Memory Networks Supporting Retrieval Effort and Retrieval Success Under Conditions of Full and Divided Attention

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Abstract. We used a multivariate analysis technique, partial least squares (PLS), to identify distributed patterns of brain activity associated with retrieval effort and retrieval success. Participants performed a recognition memory task under full attention (FA) or two different divided attention (DA) conditions during retrieval. Behaviorally, recognition was disrupted when a word, but not digit-based distracting task, was performed concurrently with retrieval. PLS was used to identify patterns of brain activation that together covaried with the three memory conditions and which were functionally connected with activity in the right hippocampus to produce successful memory performance. Results indicate that activity in the right dorsolateral frontal cortex increases during conditions of DA at retrieval, and that successful memory performance in the DA-digit condition is associated with activation of the same network of brain regions functionally connected to the right hippocampus, as under FA, which increases with increasing memory performance. Finally, DA conditions that disrupt successful memory performance (DA-word) interfere with recruitment of both retrieval-effort and retrieval-success networks.

Keywords: memory network, fMRI, recognition, divided attention, retrieval effort, retrieval success

Researchers have begun to separate the set of cognitive processes required to successfully retrieve information from long-term memory from those involved in the control, or search and monitoring, of the contents of memory. Work with brain-damaged patients suggests that the cognitive processes involved in retrieval success are related to a different set of neural structures than those related to retrieval control. Whereas patients with damage to the medial temporal lobe (MTL) show severe memory deficits in declarative (explicit) retrieval of past episodes (Milner, 1954; Scoville & Milner, 1957), individuals with damage to the frontal lobe show more subtle memory deficits, with impairments on tests that depend on the strategic control, or organization, of information (Hirst & Volpe, 1988; Incisa dela Rocchetta & Milner, 1993; Shimamura, Janowsky, & Squire, 1990; Stuss et al., 1994). This dissociation led researchers to hypothesize that the MTL contributes to processes relating to the successful access to information in long-term memory, which are distinct from those involved in strategic control processes, believed to be mediated by the frontal lobes.

Neuroimaging has also been used to separate the brain regions involved in retrieval success from those involved in retrieval control during episodic tests of memory. For example, in an early positron emission tomography (PET) study, Schacter, Alpert, Savage, Rauch, and Albert (1996) showed that right hippocampal activity was higher when participants retrieved words from a test list in which there was a high level of recall, as compared to a low level of recall, but that right anterior prefrontal cortex (PFC) activity did not differ between conditions. This work supports the hypothesis that the MTL and right PFC subserve processes relating to memory success and control, respectively.

Other research has shown that the right PFC is active during a variety of episodic retrieval tasks (Nyberg, Cabeza, & Tulving, 1996). This region is believed to be involved in control processes relating to retrieval, although the exact role of this activity has been debated. Various theories include the participation of the right PFC in the establishment of retrieval mode (REMO; Lepage, Ghaffar, Nyberg, & Tulving, 2000; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994), retrieval effort (Schacter et al., 1996), monitoring and verification processes (Cabeza, Locantore, & Anderson, 2003; Henson, Shallice, & Dolan, 1999), or post-retrieval processing (Rugg, Fletcher, Frith, Frackowiak, & Dolan, 1996). Although these models posit different roles for the right PFC, what is common is that this region is implicated in control processes relating to retrieval, rather than recovering the content of memories.

Whereas some theories propose that the right PFC serves mainly control processes relating to retrieval effort

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(i.e., attempting to retrieve information from memory whether or not this retrieval is successful; Schacter et al., 1996; Tulving et al., 1994), other work suggests that the activity supports successful retrieval of information (i.e., when successful retrieval occurs). Research has shown that activity in the right anterior PFC increases when the ratio of old to new items is increased (Rugg et al., 1996), when retrieval of deep-encoded items (high retrieval success) is compared to shallow-encoded items (high retrieval effort) (Buckner, Koustall, Schacter, Wagner, & Rosen, 1998), or when hits are compared to correct rejections (McDermott, Jones, Peterson, Lageman, & Roediger, 2000).

These varied findings have led researchers to conclude that the frontal lobes are likely involved in a multitude of retrieval processes, with different regions relating to distinct retrieval processes (Fletcher & Henson, 2001; Shallice, 2002). To help differentiate these regions, we reanalyzed a subset of a published dataset from our laboratory (Fernandes, Pacurar, Moscovitch, & Grady, 2006). We aimed to identify networks of brain activity that contribute to retrieval effort and retrieval success in a divided attention (DA) paradigm. Previous research using the DA technique has shown that it is possible to increase the resource demands of retrieval without interfering with the ability to successfully retrieve information from memory, making it an ideal paradigm with which to examine brain networks contributing to retrieval effort versus success. Specifically, when attention is divided between a free recall and a distracting task, most studies show small, or no, decrement in memory performance (Baddeley, Lewis, Eldridge, & Thompson, 1984; Craik, Govoni, Naveh-Benjamin, & Anderson, 1996; Murdock, 1965), despite the fact that participants must coordinate retrieval with another ongoing, attention-demanding concurrent task.

