

Executive Control during Episodic Retrieval: Multiple Prefrontal Processes Subserve Source Memory

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Summary

During recognition, one may sense items as familiar (item memory) and additionally recollect specific contextual details of the earlier encounters (source memory). Cognitive theory suggests that, unlike item memory, source memory requires controlled cue specification and monitoring processes. Functional imaging suggests that such processes may depend on left prefrontal cortex (PFC). However, the nature and possible anatomical segregation of these processes remains unknown. Using functional magnetic resonance imaging, we isolated distinct response patterns in left PFC during source memory consistent with semantic analysis/cue specification (anterior ventrolateral), recollective monitoring (posterior dorsolateral and frontopolar), and phonological maintenance/rehearsal (posterior ventrolateral). Importantly, cue specification and recollective monitoring responses were not seen during item memory and were unaffected by retrieval success, demonstrating that the mere attempt to recollect episodic detail engages multiple control processes with different left PFC substrates.

Introduction

Memory theorists have drawn a fundamental distinction between two ways of gaining access to past experiences: recollection of contextual details surrounding a previous encounter with a stimulus (source memory), and a general sense of familiarity that is sufficient to determine whether the stimulus was previously encountered even though contextual recollection is absent (item memory) (Atkinson and Juola, 1974; Banks, 2000; Clark and Shiffrin, 1992; Dobbins et al., 2000; Jacoby, 1991; Mandler, 1980; Tulving, 1985; Wagner et al., 1997; Yonelinas, 1994). Item memory combined with source memory failure is a common experience in everyday life and plays an important role in such problems as faulty eyewitness identification, when a face perceived as familiar is assigned the wrong source context (Schacter, 2001). The distinction also has important implications

for understanding the neural organization of memory: extensive behavioral and neuropsychological research indicates that source memory can be dissociated from memory for particular items and may heavily depend on frontal lobe executive control processes (Johnson et al., 1993; Schacter et al., 1984; Shimamura et al., 1991)

Functional imaging studies have further implicated left prefrontal cortex (PFC) by demonstrating increased activation during source relative to simple item memory judgments (Henson et al., 1999b; Nolde et al., 1998; Rugg et al., 1999). These left PFC increases have been interpreted as markers of additional “reflective” processes that operate on information other than that activated by the initial retrieval or copy cue (Nolde et al., 1998; Rugg et al., 1999). Although central to understanding the cognitive and neural computations subserving source retrieval, the nature of these reflective processes and their selectivity to recollective, as opposed to familiarity-based, memory remains largely unknown. Moreover, in contrast to the reflective hypothesis, alternative accounts contend that left ventrolateral PFC activation results from the successful retrieval of episodic details or operations contingent upon retrieval success (Henson et al., 1999a; Konishi et al., 2000). Thus, at present, there is considerable uncertainty regarding the nature of left PFC contributions to source memory.

Cognitive theory and neuropsychological evidence suggest at least two controlled operations that might be more involved in source memory than in item memory (Burgess and Shallice, 1996; Moscovitch and Melo, 1997; Norman and Bobrow, 1979; Schacter et al., 1998; Tulving, 1983). The first is retrieval cue specification, which is the systematic analysis of the possible semantic relations between the retrieval cue and the known characteristics of the potential sources. For example, if asked whether one encountered a particular friend at the library or the shopping mall, one might consider the characteristics of that friend that may make one or the other of the sources more probable. If these self-generated cues trigger explicit recollections unique to one source, then an appropriate memory judgment can be made. More generally, efficient retrieval from episodic memory critically depends on one’s ability to use semantic knowledge in order to systematically consider the most relevant characteristics of a current memory cue with regards to potential previous episodes (Moscovitch, 1995; Moscovitch and Melo, 1997; Schacter et al., 1998). The second operation especially important for source memory is recollection monitoring, which is the process of evaluating the products of memory retrieval with respect to their relevance to the retrieval task. Unlike simple item recognition tests, where subjects can endorse items based on simple familiarity, subjects during source tasks may recollect information that varies considerably in its task relevance and must therefore evaluate retrieved recollections to determine their current task relevancy.

