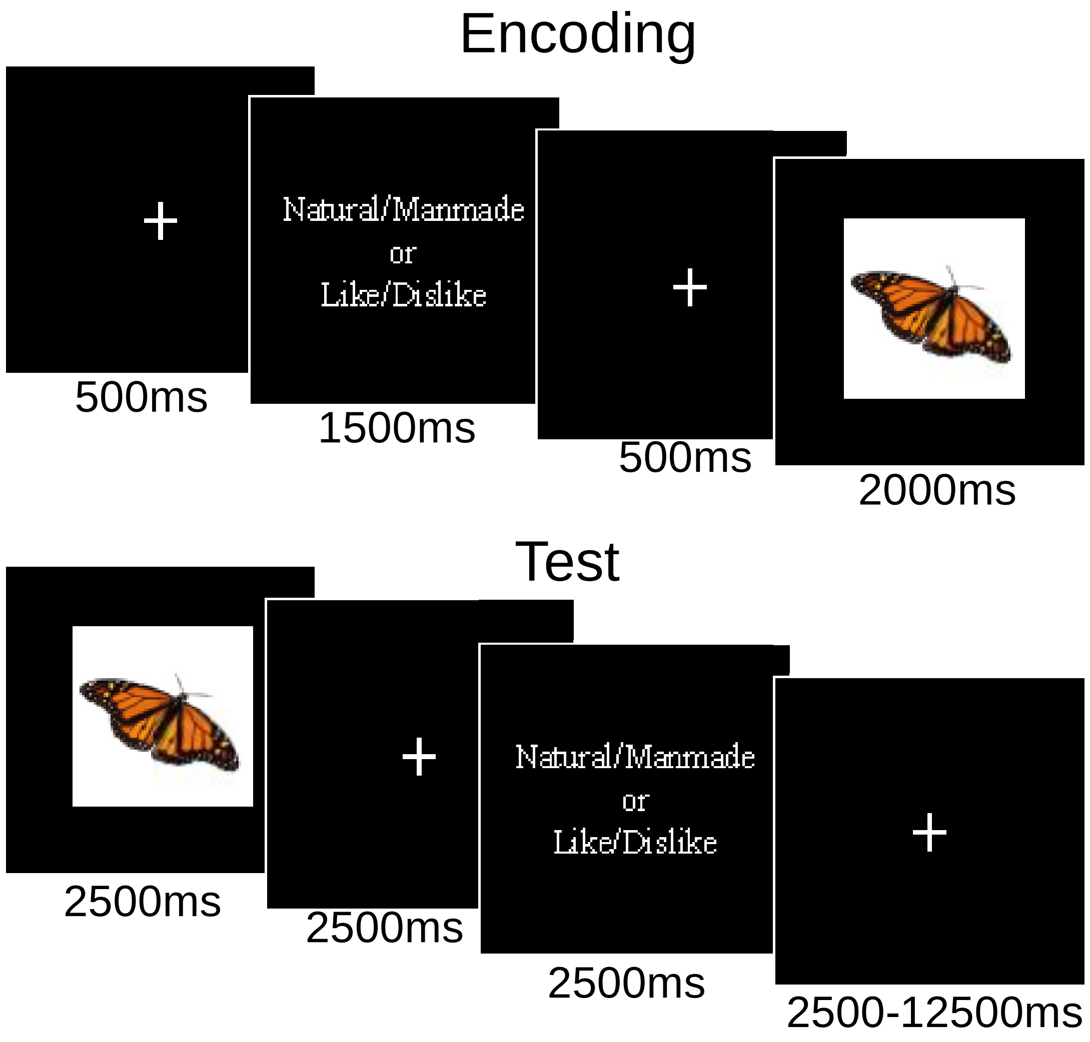

Figure 2.1. A sample trial from both the encoding and test phases. Each test trial began with a prompt for how the following object should be judged. During the memory test each item judged "old" was followed by a source memory question, how was the item judged at encoding?

fMRI data acquisition

Scanning was done using a 3T Siemens Trio MRI with a 16 channel whole-head coil. After T2-weighted anatomical scans, functional images were acquired using a gradient echo-planar pulse sequence (TR = 2.5s, TE = 25ms, 44 interleaved oblique-coronal slices, no gap, 2.5

x 2.5 x 3 mm voxels, flip angle = 90 degrees, FOV=240mm, 400 volumes per run, 6 runs). Oblique-coronal slice acquisition, perpendicular to the main axis of the hippocampus, was used to minimize susceptibility artifacts in the anterior medial temporal lobes during fMRI data acquisition. Slices were positioned to ensure complete coverage of the occipital lobe, at the expense of excluding the frontal poles for participants for whom whole-brain coverage was not possible. A high-resolution T1-weighted MPRAGE anatomical image, with 1mm isotropic voxels, was collected after the 6 experimental runs. Head motion was restricted throughout the experiment using foam inserts. Visual stimuli were projected onto a screen behind the subject and viewed through a mirror mounted on the head coil.

fMRI Data Analysis

Analyses were performed with Statistical Parametric Mapping (SPM5; Wellcome Department of Cognitive Neurology, London, UK, www.fil.ion.ucl.ac.uk) implemented in MATLAB 7.9 (The Mathworks Inc., USA). For each participant, functional images were adjusted for interleaved slice acquisition time and subjected to affine motion correction. A T2-weighted anatomical image was co-registered to the mean EPI volume across runs, and high-resolution T1 MPRAGE images was co-registered to the T2-weighted images. All images were normalized to a standard template based on the 152 subject MNI reference brain. Functional images were resampled to 3x3x3mm voxels and smoothed with a 8mm FWHM Gaussian kernel.

Event-related fMRI time-series data were convolved with the canonical hemodynamic response function, which was time-locked to the onset of each object image. These functions were then used as covariates in a general linear model, along with time-derivative basis functions for each condition, regressors for global changes both within and between blocks, and regressors of the motion-correction parameters. Least-square parameter estimates of the peak of the hemodynamic response function for each condition were computed for each participant and subjected to individual contrasts. These contrasts were then submitted to one-sample t-tests at the group level, treating subject as a random effect. All whole-brain analyses are reported at a threshold of $p < .05$, false-discovery rate corrected, unless otherwise noted.

Region of interest (ROI) analyses were performed using MarsBar 0.41 for SPM5 (Brett, Anton, Valabregue, & Poline, 2002). ROIs were submitted to finite impulse response timeseries analysis for the first eight repetition times (20 sec). The peak BOLD responses were calculated for each condition for each ROI and were then subjected to T-tests.

Results

Behavioral Results

A summary of the behavioral data from the test phase is shown in Tables 2.1 and 2.2. When hit rate was binned by item confidence, accuracy was higher for high than low confidence hits [$\underline{t}(18)=4.69$, $\underline{p}<0.001$]. However, the hit rate for low confidence responses was greater than chance [58% vs. 50%; ($\underline{t}(18)=2.63$, $\underline{p}=0.017$].

When computing source accuracy, only trials on which the item decision was correct were analyzed. Source accuracy was higher for high versus low confidence [92% vs. 74%, $\underline{t}(18)=7.01$, $\underline{p}<0.001$]. High confidence was associated with greater accuracy for both item and source judgments, and the accuracy of low confident item and source decisions was greater than chance.

Table 2.1. Mean (SE) proportion of confidence responses to old/ new item recognition query.

Study Status	**HC Old**	**LC Old**	**LC New**	**HC New**
Old	0.61(0.03)	0.21(0.02)	0.11(0.01)	0.06(0.01)
New	0.03(0.01)	0.05(0.01)	0.44(0.04)	0.47(0.04)
Accuracy	0.82	0.61	0.87	0.97

Table 2.2. Mean (SE) proportion of responses to source memory query, broken down by item confidence.

Item Memory	**HC Correct**	**LC Correct**	**LC Incorrect**	**HC Incorrect**	**Unsure**	**Other**
Overall	0.36(0.02)	0.37(0.03)	0.13(0.03)	0.04(0.01)	0.03(0.02)	0.004(0.002)
LC Item	0.09(0.02)	0.48(0.05)	0.21(0.02)	0.02(0.01)	0.18(0.04)	0.001(0.001)
HC Item	0.44(0.03)	0.33(0.02)	0.11(0.01)	0.04(0.01)	0.06(0.01)	0.005(0.002)

fMRI Results

The fMRI data was analyzed using a restricted analysis designed to minimize potential interactions between memory type (item and source) and memory strength, previously applied to ERP data (Woroch & Gonsalves, 2010). This analysis seeks to hold memory strength in one memory domain (item or source) constant while examining variations in the other. Source memory devoid of item memory is not possible to examine, since source accuracy is at chance when item memory is incorrect. The analysis strategy is to examine variations in source memory strength by reducing any potential influence of item memory strength by maintaining it at only one level.

Source Memory Strength Whole Brain Analyses

There were not enough trials to assess source memory for low-strength item memory, so we restricted our analysis of source memory to trials in which item memory was accurate with high confidence. We directly contrasted high and low confident source decisions at the whole brain level for this subset of trials.

The regions of activations from the whole-brain contrast of source memory strength are summarized in Table 2.3. Within the MTL, the right hippocampus was more active for high than low confident source hits (while keeping item memory strength constant). Additionally bilateral parahippocampal cortex was more active for high than low source confidence. Other brain regions shown to be active in other research on memory strength were also observed, most notably the ventral parietal lobe. There were no brain regions that were significantly more active for low than high confidence source memory.

Table 2.3. Regions that increase activation as source memory strength increases, while accounting for item memory strength.

Hemisphere	Region	Voxels	x	y	z	Z-score
L	Inferior Parietal	226	-48	-57	45	4.58
L	Angular		-54	-66	33	4.01
L	Supramarginal		-57	-57	30	3.98
L	Cerebellum	482	-15	-48	-42	4.53
R	Cerebellum	147	30	-81	-39	3.94
R	Parahippocampus	61	18	-42	-15	3.83
L	Parahippocampus	41	-15	-42	-9	4.23
L	Insula	33	-30	15	-18	4.32
L	Middle Temporal	19	-48	-39	-15	3.79
R	Middle Temporal	17	63	-18	-9	3.35
R	**Hippocampus**	**15**	**33**	**-18**	**-21**	**3.57**

ROI Analyses of the Hippocampus

The primary goal of the present study was to assess the role of the hippocampus in the processing of item and source memory strength respectively. Thus, we also conducted region of interest (ROI) analyses using anatomically defined masks of the left and right hippocampus, obtained from the Automated Anatomical Labeling atlas (Tzourio-Mazoyer et al., 2002) and modified slightly to fit the group average brain of our sample, and summarized the BOLD activity as percent signal change, **Fig. 2.2**. Activity of both the left and right hippocampus was greater for high confidence then low confidence source decisions (restricted to HC hits), left: [t(18)=2.25, p=0.037] right: [t(18)=2.49, p<0.023]. There was no difference in hippocampal activity between high and low confidence item trials (source incorrect) [both t(18)<0.64, p>0.540].

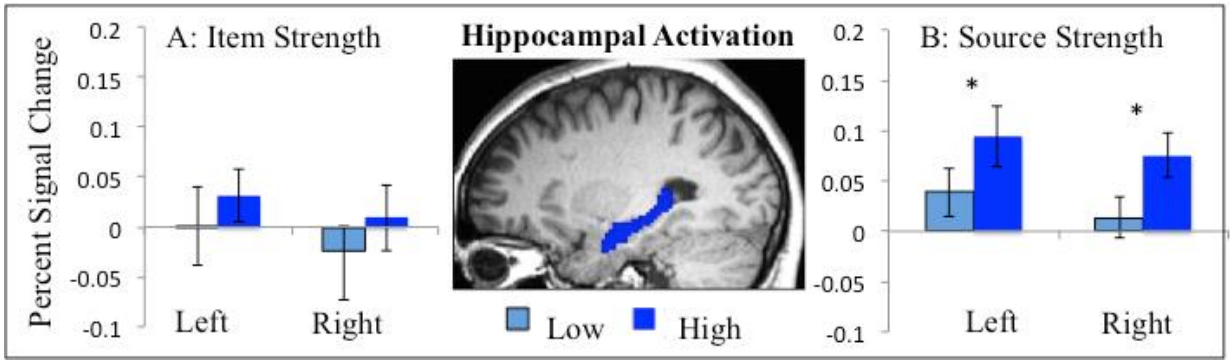

Figure 2.2. ROI analysis from anatomically-defined left and right hippocampus. The bar graphs show percent BOLD signal change in response to item (A) and source (B) memory strength conditions, with low in light bars and high in dark bars. Error bars within subject error. High source strength > Low source strength at p<0.05 for both left and right hippocampus.

Item Memory Strength Whole Brain Analyses

Brain regions that activate with item memory strength were examined in the absence of source memory strength by removing source accurate trials. We mitigated the potential influence of non-criterial recollection on item memory strength by excluding trials in which an "other" response was given. A direct contrast of high and low item trials without source memory was done at the whole-brain level.

A whole-brain contrast of high and item memory strength revealed no brain regions that changed activation in response to changes in item memory strength in the absence of source memory at a threshold $p < .05$, false-discovery rate corrected. We were sensitive to the issue of low trial counts when excluding source correct trials. We relaxed the statistical threshold to $p < .001$ with a 5 voxel extent and observed a region that was less active for high than low item strength: precuneus (peak at x=-12, y=-72, z=45, Z=3.21, 12 voxels).

Old-New Effects

The contrast of high and low item strength only one brain region that changed in activity at a very liberal statistical threshold ($p < 0.001$). Another way to examine item memory is to include correct rejections and look at old/new effects in the absence of source memory ((Jacoby, 1991; Yonelinas, 2002)). We were sensitive to the low power of the item strength contrast, so in order to examine item memory further we fit a parametric model to assess brain regions that changed in activation to increasing item memory strength that also included low and high confidence correct rejections (high confidence correct rejections, to low confidence correct rejections, to low confident item hits and then high confidence hits). Brain regions from this analysis used a statistical threshold of $p < .05$, false-discovery rate corrected. This parametric analysis of item memory strength revealed brain regions that were increasingly active to an increase in item memory strength, listed in Table 2.4 A. There were no MTL regions that showed increased activity as item memory strength increased. However several cortical regions that displayed increased activity as item memory strength increased, including the left inferior frontal gyrus and left superior parietal lobe. These areas of activation are shown in **Fig. 2.3**. The inverse analysis of regions that decrease in activity to item strength (HC item to LC item to LC correct rejections to HC correct rejection) are shown for the sake of completeness listed in Table 2.4 B, but needs mention of the caveat that it may represent increasing novelty detection regions more than decreasing item memory.

Table 2.4 Regions that parametrically increase (A) and decrease (B) in activation as item memory increases in the absence of source memory. (high confidence correct rejection – low confidence correct rejection – low confidence hit - high confidence hit).

