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Specific contributions of the posterior parietal cortex to episodic memory retrieval  
by

Jeremy Andrew Elman

A dissertation submitted in partial satisfaction of the  
requirements for the degree of

Doctor of Philosophy

in

Psychology

in the

Graduate Division

of the

University of California, Berkeley

Committee in charge:

Professor Arthur P. Shimamura, Chair

Professor William J. Jagust

Professor Matthew P. Walker

Fall 2012

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by

Jeremy Andrew Elman

## Abstract

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Jeremy Andrew Elman

Doctor of Philosophy in Psychology

University of California, Berkeley

Professor Arthur P. Shimamura, Chair

The posterior parietal cortex (PPC) has become the topic of much research regarding its role in memory over the past decade. While the medial temporal lobes and prefrontal cortex have long been studied for their contributions to memory, the PPC has been more closely associated with attention and spatial cognition. With the increasing use of functional magnetic resonance imaging (fMRI) in studies of human cognition, it has become apparent that the medial and lateral parietal cortices are consistently involved during memory retrieval tasks. The most prominent finding is that of greater activity during retrieval for previously studied items compared to new items, terms the *successful retrieval effect*. The following studies attempt to delineate the boundary conditions under which the PPC is involved during episodic memory tasks.

Study 1 examined whether PPC involvement is contingent upon directed memory retrieval or if encountering previously studied items in the context of a non-memory task would be sufficient to drive activity. The results from two experiments in Study 1 indicate that the PPC may activate in response to old items during a non-memory test, but only when determining mnemonic status is task relevant. These findings suggest that low-level retrieval processes may occur even during non-memory tasks, but that PPC activity reflects downstream processes that only come online when the retrieved information becomes relevant to the task at hand.

Continuing this line of questioning, Study 2 examined whether the PPC is activated when participants make meta-memory judgments (using a feeling of knowing paradigm) in which the retrieval of target information is not required. Furthermore, we assessed whether the PPC activity differed between metacognitive assessments of episodic and semantic memories. The resulting activations from this metacognitive task appear remarkably similar to those found in standard retrieval tasks. Furthermore, the ventral PPC appeared to be preferentially activated by episodic compared to semantic memory judgments. It is suggested that the contextually bound nature of episodic memory underlies PPC involvement.

Study 3 further considered the effect information type on PPC engagement during retrieval. Participants were tested on memory for buildings that were either personally familiar through repeated real-life encounters or linked only to a prior study session. Consistent with findings from Study 2, a specific region of the ventral PPC was found to be more active when viewing items bound to a specific context. However, the finding of a more posterior site of activity for personally familiar buildings suggests a functional heterogeneity within the PPC.

Taken together, the results of these three studies further delineate the boundary conditions under which the PPC is involved in memory tasks. These findings demonstrate that PPC contributions may depend not only on the task goal but also on the type of information being retrieved. Specifically, the PPC appears to be preferentially engaged when there is a need to bind item and context information to form an event memory. The results of the studies are further discussed in the context of current theoretical models of PPC function.

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## Dedication

To my family and friends, and in particular my wife Erin,  
for all of their love and support.

## CHAPTER 1: INTRODUCTION

In recent years the posterior parietal cortex (PPC) has become the focus of an increasing amount of research regarding its role in memory. While this region has long been associated with selective attention and spatial thinking (Corbetta and Shulman, 2002; Burgess, 2008), it had rarely been considered in the context of memory research. With the growing number of studies being conducted using fMRI, it has become apparent that the PPC shows consistently high levels of activity during tasks of memory retrieval (Wagner et al., 2005; Vilberg and Rugg, 2008; Cabeza et al., 2008). However, the specific contributions of the PPC to memory remain unclear. The following dissertation will provide a brief overview of extant research as well as three experiments that serve to further delineate PPC contributions to episodic memory. The results of these studies will then be discussed in terms of how they inform theoretical models of PPC function.

### *Neuroimaging Evidence*

In studies of episodic memory retrieval, greater PPC activity is commonly found for previously studied old items compared to unstudied new items. This finding is often termed the *successful retrieval effect* (Konishi et al., 2000; Wagner et al., 2005). Furthermore, the location of this activity is dissociated based on response confidence. Low confidence familiarity signals are localized in the dorsal PPC (dPPC; including superior parietal lobule and medial banks of the intraparietal sulcus), whereas high confidence recollection responses activate the ventral PPC (vPPC; specifically the angular gyrus, but activations often extend into supramarginal gyrus and lateral occipital cortex as well) (Wheeler and Buckner, 2004). The characterization of where memory-related activations are localized may be an important factor as recent evidence suggests that sub-regions may exist even within the vPPC itself (Nelson et al., 2010). Furthermore, the overlap of activity (or lack thereof) elicited by tasks in different domains, such as memory and attention, has served as crucial evidence in support of or against models of PPC function (see Cabeza et al., 2003, 2012; Naghavi and Nyberg, 2005; Hutchinson et al., 2009).

An interesting caveat to the successful retrieval effect is that this pattern of results occurs independent of memory accuracy, such that simply perceiving an item as old is sufficient to evoke a PPC response (Wheeler and Buckner, 2003). Furthermore, high confidence correct rejections appear to elicit high levels of activity in the vPPC as well (Cabeza et al., 2008; Kim and Cabeza, 2009). Presumably, retrieved information should not accompany these new items. Therefore, these findings have called into question whether the PPC response is an index of retrieval per se, or rather reflects peri-retrieval processes.

Studies of PPC function in the realm of memory retrieval primarily employ tests of lab-based episodic retrieval in which items from a list are studied during an encoding session. The lateral and medial parietal cortices also belong to a core network of areas implicated in autobiographical retrieval, yet it is unclear how these findings relate to those of lab-based studies (Maguire, 2001; Svoboda et al., 2006; Cabeza and St. Jacques, 2007). Direct comparisons of the two have found areas of both overlap and dissociation (Cabeza et al., 2004). However, these results are often complicated by factors of self-referential processing, vividness, and the specificity of the events being tested (Summerfield et al., 2009; Sajonz et al., 2010a). Certain evidence suggests that the degree to which memory, context and self-referential processing are emphasized in a given task may lead to subtle yet important differences in the localization of

activity within the PPC (Summerfield et al., 2009; Sajonz et al., 2010a; Burianova and Grady, 2011). It may be that the successful retrieval effect is not the reflection of a single memory process, but rather component processes mediated by a set of functionally heterogeneous sub-regions within the PPC that have heretofore been considered a unified whole. As such, differences in the foci of activation between studies should not be dismissed as trivial.

### ***Evidence from lesion and Alzheimer's literature***

The absence of the PPC from the memory literature until relatively recently is likely due to a lack of obvious memory impairment following parietal lesions (Simons et al., 2008). This stands in stark contrast to the severe deficits caused by damage to the medial temporal lobe (MTL) or prefrontal cortex (PFC) (Shimamura et al., 1990; Eichenbaum and Cohen, 1993; Squire and Zola, 1998; Aggleton and Brown, 1999). Instead, damage to the PPC may result in spatial and attentional deficits such as neglect or simultanagnosia (Mesulam, 1981, 1999; Robertson et al., 1997; Driver and Mattingley, 1998; Mattingley et al., 1998). More recent studies of memory function in patients with parietal damage have turned up mixed results. An initial report found that patients tended to lack detail in their memories and were impaired in free recall but not cued recall (Berryhill et al., 2007). Additionally, some patients described feeling as if their memories were not their own or that they had not experienced memories themselves. The authors propose a form of memory neglect in which on-going reinstatement of event details fails to draw attention away from initially retrieved information. A follow-up study found that the primary deficit in patients with bilateral lesions of the PPC was a diminished sense of confidence in their memory responses despite intact recognition and source memory performance (Simons et al., 2010). This paradox in which the PPC displays a high level of engagement during normal memory function but an apparent lack of severe deficits arising from its damage has yet to be explained.

Behavioral and neurobiological evidence from studies of Alzheimer's Disease (AD) provides more evidence for PPC contributions to memory. While memory deficits associated with AD are often ascribed to damage in the medial temporal lobe, the PPC (both lateral and medial) is also affected to a great extent. The lateral PPC is part of a network of regions (termed the default mode network, or DMN) including the medial parietal cortex, anterior cingulate and hippocampus which show high levels of amyloid build up, increased rates of cortical atrophy and disruption of both task-based and resting-state function over the course of disease progression (Buckner, 2004; Hedden and Gabrieli, 2005; Hedden et al., 2009; Morris et al., 2009; Schroeter et al., 2009). Behaviorally, there are mixed results linking PPC function to memory performance. Levels of amyloid within PPC do not correlate strongly with memory scores within a group, but they may predict sharper decreases over time within a particular subject (Storandt et al., 2009). While activity in medial temporal regions correlates with memory scores in high performing AD subjects, activity in parietal regions tends to correlate with memory only in low performing subjects (Desgranges et al., 2002). Correlations between memory performance and brain activity are often found in the form of broader network disruptions as opposed to activation differences in isolated brain regions (Pihlajamäki et al., 2008; Dickerson and Sperling, 2009; Meulenbroek et al., 2010). This, coupled with increases in activity of certain brain regions presumed to reflect compensatory mechanisms suggests that memory is supported by a complex interaction across multiple brain networks (Grady et al., 2003; Gutchess et al., 2005)

### ***Models of PPC Function***

A number of accounts describing PPC function have been proposed. Although many attribute a similar form of top-down control to the dPPC, they tend to diverge in their descriptions of vPPC function. Thus, the vPPC is often the focus of attention in the literature, as it is in the studies presented here. Two models gained prominence in the early stages of research on this topic and have been tested to a greater extent than the others. The first has been termed the *episodic buffer hypothesis* (E-BUFF), proposed by Vilberg and Rugg (2008). This hypothesis suggests that while the dPPC codes for salience, the vPPC takes on a role akin to that of the episodic buffer described in Baddeley's updated model of working memory (Baddeley, 2000). The authors propose that the left vPPC is a multi-modal store into which memory traces are temporarily held for further processing, and that the response magnitude directly tracks amount of retrieved information. The other model is termed the *Attention to Memory hypothesis* (AtoM) and was put forth by Cabeza and colleagues (Cabeza, 2008; Ciaramelli et al., 2008; Cabeza et al., 2008). This hypothesis borrows from an attentional account of PPC function in which the dPPC supports top-down attentional allocation whereas the vPPC is responsible for bottom-up attentional capture. This model posits that the dPPC guides effortful memory search while the vPPC monitors MTL output for relevant signals (whether mnemonic or novelty-based). As these signals arise, they elicit a response in the vPPC, signaling the need for greater attentional resources. While these models have provided useful frameworks to guide research, both have faced difficulty in accounting for recent findings (see Hutchinson et al., 2009; Klostermann et al., 2009; Kim and Cabeza, 2009; Simons et al., 2010; Elman and Shimamura, 2011).

More recently, Shimamura (2011) has proposed the *cortical binding of relational activity hypothesis* (CoBRA). This model draws on the ideal placement of the vPPC to act as a convergence zone for information processed in the ventral and dorsal streams. Standard consolidation theory propounds a process in which memories are initially bound within the hippocampus and, over time, form connections within the cortex itself (Eichenbaum and Cohen, 1993, 2004; Squire and Zola, 1998). CoBRA theory proposes that this final stage is facilitated by the vPPC as it binds item and contextual information to form encapsulated event ensembles. Thus far, CoBRA remains a promising model with which to describe PPC contributions to memory and is further tested in the following experiments.

### ***Overview of Included Studies***

The following three studies serve to delineate the boundary conditions under which the PPC contributes to episodic memory. While not intended to explicitly test between the models of PPC function described above, the results may nonetheless inform these theoretical endeavors.

The literature describing successful retrieval effects in the PPC is composed almost exclusively of explicit tests of episodic memory. Therefore, it has been unclear to what extent these results are a function of task specific effects arising from the paradigms used. Study 1 addresses the question of whether PPC involvement is contingent upon explicit, directed retrieval, or whether encountering previously studied items in the context of a non-memory task is sufficient to drive PPC activity. Drawing from findings in the attention literature, this study additionally explores whether the relevance of an item's mnemonic status to task goal may further modulate the PPC response. In a similar vein, Study 2 examines whether successful retrieval effects are preferentially engaged by episodic memory or if they represent non-specific memory processes that generalize to the retrieval of semantic information as well. Study 3 continues to explore whether the type of information being accessed during a memory task affects PPC activation. In the context of experiments examining the PPC's role in memory, episodic memory is often considered in a somewhat simplistic sense. That is, the memories being

assessed across studies are taken to be equivalent, yet episodic memory may be composed of multiple component processes that are co-present to varying degrees. The hallmark of episodic memories is that they are tied to a specific time and place. However, these memories are often accompanied by visuo-spatial information of differing detail. These aspects of episodic memory are dissociated in Study 3, allowing us to investigate the influence of information type on retrieval-related activity within the PPC.

Taken together, this set of studies provides evidence that PPC contributions to memory depend not only on task goal, but the type of memory being accessed. Furthermore, these results suggest that a functional-anatomic heterogeneity exists within the vPPC such that the specific sites of activation apparent during memory tests may be highly dependent upon these factors.

## CHAPTER 2: STUDY 1

### Abstract

The *successful retrieval effect* refers to greater activation for items identified as old compared to those identified as new. This effect is particularly apparent in the ventral posterior parietal cortex (vPPC), though its functional properties remain unclear. In two experiments, we assessed the activation for old and new items during explicit and implicit tests of memory. In Experiment 1, significant effects were observed during explicit recognition performance and during an implicit lexical decision task. In both tasks, determining mnemonic status provides relevant information to task goals. Experiment 2 included a second implicit task in which determining mnemonic status was not relevant (color discrimination task). In this case, vPPC activation did not distinguish between old and new items. These findings suggest that automatic or implicit processes can drive retrieval-related activation in the vPPC, though such processes are gated by stimulus relevancy and task goals.

### Introduction

In functional neuroimaging studies of episodic memory, activity in the posterior parietal cortex (PPC) is strongly correlated with successful retrieval. Specifically, PPC activity during retrieval is greater for items recognized as old (hits) compared to items recognized as new (correct rejections) (Konishi, et al., 2000). This often left-lateralized retrieval-related activity, known as the *successful retrieval effect*, has been observed using a variety of study materials and test conditions (for review see Cabeza, 2008; Vilberg & Rugg, 2008; Wagner, et al., 2005). Additional findings suggest a functional-anatomical dissociation within PPC regions, such that activity in ventral regions (vPPC: supramarginal gyrus, temporal-parietal junction, and angular gyrus) correlates with recollective responses, whereas activity in dorsal regions (dPPC: intraparietal sulcus and superior parietal lobule) correlates with weaker familiarity responses (Wheeler & Buckner, 2004).

Several models characterize the role of the PPC in episodic retrieval (Wagner et al., 2005). The *episodic buffer* model suggests that the vPPC serves as a multi-modal buffer in which the retrieved features of an episodic memory are held online for further processing (Vilberg & Rugg, 2007, 2008). In this model, vPPC activity is presumed to index the amount of information retrieved. Alternatively, an attentional account has been put forth and described as the *Attention to Memory* hypothesis (*AtoM*) (Cabeza, 2008; Ciaramelli, et al., 2008). This model draws on the finding that an analogous dorsal-ventral dissociation exists in selective attention to visual stimuli such that voluntary, goal-directed attention drives dPPC activity and involuntary, stimulus-driven attention drives vPPC activity (Corbetta & Shulman, 2002). Applying this model to episodic retrieval, *AtoM* suggests that the dPPC initiates and carries out effortful, top-down memory searches while the vPPC monitors output from the medial temporal lobe, activating in response to relevant output and signaling the need to redirect attention towards this information.

The extant research on the role of the PPC in episodic memory has focused on explicit retrieval. It is not clear to what extent this region is involved when previously studied items are encountered in the absence of directed or intentional retrieval, which we term implicit retrieval. If the vPPC is fulfilling a stimulus-driven role, whether temporarily storing or signaling the presence of unattended memory traces, one might expect activation in this region to occur even when retrieved information is accessed in an automatic or implicit manner. By this view, the

relevance of stimulus features to task goals may play a significant role in driving PPC responses. Research on the neural basis of selective attention has shown that relevant stimuli appearing in unattended locations captures attention and activates a fronto-parietal network that includes the vPPC. Yet task irrelevant stimuli, even when salient, fail to engage this network (Downar, et al., 2001; Indovina & Macaluso, 2007). Thus, it may be that stimulus filtering occurs that prevents or reduces vPPC activity (Shulman, et al., 2007).

We focus on the vPPC as its role in memory remains contested and this region appears to be susceptible to effects of task relevance. In order more directly assess ventral components of the broader successful retrieval effect, we chose to employ contrasts characterizing recollection-related activity (high confidence old responses compared to new items) when possible. While the attention-related activations mentioned previously are often right-lateralized, in contrast with the left-lateralized memory-related activations, this may be partly due to differences in stimulus features such as verbalizability rather than hard-wired hemispheric differences (Klostermann, et al., 2009). It is possible that the influence of task relevance on vPPC activation occurs in both hemispheres and across task types. Our use of the term “task relevance” here refers to whether the mnemonic status of an item carries useful information towards providing a correct response. In the following experiments, we vary the task-relevance of mnemonic status in order to evaluate relative differences in activation for old and new items during explicit and implicit retrieval. If vPPC activity may be driven an automatic fashion, that is it doesn’t require directed retrieval, we would expect to find successful retrieval effect in a non-memory task. Furthermore, if successful retrieval effects are modulated by task relevance, this would indicate that a low level of retrieval occurs prior to vPPC involvement as relevance may only be considered once mnemonic status has been determined.

## **EXPERIMENT 1:**

We assessed the *successful retrieval effect* during explicit yes/no Recognition and during an implicit Lexical Decision (LD) task. In the LD task, participants simply determined if a test item was a word or non-word. Half of the words were previously presented as study items and the other half were new words. In cross-task analyses, we compared the influence of old vs. new words for both lexical decisions and recognition memory.

## **Methods**

### ***Participants***

Twenty-one healthy subjects participated in this study (mean age 22.05 years, range 19-34 years; 14 females). One additional subject was excluded from analysis due to excessive head motion and scanner artifact. All subjects were paid for their participation and gave informed consent according to guidelines approved by the UC Berkeley Office for the Protection of Human Subjects. All subjects were native English speakers and were right-handed. None of the subjects reported a history of neuropsychiatric disorders, brain injury or having recently taken psychoactive medication.

### ***Stimuli***

Word and non-word stimuli were drawn from the English Lexicon Project database (<http://elexicon.wustl.edu/default.asp>). The entire stimulus set consisted of 280 words and 140 non-words. Words consisted of five to seven letters with an average HAL log word frequency of 6.45 (SD=1.30). The non-words were five to seven letters long and constructed by generating 140 comparable words and altering them by randomly changing one letter to produce a unique

non-word (e.g. HEPOR, SLISHTS). Non-words had an average bigram frequency of 1,201 (SD=484.72) and an orthographic neighborhood average of 1.45 (SD=0.97). Words and non-words were divided into lists and rotated across conditions such that specific items used as study and test stimuli were counterbalanced across subjects.

### ***Behavioral Procedure***

The study phase was conducted outside of the scanner. Subjects were presented 140 words divided into two blocks of 70 words each. Each study trial consisted of a central fixation cross (500 ms), a word (1500 ms), and a blank screen (1000 ms). For each word, subjects made a pleasant/unpleasant judgments using a button box. They were not informed of the later memory tasks.

Approximately 20 minutes after the study session, subjects were placed into the scanner for the test phase. The two LD blocks always preceded the two recognition blocks to help reduce memory-related retrieval strategies during the LD task. Subjects viewed stimuli projected onto a screen at the end of the magnet bore using a mirror mounted over the head coil. Stimuli were presented using E-Prime software (Psychology Software Tools, Inc, Pittsburgh, PA; <http://www.pstnet.com>).

During the LD task, a total of 70 old words (i. e., words presented during the study phase), 70 new words, and 140 non-words were presented over two runs. A single LD trial consisted of a stimulus presentation (500 ms), a blank screen (1000 ms) and a jittered inter-trial interval during which a center fixation cross was presented (ITI=250-3750 ms). Subjects were instructed to determine whether a stimulus was a word or non-word. Responses were made with either a left or right button press using the thumbs of each hand. The buttons corresponding to each response were counterbalanced across subjects.

