

Similarities and Differences in the Neural Correlates of Episodic Memory Retrieval and Working Memory

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Functional neuroimaging studies have shown that different cognitive functions activate overlapping brain regions. An activation overlap may occur because a region is involved in operations tapped by different cognitive functions or because the activated area comprises subregions differentially involved in each of the functions. To investigate these issues, we directly compared brain activity during episodic retrieval (ER) and working memory (WM) using event-related functional MRI (fMRI). ER was investigated with a word recognition test, and WM was investigated with a word delayed-response test. Two-phase trials distinguished between retrieval mode and cue-specific aspects of ER, as well as between encoding/maintenance and retrieval aspects of WM. The results revealed a common fronto-parieto-cerebellar network for ER and WM, as well as subregions differentially involved in each function. Specifically, there were two main findings. First, the results differentiated common and specific subregions within the prefrontal cortex: (i) left dorsolateral areas were recruited by both functions, possibly reflecting monitoring operations; (ii) bilateral anterior and ventrolateral areas were more activated during ER than during WM, possibly reflecting retrieval mode and cue-specific ER operations, respectively; and (iii) left posterior/ventral (Broca's area) and bilateral posterior/dorsal areas were more activated during WM than during ER, possibly reflecting phonological and generic WM operations, respectively. Second, hippocampal and parahippocampal regions were activated not only for ER but also for WM. This result suggests that indexing operations mediated by the medial temporal lobes apply to both long-term and short-term memory traces. Overall, our results show that direct cross-function comparisons are critical to understand the role of different brain regions in various cognitive functions. © 2002 Elsevier Science (USA)

INTRODUCTION

During the past decade, numerous positron emission tomography (PET) and functional MRI (fMRI) studies

have investigated the neural correlates of different cognitive functions (for a review, see Cabeza and Nyberg, 2000). Although most studies have focused on a single function (see however, LaBar *et al.*, 1999; Braver *et al.*, 2001; Nyberg *et al.*, 2002; Ranganath and D'Esposito, 2001), cross-studies comparisons indicate that different functions activate many of the same brain regions (Cabeza and Nyberg, 2000). To investigate these overlaps in activation it is critical to compare different cognitive functions within-subjects and within the same experiment. Here we present such a comparison for episodic memory retrieval and working memory, using event-related fMRI.

The standard approach in functional neuroimaging has been to focus on a single cognitive function (e.g., perception) and attribute the activations found to different aspects of this particular function (e.g., perceptual analysis, top-down perception, etc.). In contrast with this within-function approach, the cross-function approach we are advocating here asks why the same brain regions can be activated by different functions. One possible answer to this question is that the common region mediates cognitive operations that are shared by the different functions (sharing account). Another possible answer is that the common region consists of several subregions that are differentially involved in each of the functions (subdivision account). According to this last account, activation overlaps will eventually disappear as spatial resolution increases and experimental manipulations become more precise. Sharing and subdivision accounts are not incompatible, and may explain activation overlaps in different brain regions. In the present study, we use both accounts to explain similarities and differences between episodic retrieval and working memory.

Episodic retrieval (ER) was investigated with a word recognition task, and working memory (WM), with a word delayed-response task (see Fig. 1). To distinguish components of the ER task and the WM task, fMRI trials consisted of two 15-s phases (P1 and P2). In the ER task, P1 included an instruction to think back to

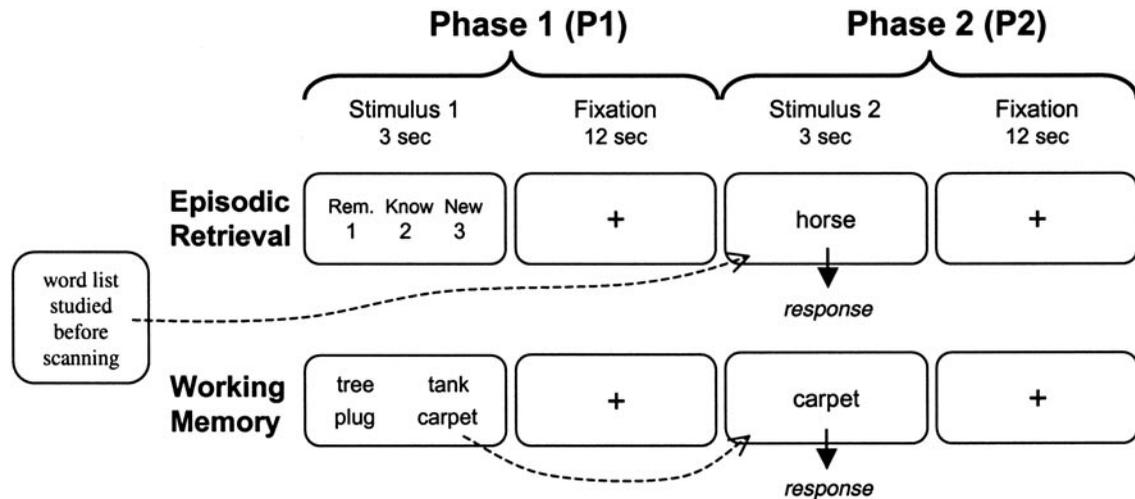


FIG. 1. Behavioral methods. Subjects studied a list of words before scanning, and during fMRI scanning they performed episodic retrieval (ER) and working memory (WM) trials in random order. Each trial consisted of two phases (P1 and P2). In the case of ER trials, P1 elicited a retrieval mode state, and P2, cue-specific ER processes. In the case of WM trials, P1 engaged WM encoding/maintenance operations, and P2, WM retrieval operations.

the study episode (which occurred before scanning), and P2 included a word cue and the associated recognition response. P1 was expected to elicit activity associated with the formation of the mental set of ER, or retrieval mode (Tulving, 1983), and P2, activity associated with cue-specific ER operations. In WM trials, P1 included a memory set of four words, and P2 included a word probe and the corresponding response. P1 was expected to elicit activity associated with WM encoding and maintenance operations, and P2, activity associated with WM retrieval operations.

In functional neuroimaging studies, the activation patterns for ER and for WM show considerable overlap, particularly in prefrontal and parietal regions. However, the frequency of ER and WM activations is not the same for different subregions of the prefrontal and parietal cortex. Subregions that are activated as often for one or the other function are more likely to reflect common processes (sharing account), whereas regions that are activated more frequently for one than for the

other function are likely processes that more specific to one of the functions.

Based on previous functional neuroimaging studies of verbal ER and WM (Table 1, Cabeza and Nyberg, 2000), we predicted similarities and differences in activity patterns across the brain. In prefrontal cortex (PFC), we predicted that dorsolateral regions (e.g., Brodmann Area, BA 9) would be involved in both ER and WM, that anterior (BA 10) and ventrolateral (e.g., BA 45) regions would be more activated for ER than for WM, and that left posterior/ventral (left BA 44, approximately Broca's Area) and bilateral posterior/dorsal regions (BA 6) would be more activated for WM than for ER. Since ER-related activity in anterior PFC (BA 10) has been attributed to retrieval mode (Nyberg, 1998; Düzel *et al.*, 1999; Cabeza and Nyberg, 2000; Lepage *et al.*, 2000), and WR-related activity in left posterior/ventral PFC (left BA 44, Broca's Area), to phonological rehearsal (e.g., Paulesu *et al.*, 1993; Awh *et al.*, 1996; Fiez *et al.*, 1996), we expected these activations to

TABLE 1

Typical PET/fMRI Activations during Verbal Episodic Memory Tasks (Including "Retrieval Success" Conditions) and Verbal/Numeric Working Memory Tasks (Adapted from Cabeza and Nyberg, 2000)

Process Brodmann areas →	Frontal		Midline				Pariet			Temporal				Occip			Subcor																
	10	11	47	45	8	9	46	4	44	6	32	24	23	31	7	40	39	38	in	42	22	21	20	MTL	37	19	18	17	bg	th	cb		
Episodic retrieval	✱			●	●						✧				✧	✱																	✱
Working memory				✱	✱		○	✱							✱	○																	✱

Note. ○, left; ●, right; ✱, bilateral; ✧, medial. Activations were displayed as lateralized if there were at least twice as many activations in one hemisphere than in the other (bilateral activations counted for both hemispheres). The size of the symbols indicate the proportion of studies showing the activation: ●, 40–50%; ●, 51–70%; ●, 71–100%.

onset during P1. We further predicted that superior parietal cortex (BA 7) would be involved in both ER and WM, that left inferior parietal (BA 40) and cerebellum would be more activated for WM than for ER, and that anterior cingulate (e.g., BA 32) and precuneus (e.g., BA 31) regions would be more activated for ER than for WM. In general, we expected that regions similarly involved in both functions would reflect common cognitive processes (sharing account), whereas regions differentially involved in one of the two functions would correspond to functionally specialized areas (subdivision account).