To examine the effect of DA at retrieval on the brain, Iidaka, Anderson, Kapur, Cabeza, and Craik (2000) and Anderson et al. (2000) used PET to measure changes in brain activation during recall of words under full attention (FA) or DA conditions. They found that although memory performance was relatively unaffected by DA at retrieval, the brain regions used to support retrieval changed. While activity in the right anterior (Iidaka et al., 2000), left dorsolateral, bilateral anterior, and right ventrolateral (Anderson et al., 2000) PFC decreased during DA conditions, the left dorsolateral, bilateral ventrolateral, (Iidaka et al., 2000), and bilateral dorsolateral (Anderson et al., 2000) PFC showed increased activity. These studies suggest that although memory retrieval can be successful when the processing demands of the memory task increase, increased activity in some frontal regions may be required to cope with the increased resource demands, or increased retrieval effort, under DA conditions.

Other work has shown that it is also possible to interfere with memory success using the DA technique. Our earlier work (Fernandes & Moscovitch, 2000, 2002) showed that retrieval of words is significantly disrupted when participants concurrently perform a word-based, compared to digit- or picture-based, distracting task during retrieval. Since memory was disrupted only when the distracting task employed words, we suggested that poor memory during retrieval in this condition arose from direct competition for access to content-specific representations, which is mediated by MTL/hippocampal structures, that are common to both the verbal memory and the word-based distracting task, rather than competition for general attentional resources.

In line with this hypothesis, our fMRI study in younger adults (Fernandes, Moscovitch, Ziegler, & Grady, 2005; Fernandes et al., 2006) showed that both memory performance and right hippocampal activity were significantly reduced when participants performed a word-based distracting task (DA-word condition) concurrently with retrieval. In contrast, neither memory, nor hippocampal activity were as affected when the concurrent task was digit-based. Maintaining successful retrieval in the DA-digit condition was hypothesized to require increased effort, and in support of this claim, we found significantly higher right anterior PFC activity in the DA-digit compared to the DA-word condition.

In the current study, we used a multivariate technique, partial least squares (PLS; McIntosh, Bookstein, Haxby, & Grady, 1996), to identify entire networks, or patterns, of brain activity contributing to task performance. This method is unique from other univariate and multivariate imaging methods in that the analysis is not based on a priori predictions of differences between tasks/behaviors, but rather considers similarities and differences in brain activation patterns across all tasks/behaviors. Using this technique, we extended our previous findings by identifying networks of brain regions (rather than single regions) active across our tasks without applying an a priori defined model, thus allowing the data itself to define which tasks show commonalities. We also examined how activity in a region of right hippocampus, shown to be involved in memory in other work (Fernandes et al., 2005, 2006; Moscovitch & Umiltà, 1991; Schacter et al., 1996), correlated with activity in other brain regions and with memory performance. In this way, we could determine the set of regions that directly predicted memory success under FA and DA, a research question not examined to date.

We analyzed a dataset consisting of three memory conditions (younger adult data from Fernandes et al., 2006): Participants engaged in a recognition memory task while performing no distracter task (FA condition), a digit-based distracter task (DA-digit condition), or a word-based distracter task (DA-word condition). Given our research questions, we limited our analysis to the younger (omitting older) adults reported in that paper. Two different analyses were performed on the dataset to investigate the set of neural regions involved in retrieval effort and retrieval success.

The first was a task PLS analysis. Because the DA conditions increase the processing demands during retrieval as compared to the FA condition, we expected the DA-digit and DA-word conditions to recruit a network of brain activity relating to retrieval effort. This effort-related network was expected to involve activity in anterior, ventrolateral, and dorsolateral PFC, similar to those regions identified as contributing to retrieval effort by Lepage et al. (2000), with emphasis on the right dorsolateral PFC, shown to increase in activity when the monitoring demands of the task increase (Henson et al., 1999).

The second was a functional connectivity PLS analysis, used to identify patterns of brain activity relating to retrieval success. Since the hippocampus is believed to be involved in accessing the content of the memory trace (Fernandes et al., 2005, 2006; Schacter et al., 1996), we examined how the right hippocampus was functionally associated with activity in the rest of the brain and whether activity in this network was correlated with successful memory performance. Based on previous work showing that retrieval success remains the same under DA-digit and FA conditions, we expected that similar success-related networks would be recruited in these conditions. The DA-word condition, however, in which memory success is disrupted, was not expected to be associated with this network.

Method

Details of the procedure used in the study of Fernandes et al. (2006) can be found in that publication, and relevant sections are included below.

Participants

Twelve healthy younger adults (7 females; 2 left handed), from 20 to 30 years of age (mean age = 26.33 years, *SD* = 3.36), with a mean of 16.5 years (*SD* = 2.33) of education, participated in the study. All procedures were approved by the ethics committee of Baycrest Centre for Geriatric Care. All participants spoke English fluently and were free from psychiatric or neurological disease.