During the recognition task, 70 old words and 70 new words were presented over two runs. All words used during the recognition task were different from those used in the LD task. A single recognition trial consisted of a stimulus presentation (750 ms), a blank screen (2250 ms) and a jittered ITI ( 500-4000 ms) during which a central fixation cross was displayed. Subjects were instructed to judge whether a word was old or new and to give a simultaneous confidence rating of their answer. Subjects were instructed to use the high confidence answers only if they were 100% sure of their response. Responses could be made during either the stimulus presentation or blank screens. The thumbs of both hands were used to make the responses (“HC-Old”, “LC-Old”, “LC-New”, “HC-New”) on a four-button response box. The buttons corresponding to each choice were counterbalanced across subject. Response times and accuracy were recorded.

### ***fMRI Acquisition***

Subjects were scanned in a 3T Siemens (Erlangen, Germany) Trio scanner at the UC Berkeley Brain Imaging Center. Each of the 4 runs acquired used a T2\*-weighted echo-planar imaging (EPI) sequence [TR=1750ms; TE=22ms; flip angle=90<sup>0</sup>; matrix=128x128; FOV=220mm; 3mm slice thickness] with GRAPPA [acceleration factor3]. 32 axial slices oriented to the AC-PC were acquired in an interleaved order giving whole brain coverage. 216 volumes were collected during each of the two LD runs and 182 volumes were collected during each of the recognition runs. The first 5 volumes of each run were to allow for magnetization preparation. A high resolution magnetization-prepared rapid-acquisition gradient echo (MPRAGE) [TR=2300ms; TE=2.98; matrix=256x256; FOV=256; sagittal plane; slice thickness=1 mm; 160 slices] and a gradient-echo multislice (GEMS) [TR=250ms; TE=22;

matrix=256x256; FOV=256; 3mm slice thickness, 32 slices] were collected for registration purposes.

### ***fMRI Data Analysis***

Data were preprocessed and analyzed with the FSL toolbox v4.1.4 (<http://www.fmrib.ox.ac.uk/fsl>; Smith et al., 2004). Motion correction was performed with MCFLIRT, aligning all images to the middle slice with rigid body transformation. Slice timing correction was performed using (Hanning windowed) sinc interpolation to shift each slice in the volume in reference to the middle of the TR period. BET (brain extraction tool) was then used to create a mask of the brain from the first volume of each time series and used to separate brain from surrounding skull and tissue in each volume. All images were spatially smoothed with a 5mm FWHM Gaussian kernel to reduce noise. Highpass temporal filtering was performed using the local Gaussian-weighted fit of a running line to remove low frequency artifacts. Subject data was registered to standard space in a two-step process using FLIRT (FMRIB's Linear Image Registration Tool). First, EPIs were registered to each subject's skull-stripped high resolution T1-weighted image. Second, subject's T1-weighted images were registered to standard (MNI) space (FSL's MNI152 template). The two registrations were then combined to take the subject's EPI images and run-level statistical maps into standard space.

A multi-level, mixed effects general linear model was run using FILM (FMRIB's Improved Linear Model) which treated subjects as random effects. Individual runs were modeled in subject space and resulting statistical maps were registered to standard space for higher level analysis. Regressors of interest were obtained by convolving stimulus onset times with FSL's canonical (gamma) hemodynamic response function and their temporal derivative. Motion parameters were included as additional confound variables and temporal autocorrelation was removed through prewhitening. Trials with no response and incorrect trials were also modeled as regressors of no interest. Contrasts were entered to compare old vs. new status, words vs. non-words, and high confidence vs. low confidence responses.

A second level analysis combined the runs for each subject using a one-sample t-test, treating runs as fixed effects. Third-level group statistics maps were created for each contrast using FLAME (FMRIB's Local Analysis of Mixed Effects). FLAME implements a Bayesian two-stage model, the first being a fast approach to the posterior probabilities of activation for each voxel and the second uses a slower Markov Chain Monte Carlo (MCMC) based analysis for all voxels identified as being near threshold in the first stage. The whole brain family-wise error was corrected to  $P < .05$  using Gaussian Random Field theory with a cluster forming threshold of  $z > 2.3$ . For visualization purposes, results from these analyses were rendered on inflated brains using CARET software (<http://www.nitrc.org/projects/caret/>).

As a follow-up analysis to assess further the cross-task results, we conducted an ROI analysis in order to perform an ANOVA on percent change of peak parameter estimates using Task (Recognition/LD) and Condition (old/new) as factors. Parameter estimates were extracted from a region defined by inclusively masking the contrasts demonstrating the *successful retrieval effect* (old > new) in both the Recognition and LD tasks. We used the clusters produced from the whole brain analysis, thus each was individually thresholded at a level of  $p < .05$ , corrected.

## **Results**

### ***Behavioral Results***

**Recognition Task:** The mean hit rate was 85% with a correct rejection rate of 81%. Reaction times were significantly faster for old items (mean=1229ms) than new items (mean=1382 ms),  $t(20)=3.917$ ,  $p<.001$ . Memory performance (hit rate) was significantly better for HC responses compared to LC responses, 90.4% vs. 72.3%  $t(20)=13.601$ ,  $p<.001$ . HC responses (mean=1212 ms) were also faster than LC responses (mean=1606 ms),  $t(20)=5.846$ ,  $p<.001$ .

**Lexical Decision Task:** Subjects correctly identified words and non-words at a similar rate, 93.6% vs. 92.4%,  $t(20)=1.05$ ,  $p=0.31$ . For words, old items were correctly identified better than new items, 95.2% vs. 89.7%,  $t(20)=3.943$ ,  $p<0.001$ . Subjects responded faster on correct Word judgments (mean=690 ms) than they did to correct non-word judgments (mean=720 ms),  $t(20)=3.455$ ,  $p<0.01$ . Examining words only, responses for old items (mean=683 ms) were significantly faster than new items (697 ms),  $t(20)=2.383$ ,  $p<.05$ .

### ***fMRI Results***

**Recognition Task:** Consistent with previous studies (Cabeza, et al., 2008; Vilberg & Rugg, 2008; Wagner et al., 2005), HC-Old items activated a neural circuit that included prefrontal cortex, parietal cortex, and the medial temporal lobe (see Table 1 for full results). Specifically, we observed increased activation for HC-Old responses compared to new responses in left vPPC, left frontal pole extending into left dorsolateral prefrontal cortex (DLPFC), bilateral posterior cingulate, bilateral precuneus and left posterior hippocampal complex (Figure 1a). Additional activations were seen in left orbitofrontal cortex (OFC), left middle temporal gyrus, and right parietal operculum. The contrast of all old items collapsed across HC and LC judgments to new items yielded similar results, with the exception of the left orbitofrontal, middle temporal gyrus and hippocampal clusters.

**Lexical Decision Task:** With respect to the basic lexical decision contrast (words vs. non-words), our findings were comparable to those observed in previous studies (Henson, 2002; Mummery, et al., 1999; Rossell, et al., 2001). A primarily left lateralized language network was activated for words > non-words, which included left middle temporal gyrus, left vPPC extending superiorly into the inferior parietal sulcus, left OFC, left middle and superior frontal gyrii, and anterior cingulate extending into frontal poles. There was also bilateral precuneus and posterior cingulate activation (see Table 2 for full list of results).

We were particularly interested in contrasts between old vs. new words presented during the LD task as in this task explicit episodic retrieval is not required. A contrast of old words > new words revealed a similar pattern of activation in the PPC as was observed in the Recognition task. Specifically, we found significant activation in bilateral vPPC, precuneus, and posterior cingulate gyrus (Figure 1b). Additionally, we observed activation in left middle frontal gyrus and a small cluster in the left lateral frontal pole (see Table 3 for full list of results). However, the more medial frontal activations that were present during the Recognition task (anterior cingulate and OFC) were absent during the LD task. These activations will be discussed later with respect to implicit memory processes.

**Cross-Task Analyses:** We performed analyses across the Recognition and LD tasks as a way to examine differences between activations during explicit (Recognition task) and implicit (LD task) retrieval. A direct comparison of the successful retrieval effect (contrast of [HC-Old>New\_Recognition] vs. [Old>New\_LD]) revealed no difference in vPPC activation. The areas that did demonstrate a greater old/new effect during the Recognition task included: left middle temporal gyrus, left DLPFC, left hippocampus, anterior cingulate and posterior cingulate, and lateral occipital cortex (see Table 4 for full list of results).

The ROI used for follow-up analysis was derived by inclusively masking the old > new contrasts from the above analysis of the Recognition and LD tasks to produce a cluster of common activation. The resulting ROI from which percent change of peak parameter estimates were extracted fell within the left vPPC, specifically the angular gyrus ( $x=-47$ ,  $y=-55$ ,  $z=37$ ; 104 voxels). Further illustrating the lack of difference between magnitude of the old/new effect between tasks, the Task x Condition interaction was not significant,  $F(1,20)=1.02$ ,  $p=.33$  (Figure 2). However, main effects of Task [ $F(1,20)=8.98$ ,  $p<.01$ ] and Condition [ $F(1,20)=12.9$ ,  $p<.01$ ] were significant. Old items showed greater activation in the Recognition task than the LD task [ $t(20)=2.68$ ,  $p<.01$ ], a finding that might be explained by the fact that more information is retrieved as part of the explicit retrieval nature of the Recognition task. However, this would not necessarily explain why new items also showed greater activation in Recognition compared to the LD task,  $t(20)=2.78$ ,  $p<.01$ . If vPPC activation indexes amount of information retrieved, the two tasks should have similarly low levels of activation in response to new items.

The findings from Experiment 1 demonstrate the similarities and differences between explicit and implicit retrieval. The successful retrieval effect was present during both tasks and while a main effect of task indicated higher activity for both conditions during Recognition, the difference between old and new items was of similar magnitudes in each task. Additional activation occurred in prefrontal areas during the Recognition task, which may represent control and monitoring processes accompanying explicit retrieval. We also found that old items produced greater vPPC activation in the Recognition task compared to the LD task. This finding may be explained by some unintentional explicit retrieval occurring during the LD task, in which subjects cannot help but process and retrieve some information when encountering old items. The intentional retrieval occurring during the Recognition task would account for the higher level of activity in response to old items. However, the same explanation does not account for the finding that new items show similarly elevated levels of activation in Recognition compared to the LD task. If vPPC activation is simply an index of retrieved information, we would not expect heightened levels of activity to accompany new items during recognition. This led us to examine alternative explanations for these patterns of activity in a second experiment.

## **EXPERIMENT 2:**

The first experiment showed that the successful retrieval effect can be observed during implicit retrieval. One explanation for this finding is that vPPC activity during the implicit task was simply a product of unintentional explicit retrieval and that the activation was a direct reflection of retrieved information. Yet, an alternative explanation is that vPPC activity is actually an index of processing relevant stimulus information, in this case mnemonic status. Under this interpretation, vPPC activity would be evoked by any relevant output from the MTL, whether arising from bound representations that have been activated during successful retrieval of old items or something akin to a novelty signal in response to new items. In both the Recognition test and the LD task, the determination of mnemonic status facilitates goal-directed behavior. To assess this factor, we included a second implicit condition that diminished the relevance of processing mnemonic status. Though the presentation of old items would still induce similar levels of unintentional explicit retrieval as may be present in the LD task, the output of these retrieval processes held little task relevance. In this Color Discrimination (CD) task, participants simply determined whether a test item was red or green.

## **Methods**

### ***Participants***

Twenty-seven healthy subjects participated in this study (mean age 21.44 years, range 18-28 years; 15 females). Two additional subjects were excluded from analysis due to excessive head motion and poor behavioral performance. All subjects were paid for their participation and gave informed consent according to guidelines approved by the UC Berkeley Office for the Protection of Human Subjects. All subjects were native English speakers and were right-handed. None of the subjects reported a history of neuropsychiatric disorders or brain injury or having recently taken psychoactive medication.

### ***Behavioral Procedure***

Procedures for the study phase remained identical to Experiment 1 with the exception being that 210 words were presented over two blocks (105 words each).

At test, the LD and Recognition tasks used identical procedures as in Experiment 1 with some minor changes to trial timing. Additionally, a Color Discrimination task was added. Two blocks of each task were run, with the order of tasks randomized across subjects. During the LD task, the jittered inter-trial interval displaying a fixation cross was changed to 500-4500 ms. Recognition trial timings were also changed slightly such that each consisted of a stimulus presentation (500 ms), a blank screen (2500 ms), and a jittered ITI displaying a fixation cross (1000-5000 ms).

In the CD task, 70 old words and 70 new words were presented over two runs. Half of each word category was presented in red font and the other half in green font. A single CD trial consisted of stimulus presentation (500 ms), a blank screen (1000 ms) and a jittered inter-trial interval during which a center fixation cross was presented (ITI=500-4500 ms). Subjects were instructed to determine whether a stimulus was printed in a red or green font. Responses were made with either a left or right button press using the thumbs of each hand.

### ***fMRI Acquisition***

Scanning was conducted using the same procedure as in Experiment 1 except for some changes to the functional sequences described below. Each of the 6 runs acquired used a T2\*-weighted echo-planar imaging (EPI) sequence [TR=2000 ms; TE=26 ms; flip angle=90°; matrix=128x128; FOV=256mm; 3mm slice thickness] with GRAPPA [acceleration factor4]. 37 axial slices oriented to the AC-PC were acquired in an interleaved order giving whole brain coverage. 224 volumes were collected during each of the two LD runs, 189 volumes were collected during each of the Recognition runs and 119 volumes were collected during each of the CD runs. Finally, the first 5 volumes of each run were removed to allow for magnetization preparation.

### ***fMRI Data Analysis***

Data analysis was conducted using the same procedure as in Experiment 1. For planned contrasts examining activation in our ventral PPC region of interest, we used a pre-threshold mask before correcting for multiple comparisons. This was defined as the angular gyrus mask in the Harvard-Oxford Cortical Structure Atlas. Additional results obtained from the non-masked, whole brain analysis are also reported.

## **Results**

### ***Behavioral Results***

**Recognition Task:** The mean hit rate was 85% with a correct rejection rate of 65%. Reaction time were significantly faster for old items (mean=1197 ms) than new items (mean=1564 ms),  $t(26)=8.296$ ,  $P<.001$ . Memory performance (correct – incorrect) was significantly better for HC responses compared to LC responses,  $t(26)=7.565$ ,  $P<.001$ . HC responses (mean=1210 ms) were also made significantly fast than LC responses (mean=1721 ms),  $t(26)=11.962$ ,  $P<.001$ .

**Lexical Decision Task:** Subjects were able to correctly identify (correct-incorrect) words and non-words at a similar rate,  $t(26)=0.29$ ,  $P=0.77$ . When looking at just words, old items were correctly identified (correct-incorrect) significantly better than new items,  $t(26)=3.519$ ,  $P<0.01$ . Subjects responded faster on correct word judgments (mean=724 ms) than they did to correct non-word judgments (mean=794 ms),  $t(26)=6.99$ ,  $P<0.001$ . Examining words only, old items (mean=712 ms) were responded to significantly faster than new items (737 ms),  $t(26)=3.477$ ,  $P<.01$ .

**Color Discrimination Task:** Memory performance (correct-incorrect) for old and new words was similar,  $t(26)=0.246$ ,  $P=0.81$ . There was also no difference in performance between red and green words,  $t(26)=0.092$ ,  $P=0.93$ . Subjects responded with similar reaction times to old (mean=523 ms) and new words (mean=527 ms),  $t(26)=0.894$ ,  $P=.38$ . However, there was a significant difference in responses between green words (mean=520 ms) and red words (mean=531 ms),  $t(26)=2.072$ ,  $P<.05$ .

### ***fMRI Results***

**Recognition Task:** The comparison of correct HC-Old items to new items revealed activations similar to those in Experiment 1. Specifically, we observed increased activation for HC-Old responses compared to new responses within the angular gyrus mask ( $x=-42$ ,  $y=-52$ ,  $z=48$ ). The global analysis revealed additional clusters in left frontal pole extending into left dorsolateral prefrontal cortex, left posterior cingulate and precuneus, and left middle temporal gyrus (Figure 3a, see Table 5 for full list of results). The contrast of all old items collapsed across HC and LC judgments to new items yielded similar results, with the exception of the right lateral occipital cortex, posterior midline, and anterior extent of the frontal pole clusters.

**Lexical Decision Task:** Our contrast of interest was to compare old words > new words. Within our angular gyrus mask, there was a significant cluster ( $x=-42$ ,  $y=-52$ ,  $z=46$  and  $x=-46$ ,  $y=-60$ ,  $z=48$ ) reflecting the successful retrieval effect (Figure 3b). The global analysis did not produce any additional clusters that survived correction for multiple comparisons.

**Color Discrimination Task:** We next looked for presence of the successful retrieval effect in the CD task in the case of activity being caused due to unintentional explicit retrieval. The contrast of old words > new words did not produce any significant clusters within the vPPC.

**Cross-Task Analyses:** We performed analyses across the three tasks in order to compare magnitudes of old vs. new differences during explicit retrieval (Recognition task), relevant implicit retrieval (LD task), and irrelevant implicit retrieval (CD task). As in Experiment 1, there were no significant clusters where old vs. new effects were different between the Recognition and LD tasks ( $[HC-Old>New\_Recognition] > [Old>New\_LD]$ ). When we directly compared old vs. new contrasts between Recognition and CD ( $[HC-Old>New\_Recognition] > [Old>New\_CD]$ ), we found significant clusters within the angular gyrus mask ( $x=-44$ ,  $y=48$ ,  $z=48$ ). Additionally, there were clusters in left frontal poles extending into DLPFC, posterior cingulate, precuneus, and left inferior and middle temporal gyrii (see Table 6 for full list of results). Critically, the comparison of implicit old vs. new contrasts when mnemonic status was relevant vs. irrelevant ( $[Old>New\_LD] > [Old>New\_CD]$ ) yielded a significant cluster within

the angular gyrus mask ( $x=-42, y=-56, z=48$ ). Furthermore, the resulting cluster overlapped with the comparison of old>new contrasts between Recognition and CD in the angular gyrus (Figure 4).

## Discussion

In two experiments, we assessed the influence of implicit and explicit retrieval on the successful retrieval effect. Experiment 1 demonstrated significant vPPC activity for old compared to new words during an explicit Recognition task and an implicit LD task. We did observe greater activation in medial prefrontal regions during explicit compared to implicit retrieval, which is consistent with previous studies (Fleck, et al., 2006) and may reflect top-down monitoring or post-retrieval processes that facilitate decision-making.

In cross-task analyses, the vPPC old-new contrast was comparable between the explicit Recognition and implicit LD tasks. Although this difference was of similar magnitudes, both old and new items evoked greater activation in Recognition than the corresponding conditions in the LD task. It could be argued that unintentional explicit retrieval mediated successful retrieval effects during the LD task. However, this interpretation cannot account for the finding of increased vPPC activity for new words during explicit retrieval compared to implicit retrieval, as novel items should not be accompanied by an episodic retrieval signal. An alternative interpretation is that vPPC activation is an index of how relevant processing mnemonic status is to completing the task. Whereas old words may facilitate correct response for both tasks, new words are only particularly relevant in the Recognition task. That is, during the LD task all studied items were words while unstudied items carried no additional task-relevant information if the goal is merely to distinguish between words or non-words. Recognition performance depends on both identifying studied items as old *and* correctly rejecting unstudied items as new. This interpretation is consistent with our finding that old items evoked vPPC activity in both tasks, although to a greater extent during explicit Recognition as the task of judging mnemonic status was the primary objective. Likewise, the mnemonic status of new items provided task relevant information in the Recognition but not LD task. The lack of differences in the magnitude of the successful retrieval effect may be explained by the fact that the different levels of activity for new items between the task created a different “baseline” to which old items were compared. Although there was greater activity for old items in Recognition, the similarly elevated levels of activity in response to new items prevented the old vs. new contrast from being significantly greater than that found in the LD task.

Experiment 2 provided evidence that the successful retrieval effect is modulated by task relevance. While it has been shown that words are automatically processed to a certain extent (e.g. Stroop task), processing mnemonic status of each item is task irrelevant during the CD task as this feature provides no additional information towards facilitating a correct response. In cross-task analyses, we replicated the finding of comparable differences between old and new items in the Recognition and LD tasks. However, the difference between old and new items during the CD task was substantially reduced. This finding argues against the role of unintentional explicit memory as driving the successful retrieval effect during the implicit LD task, because we would have expected the same unintentional processes to occur during the CD task. Instead, significant differences between old and new items were only observed when stimulus activations arising from mnemonic status were relevant to task demands, and importantly, these differences occurred in similar locations when comparing both Recognition and LD tasks to the CD task.