MATERIALS AND METHODS

Subjects

The subjects were 20 young adults (13 males) Duke University students/staff, with a mean age of 22.6 years ($SD = 3.68$). They were healthy, right-handed, English native speakers, with no history of neurological or psychiatric episodes. All subjects gave informed consent to a protocol approved by Duke University Institutional Review Board.

Behavioral Methods

Materials. The critical materials were concrete words selected from the MRC Psycholinguistic Database (<http://www.psy.uwa.edu.au/MRCDataBase/mrc2.html>). The words were four to six letters in length and of moderate frequency. Half of the words referred to living things and half to nonliving things. The words were randomly assigned to study and test lists for the ER and WM tasks, while maintaining the living/non-living proportion.

Procedure. After completing health and MRI screening questionnaires and practicing the tasks to be performed in the scanner, subjects were placed in the scanner and the anatomical scans were conducted. Following the anatomical scans and before the functional scans, subjects studied a list of 40 words (36 targets, 2 primacy fillers, 2 recency fillers), presented at a rate of 3 s/word. Subjects made a living/nonliving decision to each word, and were also instructed to remember the words for a subsequent memory test. In the scanner, all stimuli were projected using an LCD projector to a screen located at about 70 cm behind the subjects' crown, which subjects could see via an angled mirror attached to the head coil. Responses were recorded using a 3-button MR-compatible response box. During functional scanning, subjects performed ER and WM trials in a random order. Each trial lasted 30 s and had two phases, each consisting of a stimulus (3 s) followed by fixation (12 s). In both tasks, subjects made a 3-choice response to the second stimulus, which was always a single word. They were encouraged to respond

while the word was on the screen (3 s), and responses beyond this interval were not computed.

In ER trials, the first stimulus was a 3-word instruction to perform the ER task, and the second stimulus was the cue word. Subjects responded to the cue word by indicating whether they remembered having read the word in the study list before scanning (Remember response), whether they believed the word was in the study list but could not retrieve any specific detail about its occurrence within the list (Know response) or whether they thought the word was not included in the study list (New response). The Remember-Know paradigm was not included to compare Remember and Know trials, which was precluded by the total number of old words scanned (36), but to encourage subjects to use a recollection-based retrieval strategy. In WM trials, the first stimulus was a memory set of four words, presented in two columns, and the second stimulus was a probe word which subjects recognized as being in one of the two columns in the memory set or as a new word. This column-specific WM decision was used in order to match the difficulty of the ER and the WM tasks.

Functional scanning consisted of 12 runs, and each run included 6 critical trials: 3 ER trials with studied words, and 3 WM trials with words from the memory set. Additionally, each run contained several filler trials that were not included in the analyses: an average of 1.0 ER and 0.5 WM trials with new words, which functioned as "catch trials," and 3.5 sustained attention trials, which made the sequence of ER and WM trials unpredictable. Sustained attention trials involved detecting whether a letter presented at fixation blipped twice, once, or never during the fixation period. Thus, across the 12 runs there were a total of 36 ER trials and 36 WM trials. Only trials in which the word was correctly classified as part of the study list (ER trials) or the memory set (WM trials) were included in the analyses. With a level of correct ER and WM performance around 93%, most subjects contributed about 33 trials per condition.

fMRI Methods

Anatomical scanning. A T1-weighted sagittal localizer series was first acquired. The anterior (AC) and posterior commissures (PC) were identified in the mid-sagittal slice, and 34 contiguous oblique slices were prescribed parallel to the AC-PC plane. High-resolution T1-weighted structural images were acquired with a 450-ms TR (repetition time), a 9-ms TE (echo time), a 24-cm FOV (field of view), a 256^2 matrix, and a slice thickness of 3.75-mm. A second series of 46 oblique T1-weighted images perpendicular to the AC-PC was then acquired using the same imaging parameters.

Functional scanning. Thirty-four contiguous gradient-echo echoplanar images (EPis) sensitive to blood-oxygen level dependent (BOLD) contrast were acquired

parallel to the AC–PC plane, using the same slice prescription described above for the near-axial structural images. The EPIs were acquired with a 3-s TR, 40-ms TE, one radio frequency excitation, 24-cm FOV, 64^2 image matrix, and a 90° flip angle. Slice thickness was 3.75-mm, resulting in cubic 3.75-mm^3 isotropic voxels.

Image preprocessing. All image preprocessing and statistical analyses were performed using SPM99. Functional images were corrected for acquisition order, and realigned to correct for motion artifacts. Anatomical images were coregistered with the first functional images for each subject, and then both anatomical and functional images were spatially normalized to a standard stereotactic space, using the Montreal Neurological Institute (MNI) templates implemented in SPM99. Subsequently, the functional images were spatially smoothed using an 8-mm isotropic Gaussian kernel. They were proportionally scaled to the whole-brain signal, which was not significantly correlated with any of the activations identified by subsequent statistical contrasts.

Statistical analyses. Statistical analyses were separately performed for P1 and P2. For each subject, task-related activity was identified by a convolving vector of the onset times of the stimuli with a synthetic hemodynamic response (HDR) and its temporal derivative. The general linear model, as implemented in SPM99, was used to model the effects of interest and other confounding effects (e.g., session effects and magnetic field drift).

Two types of group analyses were conducted using random-effects models. First, the two conditions were compared to the fixation baseline (i.e., ER-baseline and WM-baseline), and the conjunction of the two activation maps was calculated. This was done using the ImCalc feature in SPM, and according to the following formula: $[(\text{ER-T score} > 1.95) * (\text{WM-T score} > 1.95)]$. This procedure yields a mask containing only those voxels that were significantly activated above $T = 1.95$ ($P < 0.033$) in each and both contrasts. The probability of finding a voxel that is independently significant in each and both contrasts (i.e., the joint probability) can be estimated by multiplying the probabilities for each contrast: $0.033 * 0.033 = P < 0.001$ (e.g., Allan *et al.*, 2000). Second, the two conditions were directly compared to each other (ER-baseline vs WM-baseline). In these standard pairwise contrasts, the significance threshold was set at $P < 0.001$, uncorrected ($t > 3.58$). To further reduce the risk of false positive activations in both types of analyses, activations including less than 20 contiguous voxels (each voxel = 3.75 mm^3) were not considered. On the basis of these two types of analyses, we defined common regions as those identified by the conjunction analyses, and specific regions as those that fulfilled two criteria: (1) they must be activated at $T = 1.95$ in only one of the two conditions (i.e.,

not included in the conjunction); and (2) they must show a significant difference between the two conditions in the pairwise contrasts.