A. Increase:

Hemisphere	Region	Voxels	x	y	z	Z-score
L&R	Supplementary Motor	1201	-6	12	51	5.86
L	Inferior Frontal		-48	21	21	5.86
L	Middle Frontal		-27	6	54	5.23
L	Superior Parietal	924	-33	-69	51	5.55
L&R	Precuneus		-6	-66	51	5.01
R	Angular Gyrus		39	-69	45	3.42
R	Superior Parietal		21	-66	60	4.27
L	Occipital	149	-9	-90	0	4.54

Table 2.4 cont

L	Inferior Occipital		-33	-87	-6	4.48
	Middle Occipital		-18	-90	-9	4.45
R	Occipital	65	15	-87	-3	4.96
L	Insula	29	-27	24	3	5.28
L	Middle Temporal	26	-57	-39	0	4.15

B. Decrease:

Hemisphere	Region	Voxels	x	y	z	Z-score
L	Inferior Parietal	226	-48	-57	45	4.58
L	Angular		-54	-66	33	4.01
L	Supramarginal		-57	-57	30	3.98
L	Cerebellum	482	-15	-48	-42	4.53
R	Cerebellum	147	30	-81	-39	3.94
L&R	Precuneus	98	0	-72	42	4.38
R	Parahippocampus	61	18	-42	-15	3.83
L	Parahippocampus	41	-15	-42	-9	4.23
L	Insula	33	-30	15	-18	4.32
L	Middle Temporal	19	-48	-39	-15	3.79
R	Middle Temporal	17	63	-18	-9	3.35
R	Hippocampus	15	33	-18	-21	3.57
L	Inferior Parietal	226	-48	-57	45	4.58

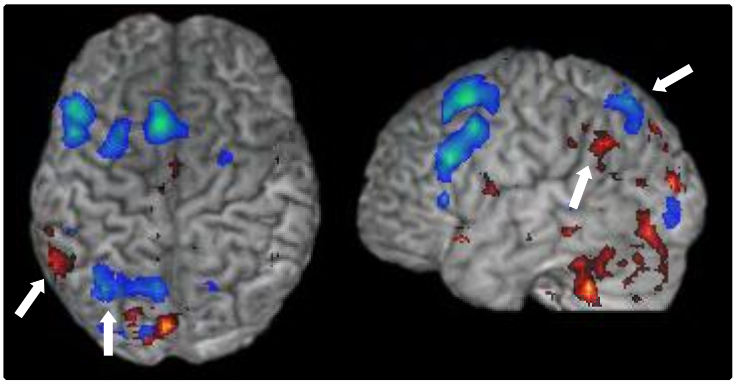

Figure 2.3. A) Brain regions that increase activity with source memory in “hot” colors and item memory in “cool" colors. The brain is the average of all subject’s normalized brains. The arrows highlight the dorsal and ventral parietal activations.

Discussion

Prior research investigating the neural correlates of item and source memory have shown the activity of the hippocampus to be specific to source memory (Cohn et al., 2009; Davachi, Mitchell, & Wagner, 2003; Diana et al., 2010; Henson, Hornberger, & Rugg, 2005; Mayes et al., 2004; Yu et al., 2012). By assuming that recollection of source information is a threshold process, not continuously graded, researchers often fail measure potential variations in source memory strength (Wixted, 2009). Recent research has shown that hippocampal activity may be reflective of overall recognition memory strength (a combination of item and source memory strength), not just source memory and may reflect changes in strength to both item and source memory (Kirwan et al., 2008; Wais et al., 2010; Wais, 2008). The conflicting results of the hippocampus are due to some studies examining memory type (item and source) and others examining memory strength. Brian regions such as the hippocampus that were previously ascribed to source memory may actually be reflective of overall recognition memory strength

(Wais, 2008).

The current study was not designed to adjudicate between models of recognition memory, but rather to address the potential confound between memory type and memory strength in the interpretation of the role of the hippocampus during source memory. Our goal was to investigate the neural correlates of item and source memory strength without assuming a specific model of recognition memory. To do so, we used an analysis strategy, previously applied to the ERP domain, which examines the neural response during item and source memory independently (Woroch & Gonsalves, 2010).

The Hippocampus Responds to Source, not Item, Strength

We hypothesized that the hippocampus would be increasingly active with increasing source memory strength, but would not be modulated by item memory strength. As predicted, we found that activity levels of the hippocampus increased with source memory strength, but not item memory strength. Hippocampal activity was highest when source memory was correct with high confidence and less active when source memory was correct with low confidence **Fig. 2.2**. The activity did not differ between high and low item memory when source memory was absent. Yu et al. (2012) also demonstrated that the activity of the hippocampus was related to the strength of source memory. However, unlike the present study, these observations were made without accounting for variations item memory strength or restricting the analysis to only one level of item confidence. Thus, the present findings strongly suggest that the hippocampus is selectively active for source memory, and shows increased activity with increasing source memory strength and not overall or item memory strength. The parametric item analysis showed the hippocampus decreasing in activity with item strength. However, this contrast includes correct rejections and likely shows hippocampal involvement in encoding (Davachi, 2006).

Prior studies found that activity of perirhinal cortex decreases as item memory strength increases (Gonsalves et al., 2005; Rubin et al., 2013). We expected that activity of perirhinal cortex might selectively decrease in response to increasing item memory strength, in the absence of source memory. However, we observed no relationship between perirhinal activity and either item memory strength or source memory strength. Since the absence of an effect is inconclusive, further research on the involvement of perirhinal cortex during item memory, ruling out the potential confound of source memory strength, is needed.

The Parietal Lobe and Item/Source Strength

A dissociation of activity to item and source memory strength within the parietal lobe was observed. Ventral posterior parietal cortex (PPC), including the angular and supramarginal gyri, increased in activity as source memory strength increased. Dorsal PPC regions showed increasing active with item memory strength (**Fig 2.3)**. The activity related to item memory strength needs the caveat that it was not observed in a direct contrast of item memory strength, but rather a parametric model of item memory strength including correct rejections. Thus, while the findings could be interpreted as continuously varying memory strength, they may also simply reflect old/new item memory effects.

The finding that activity in the ventral parietal cortex increased with source memory strength is consistent with previous work showing that ventral parietal regions are more active when more source information was retrieved (Vilberg & Rugg, 2009). Further, Kim & Cabeza (2007) found activity in ventral PPC was associated with high confidence, while dorsal regions were associated with low confidence, while Wheeler & Buckner (2004) found ventral PPC was associated with recollection and dorsal with familiarity. It should be noted that the exact functional significance of parietal engagement during recognition is unclear, whether it be accumulation of evidence (Vilberg & Rugg, 2008, 2009) or an bottom-up vs. top-down attention to memory account (Cabeza et al., 2008). That said, the present study fits well with either account, as it demonstrates that, not only is there a dissociation of PPC activity according to memory type (ventral for source, dorsal for item), but that both regions show increased activity with increasing strength of their respective memory type.

The Frontal Lobe and Item Strength

The frontal lobe is known to be involved in the monitoring of source information (Badre & Wagner, 2007; Cansino et al., 2002; Dobbins, Foley, Schacter, & Wagner, 2002; Fletcher & Henson, 2001; Mitchell & Johnson, 2009; Rugg, Henson, & Robb, 2003). In a different study, he left frontal lobe increased with familiarity (Vilberg & Rugg, 2009). This is similar to our finding of increasing left frontal activity with increasing item memory. We did not see changes in frontal activity to source memory strength. We speculate that when the item was recognized with high confidence, frontal brain regions would be recruited to aid in the additional monitoring/retrieval of source memory (Henson et al., 2005; Rugg et al., 2003). The trials when source memory was retrieved would require less processing since source memory was already retrieved.

Conclusions

This study was designed to investigate the role of the hippocampus while performing item and source memory while accounting for the potential confound between overall recognition memory strength and memory type (item and source). The obtained results are consistent with both dual-process and continuous models of source memory and does not adjudicate between the two. Source memory strength did vary in this experiment, suggesting a continuous model. However threshold models can allow recollection strength to vary once it is above threshold, which our trials were. This study used an analysis strategy that did not assume one model or another and found the hippocampus to be selectively active during correct source memory, with activity increasing with source memory strength. This supports the conclusions of previous research regarding the role of the hippocampus as selective for source memory and responds to source memory strength, not item or overall strength. Criticisms that previous findings from fMRI studies that the is selectively involved in source memory, when it really reflects overall memory strength may be unwarranted The hippocampus is involved in the retrieval of source memory, and the strength of that memory. The parietal lobes are engaged differentially depending on memory type. This may reflect differential processing of item and source memory strength, or a difference in bottom-up versus top down processing (Cabeza et al., 2008; Vilberg & Rugg, 2008). The frontal lobes are recruited when additional retrieval of source information is required.

CHAPTER 3: ACTIVATION OF STIMULUS-SPECIFIC PROCESSING REGIONS AT RETRIEVAL TRACKS THE STRENGTH OF ASSOCIATIVE MEMORY

Abstract

Many theories of episodic memory posit that the subjective experience of recollection may be driven by the activation of stimulus-specific cortical regions during memory retrieval. This study examined cortical activation during associative memory retrieval to identify brain regions that support confidence judgments of source memory in stimulus-general and stimulus-specific ways. Adjectives were encoded with either a picture of a face or a scene. During a source memory test, the word alone was presented and the participant was asked if the word was previously paired with a face or a scene. We identified brain regions that were selectively active when viewing pictures of scenes or faces with a localizer scan. We then identified brain regions that were differentially activated to words during the source memory test that had been previously paired with faces or scenes, masked by the localizer, and examined how those regions were modulated by the strength of the source memory. There were stimulus-specific perceptual processing regions for both faces and scenes that were active during source memory that increased in activity with increasing source memory confidence.

Introduction

Memory for episodes from one's past involves the coordination of multiple brain systems at the time of encoding and again during memory retrieval. These include cortical regions that process the components of an episode such as the people that were present, the time the event took place, or the setting in which the episode occurred. Structures in the medial temporal lobe (MTL), most notably the hippocampus, act to relationally bind together these various elements of experience into a coherent episodic memory (Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001). This specific episodic memory can then be retrieved in response to a cue from one aspect of the memory, allowing inspection and re-experiencing of the entire original episode. Many models of episodic memory include the idea that such remembering involves the reactivation of the brain regions that were initially engaged at the time of encoding, and that this reactivation contributes to the subjective experience of remembering (Danker & Anderson, 2010; Rissman & Wagner, 2012). However, not all components of an episodic memory are remembered with equal fidelity. It is possible to strongly remember where you were but have only a vague recollection of the people that were present or the temporal context, for example. The aim of this study was to investigate perceptual brain regions that are activated during source memory retrieval and how this activation contributes to the remembering of different stimulus types, and how activation in these regions tracks the subjective strength of memory for specific stimulus types.

Some of the brain regions involved in episodic memory retrieval are engaged in a stimulus-general manner, and contribute to episodic memory regardless of the contents of the memory. This is true of the hippocampus, which participates in the binding and retrieval of the elements of episodic memory regardless of stimulus content (Eichenbaum, Yonelinas, & Ranganath, 2007; H. Eichenbaum, Otto, & Cohen, 1994; Konkel, Warren, Duff, Tranel, & Cohen, 2008). Many neural network models of episodic memory retrieval include the idea that one role of the hippocampus is to reactivate associated memory information through a process of pattern completion (Alvarez & Squire, 1994; McClelland, McNaughton, & O'Reilly, 1995; Moscovitch et al., 2005; Norman & O'Reilly, 2003). The advent of functional neuroimaging methods has provided ways to assess the assumptions of pattern completion and cortical reactivation. Studies have generally found that perceptual processing regions that represent the specific kind of associated information tend to be active during memory retrieval in response to a cue, even when the associated information type is not presented (Khader, Burke, Bien, Ranganath, & Rösler, 2005; Nyberg, Habib, & Herlitz, 2000; Rosler, Heil, & Hennighausen, 1995; Vaidya, Zhao, Desmond, & Gabrieli, 2002; Wheeler & Buckner, 2003, 2004; Wheeler, Petersen, & Buckner, 2000; Woodruff, Johnson, Uncapher, & Rugg, 2005). For example, if a word had been encoded accompanied by a picture of an object, presenting the word alone at retrieval will often activate brain regions involved in the perception of object information. In addition to the reactivation of perceptual information, studies have also demonstrated effects associated with the reactivation of emotional associations (Maratos, Dolan, Morris, Henson, & Rugg, 2001; Smith, Henson, Dolan, & Rugg, 2004) as well as reactivation of cognitive or strategic processing engaged at encoding (Johnson & Rugg, 2007; Kahn et al., 2004; Voss, Galvan, & Gonsalves, 2011).

Several studies have taken the additional step of associating cortical reactivation effects with the process of recollection as opposed to familiarity, with the idea that reactivation of associated information is a hallmark of recollection (Johnson & Rugg, 2007; Wheeler &

Buckner, 2004; Woodruff et al., 2005). The general findings seem to confirm the notion that cortical reactivation is associated with recollection of episodic memory. However, there are fewer attempts to investigate how variations in these reactivations effects might be associated with subjective variations in the strength of recollection or variations in objective accuracy or specificity of recollection. Evidence from the behavioral recognition memory modeling literature suggests a graded recollection process and a continuous variation in the memory strength of recollection (Dodson, Holland, & Shimamura, 1998; Hicks, Marsh, & Ritschel, 2002; Mickes et al., 2009; Simons, Dodson, Bell, & Schacter, 2004; Slotnick & Dodson, 2005; Slotnick, 2010). Some studies have investigated the specificity of source retrieval (Dodson et al., 1998; Hicks et al., 2002) and variations in the amount of retrieved information (Johnson, McDuff, Rugg, & Norman, 2009; Vilberg & Rugg, 2008, 2009). Previous research has provided evidence that the activity level of hippocampus increases with source memory strength (Woroch & Gonsalves, submitted). Two other studies investigating recollection strength did not find variations in hippocampal activity with memory strength. They focused on the role of ventral parietal cortex in the strength of recollection, showing that this region is modulated by differences in subjective ratings of the amount of information recollected (Vilberg & Rugg, 2007, 2009). The precise function of this parietal region is unclear, though some have suggested that it may play a role in the orienting of attention to reactivated memory representations or may serve as an episodic buffer in working memory (Shimamura, 2011; Vilberg & Rugg, 2008). Regardless of the exact function of this region, it appears to be stimulus-general, tracking subjective memory strength regardless of stimulus type.

The aim of this study was to investigate how cortical reactivation may vary with the subjective strength of source recollection. We capitalized on the current understanding that distinct brain networks seem to be involved in processing faces and scenes. A network of regions including the superior temporal sulcus, amygdala, and fusiform cortex is more active in response to viewing faces than other types of stimuli (Ishai, 2008). In contrast, scene perception activates a network of brain regions involved in object perception, but one region dubbed the parahippocampal place area (Epstein & Kanwisher, 1998) seems to be most active to scene stimuli. These brain regions are also selectively activated during visual imagery of the respective stimulus type (O'Craven & Kanwisher, 2000). Furthermore, it has also been found that these stimulus-specific brain processing regions can be reactivated during associative memory tasks (Johnson & Rugg, 2007; Woodruff et al., 2005).

We hypothesized that stimulus-specific cortical processing regions will be activated in response to associated memory cues during retrieval. The magnitude of this cortical activation was expected to be positively related to confidence in memory for the associated, but not presented, information. To test this, we showed participants words paired with faces or scenes during encoding. At retrieval, just the word was shown and subjects were asked if it had been paired with a face or scene. We expected that stimulus-specific processing regions, identified by fMRI localizer scans, would be activated in response to words that had been previously paired with that stimulus type. The magnitude of this activation was expected increase as a function of source memory strength, indexed by subjective confidence in a source memory judgment.

Methods

Participants

Eighteen young adults participated in this study. The data from 14 participants (6 F; ages

20-35 years old, *M* = 25.6) were included in the analysis. Data from 4 participants were excluded from analysis due to excessive motion within the MRI scanner (greater than 6mm in any one plane). All participants were right-handed by self-report, had no history of psychiatric or neuropsychological disorders, and were not currently taking any psychotropic medications. All subjects gave informed consent prior to participation in the study, which was approved by the University of Illinois Institutional Review Board, and were compensated $15/hr.

Procedure

The participants performed a recognition memory experiment comprising of words, pictures of faces, and pictures of "places" (photographs of scenes) as well as a 1-back localizer task with just pictures. The words were 754 adjectives between 4 and 10 letters in length (M=7.3). The face stimuli were comprised of 300 male and 300 female color photographs faces selected from a face database used in a previous study (Althoff and Cohen,1999). There were 720 color photographs of scenes, equally represented by 6 categories (mountains, beaches, cities, forests, highways, and industry) used previously by Walther et al. (2009). The stimuli were randomly assigned to the practice, memory experiment, and localizer task for each participant, with the condition that there were equal numbers of scenes from each category in each task as well as equal numbers of male and female faces.