A few issues should be addressed regarding differences across tasks. Reaction times tended to be longer during the Recognition task than either the LD or CD tasks. It is possible that greater task difficulty (as measured by reaction time) may have contributed to higher overall activation in the Recognition task. However, this would lead us to then expect greater activation for new items which were associated with longer reactions times than old items in both Recognition and LD, a result we did not find in either experiment. Also, our main findings were drawn from comparing within-task contrasts, which should help diminish effects present across task blocks unrelated to differences in processing old vs. new items. Future studies may benefit from including a reaction time covariate in order to control for time on task effects (both within and across old/new status), although previous studies have not found vPPC activation to be significantly related to reaction time. An additional possibility is that activity in the vPPC was gated by processing lexical rather than mnemonic features of the stimuli. If one assumes that subjects perform greater levels of lexical processing during the Recognition task than the CD task, this may be the case. While lexical processing may provide a binary gating of vPPC activation, it does not appear to drive the magnitude of effects as activation levels were highest in Recognition, not the LD task which required the greatest amount of lexical processing. Furthermore, similar levels of lexical processing are needed during the LD task for both old and new items, yet we see both behavioral and BOLD response differences between these conditions. Overall, whether or not determining mnemonic status provides useful information towards completing the task goal remains a likely explanation for the pattern of results found here.

The present findings sharpen the conditions under which successful retrieval effects are observed. Implicit tasks may drive retrieval-related vPPC activity, but only if task demands substantially benefit from the detection of stored episodic features or relative novelty. With respect to extant models, our findings may be interpreted as being consistent with an attentional account such as the AtoM model, as vPPC activity is thought to index bottom-up sensory or hippocampally driven signals. The vPPC has been implicated in a gated form of stimulus-driven attention, such that only relevant stimuli produce bottom-up attentional capture (Indovina & Macaluso, 2007). In this case, the vPPC activity seen in our results may represent a target detection response to MTL outputs (of both recollection and novelty signals) that are relevant to the current task. However, it should be noted that these bottom-up activations during attention tend to be right lateralized and located more anteriorly in the supramarginal gyrus than the more posterior and strongly left lateralized recollection-related activations. This raises the possibility that while target detection may occur in response to mnemonic status, it is not the source of the successful retrieval effect. Our results also do not rule out alternative models such as the episodic buffer hypothesis. It is possible that the vPPC is serving as a passive store of information, however it does seem this transfer from MTL to vPPC must pass through a filter. vPPC activation may also represent a process other than attention to or storage of retrieved information that facilitates memory retrieval, such as the cortical binding of episodic features (Shimamura, 2011). In any event, the current study provides evidence that any such process is gated by task relevance.

## Figures and Tables

Region	Hemisphere	X (mm)	Y (mm)	Z (mm)	Z- score
Lingual Gyrus	R	30	-38	-12	3.07
Parahippocampal Gyrus	R	22	-20	-16	3.07

	R	30	-28	-14	3.39
	R	28	-34	-12	3.03
Parahippocampal Gyrus	L	-28	-42	0	3.66
Hippocampus	R	28	-22	-16	3.33
Hippocampus	L	-24	-28	-8	3.38
	L	-20	-22	-10	2.89
Temporal Occipital Fusiform Cortex	R	28	-44	-12	3.01
Thalamus	L	-14	-36	6	2.93
Inferior Temporal Gyrus	L	-52	-40	-14	3.22
	L	-52	-36	-14	3.18
	L	-48	-42	-12	3.1
	L	-58	-42	-6	4.27
Middle Temporal Gyrus	L	-56	-22	-14	3.2
	L	-54	-28	-12	3.16
Frontal Orbital Cortex	L	-26	30	-14	3.76
	L	-34	36	-10	3.67
	L	-26	18	-12	3.34
	L	-34	16	-18	3.08
Frontal Pole	L	-30	38	-12	2.99
Central Opercular Cortex	R	46	-12	14	3.34
	R	58	-10	12	3.31
	R	48	-4	8	3.28
	R	56	-6	12	3.2
Parietal Operculum Cortex	R	56	-32	22	3.37
Precentral Gyrus	R	58	8	8	3.31
Angular Gyrus	L	-50	-52	38	4.09
	L	-50	-56	30	3.49
Lateral Occipital Cortex	L	-40	-72	36	4.6
	L	-46	-62	36	4.17
	L	-44	-68	30	3.9
	L	-32	-74	42	3.77
Posterior Cingulate Gyrus	L	-4	-48	30	5.05
	L	-4	-38	32	4.42
	L	-6	42	8	3.79
	L	-2	-54	28	4.24
Precuneous Cortex	L	-6	-66	24	4.63
	L	-10	-58	20	4.2
	L	-14	-60	14	4.14
Anterior Cingulate	L	-10	38	2	3.74
Frontal Pole	L	-16	54	18	3.93
	L	-4	58	10	3.73
Paracingulate Gyrus	L	-4	54	-2	4.08

L -6 50 14 3.93

**Table 1:** Experiment 1 regions active during Recognition task for correct HC-Old > CR contrast

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z-score</b>
Middle Temporal Gyrus	L	-58	-48	6	4.55
	L	-56	-44	-6	4.06
	L	-56	-38	-6	4.04
	L	-62	-28	-6	3.18
	L	-52	-38	-2	3.1
Superior Temporal Gyrus-anterior division	L	-50	-8	-16	3.38
Lateral Occipital Cortex	L	-32	-68	36	4.49
	L	-34	-64	44	4.45
	L	-40	-64	42	4.38
	L	-46	-62	22	4.37
Angular Gyrus	L	-46	-60	28	4.12
Posterior Cingulate	L	-54	-48	32	4.12
	L	-6	-40	38	4.64
	L	-2	-36	28	4.46
	L	0	-46	22	4.29
Precuneous Cortex	L	-2	-74	34	4.02
	L	-2	-72	28	3.92
	L	-6	-80	42	3.8
Paracingulate Gyrus	L	-8	54	12	3.85
Middle Frontal Gyrus	L	-26	14	54	3.79
Frontal Pole	L	-26	38	-10	3.78
	L	-12	56	24	3.7
	L	-12	54	28	3.69
	L	-36	42	12	3.68

**Table 2:** Experiment 1 regions active during LD task for correct word > non-word contrast

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z-score</b>
Angular Gyrus	R	42	-54	48	3.04
Lateral Occipital Cortex	R	38	-68	44	3.15
	R	42	-62	42	3.46
Frontal Pole	L	-20	58	6	3.07
	L	-24	56	6	3.11
	L	-36	42	14	3.17
	L	-26	54	2	3.18
	L	-24	50	-2	3.23
	L	-28	54	-2	3.29
Middle Frontal Gyrus	L	-34	10	50	2.97

	L	-34	10	40	3.07
	L	-34	6	42	3.15
	L	-40	14	44	3.19
	L	-38	8	50	3.2
	L	-38	14	40	3.5
Posterior Cingulate	L	-2	-42	36	2.94
	L	-4	-46	22	3.43
	L	-4	-30	30	3.56
Posterior Cingulate	R	2	-42	24	3.2
	R	6	-40	22	3.52
Precuneous Cortex	L	-4	-66	38	3.4
	L	-4	-66	20	3.43
	L	-6	-64	30	3.57
	L	-6	-72	30	3.81
Precuneous Cortex	R	8	-66	26	3.4
	R	2	-66	34	3.43
Lateral Occipital Cortex	L	-42	-62	36	3.75
	L	-40	-64	32	3.85
	L	-38	-68	42	4.04
	L	-34	-74	38	4.18
	L	-34	-66	48	4.26
	L	-44	-60	42	4.32

**Table 3:** Experiment 1 regions active during LD task for correct old word > new word contrast

Region	Hemisphere	X (mm)	Y (mm)	Z (mm)	Z-score
Postcentral Gyrus	R	28	-32	56	3.22
	R	28	-34	60	2.93
Precentral Gyrus	R	36	-24	64	3.47
	R	24	-20	52	3.14
Caudate	L	-8	12	4	2.95
Caudate	R	8	8	12	3.18
	R	8	6	0	2.98
Nucleus Accumbens	L	-10	16	-4	3.35
Lateral Occipital Cortex	R	36	-82	10	3.22
	R	30	-86	24	3.13
	R	32	-86	12	3.02
	R	26	-86	24	3.01
	R	36	-88	6	2.86
Lateral Occipital Cortex	L	-38	-74	18	3.7
	L	-38	-66	26	3.44
	L	-40	-70	28	3.36
	L	-28	-84	8	3.25

	L	-44	-72	24	3.03
	L	-40	-72	34	2.99
Occipital Pole	R	24	-94	14	3
Middle Temporal Gyrus	L	-56	-48	0	3.95
	L	-58	-42	-8	3.44
	L	-48	-22	-14	3.43
	L	-56	-24	-10	3.35
	L	-52	-32	-12	3.23
	L	-58	-22	-16	3.16
Central Opercular Cortex	R	46	-12	18	3.62
Insular Cortex	R	30	-24	20	3.26
Parietal Operculum Cortex	R	34	-22	20	3.36
	R	46	-24	24	3.29
	R	40	-24	16	3.22
Precentral Gyrus	R	58	6	8	3.74
Frontal Orbital Cortex	L	-28	28	-12	3.63
	L	-34	36	-12	3.6
Frontal Pole	L	-40	48	-2	3.4
Hippocampus	L	-22	-28	-6	3.68
	L	-20	-36	12	3.59
Lingual Gyrus	L	-28	-60	-2	3.67
Posterior Cingulate	L	-2	-46	34	4.14
	L	-6	-50	28	3.79
	L	-6	-42	32	3.77
	L	-2	-50	20	3.67
Precuneous Cortex	L	-12	-58	14	4.01
	L	-10	-56	18	3.96
Anterior Cingulate	L	-6	42	8	4.3
	R	2	38	6	3.94
Paracingulate Gyrus	L	-4	54	-2	4.29
	L	-8	52	4	4.03
	L	-6	50	14	3.9
	L	-8	54	-4	3.88
Superior Frontal Gyrus	L	-24	26	48	3.21
Middle Frontal Gyrus	L	-30	16	52	3.39

**Table 4:** Experiment 1 regions active during cross-task analysis of [HC-Old>New\_Recognition] > [Old word>New word\_LD].

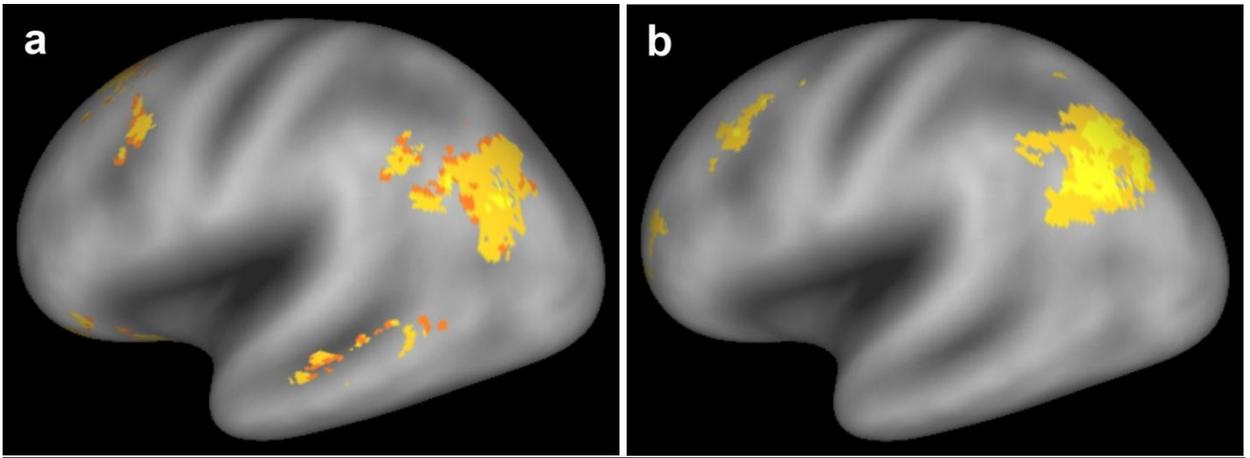
Region	Hemisphere	X (mm)	Y (mm)	Z (mm)	Z-score
Superior Frontal Gyrus	L	-2	40	56	4.73
	L	-4	30	62	4.44
	L	-22	22	62	4.21

	L	-8	16	70	4.17
	L	-10	26	50	4.08
	L	-32	16	50	4.32
Angular Gyrus	L	-42	-58	48	4.03
	L	-52	-52	30	3.91
Lateral Occipital Cortex	L	-42	-62	28	4.14
	L	-46	-66	32	3.81
	L	-50	-68	26	3.78
	L	-42	-64	52	3.63
	L	-4	-88	46	3.62
	L	-12	-84	40	3.17
	L	-12	-86	34	3.12
Lateral Occipital Cortex	R	44	-86	4	3.38
	R	34	-76	2	3.33
Posterior Cingulate	L	-2	-18	30	3.97
	L	0	-40	8	3.76
	L	-2	-30	34	3.55
Precuneous Cortex	L	-2	-40	46	3.84
	L	-12	-54	24	3.55
	L	-10	-72	28	3.39
	L	-2	-76	38	3.08
Cuneal Cortex	L	-10	-82	34	3.08
Occipital Pole	R	32	-90	32	3.63
	R	34	-90	22	3.53
	R	30	-96	18	3.52
Occipital Fusiform Gyrus	R	36	-66	-8	3.53
Precentral Gyrus	L	-10	-18	74	3.97
	L	-8	-18	50	3.92
Precentral Gyrus	R	6	-14	58	3.54
Postcentral Gyrus	R	2	-34	66	3.44
Postcentral Gyrus	L	0	-34	62	3.78
	L	-14	-32	78	3.45
Middle Temporal Gyrus	L	-60	-38	-6	3.51
	L	-68	-46	-12	3.44
	L	-64	-36	0	3.39
	L	-64	-50	-12	3.35
	L	-68	-42	-6	3.26
	L	-68	-30	-10	3.22

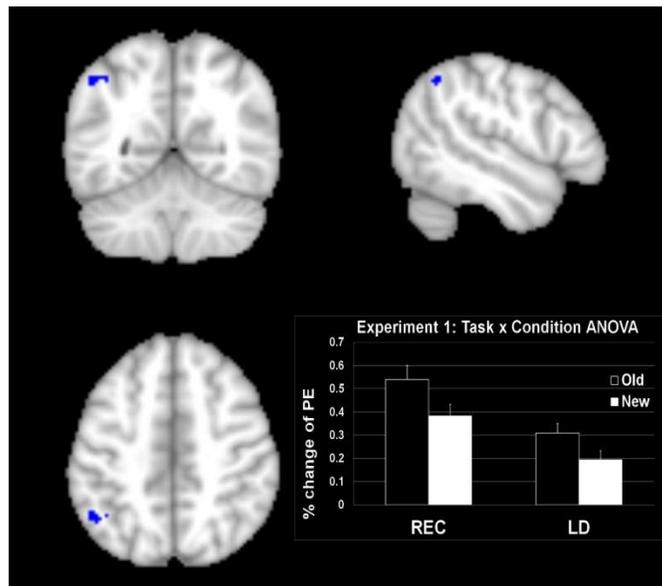
**Table 5:** Experiment 2 regions active during Recognition task for correct HC-Old > New contrast

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z- score</b>
Superior Frontal Gyrus	L	-22	22	60	3.88
	L	-4	40	54	3.83
Frontal Pole	L	-22	22	54	3.78
	L	-16	64	6	3.77
	L	-14	58	30	3.65
Lateral Occipital Cortex	L	-46	-62	48	4.01
	L	-12	58	34	3.64
	L	-36	-56	40	3.36
Lateral Occipital Cortex	L	-56	-54	44	3.28
Angular Gyrus	L	-42	-62	28	3.52
	L	-40	-70	40	3.28
Middle Temporal Gyrus	L	-38	-70	50	3.27
	L	-62	-42	-8	3.91
	L	-66	-48	-12	3.76
	L	-64	-44	-12	3.72
	L	-54	-46	-10	3.63
	L	-68	-28	-12	3.52
Posterior Cingulate	L	-58	-32	-12	3.44
	L	-4	-40	38	4.15
	L	-12	-48	30	3.24
Precuneous Cortex	L	-4	-48	34	3.21
	L	-2	-46	42	3.06
	L	-2	-48	38	2.98
Inferior Temporal Gyrus	L	-56	0	-34	3.23
	L	-50	0	-36	3.08
	L	-14	-50	34	2.9
Middle Temporal Gyrus	L	-60	-20	-32	3.3
	L	-58	-12	-32	3.1
	L	-60	-16	-32	3.07
	L	-58	-6	-32	3.03

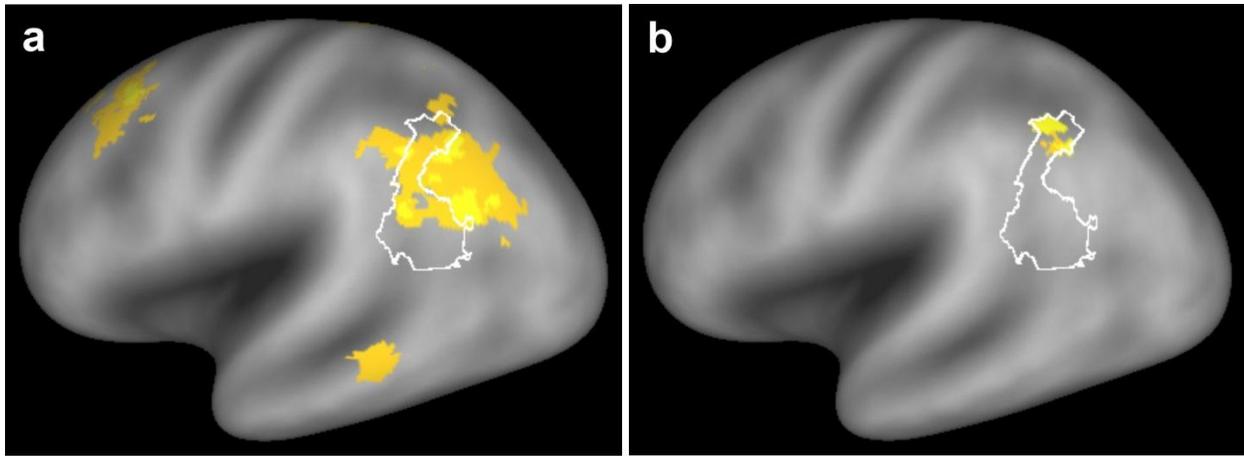
**Table 6:** Experiment 2 regions active during cross-task analysis for [HC-Old>New\_Recognition] > [Old>New\_CD] contrast



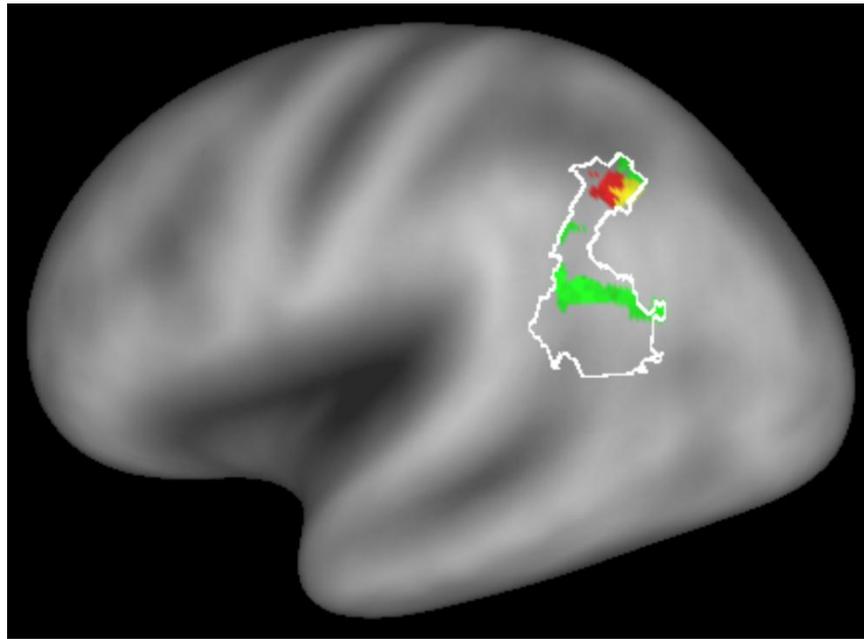
**Figure 1:** Experiment 1: a) regions active during Recognition task for correct HC-Old > New contrast. b) regions active during LD task for correct old word > new word contrast. Threshold at  $P < .05$ , corrected.



**Figure 2:** Experiment 1: ROI derived from inclusively masking HC-Old>New\_Recognition with Old word>New word\_LD shown in blue. Bar chart displays percent change of peak parameter estimates extracted from ROI. There were significant main effects for condition and task, but no interaction.