The time-courses of fMRI activations were examined by manually drawing regions-of-interest (ROIs, average size: 135.9 voxels) around the activation peaks in the T map images, and extracting the mean raw MRI signal of the voxels in each ROI for each subject and for each condition. The raw MRI signal was converted to percentage signal change from the first image in the trial. The ROI tracing and data extraction were accomplished using software developed at the Brain Imaging and Analysis Center (BIAC) of Duke University. The xyz coordinates provided by SPM, which are in MNI brain space, were converted to xyz coordinates in Talairach and Tournoux's (TT) brain space (Talairach and Tournoux, 1988) using the following formula: $[TT - x = \text{MNI} - x * 0.88 + 0.8; TT - y = \text{MNI} - y * 0.97 - 3.32; TT - z = \text{MNI} - y * 0.05 + \text{MNI} - z * 0.88 - 0.44]$. The resulting coordinates are not perfectly accurate across the whole brain, but the anatomical location of the peaks was confirmed by inspection of the activation maps overlaid on MNI-normalized structural MRI images.

RESULTS

Behavioral Data

Mean correct responses were 93.4% for ER and 91.6% for WM. A one-way ANOVA analysis indicated that this difference was not significant ($F < 1$). Most ER hits were Remember responses (76.9%). Mean reaction times (RTs) were 1711ms for ER and 1486ms for WM. A one-way ANOVA indicated that this difference was significant ($F(1,19) = 19.8, P < 0.01$). Thus, accuracy was similar for ER and WM tasks, but RTs were longer for ER than for WM.

fMRI Data

Table 2 and Figure 2 show brain regions activated during the ER task and/or during the WM task compared to baseline. Regions activated by both tasks included PFC, parietal, cerebellar, and MTL regions. In PFC, overlapping activations occurred in left dorsolateral (BA 9; Fig. 2E) and bilateral ventrolateral (BA 45; Fig. 2C) regions during P2, and in dorsomedial regions during both P1 and P2 (BA 6; Fig. 2F). In the parietal cortex, overlapping activations were found in a superior area, bilaterally during P1 and in the left hemisphere during P2 (BA 7, Fig. 2F). In the cerebellum, overlapping activations were bilateral and occurred in both P1 and P2 (Fig. 2A). In MTL, overlapping activations were found bilaterally during P1 and P2 and included the hippocampus and the anterior parahippocampal gyrus (Fig. 2C). Whereas the overlap in dor-

TABLE 2

Brain Regions Activated during ER and WM Compared to the Fixation Baseline

					ER - baseline				WM - baseline			
					x	y	z	T	x	y	z	T
		Phase	Lat	BA								
Both ER and WM												
PFC	Dorsolateral	2	L	9	-39	11	27	5.0	-42	15	27	2.4
	Ventrolateral	2	L	45	-29	26	1	4.0	-33	26	1	2.9
		2	R	45	31	26	1	4.2	31	26	1	2.4
	Dorsomedial	1	M	6	1	-2	59	4.8	1	1	60	5.8
		2	M	6	1	1	56	2.8	1	1	56	4.7
Parietal Ctx.	Superior	1	L	7	-16	-72	43	3.2	-19	-69	43	3.6
		1	R	7	23	-72	43	4.5	24	-72	43	5.9
		2	L	7	-26	-65	39	3.6	-26	-69	39	6.9
	Dorsomedial	1	M	7	4	-43	44	5.3	1	-43	44	4.3
Cerebellum		1	L		-22	-84	-25	7.5	-16	-84	-25	7.0
		1	R		21	-80	-25	6.3	21	-84	-25	6.9
		2	L		-22	-80	-25	10.2	-26	-82	-25	7.8
MTL	Hippocampus	2	R		21	-80	-25	7.0	21	-80	-25	6.8
		2	L		-19	-26	-9	3.9	-19	-26	-9	3.5
	Parahipp. Gyrus	2	R		21	-26	-9	3.9	21	-26	-9	2.0
		2	L	?	-16	-32	-5	7.0	-16	-32	-5	4.4
		2	R	?	18	-32	-5	5.4	18	-32	-5	2.5
Anterior Cingulate Ctx.		2	M	32	1	19	40	9.5	1	19	34	2.2
Medial Thalamus		2	L		-6	-21	6	8.6	-9	-22	6	10.4
		2	R		8	-18	6	6.0	10	-18	6	5.6
Lenticular Nucleus		2	L		-15	4	3	3.1	-16	4	3	3.8
		2	R		14	4	3	4.3	18	4	3	2.6
Visual Ctx.		1	L	17/18	-9	-84	2	11.8	-3	-84	2	12.9
		1	R	17/18	10	-76	3	9.1	10	-80	3	9.5
		2	L	17/18	-9	-84	2	5.6	-6	-87	2	6.4
		2	R	17/18	10	-76	3	5.7	10	-72	3	6.2
Sensorimotor Ctx.		1	L	4	-42	-11	46	3.7	-42	-11	46	7.8
		2	L	3/4	-29	-26	51	6.0	-29	-22	51	9.5
ER only												
PFC	Dorsolateral	2	R	9	47	29	24	4.3				
	Anterior	2	L	10	-32	51	16	5.2				
		2	R	10	34	51	9	3.0				
	Ventrolateral	2	L	47	-26	22	-6	6.2				
		2	R	47	40	19	-6	6.6				
Ventral Precuneus Ctx.		1	M	31	1	-69	19	5.2				
		2	M	31	1	-36	31	6.8				
Ventral Anterior Cingulate Ctx.		1	M	32	1	48	-4	4.3				
WM only												
PFC	Posterior/ventral	1	L	44					-42	8	27	4.5
	Posterior	2	L	6					-45	0	36	7.8
	Posterior/dorsal	2	R	6					24	-7	52	3.7
Inferior Parietal Ctx.		1	L	40					-49	-40	24	5.0
Dorsal Precuneus Ctx.		2	M	7					7	-65	39	2.6

Note. Lat, lateralization (L, left; R, right; M, medial); BA, Brodmann area; xyz, Talairach and Tournoux's (1988) coordinates; T, T score; Ctx., cortex.

solateral PFC and superior parietal regions were expected, the overlap in MTL was surprising because this region has been strongly associated with ER but not with WM. There were also overlapping activations in anterior cingulate, thalamic, and striatal regions, as well as in visual and sensorimotor cortices. Visual and sensorimotor activity is consistent with the sensory and motor demands of the tasks compared to the baseline.

Table 2 and Fig. 2 also show regions that were activated compared to the baseline in only one of the two tasks. Some PFC, precuneus, and anterior cingulate regions were activated only for ER. In PFC, these activations occurred in right dorsolateral (BA 9; Fig. 2E), bilateral anterior (BA 10; Fig. 2D), and some ventrolateral regions (BA 47/45; Fig. 2B). In the precuneus cortex, the ER-only activation was found in a ventral precuneus/retrosplenial region during both P1 and P2