The stimuli for the experiment were encoded on a computer outside the MRI scanner, while the test phase was performed within. Prior to the experiment, participants completed a practice version of the entire memory experiment (encoding and source test), consisting of 48 stimuli not used in the remaining experiment. During encoding, participants studied 504 words randomly presented one at a time beneath a picture of either a face or a scene for 3500ms each with a 500ms ITI (**Fig 3.1)**. While the stimuli were on the screen, the participant rated how well the word described the picture on a 6-point scale. The first and last 2 stimulus pairs were not tested, to mitigate the effects of primacy and recency. The participants entered the MRI scanner and underwent preliminary calibration and localizer scans. Approximately 30 minutes elapsed between the end of the encoding phase until the beginning of the test phase. During the memory test each word was centrally presented for 2500ms and participants were instructed to imagine the image that had been previously paired with the word. They responded if the word was previously paired with a face or a place image and simultaneously rated their confidence on a scale from one to six (sure face, think face, guess face, guess place, think place, sure place). Participants were instructed to guess face or place if they saw a word they did not remember seeing before. An additional 167.5 seconds of null fixation was randomly presented between trials, in 2.5-12.5 second intervals, throughout each block of the test to allow for deconvolution of the hemodynamic response to individual trial types. The test trials consisted of 500 words that had been previously studied (half with a face, half with a place). The remaining 100 words were new words that were not studied at encoding. The test phase was broken into 6 blocks of 100 randomly selected trials. After each block participants were shown how many times they responded sure, think, or guess, regardless of stimulus type or accuracy, and instructed to balance out their number of responses and not skew them in any one direction.

Following completion the memory task, participants performed a task with pictures of faces and places designed to localize face and place specific processing regions of the brain. The localizer was based on Walther, Caddigan, Fei-Fei, & Beck (2009) but only localized scenes and faces. To ensure attention to the pictures, participants performed a 1-back test and pressed a button whenever a stimuli was immediately repeated. The pictures used in the localizer task were randomly chosen from the set of stimuli not used in the memory task. Each picture was shown for 750ms with a 250ms ITI. Stimuli were presented in 8 blocks. Each block consisted of either 12 faces or places, followed by 12 of the other stimulus type, followed by 15 seconds of fixation. A randomly selected 9 stimuli in each block were shown once and 3 were shown twice. The order of the blocks was counterbalanced within subjects so that each block had an equal chance of beginning with faces or places and an equal chance of being followed by a block of the same order.

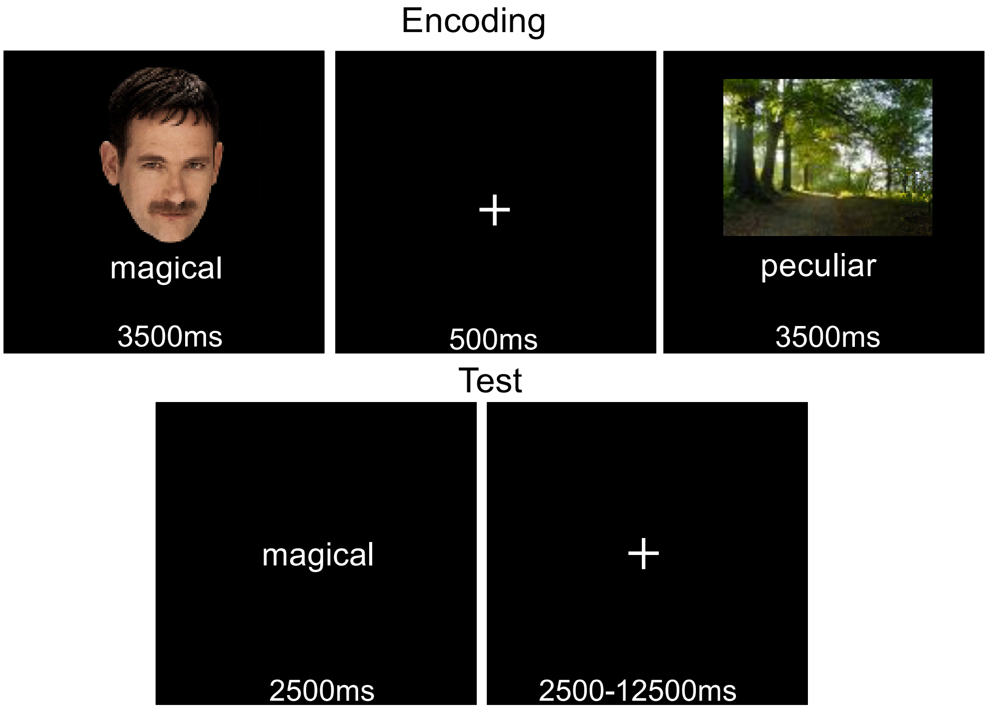

Figure 3.1. A sample trial from the source memory test. Pairs of words and pictures were shown at encoding. During the test a word was shown and participants responded with the type of stimulus, face or place.

fMRI Data Acquisition

Scanning was done using a 3T Siemens Allegra MRI with a 16-channel whole-head coil. After a T2-weighted anatomical scan, functional images were acquired using a gradient-echo echo-planar pulse sequence (TR = 2.5s, TE = 25ms, 44 interleaved oblique-coronal slices, 3.4 x 3.4 x 3 mm voxels, no gap, flip angle = 90 degrees, FOV=220mm, 274 volumes per run for 6 runs, followed by 152 volumes for one run). Oblique-coronal slice acquisition perpendicular to the main axis of the hippocampus was used to minimize susceptibility artifacts in the MTL during fMRI data acquisition. Slices were positioned to ensure complete coverage of the occipital lobe, at the expense of excluding the frontal poles for participants for whom whole-brain coverage was not possible. High-resolution T1-weighted MPRAGE anatomical images (1mm isotropic voxels) were collected after the 6 experimental runs and 1 localizer run. Head motion was restricted using foam inserts. Visual stimuli were projected onto a screen behind the subject and viewed through a mirror mounted on the head coil. Responses were made with handheld button boxes.

fMRI Data Analysis

Data analyses were performed with Statistical Parametric Mapping (SPM5; Wellcome Department of Cognitive Neurology, London, UK, www.fil.ion.ucl.ac.uk) implemented in MATLAB 7.9 (The Mathworks Inc., USA). For each participant, functional images were adjusted for interleaved slice acquisition time and then subjected to affine motion correction. T2-weighted anatomical images were co-registered to the mean EPI volume across experimental runs, and high- resolution T1 MPRAGE images were co-registered to the T2-weighted images. The localizer scan EPI volumes were co-registered to the mean EPI image from the memory runs. All functional images were then normalized to the standard template based on the 152-subject MNI reference brain, resampled to 3x3x3mm voxels, and smoothed with an 8mm FWHM Gaussian kernel.

The memory data were concatenated across runs and modeled using a general linear model. Event-related fMRI time-series data were convolved with the canonical hemodynamic response function, which was time-locked to the onset of each object image. These functions were then used as covariates in the general linear model, along with time-derivative basis functions for each condition, regressors for global changes both within and between blocks, and regressors of the motion-correction parameters. A parametric modulator based upon behavioral source confidence was included to identify brain activity that increased with increasing confidence (low-medium-high). Least-square parameter estimates of the peak of the hemodynamic response function for correct face and place responses calculated and adjusted by their respective parametric modulators. The localizer data was analyzed in a similar way, except using a blocked design and contrasting face and place blocks. The source strength effects were then submitted to one-sample *t* tests at the group level, treating subject as a random effect, and masked by the localizer contrast. These analyses are reported at a threshold of $p < .05$, false-discovery rate corrected, with a 5-contiguous-voxel extent threshold.

The parametric analysis does not reveal the activation to low, medium, and high confidence trials individually. Percent signal change analyses were performed using MarsBar 0.41 for SPM5 (Brett et al., 2002). Regions defined by the parametric memory strength analyses were submitted to a finite impulse response time-series analysis for the first eight repetition times

(20 sec). The percent BOLD signal change was calculated for each strength level separately for each ROI.

Results

Behavioral Results

The behavioral data were analyzed using a 2x3 (Face/Place x Confidence) repeated-measures ANOVA and are shown in **Fig 3.2**. Source memory accuracy in terms of percent correct was higher for places than faces overall [$F(1,13)=4.89$, $p=0.046$]. However, post-hoc t-tests at each level of confidence individually revealed no difference in accuracy between faces and places [all $t(13)<1.48$, all $p>0.161$]. There was a main effect of response confidence on accuracy; as confidence increased so did behavioral accuracy [$F(2,26)=39.71$, $p<0.001$]. There was no interaction of response confidence and stimulus type [$F(2,26)=0.67$, $p=0.521$]. While response times decreased with increasing confidence [$F(2,26)=16.41$, $p<0.001$], there was no significant difference in response time between faces and places [$F(1,13)=1.24$, $p=0.286$], and no interaction of stimulus condition and response confidence [$F(2,26)=1.23$, $p=0.309$]. The accuracy for low confidence (guess) trials was not significantly above chance for either faces [54% vs. 50%, $t(13)=2.02$, $p=0.064$] or places [53% vs. 50%, $t(13)=1.38$, $p=0.192$]. However, accuracy for medium confidence (think) trials was above chance for both faces [55% vs. 50%, $t(13)=3.96$, $p=0.002$] and places [57% vs. 50%, $t(13)=5.518$, $p<0.001$].

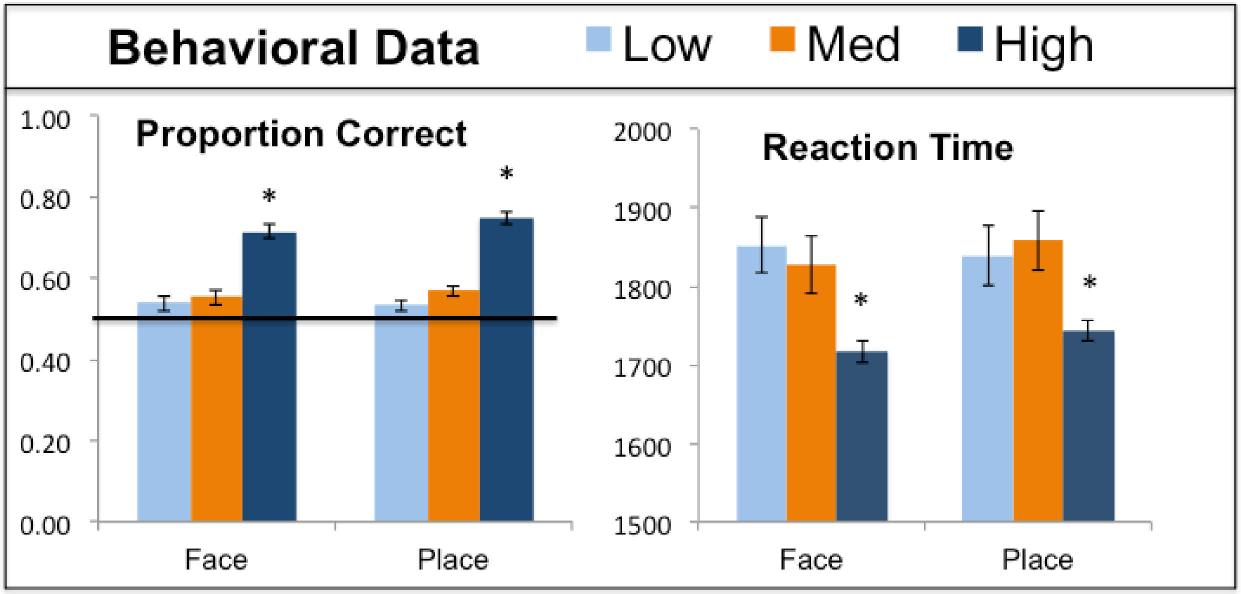

Figure 3.2. The behavioral data from the source memory test for low, medium, and high confidence responses for faces and places, with standard error bars. The black line at 50% of proportion correct represents chance performance.

fMRI results

The analysis involved two stages. First, we located stimulus-specific brain activations, face or place, using a localizer task. Second, we identified brain regions more active during the source memory task, to words alone, depending on which stimulus type was associated at encoding (places or faces) and increased in activity with increasing behavioral confidence. Those regions were masked to only include regions from the localizer scan. We then extracted the percent signal change from the local maxima of these regions to look at the activity level for each confidence level individually.

The first analysis looked at brain regions more active for places than faces that increased as a function of source memory confidence. A contrast of places minus faces from the localizer task revealed brain regions more active when viewing places, which was used as a mask for the memory test data. We then analyzed correct place trials from the source memory experiment, and identified regions that were parametrically modulated by increasing mnemonic confidence (Places by Confidence; plotted **Fig 3.3**). The only region above threshold was left parahippocampal cortex.. The percent signal change from this regions (peak at x=-30, y=-33, z=-18, *Z*=4.14, 21 voxels) is plotted in **Fig 3.3** for each level of confidence to look at the amount of activation in each condition separately.

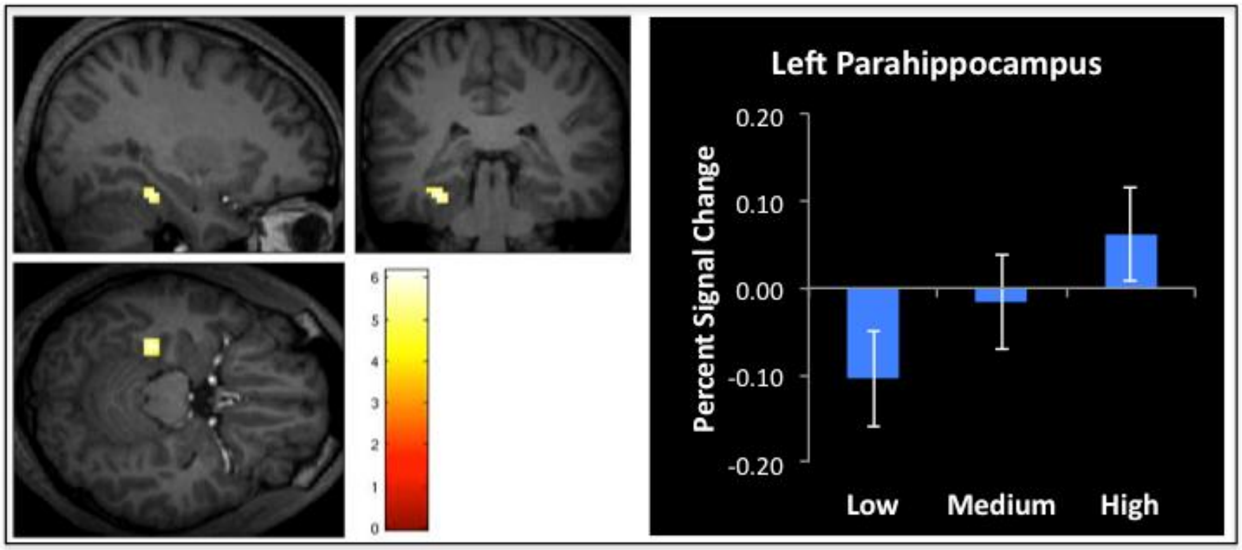

Figure 3.3. Brain activation that increases with confidence for words associated with places (left: x=-30 y=-33 z=-18), masked by regions from a place-face localizer. The graph shows the percent signal change of the parahippocampal activation to the associated word at each level of confidence with within-subject error bars.

The same strategy was employed to look for regions more active for faces than places. A contrast of faces minus places during the localizer task revealed brain regions more active when viewing faces than places. These regions were used as a mask for memory test activity. We assessed activation from the correct face memory trials that increased with increasing mnemonic confidence (faces by confidence). The only regions from this analysis that overlaps with activation from the localizer was bilateral amygdala, shown in **Fig 3.4** The percent signal change from these regions (left peak: x=-21, y=-9, z=-15, *Z*=3.42, 16 voxels; right peak: x=18, y=-3, z=-15, *Z*=3.58, 12 voxels) were plotted separately for each level of response confidence to look at the activation at each level.