To identify and specify the nature of the controlled operations that are differentially involved in source and item memory, we used functional magnetic resonance

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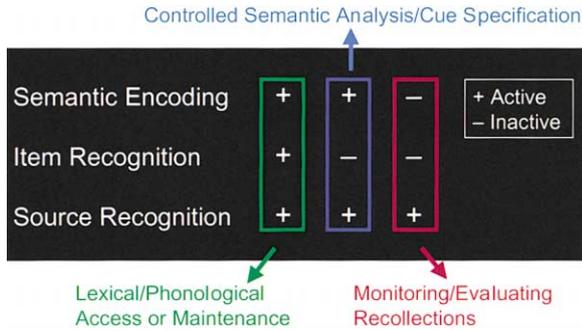


Figure 1. Logic of Cognitive Masking Procedure

Neural operations subserving lexical/phonological access or maintenance were expected to be required by all three tasks (semantic encoding, item recognition, and source recognition; green rectangle). Item recognition was not expected to depend on neural computations underlying semantic analysis or cue specification (blue rectangle). Neural computations selectively necessary for recollective/source monitoring were expected to be engaged solely by the source recognition condition (red rectangle).

imaging (fMRI) to examine activity across semantic encoding, source recognition, and item recognition. In addition, the sensitivity of these processes to the level of retrieval success was assessed. Three major questions were addressed. First, are there neural and cognitive processes engaged during both semantic encoding and source recognition that are not required during simple item recognition? If both source recognition and semantic judgments require controlled semantic analysis or the selection of semantic features (the former to specify effective retrieval cues and the latter to analyze task-relevant semantic features during encoding), then the anterior extent of left inferior prefrontal cortex (aLIPC), a region associated with controlled semantic retrieval or semantic feature selection paradigms (Buckner et al., 1995b; Kapur et al., 1994; Petersen et al., 1988; Poldrack et al., 1999; Wagner et al., 2000, 2001), should be activated in both tasks. By contrast, to the extent that item recognition judgments are based on a simple assessment of familiarity, then aLIPC should not be engaged, because controlled semantic analysis is not required (Fletcher and Henson, 2001). The second question is whether the monitoring requirements of source memory recruit unique control processes. In contrast to source memory, neither simple item recognition nor semantic encoding decisions require the monitoring or evaluation of episodic recollections, and therefore, activations that are selective to source retrieval may be indicative of monitoring operations (see Figure 1). A third pattern of activity we considered was whether there were regions that showed significant activity across semantic encoding, source recognition, and item recognition. Such activity would be predicted in posterior left inferior prefrontal cortex (pLIPC) based on research investigating phonological/lexical maintenance in working memory and rote item rehearsal (Awh et al., 1996; Davachi et al., 2001; Henson et al., 2000; Paulesu et al., 1993; Poldrack et al., 1999; Smith and Jonides, 1999). Finally, we also investigated whether left PFC responses were engaged to a greater extent during successful as opposed to unsuccessful source memory performance, thus testing

the hypothesis that activation in these regions is sensitive to episodic retrieval success.

In Experiment 1, subjects were scanned during semantic encoding and during item and source retrieval blocks. During encoding, subjects alternated between pleasant/unpleasant and concrete/abstract semantic decisions on individual items. These tasks have been shown to engage aLIPC (Demb et al., 1995; Gabrieli et al., 1996). Following encoding, subjects' memories were tested with three-alternative forced choice (3AFC) triplets consisting of a new item, and items encoded under pleasant/unpleasant and under abstract/concrete orienting. During item recognition, subjects were instructed to identify the new item in the triplet, a discrimination that can be easily made based solely on the relative item familiarities. Thus, we anticipated that subjects would predominantly rely on familiarity to make their item memory decisions, relying little (or not at all) on source memory and its associated control processes. In contrast, source recognition required selection of the item that was associated with a previous particular semantic orienting task (i.e., a specific cognitive source). We anticipated that such decisions would involve semantic cue specification as well as recollective monitoring processes not required during item recognition. Selective masking of the activation maps and region of interest (ROI) analyses were used to compare activations across the three tasks (semantic encoding, item recognition, and source recognition) and across particular regions of left PFC.