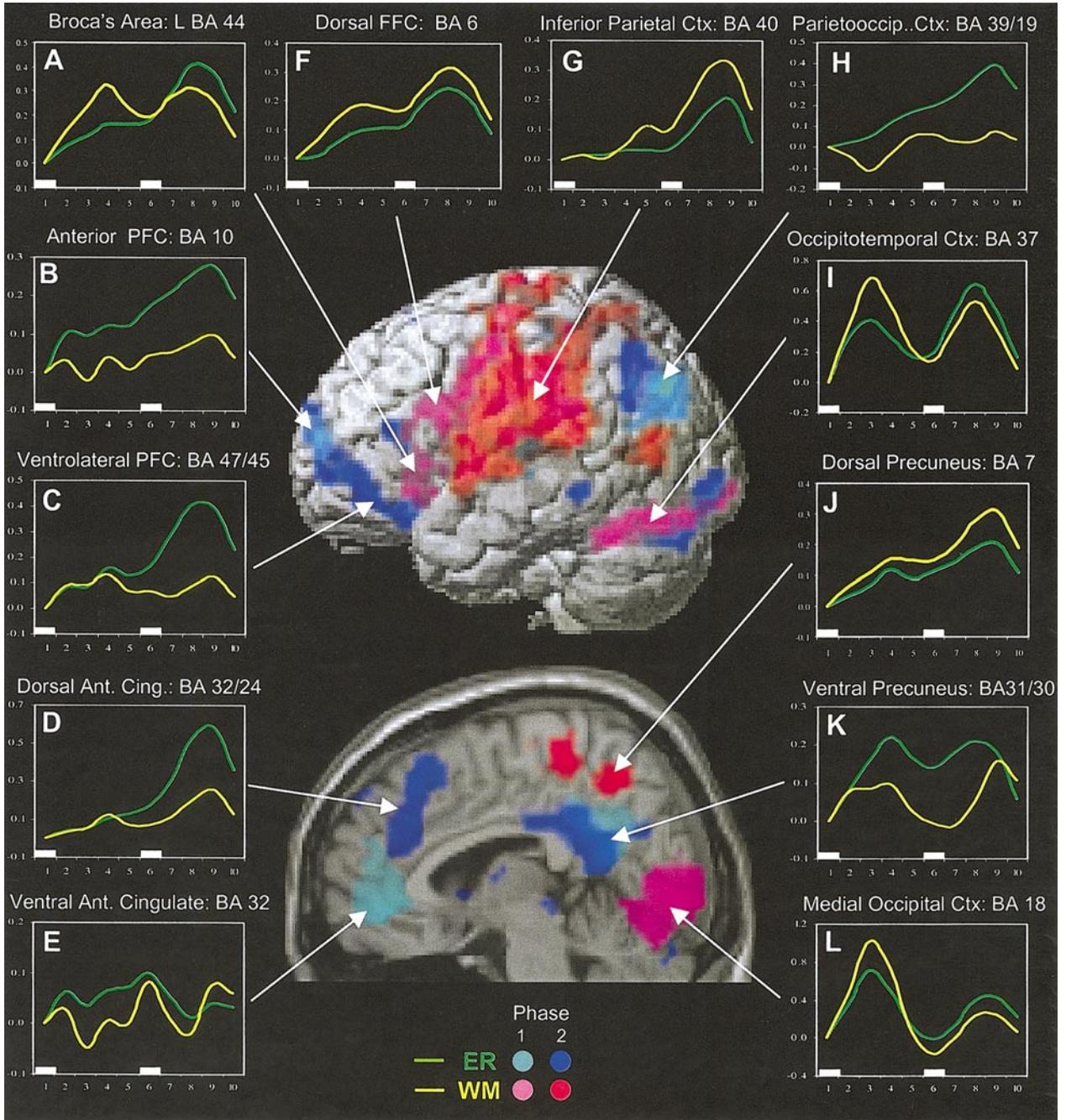


FIG. 3. Brain regions differentially involved in ER or WM, and their corresponding activation time-courses (ER: green line, WM: yellow line). Regions more activated for ER than for WM appear in cyan for P1 and in blue for P2. Regions more activated for WM than for ER appear in magenta for P1 and in red for P2. The top brain image shows left hemisphere activations (including ventral temporal activations) projected to the left lateral cortical surface of a 3-D rendered template. The time-courses correspond to the left-hemisphere activations, but homologous right-hemisphere activations had similar time-courses. The bottom brain image shows midline activations on a normalized sagittal slice. In the plots, the Y-axis indicates percentage signal change from the first image in the trial, and X-axis indicates image number within a trial (each image: 3 s; total trial: 30 s). The white squares symbolize the presentation of a stimulus at the beginning of P1 (Image 1) and P2 (Image 6).

(BA 31/23/30; Fig. 2E). In the anterior cingulate, it occurred in a ventral area during P1 (BA 32; Fig. 2E), Conversely, regions activated for WM but not for ER were found in left posterior/ventral PFC during P1 (left

BA 44; Fig. 2E), in posterior/dorsal PFC regions during P2 (e.g., right BA 6; Fig. 2F), and in the left inferior parietal cortex during P2 (BA 40; Fig. 2E). However, it is important to point out that these presence/absence

TABLE 3
Brain Regions More Activated during ER Than during WM

		Phase	Lat	BA	x	y	z	T
PFC	Anterior	1	R	10	24	51	9	4.8
		1	L	10	-19	55	12	6.0
		2	L	10	-26	51	-1	5.6
	Ventrolateral	2	R	47	31	34	-12	5.7
		2	L	47	-42	36	-8	4.8
		2	R	45	44	22	14	4.6
		2	L	45	-42	26	18	4.8
		2	R	9	44	19	37	6.0
	Dorsolateral	1	L	9	-22	26	35	5.1
		2	L	9	-35	11	40	5.0
		2	L	9	-35	11	40	5.0
	Ventral precuneus/ retrosplenial cortex	1	M	31	-3	-65	23	7.6
1		M	31	8	-47	27	5.5	
2		M	31	-3	-40	28	13.0	
2		M	23/30	-3	-51	17	9.3	
2		M	32/24	4	36	-5	10.0	
Ant. Cing. Ctx.	Ventral	1	M	32/24	4	36	-5	10.0
		2	M	32	-3	30	35	9.0
	Dorsal	2	M	6/32	-3	22	50	8.5
Parietooccipital Ctx.	1	L	39/19	-35	-80	16	5.2	
	2	L	39/19	-39	-69	32	6.9	
	1	R	39/19	40	-80	18	5.3	
Cerebellum	2	L		-19	-84	-25	6.1	
	2	R		27	-80	-25	5.6	
Lateral Temporal Ctx.	1	L	42/22	-46	-26	8	4.6	
	1	R	22	50	-11	3	6.9	
	1	R	21	34	-7	-8	4.9	
Occipital Ctx.	2	L	18	-29	-95	-12	6.2	
	2	R	18	24	-95	-2	5.9	

Note. See Table 2; Ant. Cing., anterior cingulate.

differences may reflect threshold effects, and do not prove that the corresponding regions were significantly more activated in one task than in the other. Evidence of significant differences in activation between the two tasks was provided by the results of the direct ER/WM contrasts described below.

Table 3 lists brain regions that were significantly more activated during ER than during WM, and Fig. 3 shows representative time-courses. Consistent with our predictions, PFC regions that were more activated for ER than for WM included bilateral anterior and ventrolateral PFC areas. In agreement with the retrieval mode hypothesis (Nyberg, 1998; Düzel *et al.*, 1999; Cabeza and Nyberg, 2000; Lepage *et al.*, 2000), bilateral anterior PFC (BA 10) activations started during P1, soon after the presentation of the retrieval mode instruction, and developed gradually during the rest of the trial (see Fig. 3B). The slowly rising BA 10 activity during P1 was significant in the ER-WM contrast (Fig. 3B), but not in the ER-baseline contrast (Fig. 2D), possibly because the time-course of this activation does not fit well to a canonical HDR function. Alternatively, the ER-WM difference could partially reflect a brief deactivation during the third image of the WM task (see Fig. 2B). To investigate the rise of the BA 10 activation independently of the WM condition,

an ANOVA was conducted on the BA 10 ROI, including only the first and the second images of the ER condition. This analysis yielded a significant difference in both left [$F(1,19) = 9.1, P < 0.01$] and right [$F(1,19) = 5.0, P < 0.5$] ROI, indicating a significant rise of ER-related BA 10 activity during P1. The significant rise of anterior PFC activity during P1 suggests that sustained activity in this region is not a consequence of a late onset hemodynamic response (Schacter *et al.*, 1997). In contrast with BA 10, the ER-related activation in ventrolateral PFC (BA 47) occurred in P2, after the presentation of the recognition cue (see Fig. 3C).