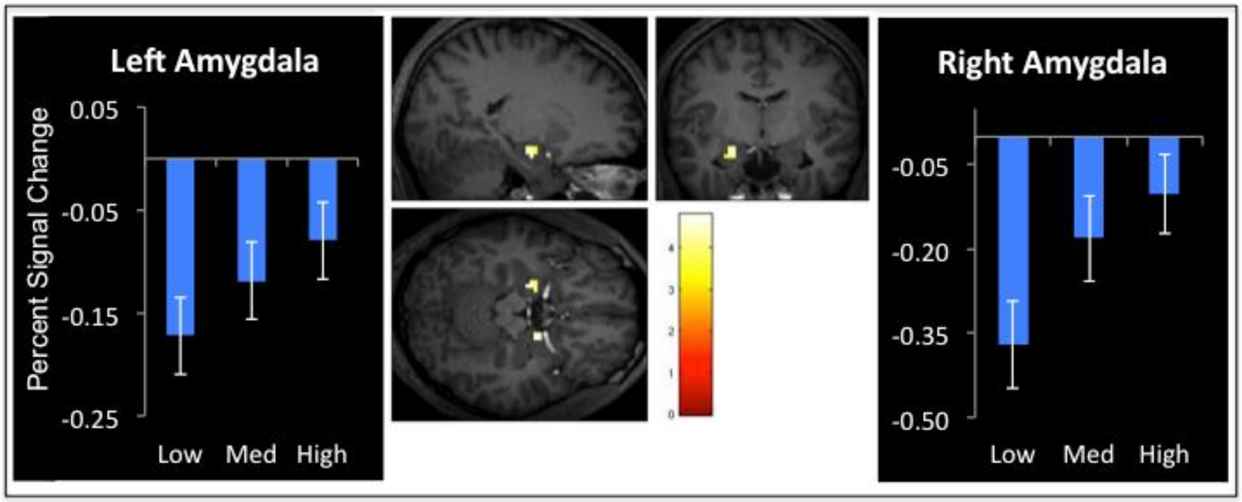

Figure 3.4. Brain activation that increases with confidence for words associated with faces (x=-21, y=-9, z=-15), masked by face-place activation from a localizer. The graphs show the percent signal change of the left and right amygdala to a word at each level of confidence with within-subject error bars.

To reveal brain regions that increase or decrease in activity as a function of memory strength in a stimulus-general way, independent of associative item identity, we performed a contrast of all correct memory trials, both faces and places, parametrically modulated by increasing memory strength compared against fixation. The brain regions that were increasingly and decreasingly active are summarized in **Table 3.1**.

Table 3.1. Brain regions that are increasingly/decreasingly active with increasing stimulus-general memory strength, regardless of whether it was encoded with a face or place.

A: Increase

Hemisphere	Region	Voxels	x	y	z	Z-score
	MTL					
L	Perirhinal Cortex	29	-27	-12	-33	4.06
L	Parahippocampus	28	-21	-39	-6	3.89
R	Hippocampus	9	27	-24	-15	3.86
	Other					
L	Superior Medial Frontal	130	-6	30	45	4.34
L	Insula	169	-30	21	-6	4.31
L	Caudate	172	-15	0	21	4.16
R	Caudate	98	12	6	18	3.68
L	Precuneus	97	-12	-69	33	3.65

B: Decrease

Hemisphere	Region	Voxels	x	y	z	Z-score
R	Supramarginal	61	63	-9	30	4.17
R	Precuneus	30	9	57	54	4.05
R	Angular	15	30	66	45	3.96
R	Middle Frontal	8	45	48	12	3.88
R	Middle Frontal	6	24	57	27	3.36

We also hypothesized that activation of stimulus-specific regions may account for how the participant responds to novel words, and incorrect response. We examined trials in which the participant responded to the face/place incorrectly as well as responses to novel words. We performed two contrasts, the incorrect trials for faces with the incorrect trials of places, and face or place responses to novel words, again masked by regions from the localizer scan. There were not enough trials to look at each level of response confidence separately, so low, medium, and high confidence were collapsed together for these analyses. We used a more liberal statistical threshold for this analysis due to low numbers of trials ($p < .0001$, uncorrected, with a 5-contiguous-voxel extent). We found no significant activation for words paired with a place during encoding and incorrectly endorsed as having been paired with a face during the source memory task or for novel word judged as having been paired with a face. However, words paired with a face at encoding but incorrectly endorsed as having been paired with a place during the source memory test produced activation in the left parahippocampus (x=-33 y=-27 z=-15, Z=4.59, 15 voxels). New words judged to have been paired with a place also elicited parahippocampal activation (x=-30 y=-48 z=-6, Z=3.53, 7 voxels).

Discussion

This study examined cortical activation during associative memory retrieval to identify brain regions that support confidence judgments of source memory in stimulus-general and stimulus-specific ways. We identified stimulus-specific processing regions using a separate localizer task. We hypothesized that the magnitude of activation of stimulus-specific processing brain regions during a source memory task would scale with confidence for that specific kind of information. Thus we expected that regions more active for faces or places during our localizer would be increasingly active with increasingly confident source memory of that stimulus type, face or places respectively. We identified brain regions that were more active during correct source memory that increased their activity parametrically with source memory confidence, masked by regions of that differed between activations from a face or place localizer task. We examined brain regions whose activity increased with source memory strength, as measured by confidence, in a stimulus-general way, independent of associated stimulus type. We also examined the brain response to novel and incorrect words.

Localizer scans for scene stimuli identified several occipital and temporal regions, including several clusters in the parahippocampal cortex that contribute to scene (place) processing. During the source memory task, when participants were correct in remembering that a word had been previously paired with a scene, the parahippocampal cortex increased in activity with increasing behavioral confidence. This parahippocampal region overlapped with regions activated in the scene localizer task, The parahippocampal regions observed in the current study included regions characterized previously as the parahippocampal place area (Epstein & Kanwisher, 1998) as well as more anterior regions. This left parahippocampal region increased in activity parametrically with increasing source confidence as shown in **Fig 3.3**.

The activation of this parahippocampal region may also be related to guessing behavior or false source memory on the memory test. The parahippocampal cortex was active for incorrect place source memory, words incorrectly judged to have been paired with a place during the memory test but were originally paired with a face during encoding. The parahippocampal cortex was also active for novel words judged to have been paired with a place. The study design did not yield enough trials to look at the contribution of confidence to this effect, so it is unclear how the magnitude of this response may relate to confidence. We found no evidence of brain regions that contribute in a similar way to incorrect face source memory, words incorrectly judged to have been paired with a face during the memory test but were actually paired with a place during encoding. A study specifically designed to examine brain regions that contribute to incorrect source judgments is needed to draw conclusions about the functional significance of these observations and to observe how this activity might interact with confidence.

The face localizer task revealed activity of several brain regions previously associated with face processing; the right fusiform cortex, right superior temporal sulcus, and right amygdala. During retrieval, when participants viewed a word that had been studied with a face, and correctly identified it as such, regions in bilateral amygdala increased in activation with increasing confidence in the "face" source memory decision, **Fig 3.3**.

Given the amygdala's role in processing emotion, we were concerned that this observed activation reflected the possibility that the words more likely correct in the face condition may have been more emotionally arousing than those in the place condition. Although the stimuli were randomly assigned to condition for each subject, we identified words across subjects that were more likely to be associated with accurate face source memory than place. We obtained the mean arousal ratings for the words used in this experiment from a normed database (Warriner, Kuperman, & Brysbaert, 2013). We found no difference in the emotional arousal ratings between words associated with accurate face source memory compared to accurate scene source memory [$t(355)=0.66$, $p=0.438$]. Although we did not collect arousal rating from the participants in the current study, this provides some evidence against the idea that amygdala activity observed in the current study was due to the emotional content of the words themselves. Our conclusion is that the amygdala activity observed is related to source memory specific to face processing.

We had expected that activation of regions typically associated with face processing, including fusiform face area (FFA) and superior temporal sulcus (STS) would be associated with face source memory confidence. However, those regions were not significantly more active during face source memory than during scene source memory in our parametric analysis. We followed up our parametric analysis by conducting region of interest analyses of these face-processing regions. There was no evidence of stimulus-specific activation that increased with source memory confidence in either the FFA or STS. The data from the ROI analysis of these regions is included in the following section of this chapter.

This study contributes data that supports the idea that activation of stimulus-specific processing regions of the brain support recollection of associated source information. The activation of different brain regions during recollection influences the source memory decision, and increasing activation of these regions is related to increasing confidence. The activation of these regions during source memory may be related to false memory of specific stimulus types, although follow-up tests are needed. Regions of the medial temporal lobe, including the hippocampus, parahippocampal cortex, and perirhinal cortex all increased their activation with increasing source memory confidence in a stimulus-general way, regardless of the associate stimulus type. These regions have been previously associated with memory strength (Diana et al., 2007; Gonsalves, Kahn, Curran, Norman, & Wagner, 2005; Wais, 2008; Woroch & Gonsalves, submitted).

A remaining question of interest is, what type of information is being represented by this cortical activation? Based on the involvement of these regions in visual imagery, we conclude that this activity reflects the recollection of the stimulus that had been studied with the word. However, an equally plausible explanation is that the activation represents access of category-level information, place or face, since that is the only information diagnostic for the source memory decision. Brain regions representing “scene” information that activate to associated cues may reflect the recollection of the exact scene stimulus that was initially studied. It may also just reflect basic category-level information such as the spatial information diagnostic of a scene compared to a face or scene category level information, such as a forest compared to a mountain. Future experiments will need to discriminate these potential interpretations.

Additional Analyses

We predicted the involvement of other face-specific processing brain regions that were not identified by our parametric model. Two additional ROIs were selected from a contrast of faces minus places during the localizer task, the right fusiform face area (FFA) (peak: x=45 y=-54 z=18, T=6.44, *voxels*=23) and right superior temporal sulcus (STS) (peak: x=57 y=-42 z=15, T=6.26, *voxels*=14). These are regions known from previous literature to be involved in selectively processing face stimuli (Ishai, 2008; Walker et al., 2014). The percent signal change from these two regions from the memory test for each condition is plotted below and was analyzed using a 2x3 (Face/Place x Confidence) repeated-measures ANOVA. The FFA was not differentially active for words paired with faces or places, nor confidence, and there was no interaction [all $F<0.59$, all $p>0.281$], **Fig. 3.5.** The activity of the STS was not different between words paired with faces and places [$F(1,13)=0.89$, $p=0.362$]. There was an effect of confidence, with activity decreasing as confidence increased [$F(2,26)=4.64$, $p=0.019$], but no interaction between condition and confidence [$F(2,26)=1.18$, $p=0.319$], **Fig. 3.6**.

Since activity in these regions did not increase with memory strength, it is not surprising that we did not identify them in the earlier parametric model. The pattern of activation identified from the ROI analyses does not show a dissociation between activity related to face or scene source memory in the FFA or STS. It is interesting to note that activity in the STS decreased with increasing memory strength.

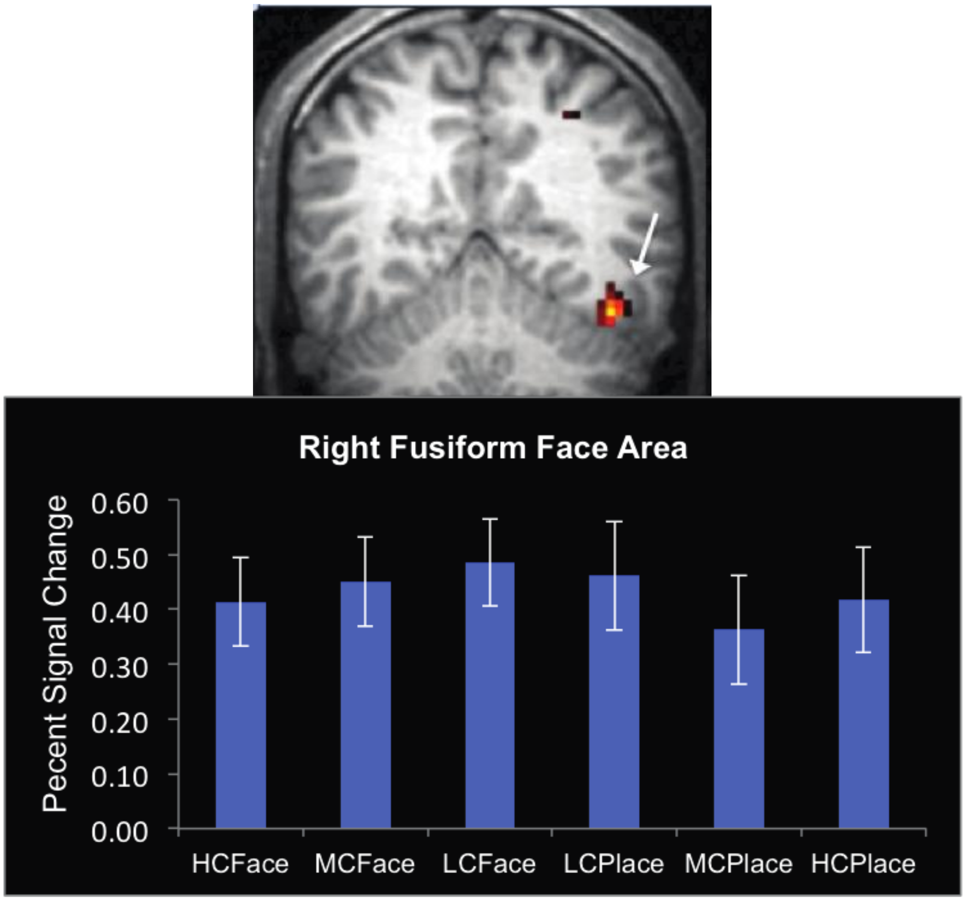

Figure 3.5. Right Fusiform Face Area activation during the localizer task (y=-52) and the percent signal change by condition high, medium, and low confidence by place and face with standard error bars).

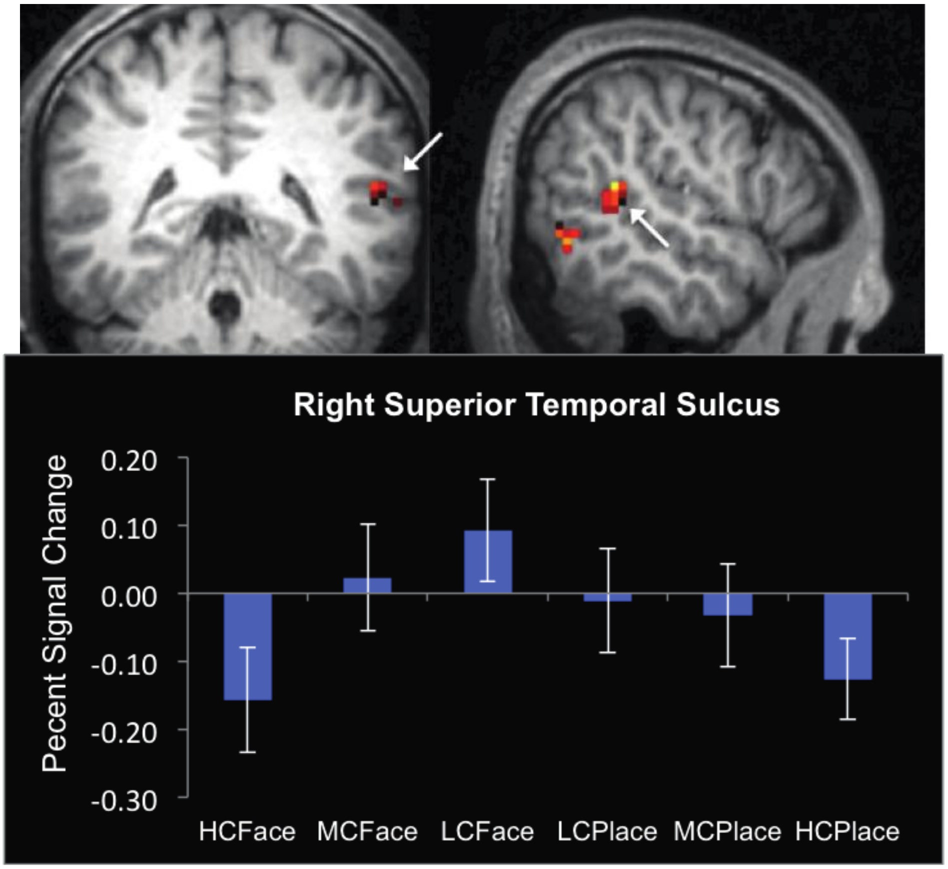

Figure 3.6. Right Superior Temporal Sulcus activation from the localizer task (x=57, y=-40) and the percent signal change by condition (high, medium, and low confidence by place and face with standard error bars).