Experiment 2 used a similar encoding procedure and scanned subjects during retrieval using an event-related fMRI design, thus permitting comparison of successful and unsuccessful retrieval trials. During source memory trials, subjects were shown two items (one associated with each semantic source) and were asked to identify the item associated with the pleasant/unpleasant source. A nonrecollective reference task used identical pairs but instead required subjects to select the item most recently encountered during the prior study list. Since the relative positions of the items in the previous study list were uncorrelated with the nature of the semantic encoding task, recency decisions were predicted to depend on retrieval processes other than those recruited during source memory.

Results

Behavioral Retrieval Data

Experiment 1

Accuracy across the three retrieval tasks significantly differed ($F(2,26) = 30.43$, $Mse = 0.006$, chance = 0.33): item recognition ("not-judged?", $M = 0.87$) was significantly higher than source recognition ("for-concrete?", $M = 0.64$; "for-pleasant?", $M = 0.69$), whereas the two source conditions did not differ reliably ($t(13) = 1.59$, $p > 0.10$). A main effect of retrieval type on median reaction times (RTs; $F(2,26) = 4.17$, $Mse = 47704$) emerged due to a significantly longer RT during concrete source retrieval ($M = 2917$ ms) than during item recognition ($M = 2682$ ms) ($t(13) = 2.56$, $p < 0.05$); RT during pleasant source retrieval ($M = 2785$ ms) did not significantly differ from either item recognition or concrete source recognition.

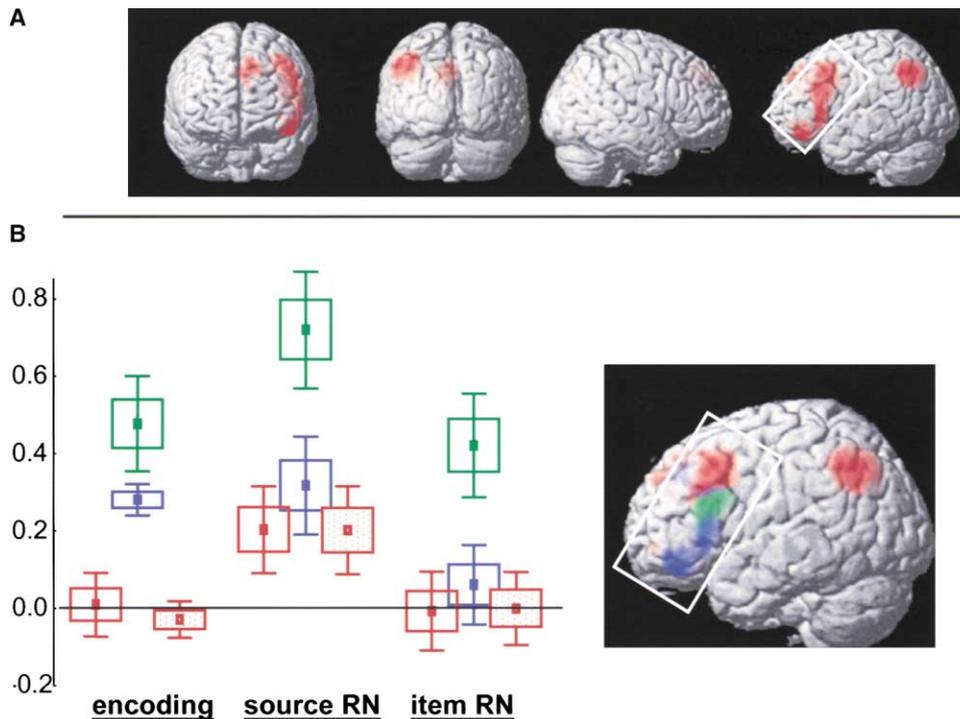


Figure 2. Selective Masking and ROI Analyses Applied to Regions Demonstrating Greater Activation during Source Relative to Item Recognition. Statistical maps are rendered onto a canonical brain. (A) Multiple left prefrontal, as well as lateral and medial parietal, regions were more active during source than during item recognition (see Table 1 for details). (B) Of these regions, left dorsolateral, frontopolar, and left parietal regions were selectively engaged during source retrieval (red regions). By contrast, the anterior and ventral extent of the left inferior prefrontal cortex (LIPC) was engaged during both semantic encoding and source recognition, but not during item recognition (blue region). Finally, the posterior and dorsal extent of the LIPC was reliably engaged by all tasks (green region). The graph renders the mean percent signal change with respect to baseline for ROIs within the four PFC regions identified by the masking analysis. Boxes reflect 1 standard error of the mean, with box-plus-stem equaling 1.96 standard errors. Note that each pair of red boxes corresponds to a dorsolateral condition. The open red box on the right denotes the dorsolateral response, while the stippled red box on the right indicates the frontopolar response.