**Figure 3:** Experiment 2: a) regions active during Recognition task for correct HC-Old > New contrast. b) regions active during LD task for correct old word > new word contrast. Threshold at  $P < .05$ , corrected.



**Figure 4:** Experiment 2 cross-task analysis. [HC-Old > New\_Recognition] > [Old > New\_CD] contrast in green and [Old > New\_LD] > [Old > New\_CD] contrast in red. Areas of overlap in yellow. Threshold at  $P < .05$ , corrected.

## CHAPTER 3: STUDY 2

### Abstract

Feeling-of-knowing (FOK) judgments were assessed for recently learned (episodic) and well-learned (semantic) facts (e.g., *The sport that is associated with Wimbledon is...*). In fMRI analyses, strong FOK responses activated ventral parietal regions, demonstrating that these sites are modulated by covert feelings of knowing as they are for overt recognition responses. Activations in these regions were greater for episodic FOKs compared to semantic FOKs, whereas semantic FOKs activated anterior temporal regions. Relative to strong FOKs, weaker responses activated dorsal parietal regions, a finding that parallels activations during effortful retrieval on tests of explicit memory (e.g., low>high confident hits). The findings implicate trace access processes during metacognitive assessment which are similarly engaged during overt

### Introduction

Metacognition refers to our ability to oversee or monitor cognitive processes (Metcalf & Shimamura, 1994; Nelson & Narens, 1990; Shimamura, 2008). With respect to memory retrieval, behavioral studies have identified two metacognitive processes—*trace access* and *inferential* processes (Allen-Burge & Storant, 2000; Koriat & Helstrup, 2007, Nelson, Gerler, & Narens, 1984). Trace access refers to retrieval of actual features (i.e. traces) of a memory, some of which may only be partially retrieved, such as knowing that the name of Dorothy's dog in the *Wizard of Oz* begins with the letter "t" or has two syllables. Findings of positive correlations between feeling of knowing (FOK) ratings and subsequent recognition performance demonstrate the validity of trace-access processes (for review, see Dunlosky & Bjork, 2008). Inferential processes do not directly tap traces but instead depend on judging the probability of retrieval based on general knowledge or familiarity of the cue. For an inferential FOK you might judge that you would likely recognize the name of Dorothy's dog because you remember having watched the movie and *think* you could recognize the dog's name. Behavioral findings demonstrate that FOK judgments can be driven solely by inferential processes, such as cue familiarity (Metcalf, Schwartz, & Joaquim, 1993).

In FOK studies, weak memories are assessed because judgments are made only for non-recallable information. Thus, if you could overtly recall the name of Dorothy's dog as *Toto*, then that item would be discarded from the FOK analysis. As a result, extant studies tend to be biased toward inferential processes because items with very strong (i.e., recallable) traces are removed from further analysis. Neurocognitive findings are consistent with the role of inferential processes for typical FOK judgments as prefrontal regions that are active during valid FOKs are also be active in tasks that involve top-down executive control. Prefrontal activations have been observed for FOK judgments about general fact knowledge (Kikyo, Ohki, Miyashita, 2002; Maril, Simons, Weaver, & Schacter, 2005) and recently learned information (Schnyer et al., 2004; Schnyer, Nicholls, & Verfaellie, 2005). Metacognitive judgments, however, do not necessarily have to assess only weak or non-recallable information. Judgments of learning (JOL), which are assessed soon after encoding, are based on all items learned, including those that are recallable (Nelson, & Dunlosky, 1991).

To assess more generally the neural correlates of FOKs, we included items that are potentially recallable. To the extent that very strong FOKs are based largely on the successful retrieval of memory traces, our FOK findings can be linked to studies of overt memory

performance. In such studies, the posterior parietal cortex (PPC) is particularly active, as evidenced on tests of old/new recognition memory when remembered items (hits) are compared with new items (correct rejections) (for review, see Vilberg & Rugg, 2008; Cabeza et al., 2008; Shimamura, 2011). Moreover, ventral regions (vPPC; particularly the angular gyrus and posterior parts of the temporo-parietal junction) are associated with high confident hits, whereas dorsal regions (dPPC; including the superior parietal lobule and the medial wall of the intraparietal sulcus) are associated with low confident hits (Wheeler & Buckner, 2004; Kim & Cabeza, 2009). Low confident hits also recruit prefrontal regions, suggesting that these areas, along with the dPPC, are involved when extensive executive (i.e., inferential) processes are required.

The neural correlates of successful retrieval have been assessed primarily on explicit memory tests, such as old/new recognition, source memory, and remember/know judgments (Wheeler & Buckner, 2004; Vilberg & Rugg, 2007; Kim & Cabeza, 2009). Analyses have shown that PPC activity also occurs for false recognitions and implicit retrieval though not as strongly as for items remembered on explicit tests (Wheeler and Buckner, 2003; Kahn et al., 2004; Elman & Shimamura, 2011). These findings are based on memory for recently learned material, such as words, faces, or pictures. Less is known about the successful retrieval of conceptual (semantic) information, such as memory for facts or general knowledge. Findings of greater vPPC activity for items associated with strong source memory or recollective responses suggest that this region may be preferentially engaged during retrieval of contextually based or episodic information (Dobbins et al., 2002; Wheeler & Buckner, 2004; Yonelinas et al., 2005; Daselaar et al., 2006).

In the present study, we addressed two questions: 1) does PPC activity monitor covert metacognitive (i.e., FOK) judgments in addition to explicit recognition decisions, and 2) does PPC activity monitor retrieval of overlearned (semantic) information as well as recently learned (episodic) information? To equate task demands across conditions we assessed memory for factual information (e.g., *The park in which Old Faithful is located is...*). For half of these items, FOKs were based on knowledge acquired prior to the experimental session and presumed to have been experienced on multiple occasions (i.e., semantic memory). The other facts were previously unfamiliar but were presented to the subjects just prior to scanning. Thus, for these recently learned facts, accurate FOKs would be based on retrieval of a specific episodic context. To our knowledge, this study represents the first to consider unrestricted FOK responses (i.e., including potentially recallable items). Moreover, few studies have compared semantically and episodically based FOKs in the same study. Our central aim concerns the neural underpinnings of very strong FOKs, which are presumed to be largely based on accessing memory traces. By evaluating the neural correlates of such covert responses—for both semantic and episodic information—we consider the degree to which PPC activity mediates covert monitoring of retrieved information. If indeed activation differences between old and new items appear similar to those resulting from standard recognition paradigms, these results would suggest that PPC contributions do not reflect retrieval per se, but rather mediate pre-retrieval processes that generalize to meta-memory in addition to explicit memory tasks. Furthermore, differences between episodic and semantic conditions would indicate that PPC activity is modulated not only by retrieval success, but by the type of mnemonic information being accessed.

## **Methods**

### *Participants*

Nineteen healthy subjects participated in this study (mean age 21.11 years, range 18-33 years; 7 females). Two additional subjects were excluded from analysis due to excessive head motion and scanner artifact. All subjects were paid for their participation and gave informed consent according to guidelines approved by the UC Berkeley Office for the Protection of Human Subjects. All subjects were native English speakers and were right-handed. None of the subjects reported a history of neuropsychiatric disorders or brain injury or having recently taken psychoactive medication.

### ***Stimuli***

We used a set of 160 fact questions presented in the form of an incomplete sentence (e.g., *The sport that is associated with Wimbledon is...* [answer: *tennis*]). Of these facts, 80 were common and generally well-known facts (henceforth identified as *semantic facts*), such as the Wimbledon question, whereas 80 other facts were more obscure (e.g., *The name of the number two wood golf club is...* [answer: *brassie*]). The answers to these obscure facts (henceforth identified as *episodic facts*), were presented to the subjects prior to scanning. Pilot tests showed that recall performance for the semantic facts were comparable to recall performance of the episodic facts after having been presented the answers. The word length of the fact sentences ranged from 7 to 24 words (mean=13.94 words).

### ***Behavioral Procedure***

Prior to scanning, subjects were presented the answers to the episodic facts. On each study trial, a fact question was presented until a subject-paced button press revealed the correct answer on-screen for 3 seconds. The presentation order of the 80 episodic facts was randomized, and the study set was repeated for a second presentation. During the initial presentation of these facts, subjects identified any that were known previously, and those items were excluded from analysis (mean number of episodic facts excluded=1.77).

In the scanner, approximately 30 minutes after the study session, subjects were presented four blocks of trials in which FOK judgments were requested. Each trial consisted of a fact question presented in the form of an incomplete sentence (4000 ms) during which subjects rated how likely they would be able to recognize the correct answer in a multiple-choice test, followed by a central fixation cross (2200-3600ms jittered). Response options were *Definitely*, *Likely*, *Maybe* and *Guess*, which were made using thumb keypresses of each hand on a four-button response box. The response mappings were counterbalanced across subjects. Each block consisted of 40 FOK trials of either episodic or semantic facts. The order of presentation (semantic or episodic blocks) alternated and their order counterbalanced across subjects.

After scanning, subjects were given a six alternative, forced-choice recognition test for all 180 facts. The facts were presented in a random order with each trial consisting of the incomplete sentence with six answer choices. The recognition test was self-paced, and subjects responded with a keypress corresponding to one of the six choices. To verify the FOK accuracy, we assessed recognition responses (correct vs. incorrect) as a function of FOK rating.

### ***fMRI Acquisition***

Subjects were scanned in a 3T Siemens (Erlangen, Germany) Trio scanner at the UC Berkeley Brain Imaging Center. For each of the four functional runs, we used a T2\*-weighted echo-planar imaging (EPI) sequence [TR=2200ms; TE=26ms; flip angle=80°; matrix=100x100; FOV=210mm; 3mm slice thickness] with GRAPPA [acceleration factor 2]. Thirty-five axial slices oriented to the AC-PC were acquired in a sequential descending order giving whole brain

coverage. A total of 118 volumes were collected during each of the functional imaging runs. The first nine volumes of each run were discarded to allow for magnetization preparation. A high resolution magnetization-prepared rapid-acquisition gradient echo (MPRAGE) [TR=2300ms; TE=2.98; matrix=256x256; FOV=256; sagittal plane; slice thickness=1 mm; 160 slices] and a gradient-echo multislice (GEMS) [TR=250ms; TE=22; matrix=256x256; FOV=256; 3mm slice thickness, 37 slices] were collected for registration purposes.

### ***fMRI Data Analysis***

Data were preprocessed and analyzed with the FSL toolbox v4.1.4 (<http://www.fmrib.ox.ac.uk/fsl>; (Smith et al., 2004). Motion correction was performed with MCFLIRT, aligning all images to the middle slice with rigid body transformation. Slice timing correction was performed using (Hanning windowed) sinc interpolation to shift each slice in the volume in reference to the middle of the TR period. BET (brain extraction tool) was then used to create a mask of the brain from the first volume of each time series and used to separate brain from surrounding skull and tissue in each volume. All images were spatially smoothed with a 5mm FWHM Gaussian kernel to reduce noise and allow group analysis. High-pass temporal filtering was performed using the local Gaussian-weighted fit of a running line to remove low frequency artifacts. Subject data was registered to standard space in a two-step process using FLIRT (FMRIB's Linear Image Registration Tool). First, EPIs were registered to each subject's skull-stripped high resolution T1-weighted image. Second, subject's T1-weighted images were registered to standard (MNI) space (FSL's MNI152 template). The two registrations were then combined to take the subject's EPI images and run-level statistical maps into standard space.

A multi-level, mixed effects general linear model was run using FILM (FMRIB's Improved Linear Model) which treated subjects as random effects. Individual runs from the FOK phase were modeled in subject space and resulting statistical maps were registered to standard space for higher level analysis. Regressors of interest were obtained by convolving stimulus onset times with FSL's double-gamma hemodynamic response function and the temporal derivative. Each correct response type was modeled separately for both conditions. Motion parameters were included as additional confound variables and temporal autocorrelation was removed through pre-whitening. Trials with no response and those corresponding to questions answered incorrectly at follow-up testing were also modeled as regressors of no interest. Contrasts were entered to compare levels of FOK and fact type (episodic vs. semantic).

A second level analysis combined the runs for each subject using a one-sample t-test, treating runs as fixed effects. Third-level group statistical maps were created for each contrast using FLAME (FMRIB's Local Analysis of Mixed Effects). FLAME implements a Bayesian two-stage model, the first being a fast approach to the posterior probabilities of activation for each voxel and the second uses a slower Markov Chain Monte Carlo (MCMC) based analysis for all voxels identified as being near threshold in the first stage. The whole brain family-wise error was corrected to  $P < .05$  using Gaussian Random Field theory with a cluster forming threshold of  $z > 2.3$ . Thresholded group maps were projected on to inflated atlases for display purposes using CARET software (<http://sumsdb.wustl.edu/sums/humanpalsmore.do>; (Van Essen, 2005).

## **Results**

### ***Behavioral Results***

Overall recognition performance was high and somewhat better for episodic facts (92.5% correct) compared to semantic facts (88.8% correct),  $t(18)=2.42$ ,  $p < 0.05$ . Response latencies

were significantly faster for episodic ratings (2140.26 ms) compared to the semantic ratings (2369.50 ms),  $t(18)=-4.62$ ,  $p<0.001$ . Subjects, however, gave more *Definitely* FOK ratings to semantic facts (69.1%) compared to episodic facts (53.9%),  $t(18)=-3.62$ ,  $p<0.01$ . Table 1 displays proportion of FOK responses elicited across the four rating categories (*Definitely*, *Likely*, *Maybe*, and *Guess*) and recognition performance within each category. FOK ratings were valid as recognition performance increased with FOK strength,  $F(3,138)=17.21$ ,  $p<0.001$ .

### ***fMRI Results***

***Feeling of Knowing:*** We grouped *Likely* and *Maybe* FOK ratings in order to increase statistical power and compared this combined set with *Definitely* FOK ratings. *Likely/Maybe* responses reflect the kind of sub-threshold or non-recallable information typically assessed in FOK studies. Items rated as *Definitely* recognizable represent strong FOK responses which have not been evaluated in previous studies, because many of these items would have been recallable and thus removed from the analysis. We first considered contrasts of *Definitely>Likely/Maybe* to reflect activations underlying very strong FOK responses. The reverse contrasts of *Likely/Maybe>Definitely* were also assessed as they represent neural processes engaged when weaker traces are evaluated and presumed to depend more on top-down inferential processes. This contrast is similar to previous analyses of low>high confidence ratings assessed during recognition judgments (Wheeler & Buckner, 2004; Kim & Cabeza, 2009). *Guess* ratings were rarely elicited and not evaluated in the following fMRI analyses.

Figure 1 shows regional activations associated with contrasts of *Definitely>Likely/Maybe* FOKs assessed separately for episodic and semantic facts. This and subsequent analyses only included correctly recognized facts. For both episodic and semantic facts, *Definitely* FOK responses activated a broad set of cortical regions (see Table 3). In particular, there were large overlapping activations in the vPPC, medial parietal cortex (mPC), and mPFC. Within the parietal cortex, lateral activations were clustered in the angular gyrus and temporo-parietal junction. Medial parietal activations were clustered in the precuneus and posterior cingulate gyrus. Within the PFC, we found significant activations in ventrolateral (vLPFC) and dorsolateral regions. These regions, evoked by strong FOK responses, are comparable to regions activated in explicit memory tests when information is successfully retrieved.

Weak FOK responses (*Likely/Maybe>Definitely*) activated a less broad set of regions (see Figure 2 and Table 4). For both episodic and semantic facts, significant activations were observed in bilateral dPPC, anterior cingulate gyrus, and right vLPFC. The dPPC and PFC activations are comparable to activations observed on explicit tests when low confident recognition hits are compared with high confident hits. For episodic FOKs, weak responses were also associated with activations in the lateral occipital cortex (bilaterally) and left medial occipital cortex. Weak semantic FOKs were associated with activations in the inferior frontal gyrus.

***Episodic vs. Semantic FOKs:*** Differences in the pattern of activation between strong episodic and semantic FOK responses were assessed by contrasting *Definitely* FOK ratings between the two sets. Figure 3 shows regional activations for the contrasts of episodic>semantic *Definitely* FOKs (in red) and semantic>episodic *Definitely* FOKs (in blue) (see also Table 5). Relative to semantic FOKs, strong episodic FOKs evoked greater activations in the left vPPC, precuneus, and frontal pole. These regions have been associated with high confident hits during explicit retrieval (Kim & Cabeza, 2009). Relative to episodic FOKs, strong semantic FOKs activated the right anterior temporal lobe, a finding consistent with previous analyses of semantic processing (Mummery et al., 2000; Martin and Chao, 2001).

One possible concern of these analyses is the small but significant difference in the behavioral performance between episodic and fact recognition. Specifically, there was a greater proportion of *Definitely* FOK responses elicited for semantic facts compared to episodic facts, though overall recognition performance for episodic facts was greater. Moreover, response latencies were faster for episodic FOK ratings than for semantic ratings. While prior work has shown that the vPPC is not modulated by the proportion of old and new items (Vilberg and Rugg, 2009), we examined the degree to which neural responses were driven by the proportion of *Definitely* responses elicited across subjects. We generated an 8 mm spherical ROI centered on the voxel with the local maximum z-score resulting from the contrast of *Definitely*>*Likely/Maybe* ratings (MNI coordinates x=-38, y=-56, z=34) and extracted parameter estimates of *Definitely* trials for each subject. We then correlated these values with each subject's proportion of *Definitely* FOK responses. The correlations were not significant for either episodic ( $r = -0.24, p = 0.43$ ) or semantic ( $r = -0.23, p = 0.35$ ) facts.

We also evaluated the possibility that brain activity was driven by differences in response latencies between episodic and semantic FOKs. This factor was not likely to impact significantly on our results for several reasons. First, the temporal derivative for each regressor allowed the model to flexibly fit the onset times by up to one second, a time larger than the difference found in response latencies. Second, longer reaction times tend to evoke greater amounts of activity, yet we observed greater vPPC activity for items with faster response latencies (episodic FOKs). To address this issue directly, we extracted the percent signal change from the vPPC ROI and generated peristimulus plots separately for strong episodic and semantic FOKs. These values were compared to the mean activity of this ROI over the entire course of each run. The onset and temporal pattern of activation were similar across conditions, with the only difference being the magnitude of the response. Thus, the temporal dynamics of the BOLD signal across conditions did not appear to be influenced by the rather small difference in response latencies.

## Discussion

Previous FOK studies have focused primarily on the PFC in mediating FOK judgments (Janowsky et al., 1989; Maril et al., 2001, 2005; Kikyo et al., 2002; Reggev et al., 2011; Schnyer et al., 2005). As mentioned above, these prior studies have restricted analyses to FOK ratings of nonrecalled information. Thus, prior studies have not considered the neural underpinnings of very strong FOK responses. The present study assessed the neural correlates of episodic and semantic facts judged as *Definitely* recognizable. Such strong FOK responses activated a broad neural circuit that included vPPC, mPC, and mPFC (see Figure 1). These same regions have been associated with recollection-related activations during explicit memory tests (see Vilberg and Rugg, 2008; Cabeza et al., 2008; Shimamura, 2011). Furthermore, we were able to compare directly metacognitive monitoring of recently learned (episodic) and well-learned (semantic) information using the same kinds of test material (i.e., general information facts). Strong episodic FOKs specifically activated vPPC, mPC, and anterior PFC, whereas strong semantic FOKs activated the right anterior temporal gyrus (see Figure 3).

The inclusion of potentially recallable information allowed us to examine more directly the contribution of trace-access processes and to link these findings to studies of explicit retrieval. Strong FOKs elicited activations similar to those observed during successful recognition (hits>correct rejections) and demonstrated the contribution of the vPPC during covert metacognitive monitoring. Whereas the vPPC was active during strong FOK judgments, the dPPC was active during weak FOK judgments (*Likely/Maybe*>*Definitely*). In two previous studies (Maril et al., 2005; Reggev et al., 2011), PPC activity was observed when subjects

elicited FOK ratings for non-recallable facts compared to *Don't Know* responses. We suggest that such PPC activity can now be distinguished between vPPC activations driven by trace access and dPPC activations driven by inferential processes. This dorsal-ventral dissociation has also been observed in comparisons of high vs low confidence ratings that follow recognition judgments (Wheeler & Buckner, 2004; Kim & Cabeza, 2009). We suggest that the dPPC, along with PFC, are particularly involved when trace access is weak or not readily available. Under such conditions, greater involvement of top-down, inferential processes is necessary.