Regions more activated for ER than for WM also included precuneus, anterior cingulate, parietal-occipital, and cerebellar areas. ER-related activity in the precuneus involved the ventral half of this region (BA 31), extending over retrosplenial cortex (BA 30), and it occurred during both P1 and P2 (see Figs. 1E and 2K). ER-related activity in the anterior cingulate showed a different time-course in two areas: in a ventral/anterior area, the ER-WM difference occurred during P1 (Figs. 2B–2E and 3E), whereas in a dorsal/posterior region, the ER-WM difference occurred during P2 (Figs. 2E and 3D). ER-related activity in the parietooccipital cortex (BA 39/19) developed gradually from P1 (see Fig. 3H). This activation is close to an area often activated

TABLE 4
Regions More Activated during WM Than during ER

		Phase	Lat	BA	x	y	z	T
PFC	Posterior/Ventral	1	L	44	-46	7	17	4.6
		1	L	44/45	-46	15	21	4.7
	Posterior	2	L	44/6	-52	1	20	7.5
		2	R	44/6	50	1	20	6.3
	Posterior/Dorsal	1	L	6	-42	-7	39	5.6
		2	L	6	-46	-7	39	7.8
		2	R	6	24	-7	52	5.4
		2	R	4/123	34	-18	48	7.9
	Dorsomedial	2	M	6	-19	-11	48	7.4
		2	M	6	21	-7	49	7.2
Inferior Parietal Ctx.	2	L	40	-35	-43	34	5.9	
Dorsal Precuneus	2	L	7	-6	-58	40	8.3	
	2	R	7	10	-62	43	7.3	
Lateral Temporal Ctx.	2	R	22	44	-3	3	6.5	
	2	L	22	-52	-3	9	7.3	
	2	R	21/37	47	-62	-3	5.4	
	2	L	21/37	-39	-69	6	5.9	
Medial Occipital Ctx.	1	L	18	-6	-101	-5	7.0	
	1	R	17	1	-91	-12	8.8	
Ventral Occipitotemp. Ctx.	1	R	19/37	31	-72	-27	5.9	
	1	L	19/37	-35	-55	-26	7.5	

Note. See Table 2; Occipitotem., Occipitotemporal.

in PET/fMRI studies of ER (BA 19; see Table 1). Finally, ER-related activity in the cerebellum occurred in a medial region that was not activated by WM during P2 (Fig. 2A). However, this region was recruited by the WM task during P1 (Table 2; Fig. 2A), suggesting it is not an ER-specific region.

Table 4 lists brain regions that were significantly more activated during WM than during ER, and Fig. 3 shows representative time-courses. Consistent with our predictions, PFC regions that were more activated for WM than for ER included left posterior/ventral (left BA 44) and posterior/dorsal areas (BA 6). As expected, left posterior/ventral PFC (left BA 44, Broca's area) showed a WM-ER difference primarily during P1 (Figs. 2E and 3A). In contrast, ER-related BA 6 activity occurred during both P1 and P2 (see Fig. 3F). During P2, dorsal BA6 activity was left lateralized for ER but bilateral for WM (Fig. 2F), and there was more right dorsal BA 6 activity for WM than for ER during P2. Dorsomedial PFC regions, including SMA, were also more activated for WM than for ER during P2.

Areas more activated during WM than during ER tasks were also found in inferior parietal, dorsal precuneus, lateral temporal, medial occipital, and ventral occipital-temporal regions. Left inferior parietal regions (e.g., BA 40) showed WM-ER differences during P2 (Figs. 1E and 2G). The dorsal precuneus region that showed more activity for WM than for ER (medial BA 7; Figs. 1F and 2J) was about 2 cm more dorsal than the ventral precuneus/retrosplenial region that showed more activity for ER than for WM (BA 31/30; Figs. 2E

and 3K). WM-related activity in lateral temporal cortex occurred primarily during P2. Medial occipital regions (e.g., BA 18) were more activated for WM than for ER during P1 (Fig. 3L). A similar time course was found more anteriorly in ventral temporooccipital regions (BA 19/37; see Fig. 3I).

DISCUSSION

The results revealed a common fronto-parieto-cerebellar network for ER and WM, as well as subregions differentially involved in each function. Specifically, there were two main findings: (i) common and specific subregions were identified within PFC, and (ii) MTL was activated for both ER and WM. These two results and other findings are discussed below.

Common and Specific Subregions within PFC

Confirming our predictions, dorsolateral PFC was involved in both ER and WM. In ER studies, dorsolateral PFC activity has been attributed to the monitoring of retrieved information (Fletcher *et al.*, 1998; Henson *et al.*, 1999; Cabeza *et al.*, 2001), and in WM studies, to the monitoring and manipulation of information within WM (e.g., Owen *et al.*, 1996; D'Esposito *et al.*, 1999). Thus, dorsolateral PFC may be involved in monitoring information in the focus of consciousness, regardless of whether the information is a transient representation of a vanished percept (WM) or the output of a memory search (ER). The overlap between ER and

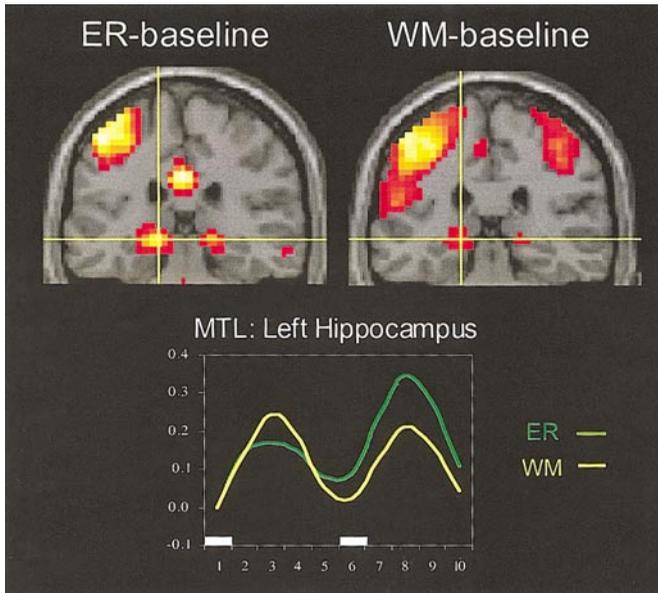


FIG. 4. Overlapping activity in the hippocampus during ER (green line) and WM (yellow line) compared to baseline.

WM occurred in left dorsolateral PFC but not in right dorsolateral PFC, where only ER showed significant activity compared to baseline (Fig. 2E). This pattern is consistent with evidence that when verbal materials are employed, PFC activity tends to be left lateralized in the case of WM (for a review, see Smith and Jonides, 1997) but is often right lateralized in the case of ER (Tulving *et al.*, 1994; Nyberg *et al.*, 1996). In a recent blocked fMRI study (Braver *et al.*, 2001), significant dorsolateral PFC activity was found during WM (N-back task) but not during ER (yes-no recognition). A possible explanation is that dorsolateral PFC is activated during ER only when the monitoring demands of the task exceed those of simple old-new recognition, as in the case of Remember/Know judgments (Rugg and Henson, in press). However, dorsolateral PFC activations are very frequent in PET/fMRI studies of ER (see Table 1) and have been found in many ER studies that used simple old-new recognition (Cabeza and Nyberg, 2000). Thus, dorsolateral PFC appears to be a basic component both WM and ER networks.

Also consistent with our predictions, anterior and ventrolateral PFC areas were more activated for ER than for WM. The aforementioned study by Braver *et al.* (2001) did not find anterior PFC to be more activated for ER than for WM, but this study did not find any PFC region to be more activated for ER than for WM at a standard significance threshold, and hence, the null finding is not particularly informative. In PET/fMRI studies of ER, anterior PFC activity has been attributed to the production and maintenance of the mental set of ER (retrieval mode: Nyberg, 1998; Düzel *et al.*, 1999; Cabeza and Nyberg, 2000; Lepage *et al.*,

2000), or to the evaluation of recovered information (postretrieval monitoring: Rugg *et al.*, 1996, 1998; Allan *et al.*, 2000). The retrieval mode hypothesis provides a better account of the present anterior PFC activity, which started early during P1 and developed gradually throughout P1 and P2 (see Fig. 3B). This time-course is consistent with the results of a combined PET-ERP (event-related potential) study (Düzel *et al.*, 1999), which associated anterior PFC with a positivity that was sustained (tonic) during the ER task, and differed between ER and semantic retrieval tasks. Whereas Düzel *et al.*'s study demonstrated the maintenance of retrieval mode activity throughout the ER task, the present study revealed the production of retrieval mode activity following a global ER instruction and before the presentation of a retrieval cue.