CHAPTER 4: EVENT-RELATED POTENTIAL INVESTIGATION OF SOURCE MEMORY CONTENT

Abstract

During retrieval of episodic memory, the details of associated information are remembered, involving the activation of the brain regions initially engaged in perceptual processing of the original experience (Danker & Anderson, 2010; Rissman & Wagner, 2012). An fMRI study of this reactivation and the relationship it has with source memory (Chapter 3) has shown that the magnitude of this reactivation increases with source memory confidence. A correct natural / manmade source decision in that experiment could be made by remembering that the associated place was a forest or by recalling the exact forest seen during encoding. The goal of this experiment was to use ERPs to examine the neural basis of the remembering of the exact stimulus compared with remembering general categorical information. In this experiment, participants were shown words paired with scenes. When shown the words during memory test, the participants were given a source question of associated scene category membership as well as a subsequent forced choice of the specific scene and similar lures. Previous ERP studies found correlations between recollection of source memory and the "LPC" component (for review see Rugg & Curran, 2007). The amplitude of the LPC has also been shown to track confidence in source memory (Woroch & Gonsalves, 2010). We found that LPC amplitude was related to confidence in the category source judgment. We also found a late frontal ERP component that predicted trials when the specific associated information was remembered. We conclude that remembering specific information involves increases source-monitoring demands indexed by the frontal ERPs

Introduction

In Chapter 3, it was revealed, using fMRI, that stimulus-specific brain regions contributed to episodic remembering of associated information and confidence in source memory. Word stimuli shown alone during the memory test activated scene and face specific processing regions of the cortex, depending on paired associates during encoding. Brain regions responsible for processing perceptual details of faces and scenes were activated when associated words were shown during a later source memory test (Chapter 3). This activity was monotonically related to the strength of this source memory, as indexed by confidence ratings. The activations were lowest for low confidence trials and increased with source memory confidence, being the greatest for high confidence trials. Brain regions within the MTL, including the hippocampus and surrounding cortical regions, also increased with source memory strength, regardless of the category membership of the associated stimuli (face or scene). This demonstrated that many different brain regions play a role in source memory confidence, and do so in many different ways. The hippocampus and adjacent MTL regions contributed to the strength of source memory in a domain-general way (all stimuli). Domain-specific neural processors, unique to the processing of faces or scenes, became active in response to a previously arbitrary word that had been randomly paired with that stimulus type. This suggests that multiple contributing brain regions contribute to the strength source memory, indexed by confidence, depending upon the content of the memory. Scene specific processing regions of the cortex are active and contribute to source memory when it involves scene stimuli.

The exact role of this activation, including what is being remembered during the source memory test and what information is represented by the cortical activation observed in the previous study, is unknown. Remembering the category membership of a stimulus' prior associates could be accomplished by remembering the category the type or remembering the individual stimulus shown before, thus revealing its category type. For example, you may remember the exact forest seen during encoding or simply remember that a forest was seen. Does the stimulus-specific brain activity observed in the previous study reflect source retrieval of the category membership of paired associates, such as whether the word was previously paired with a face or a scene? Or rather, does the brain activity instead reflect the remembering of the specific encoding episode involving the word and its associated stimuli; a replay of the original stimuli such as the specific paired scene, which would also inform the category decision? The aim of the current study was to assess if participants remember specific stimuli or simply category membership during the source category decision.

It would be possible to test whether or not the specific stimulus was recollected by presenting the participant with an alternative forced choice (AFC) test consisting of the previously studied stimuli among lures. The ability to identify the specific scene would be an indicator that the exact stimulus was remembered. However, the brain activity during this test of specific item identification would need to be separated in time, at least 1 hemodynamic response function, from assessment of the source category in order to use fMRI. Otherwise the activity during the specific item test would overlap with the category test and could not be ascribed to one process or the other. The necessary delay in time between memory tests could allow other cognitive processes to occur that are responsible for specific item identification and unrelated to the source memory decision. Thus Event Related Potentials (ERPs) were chosen to assess brain activation, as the temporal resolution would allow for the assessment of brain activity during a categorical source decision (such as scene category) unaffected by a subsequent test of specific item identification.

The experiment from Chapter 4 was designed to examine the different situations in which category source memory was correct. Participants were shown pairs of words and scenes from various categories. They were then shown a word and given two memory tests about the previously paired scene. The first was a categorical source decision: “Was the scene natural or manmade?” This was followed by a three alternative forced choice test (3AFC) consisting of the previously associated stimulus and two within-category lures. A word paired with a forest scene, would first be need to be identified as having been paired with a natural scene, and then picked out of a display of three forests (all 3 of which were seen during encoding but only one appearing with that word). If the associated stimulus was recalled during the category source decision, it would be identifiable from among these similar lures in the 3AFC. However, if only the category was recollected, the source decision would be correct, but the subsequent 3AFC may be incorrect. It is then possible to sort the brain activity during source retrieval based upon whether or not participants subsequently remembered the specific associate scene in the 3AFC. A contrast between these conditions would reveal the difference between recollection of just the associated category from recall of the specific stimulus.

Traditionally, variations in source memory strength have been largely unexplored in the cognitive neuroscience literature. This is in part due to the data being designed and interpreted in the framework of the dual-process threshold theory of recognition (Wixted, 2009). This theory is often misinterpreted as meaning that recollection, including source memory, is an all-or-none process that does not vary along a strength continuum. Thus many studies only collect a single value of recollection memory strength. Because this dual-process model of recognition actually supposes that recollection is a threshold process, describing the probability of it occurring, it does not predict the nature of memory strength above the recollection threshold (Yonelinas, 2002). Source memory may or may not be graded with strength above the recollective threshold, but many cognitive neuroscience studies fail to measure variation in source memory strength (typically assessed as a confidence judgment).

However, there have been a few studies in the ERP domain that have attempted to measure variations in source memory strength. Source memory, and recollection more generally, has been associated with what has been called the late positive complex (LPC). This is also referred to as the parietal old/new effect, an ERP component with amplitude maximal over parietal scalp channels and occurring 500-800ms after stimulus onset (Friedman & Johnson, 2000; Rugg & Curran, 2007). Amplitude in this time window is higher for trials in which source memory is accurate, and recollection has occurred, than when it is incorrect.

An adaptation of the remember-know (R/K) paradigm during EEG recording has provided evidence of graded recollection (Vilberg, Moosavi, & Rugg, 2006). This experiment had participants make different remember responses depending on the strength of their recollection. The participants responded R1 if they recollected any aspect of the study episode. They responded R2 if they could recall the specific stimulus that the test item had been paired with. It was found that the amplitude of the LPC was higher for R2 than R1 trials, and both higher than incorrect trials. However, the interpretation of the functional significance of the brain activation depends on the interpretation of the difference between R1 and R2 response. The authors posit that it may correspond to the difference in the amount or detail of information recalled. The difference between R1 and R2 amplitudes may instead reflect differences in overall recollection memory strength or a difference in the type of source memory retrieved (an episodic detail compared to a paired associate).

A previous ERP study was done to assess source memory strength directly (Woroch & Gonsalves, 2010). In this experiment, participants made a source memory decision (encoding task) with low or high confidence. We found that amplitude of the ERPs in the LPC time window (600-900ms post-stimulus) were associated with source memory strength. The amplitude was greater for high confidence than low confidence source trials, both of which were greater in amplitude then incorrect source trials. This experiment was done while attempting to control for the possible influence of item memory strength on the ERP correlates of source memory strength. The conclusion is that differences in the amplitude of the LPC may reflect variations in the strength of a source memory.

Late frontal effects are often observed in studies of source memory (Cruse & Wilding, 2009; Olichney et al., 2000; Senkfor & Van Petten, 1998; Van Petten, Luka, Rubin, & Ryan, 2002; Woroch & Gonsalves, 2010). Amplitudes in this late time window are often more positive for old items accompanied by a correct than incorrect source (context) decision (Wilding & Rugg, 1996), however this can depend on paradigm and task demands (Senkfor & Van Petten, 1998; Van Petten et al., 2000). The previously observed late-frontal positivity may be involved in a more general process than source retrieval such as post-retrieval monitoring. Our predictions regarding how our task will be connected to this effect is unclear. An a priori prediction was not given, but the results may be informative to other research.

The current study extends the paradigm of the experiment from chapter 3. Words were paired with pictures of natural or man-made scenes during encoding. The words were presented during test alone, and participants were given a categorical source test and a subsequent specific item test. Confidence judgments during the categorical source memory decision were collected to replicate the findings of previous research that LPC amplitude reflects source memory strength. The second aim of the current study was to examine the difference in brain activity between recollection of the strength of categorical information and recollection of specific perceptual details indicating the remembrance of a specific scene.

Methods

Participants

Seventeen participants comprised the final data set used for analysis. An additional nine subjects were excluded from analysis due to low trial counts (<15) in one or more conditions. All participants were right-handed by self-report, had no history of psychiatric or neuropsychological disorders, and were not currently taking any psychotropic medications. All subjects give informed consent prior to participation in the study, which was approved by the University of Illinois Institutional Review Board, and were compensated $10/hr.

Procedure

The participants performed a memory experiment comprised of a subset of the stimuli used in the experiment from chapter 3. They were 704 adjectives (4-10 letters long) and 120 pictures of scenes from each of four categories (mountains, forests, cities, and highways). The experiment was broken up into four equally long encoding/test blocks, each using unique words and scenes. Each block used 120 words and 30 scenes from each category. During each encoding block, participants studied a single, randomly chosen, word which was presented beneath a picture of a randomly selected scene for 4500ms, with a 500ms ITI consisting of a fixation cross, "+". Forty of the words presented during encoding, 10 from each scene category) would be selected for the subsequent memory test while the remaining 80 would not be. The participants were instructed to rate how well each word described the picture on a 3-point scale (low, medium, or high) and remember each pair of stimuli for the upcoming memory test. There was a 60 second break in between the encoding block and the following memory test. Each memory test consisted of 48 words (40 studied and 8 new). During the test phase, a single word was centrally presented for 2000ms. Participants were instructed to imagine the scene that was paired with the word during encoding and to withhold response. The word remained onscreen and they were then prompted to respond if the word was previously paired with a natural scene (mountain or forest) or a manmade scene (city or highway). They then made a confidence judgment about that decision on a 3-point scale (low, medium, or high). For the old words, participants were then given a 3-alternative force choice consisting of three scenes, one of which was the target scene that was encoded with the word. The two lures were within-category scenes that were not paired with the test word but were studied with an untested word from the encoding phase. Each lure was only used in one trial. Each trial was followed by a fixation cross, randomly jittered between 1250-1750ms to mitigate expectancy effects in the ERPs. For new words, the confidence judgment was followed by 1 second of null fixation. Following 10 test trials, participants were given a short break to blink their eyes.

Figure 4.1. Sample 3-AFC test

EEG data acquisition

The electroencephalogram was recorded with the ActiveTwo active electrode system from Bio-Semi (www.Biosemi.com). Sixty-four Ag/AgCl electrodes were positioned in a nylon cap according to an extension of the international 10-20 system (Chatrian, et al., 1988). Five additional electrodes were positioned on the mastoids, to the outside of each eye, and under the left eye. The EEG and electroocculogram (EOG) were continuously recorded using a reference-free procedure, amplified between 0.16 and 100Hz, and sampled at a rate of 512Hz. Offline, the data were re-referenced to an average of the left and right mastoid recordings.

EEG and ERP analysis were performed with EEGlab and ERPlab toolboxes for Matlab (Delorme & Makeig, 2004, http://erpinfo.org/erplab). The data were digitally filtered offline using a 40Hz low-pass IIR Butterworth filter. Epochs were created by taking 200ms prior to the initial onset of the word stimuli to 1500ms after. The epochs were baseline corrected to the 200ms pre-stimulus interval. EOG artifacts were corrected using an automated correction procedure (Gratton, et al., 1983). Remaining epochs with extreme voltage changes (500mv during a 200ms time window) in any of the remaining channels were discarded. ERPs were generated by averaging the remaining epochs for each condition of interest. All conditions analyzed were required to have a minimum of 15 artifact free trials; subjects who had less than 15 trials in any condition of interest were excluded from all analyses.

Results

Behavioral results

The behavioral data from the experiment are summarized in **Tables 4.1-4.3**

Table 4.1 Mean proportion correct for the category source and specific item AFC trials (SE)

Memory Test	**Forest**	**Mountain**	**City**	**Highway**	**Natural**	**Manmade**
Category (Source)	.72(.03)	.73(.02)	.63(.02)	.57(.02)	.72(.02)	.60(.02)
Specific Item (AFC)	.66(.03)	.61(.04)	.74(.04)	.70(.04)	.63(.03)	.72(.03)

Table 4.2. Mean proportion correct (SE) split by confidence in the category source decision, and RT for AFC trials in milliseconds (SE)

Source Confidence:	**Incorrect**	**Low**	**Medium**	**High**	**Overall**
Category (Source)	N/A	.49(.02)	.61(.02)	.85(.02)	.66(.01)
Specific Item (AFC)	.59(.03)	.58(.04)	.63(.03)	.76(.04)	.67(.03)
AFC Correct RT	4276(283)	4174(264)	4044(209)	3417(206)	3713(283)
AFC Incorrect RT	4639(346)	4767(394)	4680(310)	4536(272)	4634(284)

Table 4.3. Mean proportion of source category confidence responses (SE) divided by specific AFC accuracy

AFC	**Low**	**Medium**	**High**
Correct	.17(.03)	.35(.03)	.48(.04)
Incorrect	.22(.04)	.43(.04)	.35(.05)

ERP analysis

There are two principle ERP analyses, the first to identify the ERP components that reflect recollection that contributes to confidence in the category source decision. For this analysis, we compared correct categorical source decisions across confidences and source incorrect trials. The second analysis was to identify ERP components that contribute to subsequent accuracy in the AFC task above and beyond those predictive of source confidence, perhaps reflecting recollection of the specific stimulus. This analysis only included trials in which the categorical source decision was correct. The ERPs from averages of clusters of electrodes, several adjacent channels, were used to increase the signal to noise ratio. The electrodes comprising each analysis cluster are described in **Table 4.4.** The mean amplitude of over a set time period was calculated for each electrode cluster and subject to the appropriate statistical tests, t-test or repeated-measure ANOVA. A Hyun-Feldt correction was used where appropriate to adjust for non-sphericity and adjusted p values are reported.

I sought to establish a double dissociation between ERP activity that reflected just retrieval of the category source information from remembering the specific stimulus.

The amplitude of the late positive complex (LPC) is commonly associated with correct source memory. Amplitude in this time window was previously found to vary with confidence in a source decision (Woroch & Gonsalves, 2010). To assess the LPC, we chose the same electrode clusters and time windows from that study (mean amplitude from a cluster of parietal channels, 600-900ms after stimulus onset. Most subjects (10 of 17) did not have enough trials to analyze the low confidence hits, so this condition was removed from analysis. ERP amplitude from parietal electrode cluster of trials with correct high and medium confidence source decisions, and source misses were subjected to a 3x2 (condition by hemisphere) ANOVA.