Experiment 2

In contrast to Experiment 1, a reverse performance advantage between the recollective and item-based tasks was observed: accuracy was greater during source recognition (0.79) than recency recognition (0.58) ($t(10) = 6.27, p < 0.001$, chance = 0.50). In addition, RTs were longer during recency than source judgments (2371 versus 2154 ms, $t(10) = 3.74, p < 0.01$). Thus, consistent functional neuroanatomic differences between the source memory and nonrecollective retrieval tasks across experiments cannot reflect differences in accuracy or time on task since these relationships are reversed across the two experiments.

Neuroimaging Data

Experiment 1

Compared with item recognition, source recognition yielded greater activation primarily in left lateral frontal regions, including ventrolateral and posterior dorsolateral PFC, frontopolar PFC, and the medial aspect of superior PFC (Figure 2A and Table 1). Beyond frontal cortex, source recognition was associated with greater activation in posterior cingulate, left precuneus, and left lateral inferior parietal cortices.

Although clearly distinguishing the retrieval tasks, this comparison does not indicate whether functionally dis-

tinct executive control processes are subserved by separable left PFC subregions during retrieval, nor whether the differences between source and item memory are of degree or kind. This issue was explored using selective masking logic, as illustrated in Figure 1, that was designed to isolate the presence of putatively distinct control operations. Critically, three distinct patterns of activation were observed. First, left frontopolar, posterior dorsolateral, as well as lateral parietal cortex were selectively engaged, relative to baseline, during the source retrieval attempt; these regions were not engaged above baseline during either item recognition or during semantic encoding (Figure 2B, red regions). Second, the anterior ventral extent of the left inferior prefrontal cortex (aLIPC) was engaged, relative to baseline, during both source recognition and semantic encoding, but not during item recognition (Figure 2B, blue region). Finally, the posterior dorsal extent of LIPC (pLIPC) was engaged during all three conditions (Figure 2B, green). Thus, with respect to PFC, selective masking revealed four anatomically distinct regions, with three distinct activation patterns, in operation during source recognition; only one region, pLIPC, was also active during item recognition.

In order to confirm the dissociations revealed by the masking analysis, a direct test of functional separability was conducted using ROIs extracted from each of the

Table 1. Regions Demonstrating Greater Activation during Source Relative to Item Recognition

Region	Z Score	Coordinates			Voxels
		x	y	z	
Left lateral PFC					
Ant. IFG	5.51	-51	24	6	72
Ant. IFG ^a	5.27	-45	42	-18	39
Frontopolar ^a	3.40	-36	57	-3	6
Post. MFG ^a	5.07	-39	18	48	62
Post. IFG	4.82	-45	30	27	63
Post. IFG ^a	4.21	-48	15	24	64
Post. IFG	4.17	-39	24	30	70
Left medial SFG	4.22	-6	45	24	30
	4.21	-6	36	42	73
Posterior cingulate	4.88	3	-24	30	65
	4.14	-3	-39	21	54
Left lateral parietal	4.79	-48	-54	48	56
	4.53	-42	-60	48	56
	4.51	-39	-66	39	78
Precuneus	4.55	-9	-69	33	75
Left thalamus	4.44	-6	-9	6	51
	4.39	-12	-3	12	50
	4.22	-12	6	12	21
	3.80	-18	51	36	25
Brain stem	3.76	6	-15	-12	19
	3.57	-9	-18	-18	13

Ant., anterior; Post., posterior; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SFG, superior frontal gyrus.