It could be argued that, rather than retrieval mode, the anterior PFC activation reflected nonspecific attentional processes in preparation to the presentation of the cue. However, whereas many studies have associated anterior PFC with retrieval mode (Kapur *et al.*, 1995; Nyberg *et al.*, 1995; Cabeza *et al.*, 1997; Rugg *et al.*, 1997; Buckner *et al.*, 1998; Wagner *et al.*, 1998; Düzel *et al.*, 1999), very few sustained and selective attention studies have found activations in anterior PFC (Cabeza and Nyberg, 2000). Moreover, an attention study that used two-phase fMRI trials similar to the ones used in the present study (Hopfinger *et al.*, 2000), associated the effect of attention-directing cues with dorsal PFC activations rather than with anterior PFC activity.

In contrast with the anterior PFC activation, the ventrolateral PFC activation during ER occurred only during P2 (see Fig. 3C). This time course is consistent with the idea that this region is involved in cue-specification operations (see Fletcher *et al.*, 1998; Henson *et al.*, 1999). This interpretation harmonizes with evidence that ventrolateral PFC regions are activated for both high and low levels of episodic recovery (Nyberg *et al.*, 1995) and for both recall and recognition (Cabeza *et al.*, 1997). The distinction between cue-specification operations mediated by ventrolateral PFC vs. monitoring operations mediated by dorsolateral PFC fits a process-based model of PFC function (Petrides, 1994; Owen, 1997).

Finally, left posterior/ventral and bilateral posterior/dorsal PFC areas were more activated for WM than for ER. As expected, WM-related activity in left posterior/ventral PFC (Broca's area) occurred during P1 (see Fig. 3A), consistent with the notion that this area is involved in phonological rehearsal (for a review, see Smith and Jonides, 1999). In contrast, posterior/dorsal regions were more activated for WM than for ER during both phases of the trials (see Fig. 3F), suggesting they are involved in both maintenance and retrieval operations. Since BA 6 activations are most frequent in PET/fMRI studies of WM, and are not material- or

task-specific, we suggested that they reflect general WM operations (Cabeza and Nyberg, 2000). The present results are consistent with this suggestion.

MTL Activity for both ER and WM

Compared to the baseline, both ER and WM tasks activated MTL regions, including bilateral hippocampal and parahippocampal areas (see Figs. 1C and 3). This overlap was unexpected because MTL function has been strongly associated with episodic memory (for reviews, see Squire, 1992; Cohen *et al.*, 1999), but not with WM. For example, MTL lesions do not usually produce severe WM deficits (e.g., Cave and Squire, 1992), and MTL activations are infrequent in PET/fMRI studies of WM (Cabeza and Nyberg, 2000). On a closer examination, however, there are several pieces of evidence linking MTL regions and WM function. In both human (e.g., Holdstock *et al.*, 1995; Owen *et al.*, 1995; Buffalo *et al.*, 1998) and nonhuman (e.g., Murray and Mishkin, 1986; Zola *et al.*, 2000) primates, MTL lesions have been found to impair performance in trial-unique WM tasks with retention intervals longer than a few seconds. Also, there is electrophysiological (e.g., Cahusac *et al.*, 1989; Suzuki *et al.*, 1997), autoradiographical (e.g., Sybirska *et al.*, 2000), and functional neuroimaging (Haxby *et al.*, 1995; Elliott and Dolan, 1999; Curtis *et al.*, 2000; Ranganath and D'Esposito, 2001) evidence that MTL is activated during working memory tasks.

Yet, one still needs to explain why WM deficits following MTL lesions are relatively minor, and why MTL activations during WM tasks are relatively scarce. A possible answer to both questions is that WM engages MTL only when the retention interval is relatively long, such as the 12 s interval in present study. Since information in WM decays rapidly, it can be sustained for longer period only if it is rehearsed (Atkinson and Shiffrin, 1968). At the neuronal level, this rehearsal process may involve the reactivation of the WM memory representations transiently stored in the neocortex, and accessing these representations may require MTL. MTL is assumed to keep an index of stored memory representation (Damasio, 1989; Alvarez and Squire, 1994; McClelland *et al.*, 1995), and these indexes may be necessary not only to access long-term memory traces but also to access WM traces transiently stored in the neocortex. The idea is not that the WM task involved episodic memory, but that both functions may recruit the same MTL mechanism for different purposes: WM may use MTL indexing mechanism to access short-term memory representations, whereas episodic memory may use MTL indexing function to encode and retrieve long-term memory representations.

The time-courses in Fig. 4 suggest that the MTL activation was greater in P2 than in P1 in the case of

ER but not in the case of WM. To investigate this potential interaction, we conducted a task (ER, WM) x phase (P1, P2) ANOVA on the fMRI signal of Images 3 and 8. This analysis yielded a significant task x phase interaction ($P < 0.0001$), and post hoc analyses indicated that the phase effect was significant for ER ($P2 > P1$: $P < 0.0001$) but not for WM ($P > 0.05$). These results are consistent with our suggestion that overlapping MTL activations reflect MTL trace-indexing functions that are tapped by both WM and ER. In the case of WM, MTL indexing function is critical for maintaining memory traces active during P1 as well as for accessing these traces for the retrieval decision during P2. In the case of ER, in contrast, MTL indexing function is more critical for cue-specific retrieval processes during P2 than for the generation and maintenance of retrieval mode during P1.

Other Findings

In addition to PFC and MTL results, the present study yielded interesting dissociations in the lateral parietal cortex and in the precuneus region. The dissociation in the lateral parietal cortex was consistent with our predictions: superior areas were involved in both ER and WM (BA 7; Fig. 2F), whereas an inferior region was more involved in WM than in ER (BA 40; Fig. 3G). The superior parietal activation was bilateral, and could reflect attentional processes (e.g., Posner and Petersen, 1990) tapped by both ER and WM. In contrast, the inferior parietal activation was left lateralized and maximal during P2, and could reflect access to phonological storage sites during WM (Paulesu *et al.*, 1993; Awh *et al.*, 1996; Jonides *et al.*, 1998).

In the precuneus, there was a dissociation between a ventral region that was differentially engaged in ER (BA 31/30; Fig. 3K) and a dorsal region that was differentially engaged in WM (medial BA 7; Fig. 3K). The precuneus is frequently activated during ER (e.g., Cabeza and Nyberg, 2000; Rugg and Henson, in press), possibly reflecting imagery processes (Fletcher *et al.*, 1995a,b; see, however, Buckner *et al.*, 1996; Krause *et al.*, 1999). The imagery account could accommodate the present finding, if one assumes that imagery may be used not only during cue-specific operations in P2 but also during mental reconstruction of the study episode in P1 (Fig. 3K). Although the involvement of precuneus in WM was not predicted, activations in medial BA 7 have been found in several verbal working memory studies (Petrides *et al.*, 1993; Schumacher *et al.*, 1996; de Zubicaray *et al.*, 1998). The present results suggest that this region may be involved in retrieval operations specific to WM.

Caveats

Three caveats should be noted. First, since responses in the ER task were slower than responses in the WM

task, it could be argued that some differences in activation were related to differences in task difficulty. A difficulty account cannot easily explain the present results because neural activity was not greater overall in one condition than in the other. On the contrary, both conditions yielded activations that did not occur or occurred to a lesser degree in the other condition. At any rate, to test the difficulty account, we correlated the fMRI signal in the regions that were more activated for ER than for WM with the reaction times during ER, and none of the correlations (r : -0.2 to 0.2) was significant. Together with no accuracy differences, this result suggests it is unlikely that differences in activation between ER and WM reflected differences in task difficulty. Second, in the WM task subjects had to indicate which of two word columns contained the probe word. It may therefore be contended that the WM task included a spatial component. Although this possibility cannot be discarded, the left-lateralized pattern of PFC and parietal activity during WM suggests that the WM task was primarily processed as a verbal task. Finally, since ER and WM trials were randomly intermixed, it could be disputed that the activations identified reflected task-switching operations. Although it is possible that task-switching contributed to activations identified in contrasts with the baseline, since task-switching occurred for both ER and WM conditions, it cannot readily explain differences between these conditions. In sum, it is doubtful that the aforementioned potential confounds played an important role in the present study. Moreover, with the exception of the common MTL activation, the present findings are consistent with the results of dozens of PET and fMRI studies of ER and WM summarized in Table 1.