Behavioral Task Materials

During each study phase, participants heard a list of 50 unrelated words, presented while in the scanner at a rate of one word every 2 s. During the recognition phase, participants once again heard words at a rate of one word every 2 s and made a button press if the word was "old". Items in the distracting tasks were presented visually, with black letters or numbers on a white background. Items were shown centrally through MRI compatible goggles (Silent Vision™, Avotec Inc.), with the acuity adjusted for each participant. Items for the word-based distracting task were visually presented words (mean of six letters) representing animals (e.g., kitten) or man-made objects (e.g., hammer). Participants made a button press to words representing man-made objects. Items for the digit-based distracting task were two-digit numbers flanked by two Xs on either side. Participants made a button press to odd numbers. In each block, half of the items required a button press, and were presented randomly at a rate of one item every 2 s. For the auditory memory task, participants responded with their index finger of the left hand and for the visual tasks, with the index finger of the right hand, using two fMRI-compatible response pads (Lightwave Technologies, Surrey, BC, Canada).

Procedure

Participants first performed a practice session outside the scanner consisting of a block of each single and dual task condition, followed by a sample run, in which blocks were presented randomly. Blocks during both the practice and scanner sessions began with 4 s of short instructions followed by the presentation of 10 items at a rate of one item every 2 s. For the dual-task conditions, the auditory recognition and distracting task items were presented simultaneously. For the auditory recognition tasks, half of the words were old (five targets per block), and in each of the distracting tasks, half of the items were targets (five targets per block). For single-task memory conditions (recognition under FA) and single-task distracting task conditions, performance was assessed without a concurrent task, at the same rate, and with the same response frequency, as in the dual-task (concurrent) conditions.

Prior to each of the four scanning runs, while in the scanner, participants heard a study list of 50 unrelated words. These encoding phases were not scanned. Participants then counted backward silently by threes for 30 s, followed by the scanning runs. Each participant performed two "short" scanning runs, consisting of seven blocks presented pseudorandomly: Three recognition tasks performed under FA, two recognition tasks performed with the word-based distracting task (DA-word), and two of the recognition tasks performed with the digit-based distracting task (DA-digit). The FA blocks were presented in between the DA blocks. Participants also performed two "long" scanning runs, consisting of 19 blocks presented pseudorandomly: Two of the word-based distracting task performed singly, two of the digit-based distracting task performed singly, two of the FA recognition task, two of DA-word, two of the DA-digit, five of an auditory control, and four of a visual control task (see Fernandes et al., 2005, 2006). The order of runs alternated between short and long, with the presentation counterbalanced across participants.

fMRI Data Acquisition

Data were acquired with a Signa 1.5 Tesla magnet with a standard coil (CV/i hardware, LX8.3 software; General Electric Medical Systems, Waukesha, WI). Functional imaging was performed to measure brain activation by means of the blood-oxygenated level-dependent (BOLD) effect (Ogawa, Lee, Kay, & Tank, 1990) with optimal contrasts. Functional scans were acquired with a single-shot T2*-weighted pulse sequence with spiral readout (axial orientation, TR = 2500 ms; TE = 40 ms; flip angle = 80°; effective acquisition matrix = 64×26; FOV = 20 cm; number of slices = 26; slice thickness = 5.0 mm; and slice spacing = 0). Reconstruction of the data was conducted off-line and included gridding (Glover & Lai, 1998) and correction for magnetic field inhomogeneities and Maxwell gradient terms. For each participant, two short runs of 76 volumes each and two long runs of 191 volumes each were collected.

A standard high-resolution, 3D T1-weighted fast spoiled gradient echo image (axial orientation; TR = 35 ms; TE = 6.0 ms; flip angle = 35°; acquisition matrix = 256 × 124; FOV = 22 × 16.5 cm; number of slices = 124; slice thickness = 1.4 mm; and slice spacing = 0) was obtained before fMRI acquisition and was used to register brain structure and function.

fMRI Data Analysis

We used PLS to analyze the data (McIntosh et al., 1996). PLS is a multivariate analysis method that has been adapted to analyze neuroimaging data, and it identifies patterns of brain activity that covary with either some aspect of the experimental design, a behavioral measure, or activity in a reference, or "seed", region of interest. The analysis first computes the cross-covariance between two matrices, for example, one that codes the experimental design and one that contains values for each voxel of each scan of each cognitive task. This cross-covariance matrix is then decomposed using singular value decomposition to identify latent variables (LVs), or orthogonal patterns of brain activity. The LVs are ordered such that the first LV represents the greatest amount of cross-covariance between the two sets of measurements, and successive LVs account for progressively less cross-covariance. Within each LV, each voxel is given a positive or negative value (or salience), which represents how that voxel is related to the LVs. These values are then multiplied by the individual images of each task for each participant and summed across the voxels in order to derive an estimate of how robustly each participant displays that spatial pattern (a "brain score"). The different tasks or behaviors are also given a "task score", which can also be positive or negative, and these scores identify how strongly that particular task (or behavior) is related to the positively or negatively weighted voxels of that LV.