^aRegions extracted in the graph in Figure 2B.

regions (Figure 2B). Consistent with the masking results, the ROI analysis demonstrated that posterior LIPC was the only region to demonstrate an above baseline response in all three conditions, including during item recognition ($p < 0.0001$). All other frontal regions showed no appreciable response during item recognition compared to baseline (all p 's > 0.27). To determine whether these latter regions (frontopolar and posterior dorsolateral PFC, and anterior LIPC) were functionally separable, the mean level of activation across conditions was contrasted. A task (semantic encoding, source recognition, and item recognition) \times region (frontopolar, posterior dorsolateral PFC, and anterior LIPC) interaction ($F(4,52) = 7.87$, $Mse = 0.009$, $p < 0.0001$) indicated that these distinct frontal regions were differentially engaged across the tasks. Unlike the anterior LIPC, which was similarly activated during both semantic encoding and source recognition, the frontopolar and posterior dorsolateral PFC were only active during source recognition (Figure 2B, blue and red). The pattern of response in the latter two regions was statistically indistinguishable ($F < 1$). Collectively, these data point to four anatomically separate PFC regions that demonstrate one of three distinct functional patterns: (1) posterior LIPC was active across all conditions, (2) anterior LIPC was active during both source recognition and semantic encoding, and (3) frontopolar and posterior dorsolateral PFC were exclusively engaged during source recognition. These findings are consistent with our hypothesis that source retrieval depends on multiple dissociable control functions.

Experiment 2

Experiment 2 addressed the sensitivity of PFC executive control processes to levels of retrieval success. Comparison of the source and recency recognition trials

yielded a markedly similar pattern of lateral PFC responses as was observed in Experiment 1 when comparing source to item recognition. To illustrate the high degree of overlap in activations across the experiments, Figure 3 demonstrates the regions that were active in both studies at the 0.001 threshold (inclusive masking). These left PFC responses are not a function of differential task difficulty between source and item-based judgments, as the relative task difficulty was reversed across the experiments. When correct and incorrect source judgments were contrasted within these common regions, no evidence was obtained for a retrieval success effect in any of these PFC regions, even at very liberal thresholds ($p < 0.01$, uncorrected). ROI analyses on the event-related data confirm that this was not the result of low power, demonstrating equivalent or numerically greater hemodynamic response amplitudes during unsuccessful as opposed to successful source recognition trials for all the maxima observed in left lateral PFC, the reverse of what is predicted under a retrieval success account (Figure 3). Retrieval success effects were obtained in regions other than lateral PFC, including along the left hippocampal axis, which demonstrated a greater response during successful source trials in comparison to unsuccessful source and recency based responses. These success-related responses are not relevant to the current hypotheses regarding PFC contributions to source retrieval and are more fully detailed elsewhere (our unpublished data).

Discussion

The present data demonstrate that source memory, relative to item recognition, differentially requires distinct cue specification and monitoring operations that are