Identifying the ERPs associated with identifying the exact stimulus, indicated by a correct AFC decision was more exploratory. The trials analyzed will be those in which the initial category source decision was correct and the subsequent AFC was either correct or incorrect. A univariate analysis was run on the difference waveform between correct and incorrect trials using the mass univariate toolbox (Groppe, Urbach, & Kutas, 2011). The analysis was well suited to an exploratory analysis without a priori predictions such as this, as it runs a comparison between the conditions for all channels and time points simultaneously and corrects for multiple comparisons. Unfortunately, this analysis did not reveal any differences between conditions at any channels or timepoints that were statistically significant after the correction for multiple comparisons. However, sub-threshold results of this analysis as well as visual examination of the ERP waveforms revealed activation that may reflect subsequent recognition of the specific stimulus, beyond a correct category source decision. A late post stimulus positivity (900-1200ms) over frontal electrode sites appeared to differ between AFC correct and incorrect trials. The mean amplitude from frontal electrode clusters was analyzed with a 2x2 (condition by hemisphere) ANOVA.

Late Positive Complex (LPC)

The LPC was assessed by using clusters of parietal electrodes in **Table 4.4**, from each hemisphere. The mean amplitude of the ERPs was calculated from 600-900ms post-stimulus. There was a significant effect of category source confidence on LPC amplitude [$\underline{F}(2,32)=5.37$, $\underline{p}=.010$]. There was no difference in amplitude between hemispheres or interaction between hemisphere and confidence [both $\underline{p}>.131$]. Planned pairwise comparisons between confidence levels revealed that the LPC amplitude for high confident source correct trials was greater than source misses [$p=.004$]. Additionally, high confident correct was marginally higher than medium confidence [$p=.088$]. Medium confidence source correct did not differ from source incorrect [$p>.765$]. Additionally, the amplitude of the LPC was not different between trials in which the AFC was correct or incorrect [$F(1,16)=2.84$, $p=.111$]. There was no difference between hemispheres or interaction between hemisphere and confidence [both $p>.115$]

Table 4.4. Electrode clusters

Scalp Location	**10-20 Locations**
Left Frontal	F1 F3 FC1 FC3
Right Frontal	F2 F4 FC2 FC4
Left Parietal	CP1 CP3 P1 P3
Right Parietal	CP2 CP4 P2 P4

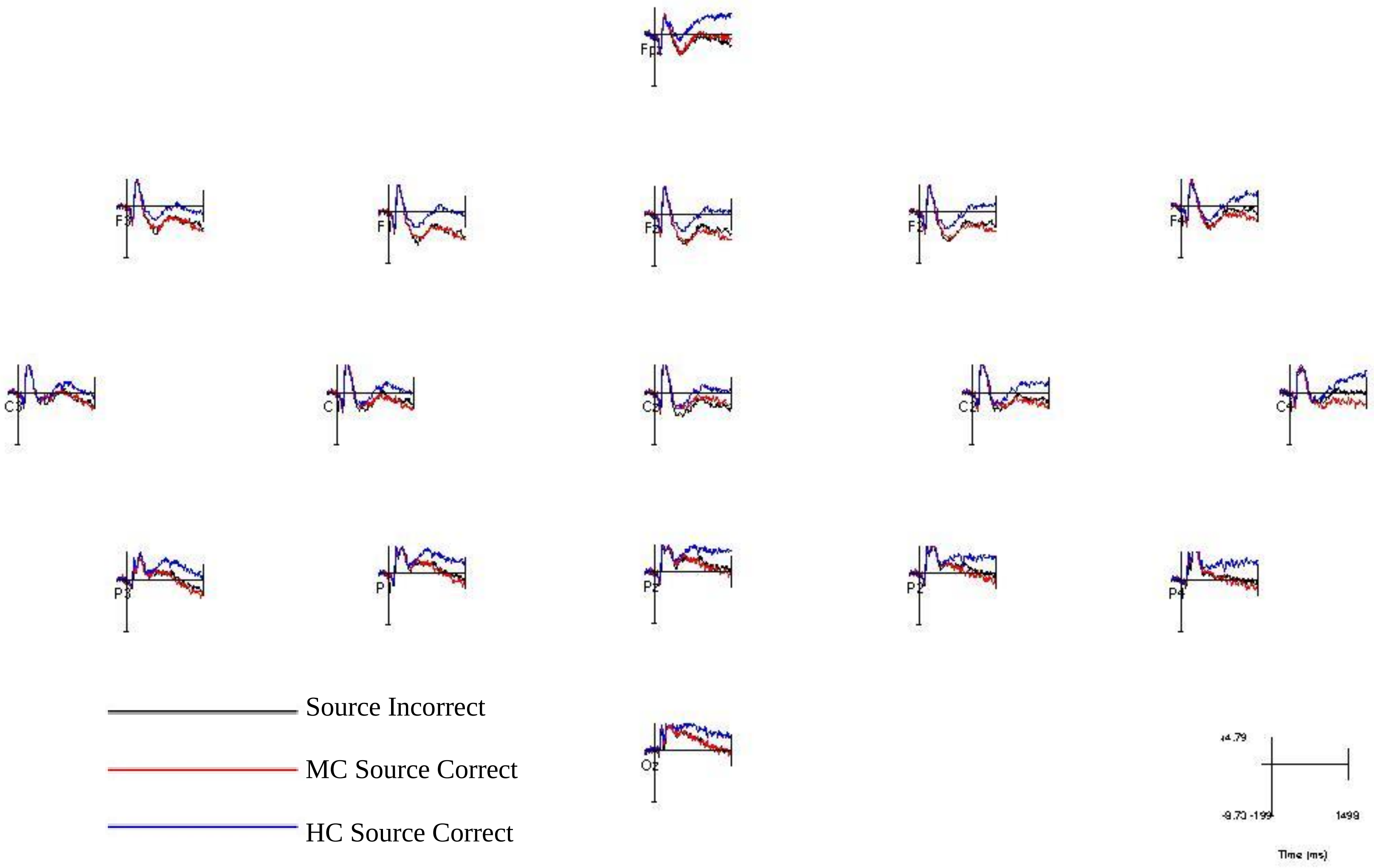

Figure 4.2 Whole head electrode montage for high and low confidence source correct and source incorrect.

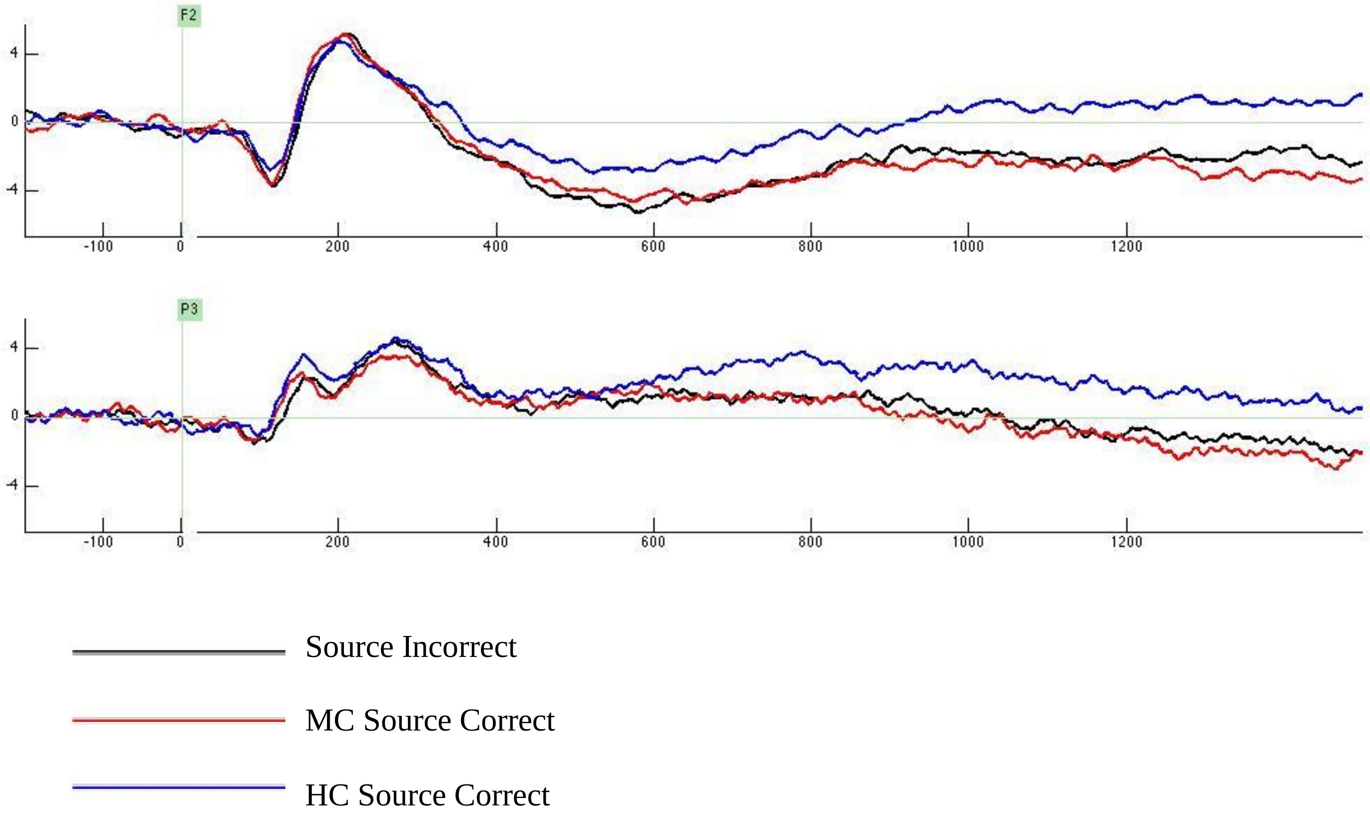

Figure 4.3 ERPs for high and low confidence source hits and source misses on channels F2 and P3.

Late Frontal

The mean amplitude of the late frontal slow wave (900-1200ms post stimulus) was higher for correct AFC trials than AFC incorrect trials [F(1,16)=5.52, p=.032]. There was no difference in amplitude between hemispheres or interaction between hemisphere and confidence [both p>.279]. Additionally, there was a significant main effect of source confidence on mean amplitude in this time window [F(2,32)=4.78, p=.015]. There was no difference between hemispheres or interaction between hemisphere and source confidence [both p>.177]. Pairwise comparison revealed that high confidence was higher than medium confidence [p=0.036] and source miss [p=0.005] but medium confidence was not different than source miss [p=.869]. The ERP results are summarized in the **Table 4.5**:

Table 4.5. ERP summary results

	Source Category Confidence	Specific Item AFC
LPC, 600-900ms	Sig *p*=0.010	NS *p*=0.111
Late frontal, 900-1200ms	Sig *p*=0.015	Sig *p*=0.032

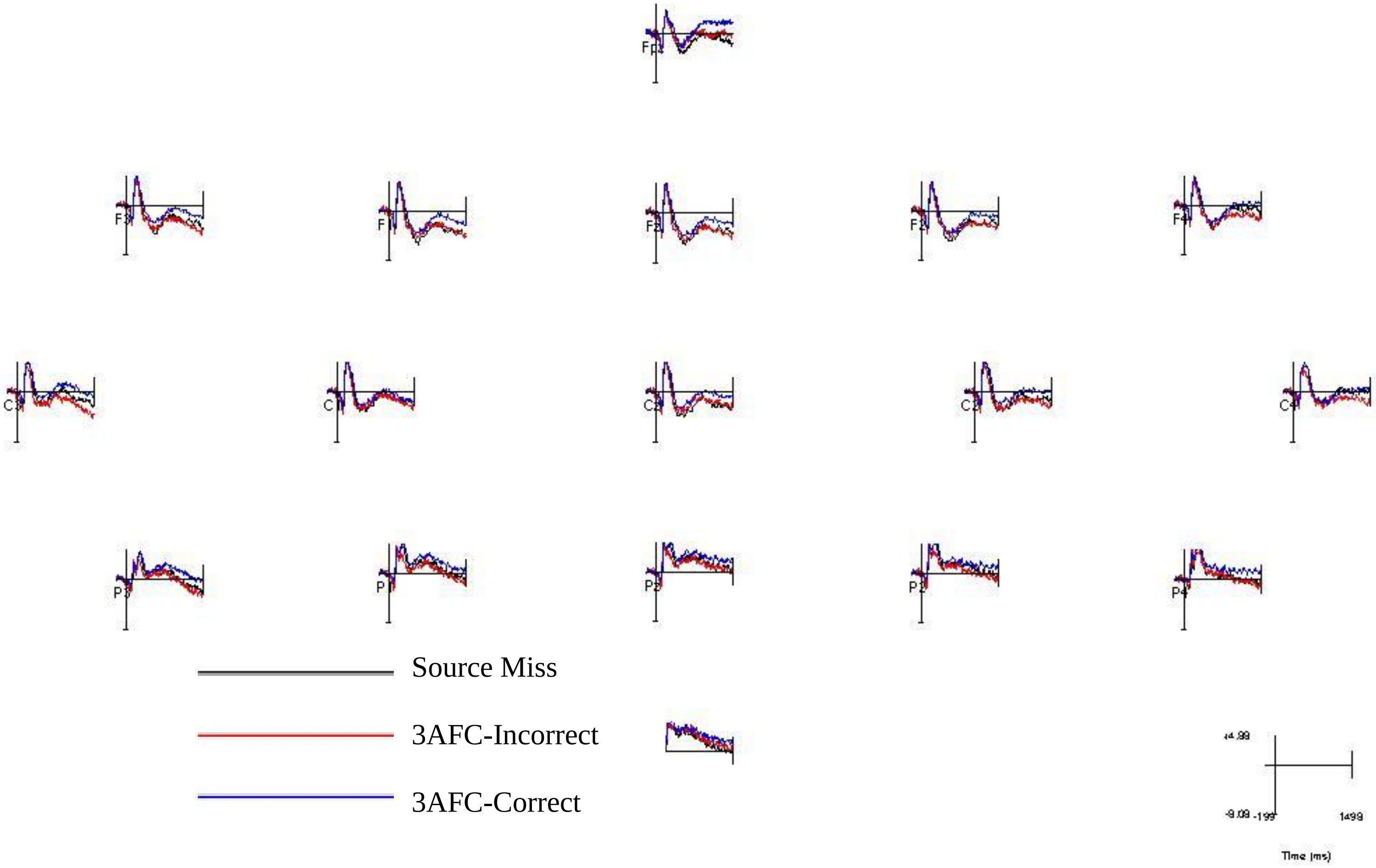

Figure 4.4 Whole head electrode montage for category source misses and category source correct trials followed by either a subsequent AFC correct or incorrect response.