PLS uses two different methods to test for statistical significance. Firstly, the LV is statistically assessed using permutation tests. We used 500 permutations and a statistical cutoff of $p < .05$. Secondly, the reliability of how each brain voxel contributes to the LV is determined by bootstrap estimation. This technique produces a bootstrap ratio (BSR: The ratio of the salience of the voxel to the standard error of that salience) and an associated approximate p value. We used 100 bootstrap estimations and a cutoff of a BSR of 4, which gives an approximate p value of .0001. For both the seed and behavior PLS analyses, bootstrap resampling is used to generate 95% confidence intervals around the obtained brain-behavior and brain-seed correlations. Significant differences between conditions are indicated when the confidence intervals between conditions are nonoverlapping, and the correlations are deemed unreliable when the confidence interval overlaps with zero (McIntosh & Lobaugh, 2004; as in West, Jakubek, Wymbs, Perry, & Moore, 2005). For the analyses, a cluster was defined as having a minimum size of 30 voxels (each voxel was 2 × 2 × 2 mm) and a minimum distance of 10 mm. Brain structures were then located using the Talairach and Tournoux (1988) atlas.

To correct for head movement, AFNI software was used to register each participant's functional scans to the first scan. Files were then converted to Montreal Neurological Institute (MNI) space and smoothed with an 8-mm filter using SPM95 software. These data were then entered into the PLS program to create datamats containing the functional images of each participant in each condition. We performed two different types of PLS analysis on the data from the FA, DA-digit, and DA-word conditions. We first performed a task PLS analysis to identify networks of activity that differed according to memory condition (FA, DA-digit, and DA-word). We then performed a combined functional connectivity and behavior PLS analysis (as in Grady, McIntosh & Craik, 2003), to examine how activity in the right hippocampus covaried with activity in the rest of the brain under FA and DA conditions, and how activity in this network covaried with memory performance. For this analysis, we used a hippocampal seed (x, y, z = 34, −27, −9) that showed greater activity during the DA-digit and FA conditions, compared to the DA-word condition, in our earlier work (Fernandes et al., 2005, 2006). We assessed connectivity and behavior simultaneously by including seed activity and a measure of performance (measured as hit rate − false alarm rate) as dependent variables to be correlated with brain activity in the analysis. This analysis allowed us to identify whether the functional connectivity of the hippocampus changes under conditions of DA, and how this network relates to retrieval success.

Results

Behavioral Results

Recognition performance was calculated as proportion of hits (out of 50 for FA and out of 40 for the DA conditions) minus proportion of false alarms (out of 50 for FA and out of 40 for the DA conditions, as in Fernandes et al., 2006; note that hit rates in Fernandes et al., 2005 were calculated out of 49 and 39 due to experimenter error, though this did not affect the pattern or magnitude of effects reported in the ANOVA results) averaging across all similar block types (FA recognition, DA-word, and DA-digit; see Table 1 for mean values). Also shown in Table 1 are the mean response times (RTs) for correctly recognized words. Recognition accuracy was analyzed with a within-participant (FA, DA-digit, and DA-word) ANOVA. There was a main effect of recognition condition, $F(2, 22) = 26.82$, $p < .001$, and post-hoc tests showed that recognition accuracy was lower in the DA-word, compared to both the FA, $F(1, 11) = 92.00$, $p < .001$, and the DA-digit conditions, $F(1, 11) = 26.35$, $p < .001$. Recognition during the DA-digit condition did not differ from that during FA condition. Using RTs as the dependent variable, there was a significant effect of recognition condition, $F(2, 22) = 17.22$, $p < .001$ (Table 1). RTs during FA were faster than during either the DA-word, $F(1, 11) = 6.74$, $p < .001$, or the DA-digit condition,

Table 1. Recognition task performance under FA and DA conditions

Measure and condition	FA	DA-digit	DA-word
Hit rate	.67 (.13)	.64 (.18)	.55 (.11)
False alarm rate	.10 (.04)	.10 (.05)	.17 (.07)
Recognition accuracy (hit rate − false alarm rate)	.57 (.14)	.55 (.20)	.38 (.14)
Response time (ms)	1114 (66)	1182 (62)	1271 (68)

Standard deviations are shown in parentheses.

$F(1, 11) = 51.67$, $p < .001$, and RT were longer in the DA-word than DA-digit condition $F(1, 11) = 7.94$, $p < .05$.

PLS Results

Task PLS on Memory Conditions

The task analysis revealed a significant LV ($p = .02$, Figure 1) that differentiated the FA from the DA conditions. The FA condition was associated with a network consisting of left medial frontal, left parahippocampal, right anterior cingulate, right postcentral, bilateral precentral, right putamen, right caudate, left cuneus, and left cerebellar regions (Table 2, positive saliences; Figure 2, areas shown in orange). Activity in right superior frontal cortex (x, y, z = 32, 30, 56) differentiated the DA-digit and DA-word conditions from the FA conditions (Table 2, negative saliences; Figure 2, areas shown in blue).

We performed a repeated measures ANOVA on individual participant brain scores, which provide a measure of how robustly each participant displayed the extracted spatial pattern. The mean brain score was −7.99 (SD = 23.55), −81.98 (SD = 29.43), and −49.63 (SD = 35.16) for the FA, DA-digit, and DA-word conditions, respectively. There was a significant effect of condition, $F(2, 22) = 20.48$, $p < .001$, and planned comparisons showed that the FA condition had a significantly higher brain score than the DA-digit, $F(1, 11) = 49.07$, and DA-word, $F(1, 11) = 10.09$, conditions, ps < .01 (also reflected by task score differences in Figure 1). Importantly, the DA-digit and DA-word conditions also differed significantly from each other, $F(1, 11) = 8.75$, $p < .05$, indicating that the right superior frontal cortex activity is more robust across participants in the DA-digit condition relative to the DA-word condition.