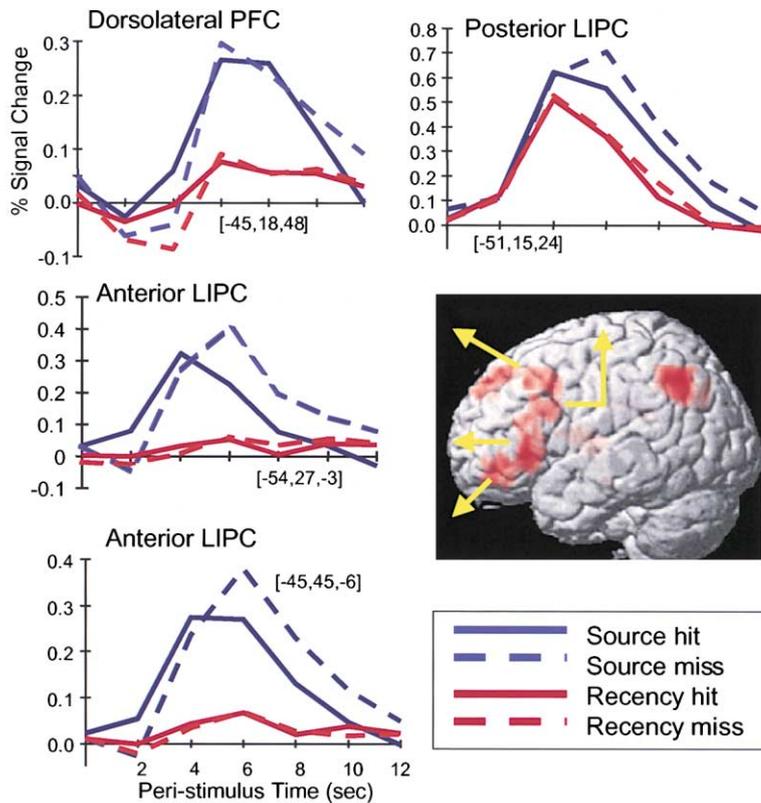


Figure 3. Regions Active in Both Experiment 1 (Source Versus Item Recognition Judgments) and the Event-Related Design of Experiment 2 (Source Versus Recency Judgments) Rendered on a Canonical Brain

Regions common to both experiments demonstrated greater activation during source recognition (blue lines) than during recency recognition (red lines) in Experiment 2 (0.001 threshold in each experiment). Comparison of correct (solid lines) to incorrect (dashed lines) source trials revealed no evidence for “success” effects in any of the lateral PFC regions. Recency trials also did not demonstrate success effects and, in addition, failed to differ from baseline response in dorsal and anterior PFC regions.

supported by anatomically separable left prefrontal regions. Furthermore, the degree of engagement of these PFC computations was insensitive to retrieval success, consistent with their role in the controlled aspects of source memory that are necessary regardless of task outcome. The pattern of responses suggested that anterior LIPC is involved in the controlled retrieval of semantic information that is necessary during semantic encoding and is a critical component of cue specification during source retrieval attempt (at least when the sources can be linked to prior semantic cognitive operations performed on verbal materials). Relative to baseline, this region showed no appreciable response during the item recognition task. In contrast, a more posterior LIPC region was recruited during all experimental conditions relative to baseline, consistent with its putative role in the short-term maintenance of, or access to, lower level phonological or lexical information. Although significantly above baseline in all three conditions, this region did show the greatest response in the source task, which, relative to the semantic encoding and item recognition tasks, required more time to execute and may have resulted in increased maintenance demands. Finally, frontopolar and posterior dorsolateral PFC regions were exclusively engaged during the source task, consistent with a role in control processes that guide the monitoring or evaluation of episodic recollections ascribed to different stimuli. Collectively, these data provide a striking demonstration that multiple, anatomically distinct regions in left lateral prefrontal cortex subserve functionally unique operations during attempted retrieval of source memories. Given that the present study exclusively used verbal materials, future research will

be needed to verify if such patterns hold for pictorial or object stimuli that are also subjected to meaningful encoding experiences.

Earlier neuropsychological investigations of prefrontal contributions to source and item recognition demonstrated that item recognition was largely intact following prefrontal damage, whereas source recognition was disrupted (Janowsky et al., 1989a, 1989b, 1989c). The current data extend this literature by pointing to a number of possible functional impairments during source memory that might arise due to frontal insult, and they lead to unique predictions for future investigation with patients or with disruption studies using transcranial magnetic stimulation. For example, damage or disruption of the anterior LIPC should result in impairments during both controlled semantic analysis tasks and during source recognition tasks that benefit from the generation of internally guided retrieval cues related to the semantic qualities of the memory probes. In contrast, damage or disruption of the frontopolar and/or posterior dorsolateral regions may result in an impairment that is only evident during source recognition; controlled semantic retrieval should remain intact. Thus, although the two different “lesion” groups would be impaired during source retrieval, they would be impaired for very different reasons.

In addition to the prefrontal regions discussed above, left lateral parietal, precuneus, and posterior cingulate regions also showed greater activity during the source compared to item recognition task in Experiment 1. Activity in the posterior cingulate and precuneus has been reliably found in numerous studies of episodic (Buckner et al., 1995a; Krause et al., 1999; Shallice et al., 1994)