With respect to PFC processes, the posterior vLPFC was active for both episodic and semantic retrieval, particularly for low FOK responses. This region has been associated the selection and maintenance of information (Shimamura, 2008; Wagner, 2002). Also, right PFC activity for weak FOK responses is consistent with conditions in which recollective processes fail and the monitoring of item familiarity becomes necessary (Henson et al., 2000; Dobbins et al., 2004). This same pattern was observed in the anterior cingulate gyrus for both episodic and semantic FOKs. It has been suggested that this region monitors response conflict and may signal a demand for further reflective processing (Raye et al., 2000). While PFC activation was largely domain general, there were some differences between conditions. Specifically, the left frontal pole was more active during episodic FOKs compared to semantic FOKs. This region has been implicated in the monitoring of context-specific retrieval, which would be more critical for recently learned (episodic) facts (Rugg et al., 1999; Dobbins et al., 2004).

In the present study, the vPPC was associated with strong FOK responses for both episodic and semantic facts, though there was significantly greater activation in this region for episodic facts. This finding is consistent with a recent theory of memory retrieval that suggests that the vPPC is involved in the *cortical binding of relational activity (CoBRA)* (Shimamura, 2011). According to CoBRA, the vPPC acts as a neocortical convergence zone that integrates or binds features associated with a past experience or event. At the time of encoding, the medial temporal cortex initially binds episodic features, as suggested by extant consolidation theories (see Eichenbaum et al., 1992; Squire and Alvarez, 1995; Shimamura, 2010). Through reminiscence or replay neocortical links between episodic features are established, many of which depend on intermodal bindings within the vPPC. During retrieval these vPPC links contribute significantly to the reinstatement or “re-collection” of event features. Retrieval tasks that depend on the recollection of contextual information are facilitated by cortical binding within the vPPC. Retrieval of semantic knowledge (and implicit memory) may also depend on such multimodal bindings, though not to the same extent as episodic recollections.

In summary, the present findings refine and extend conditions under which the parietal cortex contributes to retrieval-related processes. When individuals have strong FOK experiences vPPC regions are recruited, which are known to be involved during the explicit retrieval of episodic features or traces. Strong FOKs for well-learned semantic facts activated the anterior temporal cortex, a region associated with semantic knowledge networks. Weak FOK responses to both episodic and semantic facts were associated with increased dPPC and PFC activity, a finding which suggested a domain-general network involved in top-down executive search strategies. Thus, the results of the present findings help define and distinguish the neural correlates of trace access and inferential processes involved in metacognitive monitoring.

## **Figures and Tables**

	<b>Definitely</b>	<b>Likely</b>	<b>Maybe</b>	<b>Guess</b>
<b>Episodic</b>	.54 (98%)	.17 (94%)	.18 (86%)	.11 (74%)
<b>Semantic</b>	.69 (95%)	.13 (85%)	.10 (74%)	.08 (58%)
<b>TOTAL</b>	.62 (97%)	.15 (90%)	.14 (82%)	.09 (67%)

**Table 1.** Proportions of feeling of knowing responses by FOK strength and correct response rate (in parentheses) for Semantic and Episodic facts. These FOK strength categories refer to responses given by subjects during the scanned FOK phase and the accuracy is derived from performance during the subsequent recognition phase.

	<b>Definitely</b>	<b>Likely</b>	<b>Maybe</b>	<b>Guess</b>
<b>Episodic</b>	1946ms (64)	2577ms (150)	2580ms (91)	2555ms (87)
<b>Semantic</b>	2341ms (49)	2887ms (71)	2862ms (169)	2715ms (76)
<b>TOTAL</b>	2168ms (51)	2710ms (94)	2682ms (78)	2624ms (46)

**Table 2.** Reaction times by FOK strength category are listed with standard error in parentheses. These refer to responses given by subjects during the scanned FOK phase.

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z-score</b>
<i>Episodic Definitely &gt; Likely/Maybe contrast:</i>					
Angular Gyrus	L	-46	-50	24	3.68
	R	48	-54	18	3.88
Frontal Medial Cortex	R	8	50	-14	4.55
Frontal Orbital Cortex	L	-28	34	-20	3.87
Frontal Pole	R	6	54	-20	4.48
Inferior Temporal Gyrus	L	-62	-36	-22	3.62
	R	50	-10	-26	3.78
Lateral Occipital Cortex	L	-56	-66	-4	4.2
	R	54	-68	26	3.7
Middle Frontal Gyrus	L	-32	32	46	4.61
Middle Temporal Gyrus	L	-68	-42	-12	3.83
	R	62	-12	-10	3.64
Paracingulate Gyrus	R	4	52	2	4.62

Parahippocampal Gyrus	R	24	-20	-20	3.62
Postcentral Gyrus	R	2	-36	66	3.68
Posterior Cingulate	R	4	-52	28	3.88
Precuneous Cortex	L	-10	-58	24	4.16
Subcallosal Cortex	L	-2	8	-6	4.38
Temporal Fusiform Cortex	R	30	-36	-16	3.66

*Semantic Definitely > Likely/Maybe contrast:*

Angular Gyrus	L	-60	-54	34	3.64
Central Opercular Cortex	L	-56	-12	10	3.6
Frontal Medial Cortex	L	-2	42	-14	4.18
Inferior Temporal Gyrus	R	50	-10	-26	3.16
Lateral Occipital Cortex	L	-54	-62	-6	3.71
Middle Temporal Gyrus	L	-56	-62	-2	3.75
	R	58	0	-18	3.31
Paracingulate Gyrus	L	-10	54	-4	4.23
Posterior Cingulate	L	-4	-50	26	3.31
Precuneous Cortex	L	-4	-66	20	3.54
Subcallosal Cortex	L	0	8	-6	3.64
Superior Temporal Gyrus	R	62	-34	10	3.94
Supramarginal Gyrus	R	56	-38	8	3.45
Caudate	R	10	18	2	3.58
Parietal Operculum Cortex	L	-52	-38	24	4.02
Planum Temporale	R	58	-26	10	3.4

**Table 3.** Peak activations of significant clusters from the contrast of Definitely > Likely/Maybe. Results are separated by condition (Episodic or Semantic).

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z-score</b>
<i>Episodic Likely/Maybe &gt; Definitely contrast:</i>					
Anterior Cingulate	R	8	28	20	4.58
Frontal Operculum Cortex	R	44	14	2	3.62

Frontal Orbital Cortex	R	32	26	-4	4.08
Insular Cortex	R	30	16	8	3.4
Intracalcarine Cortex	R	12	-82	2	3.55
Lateral Occipital Cortex	L	-18	-66	46	4.23
	R	18	-72	48	5.24
Lingual Gyrus	L	-16	-88	-2	3.62
Occipital Fusiform Gyrus	R	26	-78	-8	3.43
Occipital Pole	L	-34	-92	-18	3.87
Paracingulate Gyrus	L	-6	14	40	3.69
	R	2	8	50	4.37
Precentral Gyrus	L	-26	-10	54	4.11
	R	26	-12	48	3.59
Precuneous Cortex	R	8	-66	50	3.79
Superior Frontal Gyrus	L	-22	-4	48	4.17
	R	22	-2	56	4.17
Superior Parietal Lobule	L	-34	-48	48	3.85
	R	30	-48	44	3.77
Supramarginal Gyrus	R	42	-36	42	3.73

*Semantic Likely/Maybe > Definitely contrast:*

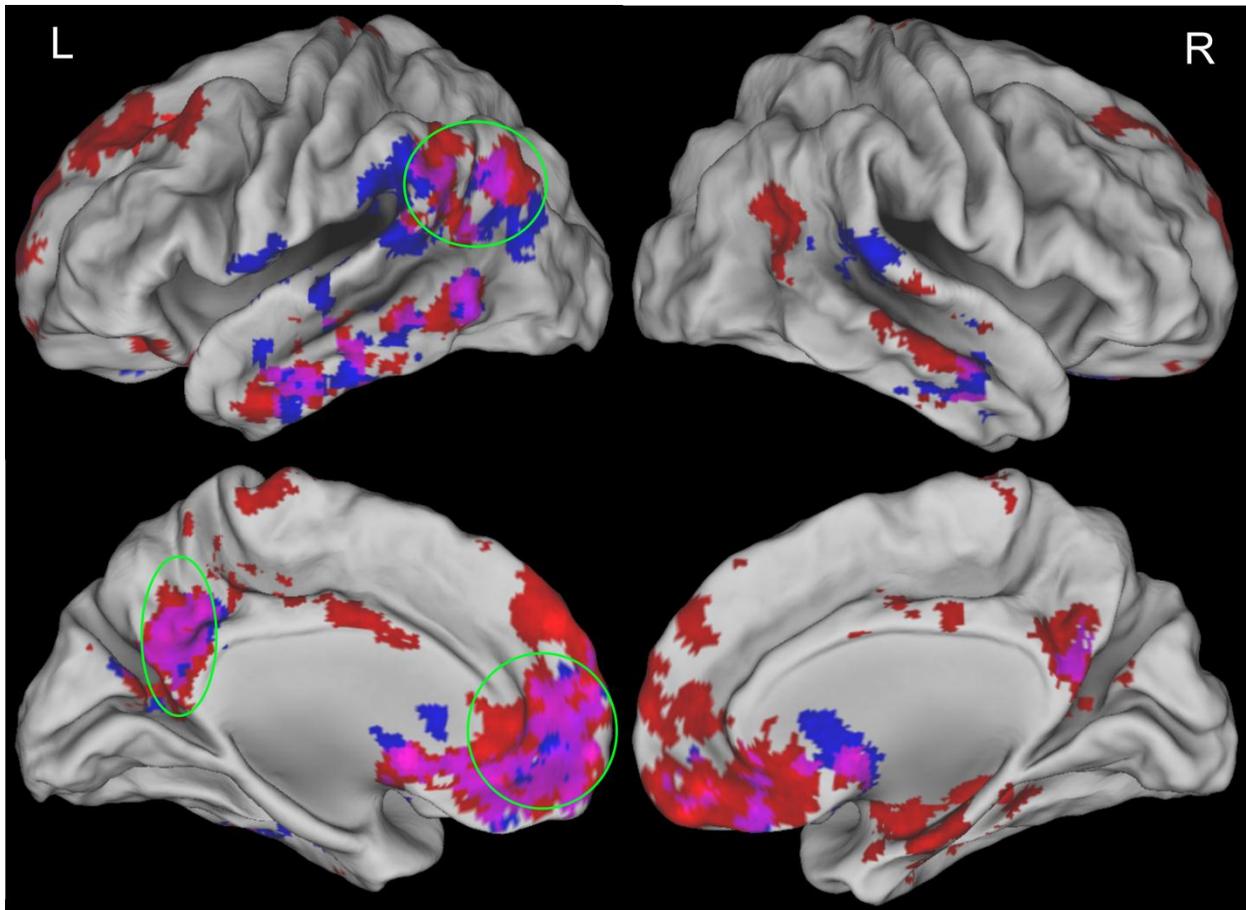
Anterior Cingulate	R	12	28	16	3.36
Frontal Orbital Cortex	R	36	22	-12	3.52
Frontal Pole	R	36	46	32	3.86
Inferior Frontal Gyrus	R	52	14	-2	2.93
Insular Cortex	R	32	18	6	3.12
Lateral Occipital Cortex	R	10	-76	52	4.76
Middle Frontal Gyrus	R	28	4	52	4.02
Paracingulate Gyrus	L	-2	28	34	3.38
	R	2	16	44	4.5
Precuneous Cortex	R	12	-66	48	4.26
Superior Frontal Gyrus	R	14	22	60	4.18

Supplementary Motor Cortex	R	4	6	50	4.5
Supramarginal Gyrus	R	48	-38	44	4.13

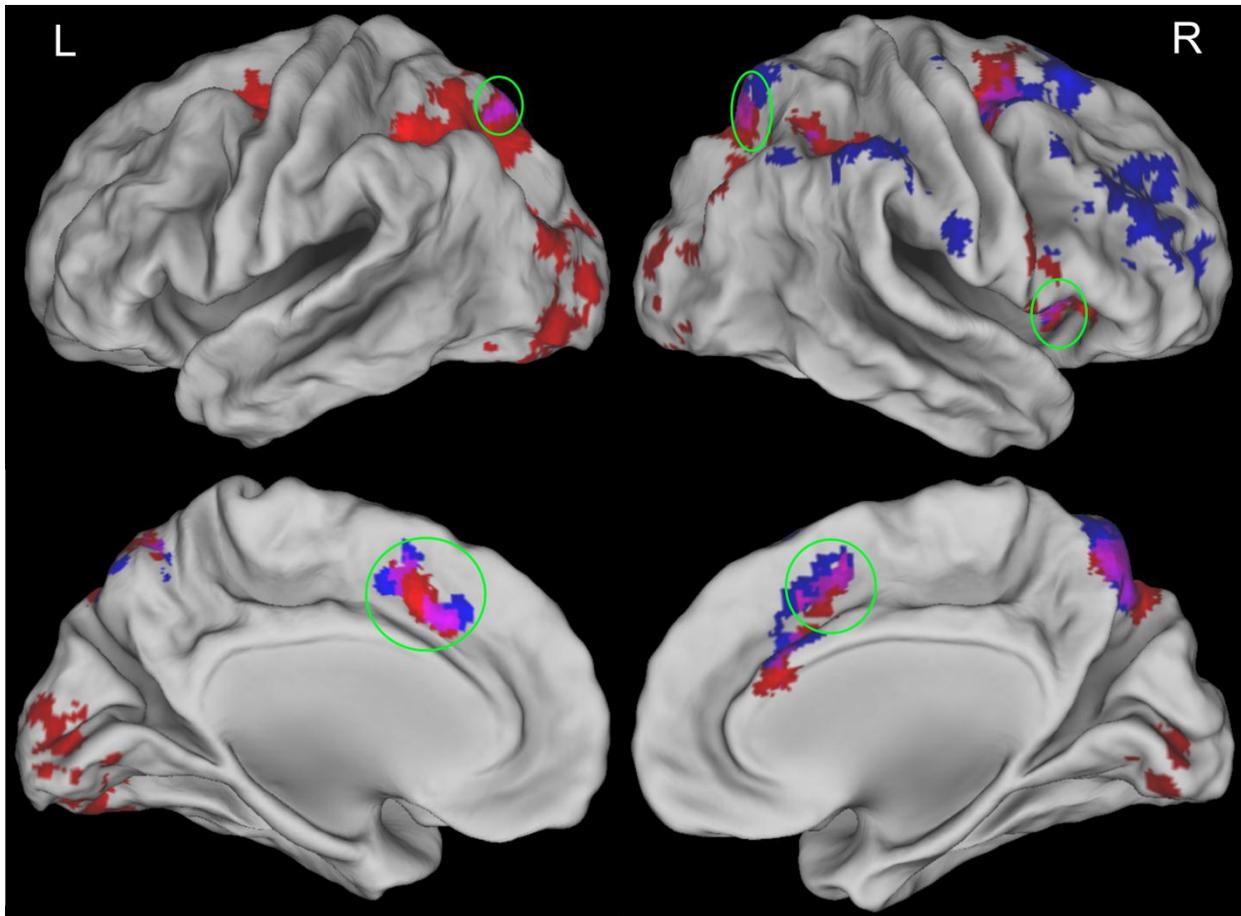
**Table 4.** Peak activations of significant clusters from the contrast of Likely/Maybe > Definitely. Results are separated by condition (Episodic or Semantic).

Region	Hemisphere	X (mm)	Y (mm)	Z (mm)	Z-score
<i>Episodic_Definitely&gt;Semantic_Definitely contrast:</i>					
Angular Gyrus	L	-40	-50	38	4.47
	R	48	-56	52	4.24
Central Opercular Cortex	L	-46	-4	4	3.49
Frontal Pole	L	-38	54	2	4.43
	R	26	60	-4	3.71
Heschl's Gyrus	L	-44	-14	4	2.97
Insular Cortex	L	-42	4	-2	3.45
Lateral Occipital Cortex	L	-42	-68	48	3.82
Posterior Cingulate	L	0	-24	26	4.11
	R	4	-20	26	4.05
Precuneus Cortex	L	-10	-78	42	4.58
	R	12	-68	42	4.32
Supramarginal Gyrus	L	-44	-42	38	3.8
<i>Semantic_Definitely&gt;Episodic_Definitely contrast:</i>					
Temporal Pole	R	50	24	-22	3.9

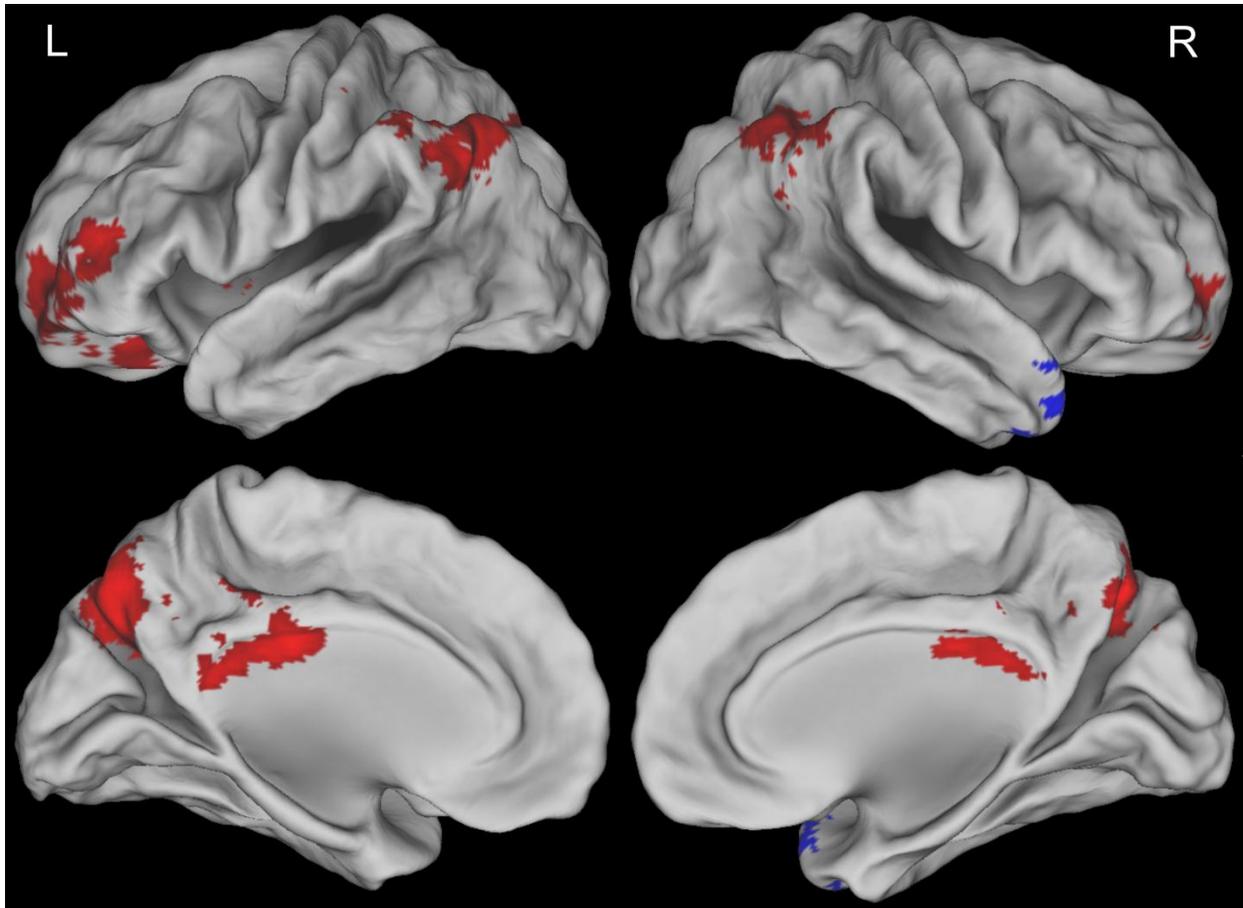
**Table 5.** Peak activations of significant clusters from the direct comparisons of Episodic vs. Semantic conditions. Only “Definitely” responses were included in order to equate FOK strength between conditions.



**Figure 1.** Regional activity associated with strong FOK ratings (*Definitely* > *Likely/Maybe*) for episodic (red) and semantic (blue) facts that were correctly recognized. Shown in purple are regions of overlap which included the left vPPC, mPC, and mPFC (circled regions). Activations are projected on to lateral (top) and medial (bottom) views of an inflated atlas using CARET software (Van Essen, 2005).