Conclusions

In summary, the present study yielded two main findings. First, the results differentiated common and specific subregions within the prefrontal cortex. Common activity in dorsolateral PFC could reflect monitoring, ER-related activity in anterior and ventrolateral areas could reflect retrieval mode and cue-specification operations, and WM-related activity in left posterior/ventral and bilateral posterior/dorsal areas could reflect phonological and generic WM operations. Second, MTL was activated for both ER and WM, suggesting that indexing MTL functions may apply to both long-term and short-term memory traces. Thus, regions that were similarly involved in ER and WM were associated with common cognitive processes (sharing account), whereas regions that were differentially involved in one of the two functions suggested functional specialization (subdivision account).

It is important to emphasize that the identification of common and specific brain regions is a continuous and long-term process, and that our interpretations are

likely to be revised by future cross-function studies. For example, future cross-function research may show that some of the regions we found to be common for ER and WM are also recruited by other cognitive functions, suggesting they mediate more general processes than the ones proposed here. Alternatively, future cross-function research may show that some of the regions we identified as common to ER and WM actually consist of subregions differentially involved in each of these functions. Future cross-function research will also clarify the cognitive role of the regions we described as specific to ER or WM. In the present article, the term "specific regions" refers only to differential involvement in ER or WM, and does not imply that these regions are "exclusive" to one of these functions. For example, reviews of the literature suggest that anterior PFC is involved in other cognitive functions besides ER (MacLeod *et al.*, 1998; Christoff and Gabrieli, 2000). In any case, our results clearly show that direct cross-function comparisons are critical to understand the role of different brain regions in various cognitive functions.

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REFERENCES

- Allan, K., Dolan, R. J., Fletcher, P. C., and Rugg, M. D. 2000. The role of the right anterior prefrontal cortex in episodic retrieval. *Neuroimage* **11**: 217–227.
- Alvarez, P., and Squire, L. R. 1994. Memory consolidation and the medial temporal lobe: A simple network model. *Proc. Natl. Acad. Sci. USA* **91**: 7041–7045.
- Atkinson, R. C., and Shiffrin, R. M. 1968. Human memory: A proposed system and its control processes. In *The Psychology of Learning and Motivation: Advances in Research and Theory*, Vol. 2 (K. W. Spence, Ed.), pp. 88–195. Academic Press, New York.
- Awh, E., Jonides, J., Smith, E. E., Schumacher, E. H., *et al.* 1996. Dissociation of storage and rehearsal in verbal working memory: Evidence from positron emission tomography. *Psychol. Sci.* **7**: 25–31.
- Braver, T. S., Barch, D. M., Kelley, W. M., Buckner, R. L., Cohen, N. J., Miezin, F. M., Snyder, A. Z., Ollinger, J. M., Akbudak, E., Conturo, T. E., and Petersen, S. E. 2001. Direct comparison of prefrontal cortex regions engaged by working and long-term memory tasks. *Neuroimage* **14**: 48–59.
- Buckner, R. L., Koustaal, W., Schacter, D. L., Dale, A. M., Rotte, M., and Rosen, B. R. 1998. Functional-anatomic study of episodic retrieval: II. Selective averaging of event-related fMRI trials to test the retrieval success hypothesis. *Neuroimage* **7**: 163–175.
- Buckner, R. L., Raichle, M. E., Miezin, F. M., and Petersen, S. E. 1996. Functional anatomic studies of memory retrieval for auditory words and visual pictures. *J. Neurosci.* **16**: 6219–6235.
- Buffalo, E. A., Reber, P. J., and Squire, L. R. 1998. The human perirhinal cortex and recognition memory. *Hippocampus* **8**: 330–339.