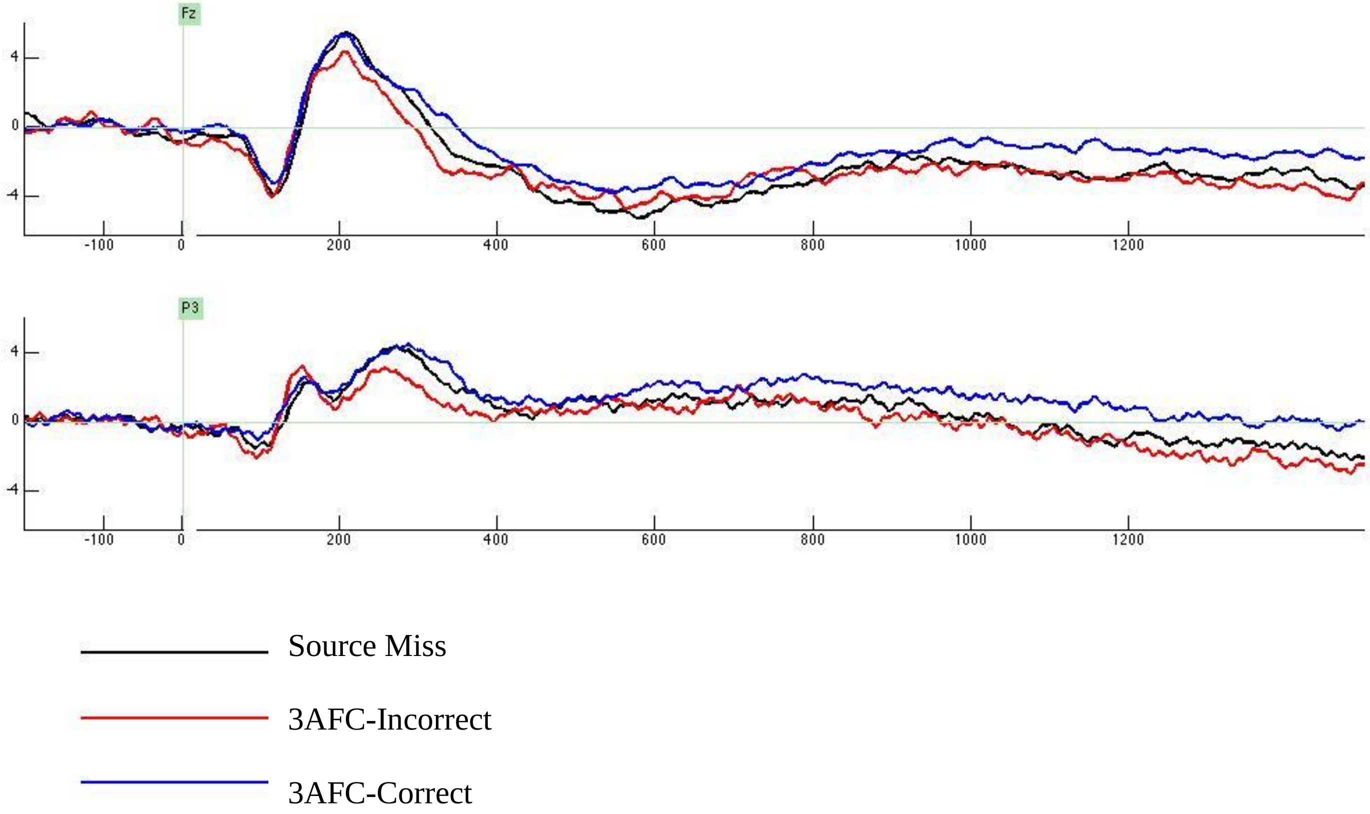

Figure 4.5 ERPs for category source misses and category source correct trials followed by either a subsequent AFC correct or incorrect response on channels F2 and P3.

Conclusion

A hallmark of recollection is the idea of re-experiencing previous episodes. Perceptual processes regions of the brain reactivate when recollection occurs, allowing inspection of the contents of memory. The previous experiment established that category-specific brain processing regions (for faces and scenes) are reactivated to word stimuli during a source memory task. Words were paired with a picture of a scene or face during encoding and later presented alone during a memory test and asked which type of picture it had been paired with. Words paired with pictures of scenes during encoding reactivated scene-specific brain processing regions in the parahippocampal gyrus, which was more active for scenes than faces. Likewise words previously paired with faces were associated with amygdala activation, which was more active for faces then scenes. The magnitude of the neural response scaled with behavioral confidence, with greater re-activation correlated with higher confidence in the behavioral response. However it is unclear if this re-activation reflects the re-imagining of the specific scene or face during recollection, or simply the re-instantiation of the category, face or scene, of the stimuli needed to answer the test question.

This experiment was designed to directly contrast circumstances in which just the stimulus category was correctly remembered from when the specific stimulus was recollected. If the specific stimulus was recollected, participants should be able identify the previously paired stimulus from among similar lures in an alternative forced choice test. The current paradigm was adapted from the previous experiment to help answer this question. Words were paired with a picture of a natural or manmade scene during encoding. During the memory test, the participants responded to both a source memory question, the category membership of the associated stimulus, as well as an alternative forced choice test consisting of the exact stimulus and within-category lures. In order to examine the neural to response to the words that predicted source and AFC accuracy separately I used event related potentials (ERPs). Thus a neuronal response correlated with confidence in category source confidence could be compared with the neural response that predicted AFC accuracy despite their temporal proximity. I identified two ERP components that were related to different aspects of source memory retrieval.

Prior studies have associated source memory with the amplitude of the late positive complex (LPC) (Rugg & Curran, 2007). The magnitude of the LPC has also been shown to scale with confidence in source memory, with amplitude increasing as confidence rises (Woroch & Gonsalves, 2010). I hypothesized that the current study would also find LPC amplitude that increased with confidence in the source category decision. Unfortunately, this study did not yield enough low confidence correct trials to create stable ERPs, so they were not examined and excluded from analysis. The present study found the amplitude of the LPC was highest when the source category question was answered correctly with high confidence and was significantly higher than when it was incorrect. This is consistent with the results of other ERP studies of source memory. The amplitude of the LPC to medium confidence correct trials was numerically less than high confidence trials and greater than source incorrect trials was not statistically significant. This pattern of results is consistent with the conclusions of Woroch & Gonsalves (2010), in which the amplitude of the LPC scaled with source confidence. The pattern of data in the current study is similar, with amplitude of the LPC at the lowest for source incorrect trials, highest for high confidence correct trails, and medium confidence correct trials in between.

Analysis of the amplitude of the LPC did not differ between trials in which the AFC choice was correct or incorrect, looking only within trials when the category source question was correct. Thus, the amplitude of the LPC was specifically related to high confidence in the category source question, not predictive of remembering the specific item, AFC accuracy. This is despite the overlap in high confidence source and AFC-correct trials (48%). The LPC has been tied to the memory process of recollection and source memory in particular (Rugg & Curran, 2007). In this paradigm, source memory strength as indexed by the LPC was not systematically predictive of subsequent identification of the specific stimulus.

In contrast, the amplitude of a late frontal positivity (900-1200ms post stimulus on frontal scalp channels) was what differentiated correct from incorrect AFC trials, with correct trials having increased amplitude. The amplitude in this time window was not associated with category source confidence (although a difference did emerge later in the trial). It is unclear what exact mnemonic processing causes this frontal positivity. An ERP positivity over frontal scalp channels, particularly over the right hemisphere, has been observed in previous studies of source memory (Cruse & Wilding, 2009; Olichney et al., 2000; Senkfor & Van Petten, 1998; Van Petten et al., 2002; Woroch & Gonsalves, 2010). It has been tied to meta-memory processes such as retrieval strategy or retrieval monitoring (Rugg & Wilding, 2000; Wilding & Rugg, 1996; Wilding, 1999). The increased frontal ERP activity observed in the current study, when participants went on to identify the exact stimulus previously paired with an associated word, may reflect the employment of a recollection strategy that allowed remembering the exact stimulus.

Early ERP studies of recognition memory observed a late-frontal old/new effect. This effect was more positive for old items accompanied by a correct than incorrect source (context) decision (Wilding & Rugg, 1996). However subsequent studies revealed that late-frontal amplitude is not necessarily tied to the accuracy of source decisions, both verbal or spatial

(Senkfor & Van Petten, 1998; Van Petten et al., 2000). This suggested that the observed late-frontal positivity may be involved in a more general process than source retrieval. It has been proposed that it reflects post-retrieval monitoring of information retrieved during a source memory task (Hayama et al., 2008; Woodruff et al., 2006). This fits with the role of cognitive processing in source monitoring (Mitchell & Johnson, 2009).

An ERP study of source memory by Cruse & Wilding (2009) also found that the late-frontal effect was not tied to source accuracy. However, they supposed that source decisions based on degraded mnemonic representations would result in a greater need to engage post-retrieval monitoring processes. They collected confidence judgments during an old/new decision and then sorted “hits” based on subsequent source accuracy. The critical comparison was between high and low confidence hits, followed by correct source decisions. They supposed that items correctly judged old with low confidence would be associated with a weaker memory representation than high confidence hits. This weaker representation would require a greater amount of post-retrieval monitoring in order to successful answer the source memory question. However they observed more positive late-frontal ERPs for high than low confidence trials. This seems at odds with a source monitoring account. Cruse & Wilding (2009) suppose there may be two cognitive processes reflected by the late-frontal effect but this was unsupported in a subsequent study (Cruse & Wilding, 2011).

The current study has a unique paradigm that informs this debate. Previous ERP studies examining the right-frontal effect have relied upon a paradigm with only one source memory decision. The current design has two source memory decisions, the first of the general category of the associated scene. The subsequent decision involves identifying the specific associated scene from among within-category lures in an alternative forced choice (AFC). It was observed that the amplitude of the LPC was related to accuracy in the correct category decision, not AFC accuracy. The amplitude of the late-frontal effect differed between AFC correct and incorrect trials, restricted to correct category trials. It is concluded that the LPC involves recollection of mnemonic information that informs the category source decision. Additional information is required to correctly identify the specific associate. A post-retrieval monitoring account could explain these effects. A weaker memory representation would allow for a correct category decision. A more perceptually specific representation would be needed to answer the subsequent AFC. Additional memory search or exploration of currently active retrieved information would be required and this is reflected by increased late-frontal amplitude.

An alternative explanation could be that the late-frontal effect is due to increased perceptual processing during memory retrieval of the AFC correct trials. Ranganath & Paller (1999) observed an ERP positivity over frontal channels during a recognition memory task that they ascribed to increased perceptual processing demands. Their participants viewed line drawings pictures of objects during encoding. Some of the previously presented objects were perceptually altered during the recognition test by having their aspect ratio adjusted, flattening or lengthening. They performed either a specific (inclusion) or general (exclusion) recognition memory test. The perceptual discrimination demands of the specific memory test were higher than the general test since the old and altered objects were visually similar to each other. They found a frontal ERP that was increased in amplitude during the specific than during the general test. Thus, enhanced perceptual recollection resulted in an ERP over frontal scalp location.

The results of the Ranganath & Paller (1999) study could possibly account for the ERP results obtained in the current study. Enhanced perceptual processing of the memory representation during source memory retrieval would allow for identification of the specific paired associate from amongst perceptually similar lures in the AFC-test. A weak or less rich perceptual recollection would allow for identification of source category, but not allow identification of the specific item. The subject may remember the test word was paired with a forest, but not recollect enough perceptual details of the forest to allow for specific identification among pictures of other forests. “I remember the word was paired with a forest, but not which one.” The scalp topography of the Ranganath and Paller (1999) study was similar to the late frontal effect observed in the present study, both maximal over frontal scalp regions. However, the onset of the ERP component was earlier in their study compared with mine (approximately 650ms vs. 900ms). This may be due to differences in experimental paradigms. Their task required increased perceptual recollection to make an old/new decision. The current study required a source category response first, which requires no perceptual details. The second decision was identification of the specific exemplar during the AFC, which required much higher perceptual detail for an accurate response. This delay in the requirement of perceptual detail may account for the latency difference observed between studies. A likely explanation is that post-retrieval monitoring mechanisms are engaged that allow the participant to correctly identify the exact associated stimulus. These monitoring mechanisms are likely engaged in gathering information that will be diagnostic for any upcoming decisions, which in this paradigm is highly perceptual.

ERP components previously associated with recollection confidence do not fully capture the richness of remembering associated with a recollective experience. The current study observed a double dissociation between the ERPs of source confidence (LPC) and remembering of a specific paired associate (late frontal). Additional brain processes, perhaps related to the retrieval of perceptual details or post-retrieval monitoring, add to the completeness of source memory to create a more rich and detailed recollection of the original encoding experience.

CHAPTER 5: ADVANCEMENTS ON THE UNDERSTANDING OF SOURCE MEMORY AND THE BRAIN

The hippocampus has long been considered the seat of recollection. The implication is that it is critical for the retrieval of source memory and indeed studies of amnesia patients with hippocampal damage (Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001; Spiers, Maguire, & Burgess, 2001; Squire et al., 2008; Squire & Wixted, 2011) and many functional brain-imaging studies (Eichenbaum et al., 2007; Squire et al., 2004b) have supported this view. However, we also know that the hippocampus is not the only brain region that contributes to source memory and both parietal and frontal regions have been implicated as well (Cabeza et al., 2008; Donaldson, Wheeler, & Petersen, 2010; Duarte, Ranganath, & Knight, 2005; Fletcher & Henson, 2001; Henson et al., 2005; Rugg et al., 1999; Vilberg & Rugg, 2009; Wagner, Shannon, Kahn, & Buckner, 2005). The experiments detailed in this dissertation offer unique contributions to the current understanding of the brain basis of source memory, and recollection more generally.

Cognitive Modeling & the Cognitive Neuroscience of Source Memory

There has been a long-standing debate in the literature about the cognitive model that best describes recognition memory. Within the field of cognitive neuroscience, there are two primary camps promoting dual-process (Yonelinas, 2002) and single memory strength (Wais, 2008) theories. A single memory strength account supposes that a unitary memory strength signal serves as the basis of recognition decisions (Wixted, 2007a). The modern instantiations of these theories leave open the possibility that many different mnemonic processes (such as familiarity and recollection) may contribute to the unitary dimension of overall strength of recognition memory (Slotnick & Dodson, 2005; Wixted & Stretch, 2004). A memory strength signal from each contributing memory process is aggregated into a single memory strength signal upon which old/new recognition decisions are made. Alternatively, dual-process theories suppose that familiarity and recollection are separate processes and that recognition is based upon either one process or the other and a dominant theory is that recollection is a threshold rather than continuous process (Yonelinas, 2002). Many initially took this to mean that recollection was all-or-none, either occurring or not, and did not vary in strength (Parks & Yonelinas, 2007). Behavioral studies have shown that source memory strength is indeed continuous (Mickes et al., 2009; Slotnick & Dodson, 2005; Slotnick, 2010). Unfortunately most cognitive neurosciences studies of memory processes have not measured the strength of recollection.

Cognitive Neuroscience has attempted to provide evidence of two processes using source memory paradigms and mapping the processes of familiarity and recollection to separate brain signals that support recognition of a single item with or without recollection of source information . This has been attempted with a variety of methods including study of neuropsychological patients with MTL damage (for review see Cohen, Poldrack, & Eichenbaum, 2007; Eichenbaum, Otto, & Cohen, 1994), ERPs (for review see Rugg & Curran, 2007), and fMRI (for review see Davachi, Mitchell, & Wagner, 2003; Diana, Yonelinas, & Ranganath, 2007; H Eichenbaum et al., 2007). The goal of such studies was to find dissociable neural substrates of familiarity and recollection, indicating the presence of more than one process. There has been a good deal of converging evidence that recognition is based upon at least two distinct memory processes, most commonly conceptualized as familiarity and recollection. It should be noted that there are many other studies that have also found evidence of a unitary process account (Jeneson et al., 2010; Kirwan et al., 2010; Shrager et al., 2008; Wais et al., 2010; Wais, Wixted, Hopkins, & Squire, 2006; Wais, 2008, 2011). A likely reason that discrepant results have been reported is that different models make different assumptions that shape the analyses performed. Experimental design and analyses focused on localizing memory processes to dissociable neural substrates differ greatly from those seeking to investigate the strength of memory representations (for review see Wixted, 2009). For example, studies based upon dual-process theories do not measure variations in source memory strength and studies in favor of a single memory process tend to make one measure of memory strength. The studies of this dissertation aim to describe variations in source memory strength without ascribing to a dual or single process theory. The experiment from chapter 2 measured both item memory strength and source memory strength to assess brain regions that contribute to one memory type and not the other in an attempt to reconcile the findings in favor of dual and unitary processes of recognition. Experiments 2 & 3 assess the contribution of memory re-activation to assess other brain regions that contribute to source memory strength.