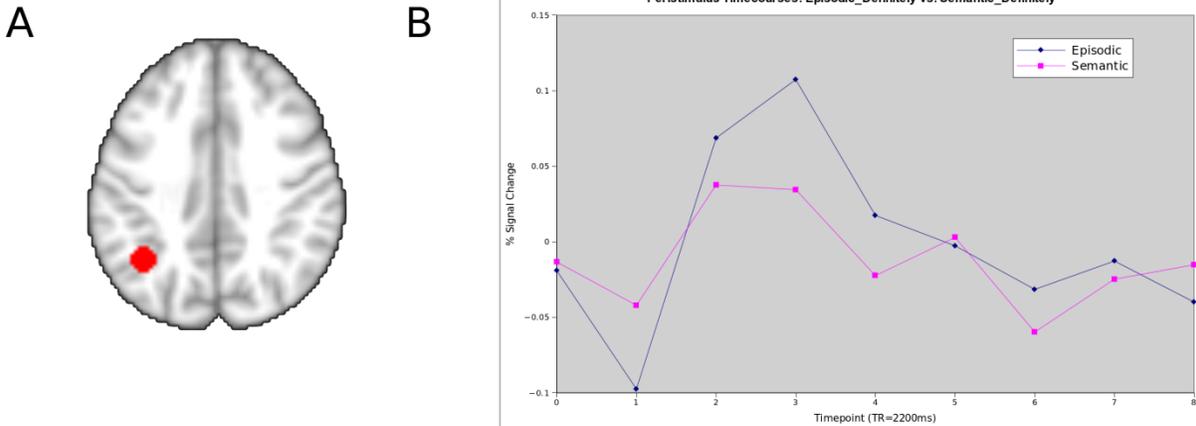


**Figure 2.** Regional activity associated with weak FOK responses (*Likely/Maybe* > *Definitely*) for episodic (red) and semantic (blue) facts that were correctly recognized. Shown in purple are regions of overlap which included bilateral dPPC, anterior cingulate and right vLPFC (circled regions). Activations are projected on to lateral (top) and medial (bottom) views of an inflated atlas using CARET software (Van Essen, 2005).



**Figure 3.** Direct contrasts of strong (*Definitely*) FOKs for correctly recognized episodic and semantic facts. Shown in red are regions evoked specifically by strong episodic FOKs (episodic>semantic), which included bilateral vPPC, mPC and left anterior PFC. Shown in blue are regions evoked specifically by strong semantic FOKs (semantic>episodic), which include the right anterior temporal gyrus. Activations are projected on to lateral (top) and medial (bottom) views of an inflated atlas using CARET software (Van Essen, 2005).

## Supplementary Material



**Supplementary Figure 1.** Peristimulus timecourses for Definitely responses were examined in each condition to determine whether response times differences may have reflected poorer fit in the Semantic condition due to delayed response onset. (A) An 8-mm ROI was derived from the peak local maximum z-score resulting from the contrast of *Definitely* > *Likely/Maybe* (MNI coordinates  $x=-38, y=-56, z=34$ ). Percent signal change over the course of 8 TRs (TR=2200ms) was extracted from Definitely trials for each subject. (B) Timecourses show that the primary difference between conditions was in the response magnitude rather than onset.

## CHAPTER 4: STUDY 3

### Abstract

In fMRI analyses, successful retrieval of episodic memories (hits > correct rejections) activates broad regions in the posterior parietal cortex (PPC). To distinguish more succinctly retrieval-related PPC activity, we compared memory for recently learned locations with familiar locations. Participants studied photographs of previously unfamiliar buildings, and later made recognition judgments with confidence ratings for these recently learned items, personally familiar buildings (frequently encountered campus buildings), and new buildings. Retrieval-related activation for recently studied locations was observed in the anterior angular gyrus and posterior precuneus, whereas retrieval of familiar locations activated more posterior regions of the angular gyrus and an anterior region of the precuneus. These findings of dissociable activations for information acquired during a specific learning episode and those occurring during retrieval of familiar locations demonstrate the existence of functionally heterogeneous areas within the lateral and medial PPC which are engaged during memory retrieval.

### Introduction

In neuroimaging studies of memory, retrieval-related activity is prominent in the posterior parietal cortex (PPC). Such activity has been associated with the *successful retrieval effect* in which correctly recognized items (hits) are compared to correct rejections (CRs) (Henson et al., 1999; Konishi et al., 2000). Retrieval-related activity has been further dissociated within the PPC with highly confident recollections localized in the ventral PPC (vPPC) and activity associated with weaker, more effortful retrieval localized in the dorsal PPC (dPPC) (Wheeler and Buckner, 2003; Spaniol et al., 2009; Kim and Cabeza, 2009).

The successful retrieval effect has almost exclusively been assessed using explicit memory tests of recently learned material. Yet vPPC activations does occur during implicit tests (Elman and Shimamura, 2011), as well as for false recognitions (Wheeler and Buckner, 2003; Kahn et al., 2004). Also, Elman et al. (2012) compared retrieval of well-learned (semantic) facts with retrieval of recently learned (episodic) facts. Activity in the vPPC was greater for episodic facts than semantic facts, suggesting that this region plays a particular role in recollecting specific episodic events.

Several theories have been proposed to account for the role of the PPC in episodic retrieval. The *Attention to Memory* theory (*AtoM*, Ciaramelli et al., 2008; Cabeza et al., 2008) suggests that the dPPC is part of a frontoparietal circuit involved in top-down or goal-directed retrieval processes, whereas the vPPC reacts to a “bottom-up” feed of activated memories. These bottom-up activations are initiated by sensory cues or by episodic features retrieved by way of medial temporal lobe (MTL) bindings. The *Episodic Buffer* theory (*E-BUFF*, Vilberg and Rugg, 2008) draws on Baddeley’s working memory model (Baddeley, 2000) in which a short-term store acts as a temporary repository of multimodal episodic features. According to E-BUFF, the vPPC acts as an episodic buffer which is particularly involved during recollective responses as this buffer maintains online event features during retrieval (Vilberg and Rugg, 2008). The dPPC is presumed to reflect non-specific processes involved in both recollection and familiarity.

Recently, Shimamura (2011) proposed CoBRA theory in which the vPPC acts as a convergence zone involved in the *cortical binding of relational activity*. At the time of initial encoding, relevant event features are monitored and activated by the prefrontal cortex (PFC) (see Shimamura, 2000; Miller and Cohen, 2001), with the binding of these features initiated by links

to the MTL (Eichenbaum et al., 1992; Squire and Alvarez, 1995; Shimamura, 2010). Through reminiscence or replay, vPPC bindings are established across event features, such that an episodic memory becomes less dependent on MTL bindings and develops (i.e., consolidates) as a cortically encapsulated representation. At retrieval, strong episodic recollections depend upon vPPC bindings for the reinstatement of event features specific to a prior episode or experience.

To explore further the role of the vPPC in retrieving specific episodic features, we compared memory for locations that were learned during a recent episode (photographs of previously unfamiliar buildings) with memory for familiar locations (campus buildings encountered many times during a student's daily experience). Recognition of frequently encountered buildings, though autobiographical in nature, are likely represented widely as spatial knowledge, whereas memory for studied material is tied to a specific episodic event (i.e., the learning session). The present study addressed the degree to which vPPC activity associated with retrieval of spatial information learned during a single episodic event is the same or different from retrieval of memory for frequently encountered locations. If indeed the vPPC is involved in binding item information with contextual information from a specific event, we would expect greater activity within the angular gyrus for the studied buildings.

## **Methods**

### ***Participants***

Nineteen healthy subjects were included in this study (mean age 21.63 years, range 19-29 years; 10 females). Four additional subjects were excluded from analysis due to excessive head motion and scanner artifact, and a further four subjects were excluded due to poor behavioral performance. Recruitment was conducted via advertisement on the Department of Psychology website (<http://psychology.berkeley.edu/rsvp>), with the criterion that they had been enrolled at UC Berkeley for at least two years and were familiar with the campus. All subjects were native English speakers and were right-handed. None of the subjects reported a history of neuropsychiatric disorders or brain injury or having recently taken psychoactive medication. Subjects were paid for their participation and gave informed consent according to guidelines approved by the UC Berkeley Office for the Protection of Human Subjects.

### ***Stimuli***

Ninety photographs of buildings were used in this study. Of these, 30 consisted of buildings from the UC Berkeley campus considered to be very familiar amongst students were used for the “Personally Familiar” locations. The remaining 60 photographs consisted of unfamiliar buildings taken at the CSU East Bay and Mills College campuses and downloaded from the web. Both the familiarity of the UC Berkeley buildings and the unfamiliarity of the other set of buildings were verified by a follow-up questionnaire at the end of the experiment. Half of the unfamiliar buildings were presented during a study phase and comprised the “Studied” items, while the other buildings were presented only at test and used as “New” items in a recognition test. Buildings used in the “Studied” and “New” sets were counterbalanced across subjects.

### ***Behavioral Procedure***

All trials were presented using *E-Prime 2 Professional* software (<http://www.pstnet.com/eprime.cfm>). Prior to scanning, participants were presented a study phase in which the 30 study buildings were presented two times each in a pseudo-random order.

On each trial, participants were shown a building and given 4000ms to determine whether it was the first or second presentation. Trials were separated by a 1000ms blank screen (see Figure 1).

In the scanner, approximately 30 minutes after the study phase, participants were given a recognition test. A total of 90 test items (30 Studied, 30 Personal, 30 New) were presented in two scanning blocks (see Figure 1). Each trial consisted of a photograph of a building for 3500ms followed by a central fixation cross presented for a jittered ITI (900-5300ms, mean=1975.5ms). Participants were asked to rate each item with respect to having “*Definitely seen the building before*” (referred to as high confidence (HC) hits), “*Maybe seen the building before*” (referred to as low confidence (LC) hits), or “*Definitely not seen the building before*” (referred to as “new”). These response options map onto those associated with the Remember/Know paradigm, though they are less theoretically motivated, as they do not necessarily imply a discrete, dual-process interpretation (see Shimamura, 2010). Responses were made using key-presses on a response box with finger-key-press mappings counterbalanced across subjects.

After scanning, we administered a questionnaire regarding how long participants had been enrolled at UC Berkeley and whether they had previously visited the CSU East Bay campus or Mills College. No participants reported having visited these other campuses.

### ***fMRI Acquisition***

Subjects were scanned with a 3T Siemens (Erlangen, Germany) Trio scanner housed at the UC Berkeley Brain Imaging Center. For each of the two functional runs, we used a T2\*-weighted echo-planar imaging (EPI) sequence [TR=2200ms; TE=26ms; flip angle=80°; matrix=100x100; FOV=210mm; 3mm slice thickness] with GRAPPA [acceleration factor 2]. Thirty-five axial slices oriented to the AC-PC were acquired in a sequential descending order giving whole brain coverage. A total of 130 volumes were collected during each of the functional imaging runs. The first nine volumes of each run were discarded to allow for magnetization preparation. A high resolution magnetization-prepared rapid-acquisition gradient echo (MPRAGE) [TR=2300ms; TE=2.98; matrix=256x256; FOV=256; sagittal plane; slice thickness=1 mm; 160 slices] and a gradient-echo multislice (GEMS) [TR=250ms; TE=22; matrix=256x256; FOV=256; 3mm slice thickness, 37 slices] were collected for registration purposes.

### ***fMRI Data Analysis***

Data were preprocessed and analyzed with the FSL toolbox v4.1.7 (<http://www.fmrib.ox.ac.uk/fsl>; (Smith et al., 2004). Motion correction was performed with MCFLIRT, aligning all images to the middle slice with rigid body transformation. Slice timing correction was performed using (Hanning windowed) sinc interpolation to shift each slice in the volume in reference to the middle of the TR period. BET (brain extraction tool) was then used to create a mask of the brain from the first volume of each time series and used to separate brain from surrounding skull and tissue in each volume. All images were spatially smoothed with a 5mm FWHM Gaussian kernel to reduce noise and allow group analysis. High-pass temporal filtering was performed using the local Gaussian-weighted fit of a running line to remove low frequency artifacts. Subject data was registered to standard space in a two-step process using FLIRT (FMRIB's Linear Image Registration Tool). First, EPIs were registered to each subject's skull-stripped high resolution T1-weighted image. Second, subject's T1-weighted images were registered to standard (MNI) space (FSL's MNI152 template). The two registrations were then combined to take the subject's EPI images and run-level statistical maps into standard space.

A multi-level, mixed effects general linear model was run using FILM (FMRIB's Improved Linear Model) which treated subjects as random effects. Individual runs from the test phase were modeled in subject space and resulting statistical maps were registered to standard space for higher level analysis. Regressors of interest were obtained by convolving stimulus onset times with FSL's double-gamma hemodynamic response function and the temporal derivative. Each correct response type was modeled separately for both "Studied" and "Personal" conditions of both confidence levels (HC or LC) and for correctly identified "new" items. Incorrect responses and trials with no response were modeled as regressors of no interest. Motion parameters were included as additional confound variables and temporal autocorrelation was removed through pre-whitening. Contrasts were entered comparing both Studied and Personal items to new items as well as direct comparisons of Studied and Personal items to each other.

A second level analysis combined the runs for each subject using a one-sample t-test, treating runs as fixed effects. Third-level group statistical maps were created for each contrast using FLAME (FMRIB's Local Analysis of Mixed Effects). FLAME implements a Bayesian two-stage model, the first being a fast approach to the posterior probabilities of activation for each voxel and the second uses a slower Markov Chain Monte Carlo (MCMC) based analysis for all voxels identified as being near threshold in the first stage. The whole brain family-wise error was corrected to  $P < .05$  using Gaussian Random Field theory with a cluster forming threshold of  $z > 2.3$ .

## Results

### *Behavioral Results*

Recognition performance was comparable between Studied (85.6% correct) and Personal (90.5% correct) items [ $t(18) = -1.551, p = 0.13$ ] (see Table 1). HC ratings were given to 71.5% of Studied items and 80.8% of Personal items, suggesting that participants often judged that an item was "definitely" recognized. Response latencies were also comparable between the two sets (Studied = 1532 ms; Personal = 1469 ms, [ $t(18) = 1.095, p = 0.28$ ]). However, response latencies for New items (1800 ms) were significantly slower than latencies for the Studied and Personal sets ( $t(18) > 5.2, p < 0.001$ ).

### *fMRI Results*

Retrieval-related activations (Hits-CRs) were assessed separately for Studied and Personal items (see Figure 2). Within the vPPC, Studied items activated a large cluster centered on the anterior angular gyrus and extending into adjacent regions in the supramarginal gyrus and intraparietal sulcus (IPS). In the PFC, active regions included the left dorsolateral prefrontal cortex (dlPFC), frontal pole, and medial prefrontal cortex (mPFC). Significant activations also occurred in medial regions, including the anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), and precuneus (see Table 3 for full set of activations).

For Personal items, retrieval-related activations within the vPPC occurred in more posterior regions than those observed for Studied items. Specifically, Personal items activated the posterior angular gyrus and adjacent regions in the lateral occipital complex (LOC). Within the angular gyrus, mid-regions were activated by both Personal and Studied items (see Figure 2). Within the PFC, Personal items activated left dlPFC (inferior frontal gyrus) and polar regions. Particularly extensive regions of activation were observed in medial regions, including ventromedial PFC, anterior precuneus and adjacent regions in the retrosplenial cortex (see Table 3).

To assess retrieval-related activations specific to Studied and Personal items, we performed bidirectional contrasts between these two conditions for HC hits. We interpreted these HC contrasts to define regions associated with very strong, "recollective" responses distinct to each condition. As was shown for overall hits>CRs, HC hits for Studied items relative to Personal items activated bilateral regions in the anterior angular gyrus and adjacent regions in the supramarginal gyrus and IPS, whereas the reverse contrast (HC Personal items>HC Studied items) activated posterior angular gyrus and LOC. Dissociable activations were also observed in medial regions, as HC Studied items specifically activated right dlPFC, anterior PFC (aPFC), and posterior cingulate, whereas HC Personal items activated primarily left superior and bilateral medial frontal cortex as well as bilateral activations in the anterior precuneus, retrosplenial cortex, medial PFC, and parahippocampal gyrus (for full set of activation sites, see Table 3). We additionally compared Studied and Personal items collapsed across confidence levels to assess more broadly retrieval-related activity. This contrast resulted in similar areas of activity with the addition of clusters in the dPPC and posterior precuneus for the Studied > Personal contrast (see Supplemental Figure S1 and Table S1 for full set of activations).

## Discussion

Recognition memory was assessed for recently studied locations (photographs of unfamiliar buildings) and for personally familiar locations (campus buildings). For each test item, participants judged whether they had previously seen the item and rated their confidence (HC hits= definitely seen the building before). With respect to the successful retrieval effect (hits>CRs), Studied items activated a vPPC region centered in the anterior angular gyrus and extending into the supramarginal gyrus and IPS. This region was distinct from retrieval-related activations for Personal items, which activated posterior angular gyrus and adjacent regions in the LOC. The dissociation of vPPC activity for Studied and Personal items was particularly apparent when HC hits were contrasted between conditions (see Figure 3). Previous findings have implicated the vPPC during recollection-based episodic retrieval (Vilberg and Rugg, 2008; Cabeza, 2008; Shimamura, 2011). The present findings point to a more focal region centered on the anterior angular gyrus as being particularly associated with retrieval of information from a specific episodic context (see also Hutchinson et al., 2009; Wheeler and Buckner, 2004; Vilberg and Rugg, 2008).

Unlike Studied items, retrieval of personally familiar locations activated more posterior vPPC regions centered on the posterior angular gyrus and extending into the LOC. Such dissociable activations can be related to extant findings, such as those by Nelson et al. (2010) in which a combined resting state/fMRI functional connectivity analysis was used to parcellate the left PPC into functionally distinct sub-regions. They found functional networks linked to the anterior and posterior inferior parietal lobule adjacent to the IPS and that were dissociable from another network tied to more inferior and posterior angular gyrus and extending into LOC. In a meta-analysis of memory retrieval tasks, McDermott et al. (2009) found that retrieval-related activity for recently studied, lab-based material was localized in anterior regions of the angular gyrus, whereas retrieval of autobiographical information was localized more posteriorly into the LOC. Finally, our results are consistent with findings of an anterior-posterior dissociation in which successful episodic retrieval was linked to anterior and superior vPPC regions, whereas self-referential processing activated inferior and posterior regions (Sajonz et al., 2010b).

Personal items activated broad regions on the medial surface bilaterally. Yet as in the vPPC, these medial activations were dissociable from those related to Studied items. Specifically, Personal items activated anterior precuneus and retrosplenial cortex, whereas

Studied items activated posterior cingulate gyrus and, when collapsing across confidence levels, posterior precuneus (see Figure 3 and Supplementary Figure S1). In a recent review of the neurobehavioral correlates of the precuneus, the posterior precuneus was associated with retrieval processes regardless of imageable characteristics (Cavanna and Trimble, 2006; see also Summerfield et al., 2009). Such findings suggest a posterior-anterior distinction on the medial surface in which posterior activations (posterior precuneus, posterior cingulate gyrus) reflect successful episodic retrieval, whereas more anterior activations (anterior precuneus; retrosplenial cortex) reflect self-referential or visuo-spatial processing, including autobiographical memory and mental imagery from a first-person perspective (Maguire, 2001; Cabeza et al., 2004; Svoboda et al., 2006; Summerfield et al., 2009; Sajonz et al., 2010b).

Interestingly, significant bilateral activity was observed in the parahippocampal gyrus for Personal items but not for Studied items. Such activations may reflect the contribution of this region to spatial processing, such as scene reconstruction and spatial integration (Gilboa, 2004; Cabeza and St. Jacques, 2007; Henderson et al., 2008; Vann et al., 2009; Summerfield et al., 2010). This region has also been linked to activity in the PPC and retrosplenial cortex, forming a proposed circuit related to processing spatial coordinates (Maguire et al., 1998; Burgess et al., 2001a, 2001b). It is likely that recognition of personally familiar buildings, such as the ones presented in our study, activated these broad cortical networks associated with scene integration and egocentric spatial representation of the surrounding environment each building was located within.

With respect to retrieval-related activity in the PFC, the right aPFC and dlPFC were more active for Studied items, whereas the mPFC and vmPFC were more active for Personal items (see Figure 3). These findings are broadly consistent with meta-analytic comparisons of lab-based vs. autobiographical memory (Gilboa, 2004; Svoboda et al., 2006; McDermott et al., 2009). From these extant findings, medial prefrontal activation reflects self-referential processing, which is consistent with our conceptualization that personally familiar locations depend more on indexing autobiographical memory. Furthermore, Moscovitch and Winocur (2002; see also Gilboa, 2004) proposed that this region underlies “felt rightness,” the ability to gauge quickly the accuracy of a response without the need for in-depth monitoring or verification which may arise from subjects’ strong familiarity. This proposal, however, is in contrast to aPFC and dlPFC activations in the Studied condition which are thought to reflect the greater need for monitoring and verification of accuracy in lab-based tests (Gilboa, 2004; Svoboda et al., 2006), a view further supported by the lower proportion of high confidence responses and greater engagement of the dPPC during the Studied condition.