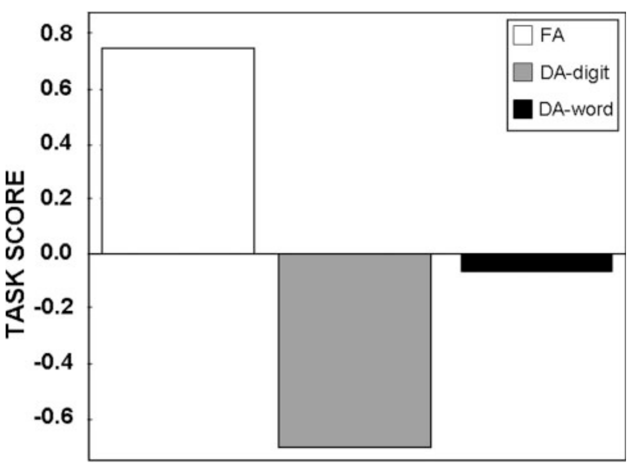

Figure 1. Task PLS results showing task scores for each of the three conditions.

Functional Connectivity of the Hippocampus

The functional connectivity analysis resulted in one significant LV ($p = .01$) that identified a network of regions whose activity correlated significantly with the activity in the hippocampal seed (x, y, z = 33, −27, −9) (see Figure 3). This network included bilateral middle and medial frontal cortex, left superior and inferior frontal cortex, right inferior parietal lobe, right precuneus, right precentral gyrus, left superior and medial temporal regions, as well as bilateral anterior cingulate gyrus (see Table 3, positive saliences; Figure 4, areas shown in orange). As shown in Figure 3, panel A, this pattern of activity was positively correlated with hippocampal seed activity across all three memory conditions, although this correlation was not reliable (confidence interval overlaps zero) in the DA-word condition (see Figure 3, panel A).

Activity in this network also increased with retrieval success in the FA and DA-digit conditions (Figure 3, panel B). That is, memory accuracy increased during the FA and DA-digit conditions as activity in this hippocampal network increased. In contrast, memory accuracy for the DA-word condition was negatively correlated with activity in this network, although again the correlation was not reliable (confidence intervals overlap zero; see Figure 3).

Discussion

We used a multivariate analysis technique, PLS, to identify effort-related and success-related networks recruited under FA or DA conditions during retrieval. Analysis of recognition performance showed that the word-based distracter task interfered with memory performance to a greater degree than did the digit-based distracter task. The task PLS analysis showed that the DA-digit condition was strongly associated with activity in the right dorsolateral frontal cortex, suggesting that although there is no difference in memory output, relative to FA, this region is recruited during conditions in which retrieval requires increased retrieval effort. The functional connectivity analysis showed that successful memory performance in the FA and DA-digit conditions was associated with activation of the same network of brain regions, functionally connected to the right hippocampus. To our knowledge, this is the first study to show such a functional association between a hippocampal network and memory performance for item recognition (for a similar

Table 2. Brain regions associated with different memory conditions, as measured by task PLS analysis

Region	Hem	BA	*X*	*Y*	*Z*	Ratio
Positive saliences (FA condition)						
Inferior frontal	L	44	−66	14	26	6.36
Medial frontal	L	6	−8	−8	62	6.14
Medial frontal	L	6	−6	−24	68	5.08
Precentral	R	6	54	−6	38	5.47
Precentral	R	4	38	−22	52	5.75
Postcentral	R	3	52	−14	56	5.14
Postcentral	L	3	−24	−32	68	9.07
Anterior cingulate	R	24	6	28	0	6.72
Parahippocampus	L	27	−22	−36	−4	8.01
Cuneus	L	19	−2	−96	26	6.11
Cuneus	L	17	−8	−84	2	7.81
Caudate head	R	–	10	10	4	6.95
Putamen	R	–	22	16	−4	8.23
Cerebellum (culmen)	L	–	0	−48	−4	6.16
Negative saliences (DA-digit condition)						
Superior frontal	R	8/9	32	30	56	−9.11

The MNI coordinates represent the peak for the given region; Hem, hemisphere; R, right; L, left; BA, Brodmann area; Ratio, salience/standard error, from the PLS bootstrap analysis, which is a measure of how strongly each region covaries with the pattern of activity seen on the LV; *X* (right/left), negative values are in the left hemisphere; *Y* (anterior/posterior), negative values are posterior to the zero point (located at the anterior commissure); *Z* (superior/inferior), negative values are inferior to the plane defined by the anterior and posterior commissures.