Source Memory & The Medial Temporal Lobe

One of the reasons that a unitary recognition process has not been ruled out entirely is because the data from many studies supporting a dual-process model can be re-interpreted as arising from a single memory strength dimension (Squire, Wixted, & Clark, 2007; Wais, 2008; Wixted, 2009). The reason comes from the difference in how recognition is measured; some studies measure the mnemonic processes that allow recognition (familiarity and recollection) while others measure the strength of memory representations themselves. A single recognition's strength may arise from a single underlying memory process (Slotnick & Dodson, 2005). It may also be a summation (or non-additive combination) of the memory strengths from a variety of processes (Wixted, 2007a). This ambiguity over the nature of the memory processes that underlie recognition memory and the strength of the representations has cast a shadow of doubt over the interpretation of studies showing a difference in brain activity between processes. This line of research highlights that memory processes and memory strength should not be confounded and need to be measured individually. The studies of this dissertation aims to integrate these two lines of research by measuring memory strength in multiple dimensions. While the studies in this dissertation were not specifically designed to, and therefore cannot, adjudicate between dual process and single decision strength models of recognition, they do add relevant data to the ongoing discussion of underlying processes and memory strength. The strength of the processes of familiarity and recollection is not the same as the strength of the individual representation of the memory itself.

The potential confound between memory process and memory strength was previously assessed in the ERP domain. While controlling for memory strength in the item and source domains separately, dissociable ERP components that correlated with item and source strength were still identified (Woroch & Gonsalves, 2010). This supported all of the previous work showing dissociable ERP components related to familiarity and recollection, showing that the interpretation was likely correct despite the potential confound from not measuring recollective strength. The experiment in chapter 2 of this dissertation was designed to investigate the functional heterogeneity of the subcomponents of the MTL as they relate to this issue of memory process versus memory strength. When data from fMRI studies supporting dual processes of recognition were reanalyzed using a single strength model, it was found that the hippocampus may be involved in both individual item and source memory and by extension both familiarity and recollection (Wais, 2008).

Experiments 1 & 2 both show evidence of the hippocampus's involvement in source memory strength. Specifically the activity in the hippocampus increases as the confidence in a source memory increases. This is interpreted as evidence that the activity of the hippocampus tracks source memory strength. These findings are predicted by both dual and single process models of recognition memory and are not novel on their own. Previous findings from fMRI that have found the hippocampus to be selectively involved in recollection can also be shown to be involved in memory strength more generally (Wais, 2008). Since previous studies have not measured the strength of item and source memory separately, these interpretations could not be adjudicated. The unique finding from the experiment in chapter 2 is that the hippocampus does not increase in activity as item memory strength increases in the absence of source memory. Additionally the variation of memory strength was observed even when the strength of item memory was held constant. Furthermore, hippocampal activity does not track overall recognition memory strength, rather the activity level tracks the strength of source memory specifically and not item memory strength. These data, therefore, support a dual-process account of memory, showing that the hippocampus is involved in memory strength for one type, but not all. This is in contrast to theories that the hippocampus responds to memory strength in general, regardless of memory type (Kirwan et al., 2008, 2010; Wais et al., 2008, 2010). The experiment from chapter 3 replicates the finding that the hippocampus is involved in source memory strength using a different paradigm and type of source information. This study found that hippocampal activity increases as source memory strength increases, independent of different categories of source information.

The experiment from chapter 2 did not identify regions within the MTL, beyond the hippocampus, that were engaged in item or source memory strength. The experiment from chapter 3 identified several regions, including parahippocampal cortex and the amygdala, that were active in support of source memory and responded to variations in the strength of that memory. As opposed to the hippocampus whose activity increases with source memory strength regardless of stimulus content, these regions were more active to stronger source memory of certain categories depending upon the stimuli at encoding. The paradigm used in that study did not explicitly control for variations in item memory strength, but theses regions were not identified as being involved in item strength in the experiment from chapter 2. In the experiment from chapter 3, the right amygdala was found to be active during face perception, source memory retrieval of information involving faces. The activity level increased as the strength of that memory increased. Conversely, the parahippocampal cortex was more active during source memory retrieval of scene information. This pattern highlights that different brain regions are differentially active during different aspects of source retrieval, depending on the content of the information retrieved.

Using our example from the beginning about bumping into an acquaintance, the activity of the brain at the time of recognition is different according to what is remembered. The hippocampus is increasingly active with the strength of the memory when memory strength is quantified using your confidence in what you are remembering. This increase is regardless of the content of the memory and happens in a domain general way. The amygdala likely becomes increasingly active when recalling the faces of mutual acquaintances. Activity of the parahippocampal cortex may allow you to remember the scene or context in which you initially met the person.

Parietal Lobe Contributions to Source Memory

The MTL does not work in isolation to accomplish source memory. The experiment from chapter 2 also includes evidence of the parietal lobe's involvement in recognition memory strength. This includes memory for individual items as well as retrieval of source information. The Attention to Memory model hypothesizes that the role of the parietal lobe in recognition and source memory is in attention and orienting to mnemonic information generated by the MTL (Cabeza et al., 2008). As the brain retrieves memory strength signals, the parietal lobe focuses attention on that information. Another perspective is that the parietal lobe reflects the accumulation of mnemonic evidence, predicting that regions would increase their activity as evidence increase. A study of the neural correlates of familiarity and recollection found a ventral/dorsal dissociation within the posterior parietal cortex. Know (familiarity) responses were associated with dorsal regions, while ventral regions were associated with Remember (recollection) responses (Wheeler & Buckner, 2004). Another study found a similar dissociation in parietal activation in response to confidence (Kim & Cabeza, 2009), with dorsal regions more active for low confidence and ventral regions more active for high confidence.

The experiment from chapter 2 provided evidence that activity of different regions within posterior parietal cortex (PPC) were associated with memory for different types of information, but those same regions responded to the strength of those representations. Ventral regions of PPC were more active for item memory and activity increased with the strength of that memory.

Dorsal regions of PPC were more active during source memory and activation increased as source memory strength increased. The findings of this dissertation integrates the two findings of the dorsal/ventral dissociation between memory process and memory strength. The process of familiarity allows for recognition of individual items and is associated with dorsal regions (Wheeler & Buckner, 2004), but the level of activity also correlates to confidence in item memory with greater activity for high confidence (chapter 2). Critically, this finding emerges when trials are limited to source memory incorrect trials, so the high confidence responses on these trials cannot be attributed to recollection of source memory. The activity reflects high confidence in the memory for the individual item. Source memory trials are associated with higher levels of overall recognition confidence (Mitchell & Johnson, 2009; Parks & Yonelinas, 2007; Slotnick & Dodson, 2005; Yonelinas, 2002). Kim & Cabeza (2009) observed ventral regions of PPC active for high confidence trials, which are more likely to be the result of recollection. It is unclear if the ventral activation during these studies are specific to recollection or associated overall memory strength. The potential ambiguity over the interpretation between process and memory strength (confidence) is mitigated by my analysis strategy of the experiment from chapter 2. My finding that ventral regions of PPC are engaged in source memory strength and not item strength, suggests that this region is specific to the strength of source memory. This region responds to high confidence in source memory and thus high confidence overall. However, this region also responds to low confidence in the source decision while confidence in the item decision is high; restricted to low confidence in the in the source domain (and high confidence in memory for the item). Together these findings suggest that activity of the parietal cortex dissociates memory for types of information, and that the level of activity within that region responds to confidence of that type.

The PPC activation may reflect attention to different aspects of memory such as item or source (Cabeza et al., 2008). The stronger the memory strength signal, the more the parietal lobe allocates attention to these regions. An alternative interpretation is that the PPC accumulates mnemonic evidence in the service of a memory decision (Vilberg & Rugg, 2009)In this perspective, the ventral/dorsal dissociation observed in the experiment from chapter 2 suggests that the PPC accumulates evidence of different types of memory in different regions, dorsal for item and ventral for source. Although data from my experiments to do not add credence to one theory over another, they do show that the ventral/dorsal split is related to both type of information and memory strength.

Frontal Lobe Contributions to Source Memory

In addition to the MTL and parietal lobe contributions, the frontal lobes are also involved in source memory. Damage to the frontal lobe often results in deficits on source memory tasks (Duarte et al., 2005; Janowsky, Shimamura, & Squire, 1989; Schacter, Harbluk, & McLachlan, 1984; Simons & Spiers, 2003). Some models of source memory retrieval include post-retrieval monitoring, a process that is engaged in the service of monitoring and evaluating the contents of episodic retrieval (Johnson & Rugg, 2007; Johnson et al., 1993; Mecklinger, 2000). This additional processing can be utilized to accomplish the goal of the particular source memory paradigm. The prefrontal cortex (PFC) has been found to be critically in post-retrieval monitoring in service of source memory using fMRI (Fleck, Daselaar, Dobbins, & Cabeza, 2006; Han, Huettel, & Dobbins, 2009; R. N. a Henson, Shallice, & Dolan, 1999; R. N. Henson, Rugg, Shallice, & Dolan, 2000; Rugg, Henson, & Robb, 2003; for review see Mitchell & Johnson, 2009). ERP studies of source memory often observe late-frontal ERP old/new effects (Cruse & Wilding, 2009; Olichney et al., 2000; Rugg & Curran, 2007; Senkfor & Van Petten, 1998; Van Petten et al., 2002; Woroch & Gonsalves, 2010) which are thought to reflect post-retrieval monitoring (Henson, Rugg, et al., 1999; Rugg & Wilding, 2000; Wilding & Rugg, 1996; Wilding, 1999). While the studies of this dissertation were not designed to assess the role of the PFC in recognition memory, the obtained results help inform our current understanding and are germane to the current literature.

The hippocampus provides a mechanism for retrieval of source information from memory. The PFC, however, is thought to play a role in the systematic monitoring and evaluation of retrieved information that needs to be further differentiated (Badre, Poldrack, Paré-Blagoev, Insler, & Wagner, 2005; Dobbins & Wagner, 2005; Donaldson et al., 2010; Dulas & Duarte, 2013; Fleck et al., 2006; Fletcher & Henson, 2001; Henson, Shallice, et al., 1999; Mitchell & Johnson, 2009; Mitchell et al., 2008; Mitchell, Johnson, Raye, & Greene, 2004; Ranganath & Paller, 2000; Rugg et al., 2003; Simons & Spiers, 2003; Turner, Simons, Gilbert, Frith, & W, 2008). Some information is retrieved during recognition, when that information needs to be monitored for more questioning or fine-grained evaluation, the PFC becomes more active. This activity is not always tied to source accuracy; many studies find more PFC activity for source incorrect than correct trials. The hypothesis is that those trials in which the *source* information was readily available would require less additional processing than when it was not (Dulas & Duarte, 2013). A participant would spend more time searching and evaluating their memory if it the source was not already retrieved.

The experiment from chapter 2 revealed left dorsal and middle lateral PFC activations that increased as item memory strength increased, in the absence of correct source memory.

Individual items remembered with high confidence in the absence of source memory may be more likely elicit effortful examination and monitoring of the details of memory associated with that item in order to prepare an answer for the upcoming source memory question than individual items remembered with low confidence. When these items are confidently remembered it is due to a strong item memory representation, the next decision the participant faces is the source of the item (in this case the encoding context). The PFC is engaged in an effort to retrieve and reveal the source of the item, although ultimately unsuccessfully. Items recognized with low confidence may not be further scrutinized to attempt to identify their source because even the individual item was not remembered well. Because the item response was based on a weak item representation, it was not worth engaging the PFC to examine the contents of memory further. This finding is consistent with the hypothesis that trials in which more post-retrieval processing is required would elicit more PFC activity.

The experiment from chapter 3 adds evidence in favor of this interpretation. It was found that hippocampal activity increased with source memory strength regardless of stimulus category membership. However, right PFC activity decreased as source memory strength increased. Presumably the trials required less post-retrieval monitoring of re-activated memory information from the hippocampus, parahippocampal cortex, and/or amygdala.

A contradictory explanation is that the PFC is more involved in item memory strength than source memory strength. The data from this dissertation would not rule out this explanation given the observation of item strength related activity of the left PFC in the experiment from chapter 2, but it is inconsistent with other research in the field (Cansino et al., 2002; Dobbins et al., 2002, 2003; Dobbins & Han, 2006; Dobbins & Wagner, 2005; Dudukovic & Wagner, 2007; Henson, Shallice, et al., 1999; Mitchell et al., 2008, 2004; Nolde, Johnson, & Raye, 1998;

Ranganath & Paller, 2000; Rugg et al., 1999; Simons, Gilbert, Owen, Fletcher, & Burgess, 2005; Slotnick et al., 2003).

The experiment from chapter 4 used ERPs and identified a late positive component that was predictive of memory for a specific item, independent of a categorical source judgment. The observed differences were distributed across the scalp, but were maximal on right frontal scalp channels. An ERP positivity over frontal scalp channels, particularly over the right hemisphere, has been observed in previous studies of source memory (Cruse & Wilding, 2009; Olichney et al., 2000; Senkfor & Van Petten, 1998; Van Petten et al., 2002; Woroch & Gonsalves, 2010; for review see M. D. Rugg & Curran, 2007). It has been tied to meta-memory processes involved in post-retrieval monitoring (Rugg & Wilding, 2000; Wilding & Rugg, 1996; Wilding, 1999). The experiment from chapter 4 only examined trials in which source memory was correct. The novel part of this experiment was dividing knowledge of the associated information into two parts, the identity of the general category of the source information from the memory for the specific associated item. Participants' ability to remember the categorical source information was represented by the LPC (an ERP component occurring before the frontal effects and maximal over parietal scalp locations thought to index recollection or source memory strength). However participants' ability to identify the specific associated stimuli from among lures was predicted by late frontal activity when participants were making the category decision. This study is novel in that all trials analyzed involved a correct source decisions. However, in order to identify the exact paired stimulus, a memory representation with greater perceptual detail was required. The late frontal ERP effects observed in the experiment from chapter 4 may reflect increased post-retrieval monitoring and evaluation of the contents of the memory in preparation for the subsequent identification of the specific item. The LPC reflected the initial recall of the source of the item. However additional processing of the contents of the memory, likely by the frontal lobes, was needed to identify more detailed information diagnostic of the exact identity of associative information.

There has been much work on the role of the left versus right PFC during source memory. The experiment from chapter 2 found areas of left PFC that responded to item memory strength. The experiment from chapter 3 found the right dorsolateral PFC decreased in activity as overall source memory strength increased. This was not seen in the experiment from chapter 2 when variations in item memory strength were accounted for. A possible explanation is that high source memory strength trials in the experiment from chapter 3 did not require as much PFC activity for monitoring source information for a correct response than low source strength trials. The experiment from chapter 4 observed an increase in ERP amplitude related to detailed source memory over right scalp channels. However a direct comparison of the ERP and fMRI results may not be appropriate. Additionally, the PFC activity in the experiment from chapter 2 was observed during source absent trials and experiments 2&3 involved analysis of trials in which source memory was recalled. However all experimental conditions in which frontal activity was observed involved an increased need to monitor memory for information that would be diagnostic for an upcoming memory decision. The PFC activity may be triggered by a strong item representation (chapter 2), a weak source representation (chapter 3), or reflect additional processing that predicts future responses (chapter 4).

Final Conclusions

Successful source memory involves multiple brain regions that contribute to the strength of the memory and depend upon task demand. Some brain regions appear to be involved in source memory strength regardless of task and stimulus content. The hippocampus is one such region that is specifically engaged for source memory strength, not item memory strength (chapter 2). The hippocampus is involved in source strength for a variety of source types, both contextual (chapter 2) and associative (chapter 3). The neural generators of generic categorical source information are different than those of remembering specific stimuli (chapter 4).

Other brain regions are engage depending upon task demands. The posterior parietal cortex is involved in source memory strength, specifically ventral regions (chapter 2). The activity of the left frontal lobes was shown to increase with the strength of an item memory decision when source memory was absent (chapter 2). The right dorsolateral PFC decreases in activity with the need for less source monitoring (chapter 3). There are also brain regions that contribute to source memory strength depending upon the perceptual content of the encoded memory. Specifically, the parahippocampal cortex, which is involved in scene perception, contributes to source memory strength when the source is a scene, while the amygdala, which is involved in face perception, contributes to source memory strength when it involves faces (chapter 3). Frontal ERPs were greater when remembering a specific stimulus as opposed to categorical source strength (chapter 4). Thus, the data presented in this dissertation emphasize the importance of many brain regions for successful source memory. These regions contribute differentially depending on task demands and memory content.

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