As task instructions and stimuli (i.e., photographs of buildings) were identical between Personal and Studied conditions, the essential distinction between the two conditions is that retrieval of Studied items was based on accessing a specific episodic context, whereas retrieval of Personal items was based on accessing more widely represented spatial knowledge and personal past. As such, the present findings can be related to CoBRA theory (Shimamura, 2011), as both Studied and Personal items should depend on cortical binding, though by nature of retrieving from a specific episodic event, Studied items should activate vPPC regions more than Personal items. In particular, a Studied item judged as a high confidence hit would depend greatly on vPPC bindings as such a response would be based on an item that was definitely recognized as being presented during the study episode. As shown in Figure 3, the anterior angular gyrus was specifically involved in the binding of items tied to the study episode. As mentioned in the introduction, we previously contrasted retrieval-related activity for recently

learned and familiar facts and found greater vPPC activity for the contextually-bound, episodically based facts compared to previously familiar facts (Elman et al., 2012). In contrast to CoBRA, the E-BUFF and AtoM models do not easily account for the pattern of results found here. According to E-BUFF, the vPPC acts upon memories independent of modality. Therefore, activation should not vary based on the type of memory being accessed, but rather the amount of successfully retrieved information. Similarly, AtoM posits that the vPPC responds primarily to relevance, but is presumably independent of memory type. Under these models, we might then expect greater activation within the vPPC during the Personal condition as there is almost certainly more information retrieved for these items. That is, participants are likely have more knowledge of the buildings used in the Personal condition through repeated real life encounters compared to the relatively impoverished information available for encoding during the two viewings of pictures used in the Studied condition. Memories for items used in the Personal condition may include detailed knowledge of a building’s appearance from multiple viewpoints, personal associations with the building (e.g. classes held in the building) and knowledge of the surrounding environment. That they have strong memories for Personal items is further supported by the greater amount of high confidence responses given for this condition. Of the three models, only CoBRA would predict that the type of memories being retrieved (e.g. a memory bound to a specific context) may be a better predictor of vPPC activity than the amount of information retrieved.

In summary, the present study delineates the boundary conditions underlying retrieval-related activity associated with episodic memory. Dissociable activity was observed during retrieval of recently learned and familiar locations. In the vPPC, retrieval of recently learned locations activated anterior angular gyrus, whereas retrieval of personally familiar locations activated posterior angular gyrus and LOC. In the medial parietal cortex, recently learned items activated posterior cingulate and anterior precuneus, whereas familiar items activated more anterior regions in the posterior cingulate and retrosplenial cortex. Often, episodic memory contains a mixture of contextually-bound details and visuo-spatial or self-referential information which may vary in proportion based on task-specific characteristics. While the relative degree to which these elements are present may help differences in activation foci across previous studies, we have attempted to isolate these component processes. As both task demands and stimulus features were comparable across conditions, these dissociable effects point to the role of the anterior angular gyrus and posterior medial parietal cortex in mediating the retrieval of information from a specific episodic context.

## Figures and Tables

	High	Low	Old*	New
Studied	71.3%	14.3%	85.6%	14.4%
Personal	80.5%	10%	90.5%	9.5%
New	28.2%	38.3%	33.5%	66.5%

**Table 1.** Behavioral results from the test phase of the experiment. Proportion of response types for each condition is listed. The “Old” column refers to the combined percent of “High” and “Low” confidence responses. Recognition performance was similar for Studied and Personal items. However, subjects were significantly more likely to give high confidence responses for Personal items than Studied items.

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z-score</b>
<i>Studied Items (Hits &gt; CRs)</i>					
Angular Gyrus	L	-54	-56	30	4.14
	L	-38	-54	34	3.53
	L	-52	-54	52	3.38
	R	44	-50	48	3.45
Anterior Cingulate	R	10	40	16	3.74
Frontal Orbital Cortex	L	-24	22	-24	3.91
	L	-32	16	-22	3.52
	L	-14	34	-22	3.25
	L	-18	32	-24	3.13
	L	-28	20	-12	2.78
Frontal Pole	L	0	58	20	3.77
	L	-28	46	-18	3.66
	L	-40	44	-10	3.56
	L	-42	56	4	3.24
	L	-42	54	8	3.19
	L	-40	50	2	3.16
	L	-48	38	16	3.16
Inferior Temporal Gyrus	R	56	-36	-14	3.31
Insular Cortex	L	-30	8	-16	3.27
Lateral Occipital Cortex	L	-42	-60	44	3.69
	L	-42	-70	34	3.48
	R	40	-66	46	3.54
Middle Temporal Gyrus	L	-66	-36	-18	3.89
	L	-60	-34	-8	3.78
	L	-60	-30	-8	3.6

	L	-66	-32	-14	3.45
	L	-56	-34	-6	3.37
	L	-66	-28	-10	3.18
	R	60	-44	-2	3.82
	R	64	-26	-16	3.46
	R	72	-28	-16	3.44
	R	66	-42	-6	3.34
	R	72	-24	-12	3.24
Paracingulate Gyrus	L	-2	48	10	3.49
	L	-6	34	26	3.45
	R	2	44	18	3.66
	R	6	50	-2	3.55
Posterior Cingulate	L	-4	-30	44	3.68
	L	-2	-40	40	3.65
	L	0	-28	44	3.61
	L	0	-50	32	3.53
	R	4	-26	44	3.64
Precuneous Cortex	L	-8	-72	28	3.73
Supramarginal Gyrus	L	-56	-50	24	3.5
	R	42	-44	34	3.55
	R	46	-42	48	3.54
	R	54	-36	48	3.52
	R	56	-38	42	3.31
<i>Personal Items (Hits&gt;CRs)</i>					
Frontal Medial Cortex	L	-6	54	-16	4.76
	L	-8	38	-16	4.75
	L	-50	28	-12	3.48
Frontal Pole	L	-4	58	6	5.27

	L	-4	58	0	4.98
	L	-2	56	-12	4.78
	L	-52	38	-2	3.76
Inferior Frontal Gyrus	L	-52	28	14	3.91
	L	-52	34	10	3.66
	L	-52	30	8	3.6
	L	-44	22	22	3.39
Lateral Occipital Cortex	L	-50	-72	30	5.11
	L	-38	-76	32	4.65
	L	-46	-80	30	4.47
	L	-54	-72	32	4.16
	L	-32	-86	32	4.12
	L	-38	-84	36	3.94
	R	52	-64	18	3.91
	R	50	-64	22	3.87
	R	56	-64	18	3.87
	R	40	-78	42	3.55
	R	44	-72	28	3.29
	R	40	-78	34	3.08
Middle Temporal Gyrus	L	-62	-8	-20	4.42
	L	-54	0	-26	4.35
	L	-52	-8	-24	3.92
	L	-56	-8	-14	3.52
Paracingulate Gyrus	L	-8	32	-12	4.84
Posterior Cingulate	L	-6	-56	28	5.39
	L	-2	-54	20	4.92
Precuneous Cortex	L	-2	-64	34	5.22
	L	-4	-54	12	4.86
	L	-14	-58	18	4.68
	L	-4	-62	42	4.67

Temporal Pole	L	-54	4	-30	3.37
	L	-50	18	-34	3.1

**Table 2.** Successful retrieval effect as indicated by peak activations of significant clusters from the contrasts for Studied Items (Hits>CRs) and Personal Items (Hits>CRs). Regions were derived from the Harvard-Oxford Cortical Atlas.

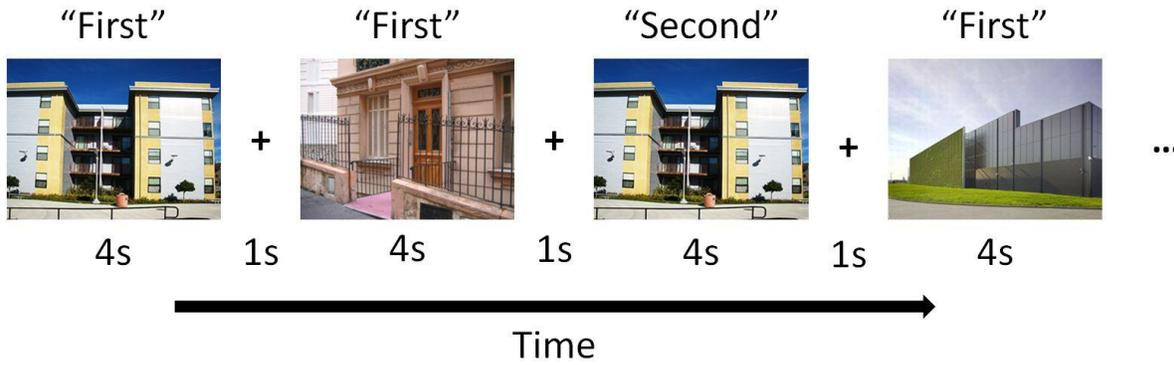
Region	Hemisphere	X (mm)	Y (mm)	Z (mm)	Z-score
<i>High Confidence Studied &gt; High Confidence Personal</i>					
Angular Gyrus	L	-40	-58	48	5.14
	L	-42	-48	36	3.34
	R	44	-50	46	5.17
Central Opercular Cortex	L	-48	-12	18	3.64
	R	58	-14	20	3.21
	R	68	-12	10	3.17
	R	60	-12	12	3.11
Frontal Orbital Cortex	R	46	20	-6	3.16
Frontal Pole	L	-36	50	0	3.62
	L	-40	56	6	3.42
	L	-34	58	-4	3.33
	L	-38	60	10	3.24
Frontal Pole	R	44	54	4	3.97
	R	42	58	8	3.71
	R	36	40	10	3.59
	R	38	56	-2	3.48
	R	38	46	12	3.25
	R	40	44	4	3.2
Heschl's Gyrus	L	-50	-26	10	3.21
Insular Cortex	R	28	16	8	3.65
	R	44	16	-10	3.4
	R	42	-2	-10	3.08

Lateral Occipital Cortex	L	-40	-66	52	3.66
Middle Frontal Gyrus	L	-40	38	30	3.7
	L	-42	30	28	3.4
Parietal Operculum Cortex	R	58	-22	16	3.79
	R	52	-20	22	3.6
Planum Polare	R	54	2	-2	3.6
Planum Temporale	L	-58	-24	12	3.41
Posterior Cingulate	L	-2	-36	24	3.44
	R	4	-20	26	4
	R	8	-26	26	3.99
	R	6	-40	22	2.57
	R	10	-36	22	2.49
Superior Parietal Lobule	L	-36	-54	52	4.33
	L	-32	-58	56	3.77
	L	-42	-48	50	3.63
	R	38	-44	54	3.71
	R	34	-52	54	3.12
Supramarginal Gyrus	L	-64	-32	26	4
	L	-60	-26	26	3.85
	L	-62	-28	20	3.81
	R	54	-22	26	3.86
	R	48	-28	44	3.29
	R	48	-38	48	3.26
	R	52	-34	56	3.16
Temporal Pole	R	46	12	-10	3.23
<i>High Confidence Personal &gt; High Confidence Studied</i>					
Angular Gyrus	L	-44	-62	16	2.85
Frontal Medial Cortex	L	-6	54	-10	5.83
	L	-8	46	-12	5.42
	L	-4	34	-16	5.38

	L	-2	50	-14	5.08
	R	4	48	-10	5.18
Frontal Pole	L	-18	40	44	4.18
	L	-18	44	42	3.98
Hippocampus	L	-24	-16	-20	3.56
	R	32	-20	-16	3.71
Lateral Occipital Cortex	L	-36	-82	30	5.38
	L	-50	-72	22	4.93
	L	-46	-78	24	4.49
	L	-40	-70	20	4.23
	L	-50	-76	34	3.63
	R	42	-82	28	4.34
	R	36	-82	32	4.25
	R	48	-68	22	3.89
	R	32	-88	32	3.66
	R	44	-62	22	3.54
	R	48	-74	24	3.5
Lingual Gyrus	L	-8	-58	4	5.7
	L	-12	-62	4	5.35
Middle Frontal Gyrus	L	-26	36	44	3.3
Paracingulate Gyrus	L	0	46	-10	5.46
Parahippocampal Gyrus	L	-20	-38	-18	4.57
	R	26	-38	-14	3.73
Precuneous Cortex	L	-6	-62	12	5.44
	L	-12	-60	14	5.31
	L	10	-52	4	5.17
	R	14	-58	16	6.1
Superior Frontal Gyrus	L	-22	22	44	4.01
	L	-16	38	34	3.38
	L	-22	22	34	2.94

**Table 3.** Peak activations of significant clusters from the contrasts of High confidence Studied vs. High confidence Personal responses. Regions were derived from the Harvard-Oxford Cortical Atlas.

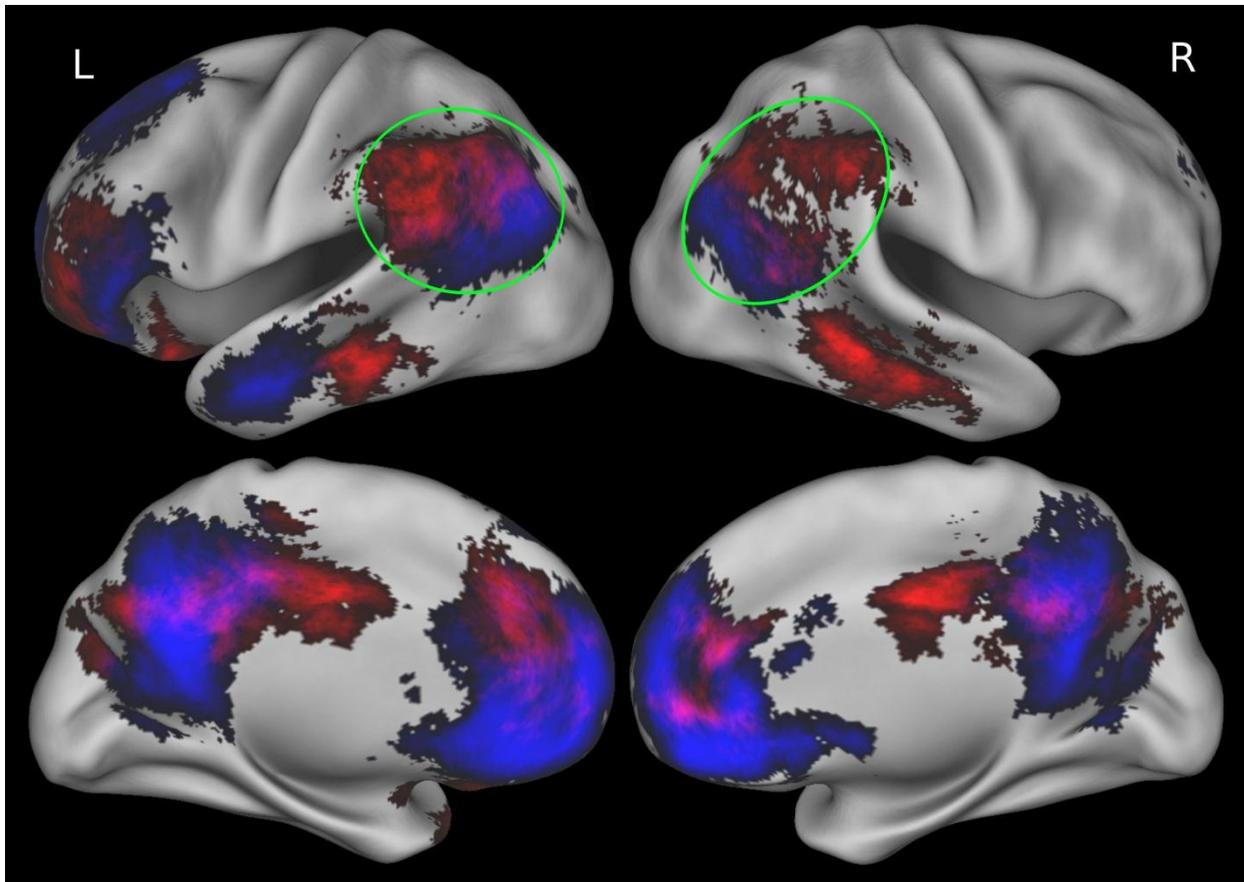
## Study Session:



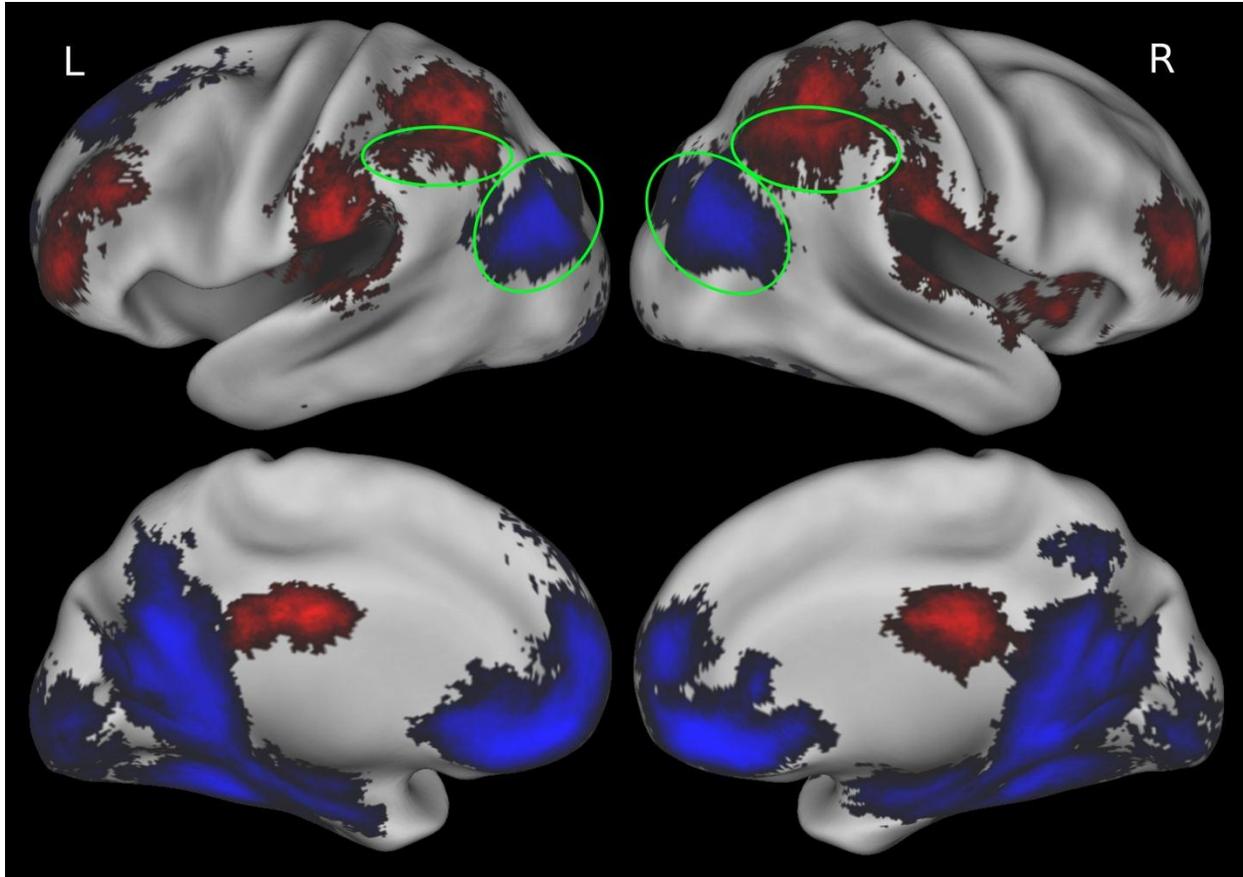
## Test Session:



**Figure 1.** The study session presented 30 photographs of previously unfamiliar buildings, each shown twice in a pseudo-random order. Subjects responded whether it was the first of second presentation for each. The test session took place approximately 30 minutes later in the fMRI scanner. Subjects were presented 30 Studied buildings, 30 Personally Familiar (from the UC Berkely campus), and 30 New buildings over two blocks. For each photograph, subjects were asked to respond whether they had “*Definitely seen the building before,*” “*Maybe seen the building before*” or “*Never seen the building before.*”



**Figure 2.** The successful retrieval effect (Hits>CRs) for Studied (red) and Personal (blue) Items with areas of overlap shown in purple. Within the vPPC (circled), Studied items activated anterior regions, whereas Personal items activated more posterior regions (with overlapping areas in mid-regions of the angular gyrus). Note extensive retrieval-related activations for Personal items in medial regions. Activations are projected on to lateral (top) and medial (bottom) views of an inflated atlas using CARET software (Van Essen, 2005).