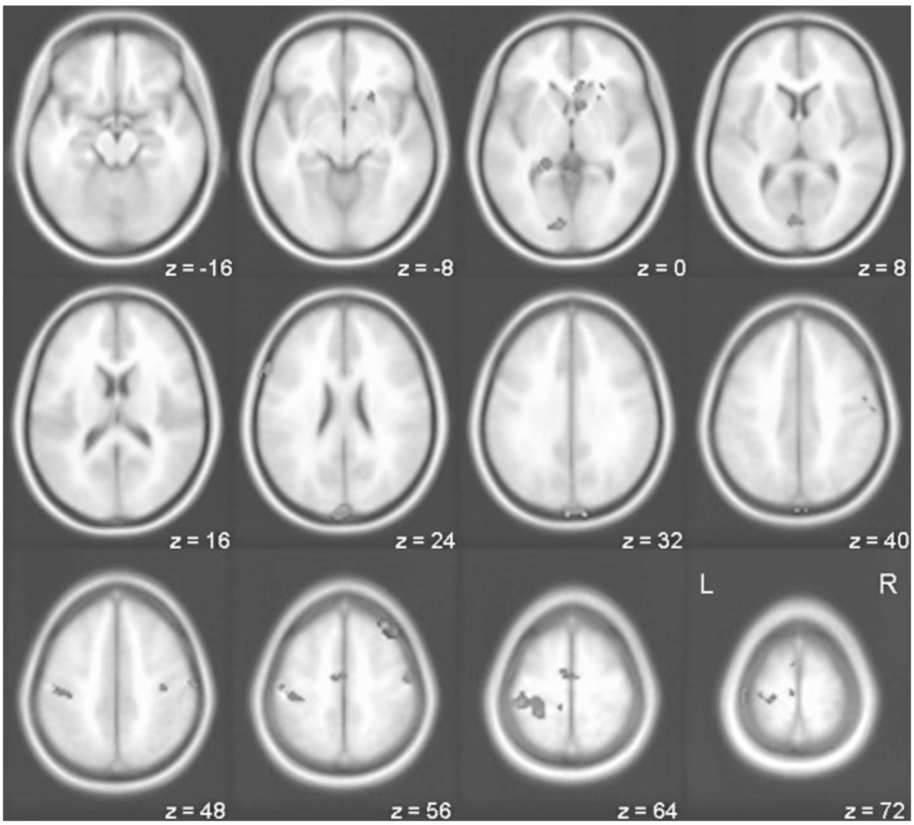

Figure 2. Regions showing task-related activity are shown on standard MNI brain slices at $z = -22$ through +76, relative to the AC-PC line (anterior commissure-posterior commissure line). The right side of the brain is shown on the right in each brain slice. Areas shown in orange represent the brain network related to the FA condition and those shown in blue represent the network related to the DA-digit condition (color figure available online).

Table 3. Brain regions whose activity covaried with right hippocampal activity, and memory accuracy, in the functional connectivity PLS analysis

Region	Hem	BA	*X*	*Y*	*Z*	Ratio
Positive saliences (FA and DA-digit conditions)						
Inferior frontal	L	46	−52	32	14	7.30
Superior frontal	L	8	−2	30	52	8.22
Medial frontal	L	32	−14	8	50	11.99
Middle frontal	L	10	−30	44	0	11.85
Medial frontal	L	10	−16	46	18	11.57
Medial frontal	R	9	14	26	36	6.37
Middle frontal	R	6	38	−8	48	5.65
Middle frontal	R	6	26	−10	50	6.76
Precentral	L	4	−32	−20	52	7.88
Anterior cingulate	R	–	12	36	8	6.77
Cingulate	R	32	16	6	40	7.83
Cingulate	L	31	−6	−28	36	7.65
Cingulate	L	31	−22	−40	40	5.66
Posterior cingulate	L	31	12	−56	20	8.42
Hippocampus	R	–	36	−28	−12	10.15
Superior temporal	L	38	−48	8	−22	8.23
Superior temporal	L	22	−52	−56	16	7.42
Middle temporal	L	20	−66	−26	−16	5.99
Inferior parietal	R	40	58	−32	44	8.77
Precuneus	R	7	10	−38	46	7.09
Cerebellum	R	–	14	−50	−36	6.16
Negative saliences (DA-word condition)						
Precuneus	L	7	−6	−70	68	−5.52

The MNI coordinates represent the peak for the given region; Hem, hemisphere; R, right; L, left; BA, Brodmann area; Ratio, salience/standard error, from the PLS bootstrap analysis, which is a measure of how strongly each region covaries with the pattern of activity seen on the LV; *X* (right/left), negative values are in the left hemisphere; *Y* (anterior/posterior), negative values are posterior to the zero point (located at the anterior commissure); *Z* (superior/inferior), negative values are inferior to the plane defined by the anterior and posterior commissures.