and autobiographical retrieval (Conway et al., 1999; Fink et al., 1996; Maddock et al., 2001; Maguire and Mummery, 1999), and there is some evidence that damage proximal to these regions can cause severe memory impairment (Rudge and Warrington, 1991; Valenstein et al., 1987). This observation has led some researchers to suggest that one and/or the other region is critically involved in episodic recovery. Consistent with this idea, both Eldridge et al. (2000) and Henson et al. (1999a) found that activity in posterior cingulate during successful memory judgments varied as a function of the reported presence of recollection. When subjects claimed to recollect or remember elements of the prior study context, there was greater activity in posterior cingulate than when items were endorsed based solely on feelings of familiarity (Eldridge et al., 2000; Henson et al., 1999a). In the current study, neither left lateral parietal nor prefrontal regions showed any evidence of a retrieval success effect at a lenient threshold of 0.01. However, this was not the case for the midline posterior regions. Both the precuneus (MNI coordinates of 3, -75, 30) and posterior cingulate (0, -39, 27) demonstrated increased activity for successful compared to unsuccessful source memory at this lenient threshold. Taken in consideration with the prior imaging evidence and with the known interconnectivity between posterior cingulate and MTL structures (Suzuki and Amaral, 1994), this finding further suggests that posterior cingulate may critically contribute to memory function.

The idea that source and item memory may involve different retrieval operations has a long history in cognitive theory, computational models, statistical decision models, and neuropsychology (Banks, 2000; Janowsky et al., 1989a; Johnson et al., 1993; Moscovitch and Melo, 1997; Schacter et al., 1984; Yonelinas, 1999). However, the ability to delineate different retrieval operations involved in source and item memory has been limited by the difficulty of drawing such distinctions purely on the basis of behavioral data and by the large and indiscriminate nature of opportunistic lesions in human prefrontal cortex. Current neuroimaging techniques now offer researchers the chance to tease apart the different strategic and monitoring processes that are vital to our ability to situate current experiences within the framework of our personal episodic past.

Experimental Procedures

Subjects

Fourteen (Experiment 1) and eleven (Experiment 2) right-handed, 18- to 35-year-old, native English speaking volunteers were paid \$50 for participating in the study. Informed consent was obtained in a manner approved by the Human Studies Committee at Massachusetts General Hospital, the Committee on the Use of Humans as Experimental Subjects at MIT, and the Harvard University Committee on the use of Human Subjects in Research.

Study Materials

For Experiment 1, 576 nouns were drawn from the Oxford English Dictionary. Nine lists were constructed for use in three separate study/test cycles (three lists/192 words per cycle); mean item length and word frequency were controlled across lists. For each 128 item study phase, subjects studied two of the three assigned lists. The third list constituted the 64 novel lures during the subsequent 3AFC test. Across subjects, lists were counterbalanced across condition and scans.

For Experiment 2, 640 nouns were drawn from the Oxford English Dictionary. Four lists of 160 items were constructed for use in four separate study/test cycles; mean item length and word frequency were controlled. Within each list, across subjects, blocks of 40 words were serially rotated to counterbalance across conditions.

Study Procedure

In both experiments, stimuli (32 point Geneva font) were back-projected onto a screen at the rear of the magnet bore and were viewed via a rearward facing mirror placed above the eyes. During the study phases of Experiment 1, subjects were scanned while alternating between blocks of two different semantic orienting tasks ("concrete<>abstract?" or "pleasant<>unpleasant?"); alternations occurred after every eight words interspersed with fixation blocks lasting from 8 to 14 s. In the study phases of Experiment 2 (not scanned), subjects alternated between these two semantic tasks on every trial. In both experiments, each word appeared immediately below the cue, and responses were made with either a left or right key press. The stimulus onset asynchrony (SOA) for items was 2.5 s for Experiment 1, and 3 s for Experiment 2. Critically, the two semantic encoding tasks constituted the two sources that subjects would have to recollect during subsequent source memory testing.