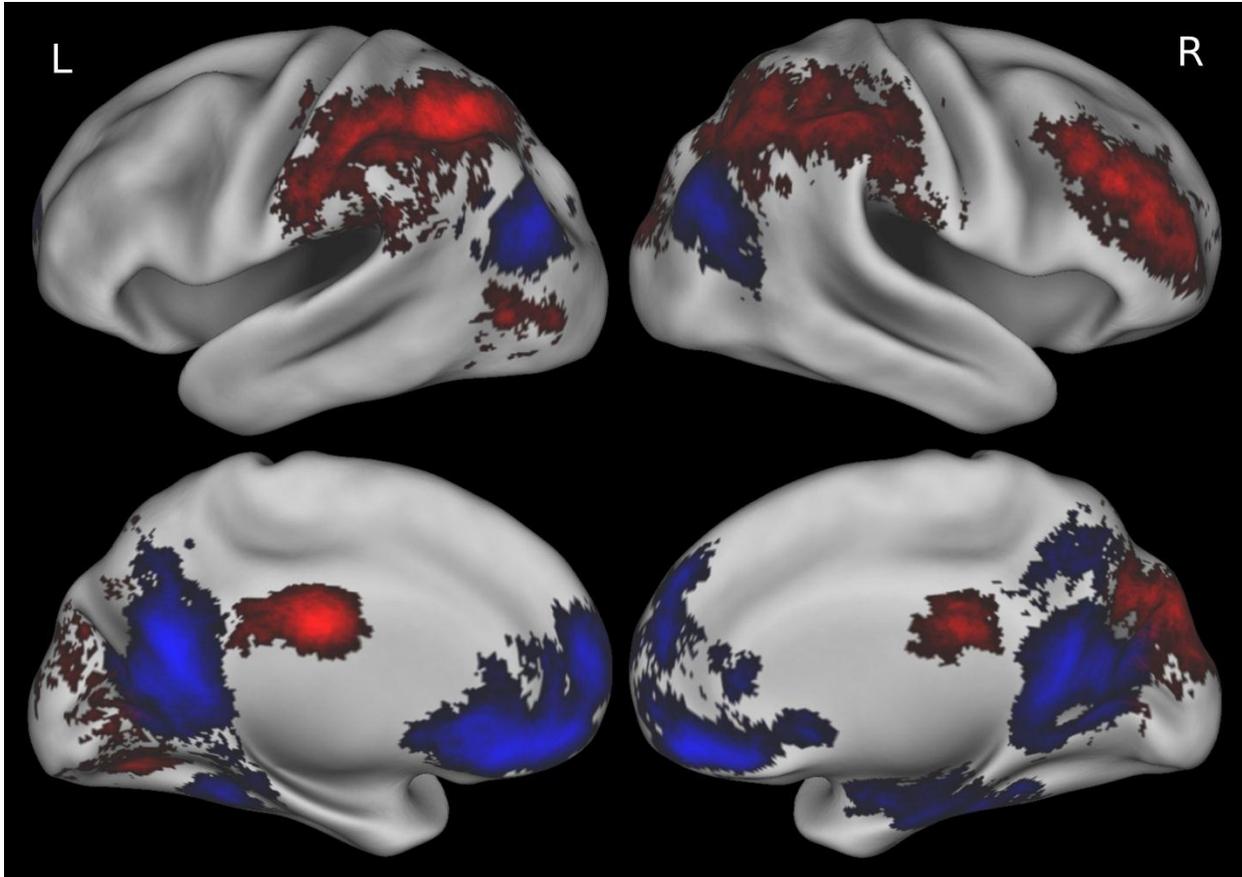
**Figure 3.** Clusters in which there was greater activity for Studied compared to Personal items (red) and Personal compared to Studied items (blue) when only assessing high confidence responses. Of particular interest are the anterior posterior dissociations within lateral vPPC (circled) and medial parietal cortices. All clusters were significant after correction for multiple comparisons. Activations are projected on to lateral (top) and medial (bottom) views of an inflated atlas using CARET software (Van Essen, 2005).

## Supplementary Material

<b>Region</b>	<b>Hemisphere</b>	<b>X (mm)</b>	<b>Y (mm)</b>	<b>Z (mm)</b>	<b>Z-score</b>
<i>Studied &gt; Personal</i>					
Angular Gyrus	L	-40	-56	40	4.01
	R	44	-50	48	4.31
Anterior Cingulate	L	-4	-16	26	4.04
Caudate	L	-14	-14	24	3.26
	L	-18	-20	26	2.62
Cuneal Cortex	R	16	-72	32	4.08
Frontal Pole	R	46	44	18	3.87
	R	44	40	20	3.82
Lateral Occipital Cortex	L	-40	-70	4	3.46
Lingual Gyrus	L	-24	-66	-4	4.37
	L	-30	-58	-2	3.58
	L	-20	-76	0	3.53
	L	-16	-86	-4	3.14
Middle Frontal Gyrus	R	46	22	32	3.8
	R	46	28	28	3.65
	R	46	18	38	3.47
	R	48	34	24	3.44
Occipital Fusiform Gyrus	L	-36	-60	2	3.17
Occipital Pole	R	12	-88	38	3.9
	R	24	-92	20	3.79
	R	8	-88	38	3.77
	R	12	-94	24	3.58
Postcentral Gyrus	L	-42	-34	42	3.99
	L	-44	-30	44	3.88
Posterior Cingulate	L	-2	-30	26	3.27
	R	4	-24	26	3.79
Precuneous Cortex	R	14	-68	32	4.19
Superior Parietal Lobule	L	-36	-50	54	3.83
	L	-36	-54	52	3.82
	L	-26	-58	50	3.82
	R	44	-38	56	4.35
Supramarginal Gyrus	R	48	-38	48	4.02
	R	52	-28	48	3.98
	R	50	-38	52	3.87
	R	54	-20	26	3.86
<i>Personal &gt; Studied</i>					
Frontal Medial Cortex	L	-6	42	-18	4.76
	L	-2	32	-20	4.48

	R	2	42	-18	4.46
	R	2	48	-14	4.41
	R	8	48	-16	4.17
Frontal Pole	R	2	56	-12	5.26
Lateral Occipital Cortex	L	-38	-80	30	4.51
	L	-44	-78	26	4.47
	L	-48	-78	20	4.29
	L	-52	-72	22	4.17
	L	-40	-76	22	4.14
	L	-34	-74	20	3.12
	R	44	-74	26	4.17
	R	48	-72	26	4.09
	R	56	-70	20	3.21
	R	52	-64	16	3.06
	R	48	-66	14	3.03
	R	42	-76	38	2.88
Parahippocampal Gyrus	R	24	-14	-24	3.3
	R	30	-10	-22	3.07
Precuneous Cortex	L	-6	-58	10	5.08
	L	-12	-60	6	5.04
	L	-10	-58	12	4.93
	L	-4	-60	16	4.69
	R	10	-58	14	5.2
	R	10	-52	8	4.78
Temporal Fusiform Cortex	R	38	-32	-24	3.51
	R	32	-26	-24	3.31
	R	32	-26	-30	3.06
Temporal Occipital Fusiform Cortex	R	26	-40	-18	3.12

**Table S1.** Peak activations of significant clusters from the contrasts of Studied vs. Personal collapsing across responses of high and low confidence. Regions were derived from the Harvard-Oxford Cortical Atlas.



**Figure S1.** Clusters in which there was greater activity for Studied compared to Personal items (red) and Personal compared to Studied items (blue) when collapsing across high and low confidence responses. Of particular interest are the anterior posterior dissociations within lateral vPPC and medial parietal cortices. All clusters were significant after correction for multiple comparisons. Activations are projected on to lateral (top) and medial (bottom) views of an inflated atlas using CARET software (Van Essen, 2005).

## CHAPTER 5: GENERAL DISCUSSION

The studies presented here serve to delineate the boundary conditions under which the PPC is involved in episodic memory retrieval. These results help to inform current models of PPC function by dissociating the component processes often involved in episodic memory that specifically engage this region. Furthermore, these results suggest a previously neglected functional heterogeneity within the PPC such that the expected location of activation may depend to a large degree on the task and information being assessed.

### *Effect of task and information type*

Study 1 set out to determine whether an effortful memory search is required to elicit a PPC response. While it was apparent that PPC activity may be present when retrieval is not the primary goal of a task, it does depend on the degree to which mnemonic status is relevant to task goals. Thus, a low-level form of retrieval likely occurs regardless for all items regardless of task, yet only those holding high task relevance are sufficient to engage the PPC. This would suggest that while the PPC is involved in memory, it is downstream of initial retrieval attempts.

A peri-retrieval role is further supported by the results of Study 2. Although subjects were not required to explicitly recall remembered information, the PPC appeared to be more engaged during trials in which subjects were likely assessing knowledge for the context in which information was learned. As the item information potentially recallable was matched between conditions, the differences in PPC activity presumably arise from the extent to which retrieval cues are associated with contextual cues from the learning event. Study 3 provided further evidence for the importance of reinstating contextual information. An event memory contains many visual and spatial details, but crucially, is bound to a particular time and place. It is this memory for a unique occurrence of an encapsulated event which appears to drive PPC activity. Furthermore, the amount of cross-modal association may be particularly important to engaging this region. There is additional evidence that a more posterior area extending into lateral occipital cortex is responsible for processing the visuo-spatial information often accompanying episodic memories.

These results are consistent with recent meta-analytic findings that the anterior angular gyrus shows greater activity for lab-based tests of recently learned material compared to more distant autobiographical memories (McDermott et al., 2009). Whereas visuo-spatial detail may be similar between these two forms of memory, recently learned material tends to have more defined boundaries within one's memory. The difference between these forms of memory may be roughly aligned with findings of greater vPPC involvement during recollection compared to familiarity (Wheeler and Buckner, 2004). It is often assumed that this increase in activity is driven by greater amounts of retrieved information associated with recollection (Vilberg and Rugg, 2007). However, the alternative is that it is the linking of item information to a distinct time and place which is responsible for this pattern of results. Indeed, it is the presence of both item and contextual details which distinguishes recollection from familiarity. This integrative mechanism may also serve to elucidate underlying causes for the curious finding that simply perceiving an item as old is sufficient to drive PPC activity, regardless of accuracy (Wheeler and Buckner, 2003). As shown in Study 2, it is not necessary to recall specific item information in order to elicit a PPC response. Reinstated contextual information relating to a previous learning event may be incorrectly bound to a novel item, leading to a perceived quality of "oldness" in the

absence of actual item retrieval. Thus, perceived oldness effects may be explained by this associative binding process without requiring any spurious item retrieval.

#### *Neuroanatomical distinctions within the ventral posterior parietal cortex*

Recently, the neuroanatomical divisions within the parietal cortex have gained more attention (Summerfield et al., 2009; Sajonz et al., 2010b; Nelson et al., 2010). An initial distinction between dorsal and ventral parietal cortex was expanded to include distinctions between anterior and posterior divisions, with activity in the supramarginal gyrus associated with attentional tasks and memory-related activity localized to the angular gyrus (Wheeler and Buckner, 2004; Hutchinson et al., 2009; Kim and Cabeza, 2009). However, results from Studies 2 and 3 support claims of further sub-divisions even within the angular gyrus (McDermott et al., 2009; Sajonz et al., 2010b; Nelson et al., 2010). Taken together the findings here suggest that the anterior angular gyrus is more specifically involved in the retrieval of encapsulated event memories bound to a particular time and place. In contrast, the posterior angular gyrus may process visuo-spatial details and self-referential processing associated with a memory, particularly from an egocentric perspective (Burgess et al., 2001a; Summerfield et al., 2010). Thus, the extent to which a task may emphasize information processed by dissociable yet neighboring regions must be taken in to account when comparing results across studies. Future work may also benefit from more spatially specific reporting of results.

#### *Links to neuropsychological findings*

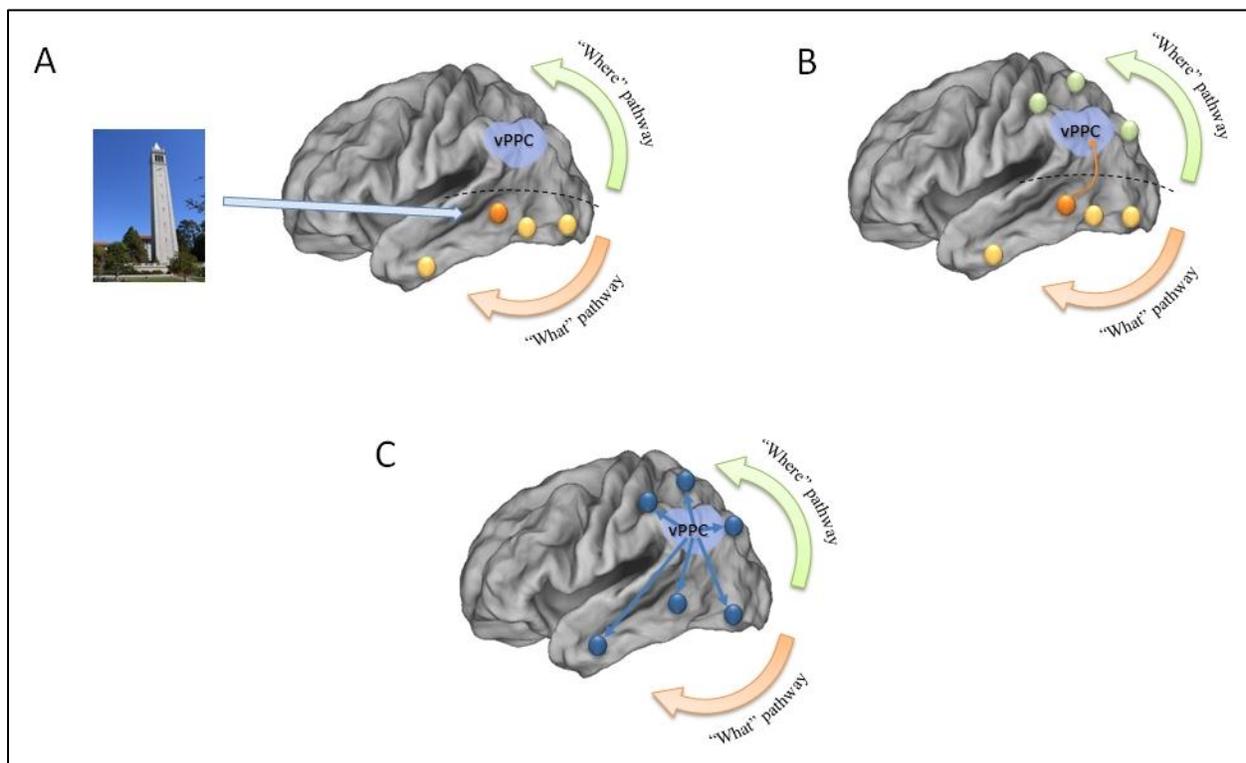
A functional heterogeneity within the PPC would serve to explain the seemingly variable patterns of results derived from lesion studies if different processes are disrupted due to relatively small differences in the origin and extent of damage. One of the more compelling results arising from patient work is that subjective confidence in memory may be lower following bilateral PPC damage despite normal memory accuracy (Simons et al., 2010). Additionally, patients tend to produce fewer event details during free recall, yet perform normally when cued given cues. A peri-retrieval role in which the vPPC facilitates the binding of item and context information may provide insight into these behavioral deficits. The results from Study 1 would suggest that retrieval processes occur independently of vPPC activation (at least initial). Therefore, damage to the anterior angular gyrus should not be expected to disrupt retrieval per se, but rather downstream processes. Results from Studies 2 and 3 indicate that the vPPC helps form a coherent and distinct event representation out of individual pieces of information. While the full set of encoded information remains available in memory, an inability to bind these ensembles to a specific time and place may cause event memories to be experienced as particularly weak.

Evidence from the spatial cognition literature may provide further evidence for a peri-retrieval binding role. For example, PPC lesions in rats have been found to not impair memory for object or locations individually, but rather the combination of these two types of information (Long et al., 1998). Turning to humans, bilateral damage to the angular gyrus may result in Balint's syndrome, a severe form of spatial impairment. Patients with Balint's syndrome are unable to perceive multiple objects at the same time (Treisman, 1996, 1998; Robertson et al., 1997). It is thought that the underlying cause of the deficit is an inability to properly bind object features such as color and shape to a particular point in space. It is plausible that this binding mechanism may act similarly upon internally generated information arising from memory as it does with externally perceived information.

One of the hallmark symptoms of Alzheimer’s Disease is a severe impairment in memory, although this is often attributed to medial temporal lobe damage. However, extensive functional abnormalities and neurological damage appear throughout the default mode network, including the angular gyrus (Desgranges et al., 2002; Lind et al., 2006; Fjell et al., 2009; Sperling et al., 2009). While episodic memory as a whole is affected, it appears that recollection memory is particularly impaired (Westerberg et al., 2006), which may be a function of reduced vPPC and hippocampal contributions. Autobiographical memory seems to be similarly affected in AD (Eustache et al., 2004). However, remote autobiographical memories appear to be spared when patients are able to rely on more semantic representations of these events (Meulenbroek et al., 2010). Study 3 demonstrates memories for specific occurrences may rely on anterior angular gyrus regions susceptible to damage in AD, autobiographical memories of a more semantic form may be supported by additional posterior areas such as the lateral occipital cortex.

*Relation to current models of parietal function*

While not intended to test between competing models of PPC function, the results from these studies do provide valuable evidence that may be used to evaluate the models as they are currently construed. As mentioned previously, three models stand out as particularly compelling descriptions of PPC contributions: the Episodic Buffer Hypothesis (E-BUFF; Vilberg and Rugg, 2008), the Attention to Memory Hypothesis (AtoM; Cabeza et al., 2008), and the Cortical Binding of Relational Activity Hypothesis (CoBRA; Shimamura, 2011).



**Figure 1.** An overview of how the three studies described here may be interpreted under the CoBRA Model. A.) When a cue is presented, low-level retrieval of item information occurs in an automatic fashion, presumably driven by processes within the medial temporal lobe. B.) Item and context memory traces may arise in disparate posterior areas, but at this stage they remain independent of each other. The dashed line represents the filtered nature in which the vPPC seems to respond to retrieved information. That is, mnemonic information only seems to elicit a vPPC

response when it is relevant to the task. C.) Relevant memory traces elicit a vPPC response. Associated item and context information are reinstated to produce a complete event memory. In contrast to E-BUFF which proposes memories are transferred to the vPPC, CoBRA proposes that binding occurs through reactivation of cortical sites responsible for representing associated information. The details that constitute an event memory may be accessed in an isolated form (as in familiarity-based retrieval), but when bound together they give rise to a unique ensemble that may be linked to a specific experience that is discriminable from all other occurrences. This ability to re-experience an event linked to a particular time and place is a hallmark of episodic memory.

The results from Study 1 arguably support all three to a similar extent. PPC responses to items during non-memory tasks may be construed as target detection of relevant mnemonic information under the AtoM model. Likewise, these results are equally consistent with the E-BUFF and CoBRA models if buffering or binding processes are gated (presumably by prefrontal regions), such that these operations are only performed upon reinstated memory traces when relevant to the task at hand.

In contrast, the results from Studies 2 and 3 appear to be more consistent with CoBRA than either of the other two models. Although the vPPC does seem track the amount of information retrieved (Guerin and Miller, 2010), a pattern of results predicted by all three models, neither E-BUFF nor AtoM would predict differences in activity based on the information type insofar as information amount is matched. The common factor underlying conditions of heightened vPPC activity in both Studies 2 and 3 was the need to integrate item information (either the target itself or an associated retrieval cue as in the case of Study 2) with contextual details, particularly those associated with a unique event occurrence. E-BUFF posits that the vPPC acts as a modality independent buffer and AtoM attributes a target detection role to the vPPC, yet these actions should be performed to a similar extent on retrieved information of all types. However, differences in vPPC activity were found despite the use of fact questions containing similar amounts of information in Study 2. Similarly, in Study 3, the context-free condition was likely accompanied by an even greater amount of retrieval than the context-specific condition (due to repeated exposure and familiarity). Indeed, the cross-modal binding processes necessary for these tasks is proposed to be the central contribution of the vPPC as described by CoBRA.

In light of these recent findings, the CoBRA model remains a likely candidate to accurately describe vPPC function in memory. However, it should again be noted that these experiments were not conducted with the intention testing predictions from each of these models. The studies described here do however provide valuable insight into the boundary conditions under which the PPC is active during memory tasks. Further work delineating these conditions will help develop a mechanistic model that sufficiently accounts for PPC to domains such as spatial cognition and attention with which it is traditionally associated as well as its more recently appreciated role in episodic memory.

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