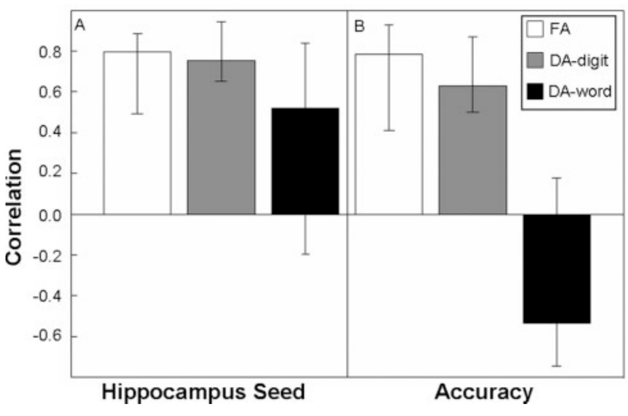

Figure 3. Functional connectivity PLS results showing correlations between brain scores and activity in the right hippocampus seed (in panel A) and memory accuracy (in panel B) for each of the three memory conditions. Error bars represent the 95% confidence interval.

analysis in a source memory paradigm using emotional contexts, see Smith, Stephan, Rugg, & Dolan, 2006). Moreover, we have shown that despite changes in effort-related networks, successful memory performance in the DA-digit condition relied on activation of the same set of brain regions as in the FA condition. Lastly, the DA-word condition, in which successful memory performance was disrupted, was not strongly associated with either network, indicating interference with the recruitment of both retrieval-effort and retrieval-success networks.

Effort-Related Activity

The task PLS identified a pattern of activity that differentiated the FA conditions from the more effortful DA conditions. The FA condition was related to a network of left medial frontal, left parahippocampal, right anterior cingulate, right postcentral, bilateral precentral, right putamen, right caudate, left cuneus, and left cerebellar regions. A region in the right superior frontal lobe, bordering Brodmann areas (BAs) 8 and 9, characterized the DA-digit condition. The focus of this right dorsolateral PFC region is more superior to the right anterior PFC region found to increase during the DA-digit condition in our earlier work,

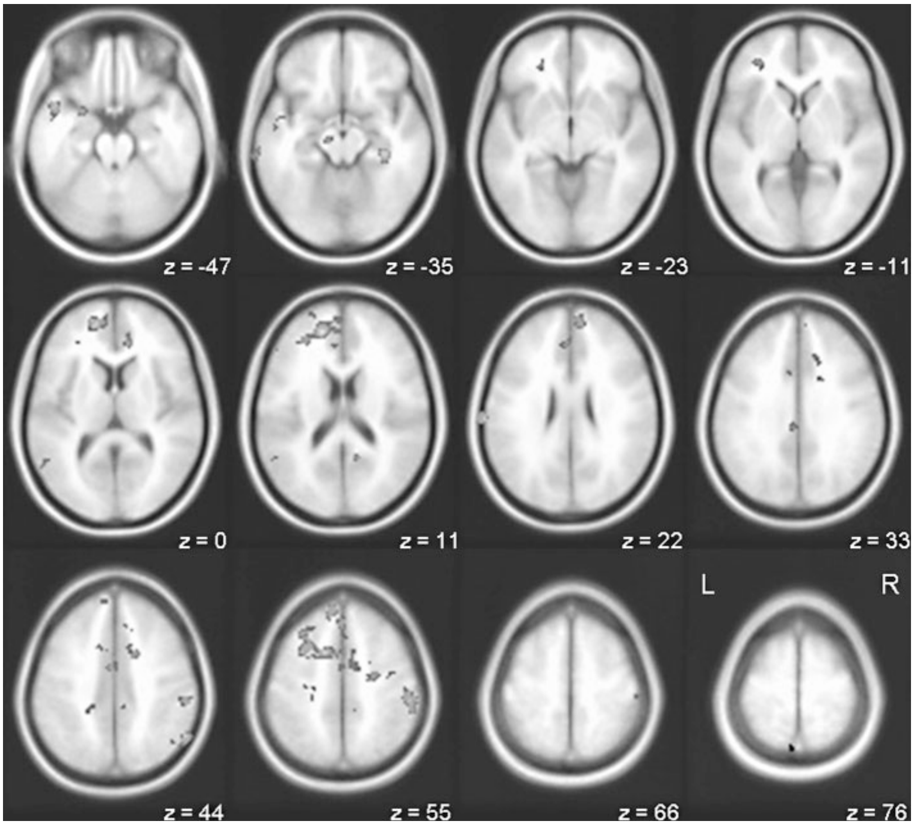

Figure 4. Regions significantly correlated with the right hippocampus and memory accuracy are shown on standard MNI slices at z = −47 through +76. Memory accuracy in the FA and DA-digit conditions increased, as activity in brain regions shown in orange increased, and memory accuracy decreased when activity in the brain regions shown in blue increased (color figure available online). These regions were not reliably correlated with the right hippocampus in the DA-word condition, and accuracy in the DA-word condition was not correlated with activity in this network.

(Fernandes et al., 2005, 2006). This is likely due to differences in analysis technique: In our earlier work, we contrasted activity in the DA-digit and DA-word conditions, whereas the current task PLS instead differentiated patterns of activity across all three memory conditions. The current analysis should be considered a better indicator of the PFC regions involved in the retrieval effort under DA conditions, as the current analysis differentiated the three memory conditions without a priori contrasts selected by the experimenter.