Test phases immediately followed each study phase. For Experiment 1, test probes consisted of a task cue above 3AFC triplets arrayed from left to right; each triplet contained an item from all three possible classes (novel, rated for pleasantness, and rated for concreteness). Across test blocks, the nature of the retrieval cue varied: "not-judged", "pleasant-task", or "concrete-task". During "not-judged" blocks, subjects were to indicate which of the test probes was novel; during "for-pleasant" and "for-concrete" blocks, subjects indicated which of the probes was studied with that cognitive source. Subjects were informed that every trial contained an item from each of the three classes; responses were indicated by a left, middle, or right key press, and the location of the correct response was pseudo-randomized. Each retrieval block contained four trials with an SOA of 5 s, with each scan consisting of eight blocks of item recognition ("not-judged") and eight blocks of source recognition (four of "for-pleasant" and four of "for-concrete"). Interspersed among retrieval blocks were passive fixation blocks ranging from 8 to 14 s; for these blocks, the orienting cue was replaced by a row of crosses. Each study and test scan contained 248 image-volumes.

For each test phase of Experiment 2, a two-alternative forced choice (2AFC) recognition test assessing source and recency was administered. Test pairs were constructed by systematically crossing the items from each half of the study list with the type of encoding that each received, yielding 80 test pairs in which one item was encoded for pleasantness, one for concreteness, and each differed in recency. The side of the correct response was pseudo-randomized. For relative recency trials ("most-recent?"), subjects were to select the member of the pair seen most recently during the immediately preceding study list. For source retrieval trials ("pleasant-task?"), subjects were to select the member of the pair that was rated as pleasant or unpleasant in the preceding study list. The test cue and item pairing was reversed for half of the subjects. The order of the test trial types (recency and source: 4 s), along with fixation periods (2-10 s), was determined using an optimal sequencing program designed to maximize the efficiency of recovery of the bold response (Dale et al., 1999). During fixation trials, positions were replaced by rows of crosses of approximately the same length as the stimuli. Each test scan contained 240 image-volumes.

fMRI Data Acquisition

Scanning was performed on a 3T Siemens Allegra system using a standard whole-head coil. Functional data were acquired using a gradient-echo echo-planar pulse sequence (TR = 2 s, TE = 30 ms, 21 axial slices parallel to the AC-PC plane, 3.125 × 3.125 × 5 mm, 1 mm interslice gap). Prior to functional data collection, four dummy volumes were collected and discarded to allow for T1 equilibration effects. High-resolution T1-weighted (MP-RAGE) anatomical images were collected for visualization. Head motion was restricted using a pillow and foam inserts.

fMRI Data Analysis

Data were preprocessed using SPM99 (Wellcome Department of Cognitive Neurology, London). Slice acquisition timing was corrected by resampling all slices in time relative to the first slice, followed by rigid body motion correction across all runs. Functional data were spatially normalized to an EPI template using a 12 parameter affine and nonlinear cosine basis function transformation. Volumes were resampled into 3 mm cubic voxels and spatially smoothed with an 8 mm FWHM isotropic Gaussian kernel. Each session was rescaled such that the mean signal was 100.

The data were statistically analyzed, treating subjects as a random effect. For the analyses, volumes were treated as a temporally correlated time series and modeled by convolving a synthetic hemodynamic response function and its first-order time derivative using the onset times for the blocks/events. The resulting functions were used as covariates in a general linear model, along with a basis set of cosine functions that were used to high-pass filter the data, and a covariate representing session effects. The least squares parameter estimates of height of the best fitting synthetic HRF for each condition of interest (averaged across scans) were used in pairwise contrasts and stored as a separate image for each subject. These images were then tested against the null hypothesis of no difference between contrast conditions using one-sided *t* tests, resulting in repeated measures *t* tests across subjects. Regions were considered significant if they consisted of five or more contiguous voxels and exceeded an α threshold of 0.001 ($Z > 3.09$, uncorrected). This threshold has been demonstrated to adequately control for family-wise error in similar studies and is comparable to that typically used in fMRI studies of memory, enabling meaningful across study comparisons (e.g., Buckner et al., 1998; Donaldson and Buckner, 1999). In addition, the left PFC regions discussed replicated across Experiments 1 and 2, each of which employed a 0.001 threshold, resulting in an exceedingly stringent joint probability of 0.001².

ROIs were extracted by selectively averaging the conditions of interest from 4 to 20 s post-block onset in the blocked design and using peristimulus time averaging for the event-related fMRI data. Percent signal averages were obtained for above-threshold voxels within an 8 mm radius of each of the SPM-identified maxima for the source greater than item memory contrast in Experiment 1, and the source greater than recency memory contrast in Experiment 2.

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