The right PFC region in our study differs from the bilateral ventrolateral and more inferior dorsolateral prefrontal regions found to increase during DA in the studies by Iidaka et al. (2000) and Anderson et al. (2000), respectively. This difference may relate to the specific task and populations used in each study. Iidaka et al. and Anderson et al. both used cued-recall, rather than recognition memory tasks, and Anderson et al. examined memory in both younger and older adults. This suggests that different memory tasks, and populations, may recruit different subregions of the PFC under DA conditions; however, this work converges on the notion that additional prefrontal processes are required to cope with increased processing demands under DA conditions. In addition, the frontal region in our study is similar to the region identified by Lepage et al. (2000), bordering BAs 8 and 9, believed to be a part of the REMO network. We thus interpret the increased activity in right dorsolateral PFC identified by the current PLS analysis to reflect the increased resource demands of DA conditions needed to help maintain REMO, rather than retrieval success. It should also be noted that superior frontal cortex activity has been found during numerical processing (Hanakawa, Honda, Okada, Fukuyama, & Shibasaki, 2003; Zago et al., 2001), which may account for the increased superior PFC activation observed during the DA-digit condition in our study. However, whereas the activation associated with the DA-digit condition was in the right hemisphere, numerical processing is usually lateralized to the left (in right-handed participants; Burbaud et al., 1995).

We predicted that the DA-word condition would activate a similar effort-related network as the DA-digit condition. Instead, we found that the DA-word condition was not strongly associated with activity in any set of brain regions. This finding may suggest that maintaining REMO is hampered in that condition because of difficulties in reactivating any potential words from memory. This possibility is discussed further below.

In contrast to the right PFC activity associated with our DA-digit condition, activity in left medial (BA 6) and inferior (BA 44) PFC was associated with the FA network.

Buckner and Wheeler (2001) hypothesized that retrieval-related activity in these regions might reflect control processes relating to verbal elaboration, and work shows that activation in BA 44 increases as the controlled processing demands of a word-based memory retrieval task increase (Wheeler & Buckner, 2003). Our finding that activity in left medial and inferior PFC increased under FA, as compared to DA, conditions suggests that participants can better engage in control processes relating to verbal elaboration under FA.

Success-Related Patterns

Using PLS, we were able to extend our previous findings (Fernandes et al., 2006) by identifying brain regions whose activity covaries with retrieval success (recognition accuracy) in each condition. The functional connectivity analysis revealed a network consisting of left anterior prefrontal, bilateral dorsolateral prefrontal, right premotor, bilateral cingulate, right parietal, and right cerebellar regions, which correlated significantly with activity in the right hippocampus during all three memory conditions. Most importantly, activity in this network increased as memory performance increased in the FA and DA-digit conditions. That the DA-word condition was not reliably associated with this pattern, but the DA-digit and FA conditions were, suggests that this network is related specifically to retrieval success. The predominance of left PFC activity in the success network stands out against the right PFC activity found in the effort-related analysis. This is consistent with other work showing that the left PFC is involved more in the successful retrieval of information than is the right PFC (Dobbins, Foley, Schacter, & Wagner, 2002; Mitchell, Johnson, Raye, & Greene, 2004).

While the success-related network also included a right dorsolateral PFC region, this region is more inferior and posterior to that identified in the effort-related analysis, and is not closely situated to those regions identified by Lepage et al. (2000), Iidaka et al. (2000), and Anderson et al. (2000) as involved in effort-related processes. Rather, the right medial frontal region identified in the success-related network is similar to the medial frontal region identified by Rugg et al. (1996) to increase in activity with increased retrieval success, supporting the idea that different frontal lobe regions support different retrieval processes.

Right inferior parietal and right precuneus regions were also part of the success-related network. Various studies have found parietal activation during episodic retrieval. These activations are largely lateralized to the left hemisphere (for reviews see Ciaramelli, Grady, & Moscovitch, 2008; Vilberg & Rugg, 2008); the right parietal activity found in our study may reflect the fact that we used a right hippocampal seed, leading to functional connections that are lateralized in the retrieval success network. Vincent et al. (2006) found that fluctuations in the BOLD response in the left and right hippocampus were correlated with activity in bilateral parietal regions and that these parietal regions, functionally connected to the hippocampus, were activated during successful recollection. Our analysis also shows that parietal lobe activity, functionally connected to the hippocampus, increases with retrieval success.

Finally, we found that the brain-seed and brain-behavior correlations in the DA-word condition were not reliable. This suggests that the lower memory performance observed during the DA-word condition is associated with a dampening of activity in the network of brain regions relating to retrieval success. This finding lends support to Moscovitch and Umiltà's (1990, 1991) model of retrieval and provides strong evidence for our earlier suggestion (Fernandes & Moscovitch, 2000) that the hippocampus is unable to engage in processes involved in indexing the content of the memory trace during memory interference brought on under certain DA conditions. Our findings additionally indicate that difficulties in activating a success-related network co-occur with difficulties in activating a network relating to retrieval effort. This suggests that when retrieval success is hindered during DA, the ability to engage in REMO is similarly disrupted.

In summary, using multivariate imaging methods we found that a DA condition that did not disrupt memory performance (DA-digit condition) was associated with a different retrieval-related, but similar performance-related network of activity, as under FA conditions. Specifically, we found that a right superior PFC region increased in activity with increased retrieval effort, whereas bilateral PFC and right parietal regions were functionally connected to the hippocampus and contributed to a network of activity related to retrieval success. A DA condition that disrupted memory performance (DA-word condition) was not associated with either the retrieval- or performance-related networks, suggesting that similar material in the memory and distracting tasks disrupts engagement of both networks.

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