- Cabeza, R., Kapur, S., Craik, F. I. M., McIntosh, A. R., Houle, S., and Tulving, E. 1997. Functional neuroanatomy of recall and recognition: A PET study of episodic memory. *J. Cogn. Neurosci.* **9**: 254–265.
- Cabeza, R., and Nyberg, L. 2000. Imaging Cognition II: An empirical review of 275 PET and fMRI studies. *J. Cogn. Neurosci.* **12**: 1–47.
- Cabeza, R., Rao, S. M., Wagner, A. D., Mayer, A. R., and Schacter, D. L. 2001. Can medial temporal lobe regions distinguish true from false? An event-related fMRI study of veridical and illusory recognition memory. *Proc. Natl. Acad. Sci. USA* **98**: 4805–4810.
- Cahusac, P. M. B., Miyashita, Y., and Rolls, E. T. 1989. Responses of hippocampal formation neurons in the monkey related to delayed spatial response and object-place memory tasks. *Behav. Brain Res.* **33**: 229–240.
- Cave, C. B., and Squire, L. R. 1992. Intact verbal and nonverbal short-term memory following damage to the human hippocampus. *Hippocampus* **2**: 151–164.
- Christoff, K., and Gabrieli, J. D. E. 2000. The frontopolar cortex and human cognition: Evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. *Psychobiology* **28**: 168–186.
- Cohen, N. J., Ryan, J., Hunt, C., Romine, L., Wszalek, T., and Nash, C. 1999. Hippocampal system and declarative (relational) memory: Summarizing the data from functional neuroimaging studies. *Hippocampus* **9**: 83–98.
- Curtis, C. E., Zald, D. H., Lee, J. T., and Pardo, J. V. 2000. Object and spatial alternation tasks with minimal delays activate the right anterior hippocampus proper in humans. *Neuroreport* **11**: 2203–2207.
- Damasio, A. R. 1989. Time-locked multiregional retroactivation: A systems-level proposal for the neural substrates of recall and recognition. *Cognition* **33**: 25–62.
- de Zubicaray, G. I., Williams, S. C., Wilson, S. J., Rose, S. E., Brammer, M. J., Bullmore, E. T., Simmons, A., Chalk, J. B., Semple, J., Brown, A. P., Smith, G. A., Ashton, R., and Doddrell, D. M. 1998. Prefrontal cortex involvement in selective letter generation: A functional magnetic resonance imaging study. *Cortex* **34**: 389–401.
- D'Esposito, M., Postle, B. R., Ballard, D., and Lease, J. 1999. Maintenance versus manipulation of information held in working memory: An Event-Related fMRI study. *Brain Cogn.* **41**: 66–86.
- Düzel, E., Cabeza, R., Picton, T. W., Yonelinas, A. P., Scheich, H., Heinze, H.-J., and Tulving, E. 1999. Task- and item-related processes in memory retrieval: A combined PET and ERP study. *Proc. Natl. Acad. Sci. USA* **96**: 1794–1799.
- Elliott, R., and Dolan, R. J. 1999. Differential neural responses during performance of matching and nonmatching to sample tasks at two delay intervals. *J. Neurosci.* **19**: 5066–5073.
- Fiez, J. A., Raife, E. A., Balota, D. A., Schwarz, J. P., Raichle, M. E., and Petersen, S. E. 1996. A positron emission tomography study of the short-term maintenance of verbal information. *J. Neurosci.* **16**: 808–822.
- Fletcher, P. C., Frith, C. D., Baker, S. C., Shallice, T., Frackowiak, R. S. J., and Dolan, R. J. 1995a. The mind's eye—Precuneus activation in memory related imagery. *Neuroimage* **2**: 195–200.
- Fletcher, P. C., Frith, C. D., Grasby, P. M., Shallice, T., Frackowiak, R. S. J., and Dolan, R. J. 1995b. Brain systems for encoding and retrieval of auditory-verbal memory: An *in vivo* study in humans. *Brain* **118**: 401–416.
- Fletcher, P. C., Shallice, T., Frith, C. D., Frackowiak, R. S., and Dolan, R. J. 1998. The functional roles of prefrontal cortex in episodic memory. II. Retrieval. *Brain* **121**: 1249–1256.
- Haxby, J. V., Ungerleider, L. G., Horwitz, B., Rapoport, S. I., and Grady, C. L. 1995. Hemispheric differences in neural systems for face working memory: A PET-rCBF study. *Hum. Brain Mapp.* **3**: 68–82.
- Henson, R. N. A., Shallice, T., and Dolan, R. J. 1999. Right prefrontal cortex and episodic memory retrieval: A functional MRI test of the monitoring hypothesis. *Brain* **122**: 1367–1381.
- Holdstock, J. S., Shaw, C., and Aggleton, J. P. 1995. The performance of amnesic subjects on tests of delayed matching-to-sample and delayed matching-to-position. *Neuropsychologia* **33**: 1538–1596.
- Hopfinger, J. B., Buonocore, M. H., and Mangun, G. R. 2000. The neural mechanisms of top-down attentional control. *Nature Neurosci.* **3**: 284–291.
- Jonides, J., Schumacher, E. H., Smith, E. E., Koeppe, R. A., Awh, E., Reuter-Lorenz, P. A., Marshuetz, C., and Willis, C. R. 1998. The role of parietal cortex in verbal working memory. *J. Neurosci.* **18**: 5026–5034.
- Kapur, S., Craik, F. I. M., Jones, C., Brown, G. M., Houle, S., and Tulving, E. 1995. Functional role of the prefrontal cortex in retrieval of memories: A PET study. *Neuroreport* **6**: 1880–1884.
- Krause, B. J., Schmidt, D., Mottaghy, F. M., Taylor, J., Halsband, U., Herzog, H., Tellmann, L., and Müller-Gärtner, H.-W. 1999. Episodic retrieval activates the precuneus irrespective of the imagery content of word pair associates: A PET study. *Brain* **122**: 225–263.
- LaBar, K. S., Gitelman, D. R., Parrish, T. B., and Mesulam, M. 1999. Neuroanatomic overlap of working memory and spatial attention networks: a functional MRI comparison within subjects. *Neuroimage* **10**: 695–704.
- Lepage, M., Ghaffar, O., Nyberg, L., and Tulving, E. 2000. Prefrontal cortex and episodic memory retrieval mode. *Proc. Natl. Acad. Sci. USA* **97**: 506–511.
- MacLeod, A. K., Buckner, R. L., Miezin, F. M., Petersen, S. E., and Raichle, M. E. 1998. Right anterior prefrontal cortex activation during semantic monitoring and working memory. *Neuroimage* **7**: 41–48.
- McClelland, J. L., McNaughton, B. L., and O'Reilly, R. C. 1995. Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* **102**: 419–457.
- Murray, E. A., and Mishkin, M. 1986. Visual recognition in monkeys following rhinal cortical ablations combined with either amygdalotomy or hippocampectomy. *J. Neurosci.* **6**: 1991–2003.
- Nyberg, L. 1998. Mapping episodic memory. *Behav. Brain Res.* **90**: 107–114.
- Nyberg, L., Cabeza, R., and Tulving, E. 1996. PET studies of encoding and retrieval: The HERA model. *Psychonomic Bull. Rev.* **3**: 135–148.
- Nyberg, L., Forkstam, C., Petersson, K. M., Cabeza, R., and Ingvar, M. 2002. Brain imaging of human memory systems: Between-systems similarities and within-system differences. *Cogn. Brain Res.* **13**: 281–292.
- Nyberg, L., Tulving, E., Habib, R., Nilsson, L.-G., Kapur, S., Houle, S., Cabeza, R., and McIntosh, A. R. 1995. Functional brain maps of retrieval mode and recovery of episodic information. *Neuroreport* **7**: 249–252.
- Owen, A. M. 1997. The functional organization of working memory processes within human lateral frontal cortex: The contribution of functional neuroimaging. *Eur. J. Neurosci.* **9**: 1329–1339.
- Owen, A. M., Evans, A. C., and Petrides, M. 1996. Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: A positron emission tomography study. *Cerebral Cortex* **6**: 31–38.
- Owen, A. M., Sahakian, B. J., Semple, J., Polkey, C. E., and Robbins, T. W. 1995. Visuo-spatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia* **33**: 1–24.

- Paulesu, E., Frith, C. D., and Frackowiak, R. S. J. 1993. The neural correlates of the verbal component of working memory. *Nature* **362**: 342–345.
- Petrides, M. 1994. Frontal lobes and working memory: Evidence from investigations of the effects of cortical excisions in nonhuman primates. In *Handbook of Neuropsychology*, Vol. 9 (F. Boller and J. Grafman, Eds.), pp. 59–82. Elsevier, Amsterdam.
- Petrides, M., Alivisatos, B., Meyer, E., and Evans, A. C. 1993. Functional activation of the human frontal cortex during the performance of verbal working memory tasks. *Proc. Natl. Acad. Sci. USA* **90**: 878–882.
- Posner, M. I., and Petersen, S. E. 1990. The attention system of the human brain. *Annu. Rev. Neurosci.* **13**: 25–42.
- Ranganath, C., and D'Esposito, M. 2001. Medial temporal lobe activity associated with active maintenance of novel information. *Neuron* **31**: 865–873.
- Rugg, M. D., Fletcher, P. C., Allan, K., Frith, C. D., Frackowiak, R. S. J., and Dolan, R. J. 1998. Neural correlates of memory retrieval during recognition memory and cued recall. *Neuroimage* **8**: 262–273.
- Rugg, M. D., Fletcher, P. C., Frith, C. D., Frackowiak, R. S., and Dolan, R. J. 1996. Differential activation of the prefrontal cortex in successful and unsuccessful memory retrieval. *Brain* **119**: 2073–2083.
- Rugg, M. D., Fletcher, P. C., Frith, C. D., Frackowiak, R. S., and Dolan, R. J. 1997. Brain regions supporting intentional and incidental memory: A PET study. *Neuroreport* **8**: 1283–1287.
- Rugg, M. D., and Henson, R. N. A. in press. Episodic memory retrieval: An (event-related) functional neuroimaging perspective. In *The Cognitive Neuroscience of Memory Encoding and Retrieval* (A. E. Parker, E. L. Wilding, and T. Bussey, Eds.), Psychology Press, Hove.
- Schacter, D. L., Buckner, R. L., Koutstaal, W., Dale, A. M., and Rosen, B. R. 1997. Late onset of anterior prefrontal activity during true and false recognition: An event-related fMRI study. *Neuroimage* **6**: 259–269.
- Schumacher, E. H., Lauber, E., Awh, E., Jonides, J., Smith, E. E., and Koeppe, R. A. 1996. PET evidence for an amodal verbal working memory system. *Neuroimage* **3**: 79–88.
- Smith, E. E., and Jonides, J. 1997. Working memory: A view from neuroimaging. *Cogn. Psychol.* **33**: 5–42.
- Smith, E. E., and Jonides, J. 1999. Storage and executive processes in the frontal lobes. *Science* **283**: 1657–1661.
- Squire, L. R. 1992. Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychol. Rev.* **99**: 195–231.
- Suzuki, W. A., Miller, E. K., and Desimone, R. 1997. Object and place memory in the macaque entorhinal cortex. *J. Neurophysiol.* **78**: 1062–1081.
- Sybirska, E., Davachi, L., and Goldman-Rakic, P. S. 2000. Prominence of direct entorhinal-CA1 pathway activation in sensorimotor and cognitive tasks revealed by 2-DG functional mapping in non-human primate. *J. Neurosci.* **20**: 5827–5834.
- Talairach, J., and Tournoux, P. 1988. *A Co-planar Stereotactic Atlas of the Human Brain*. Thieme, Stuttgart, Germany.
- Tulving, E. 1983. *Elements of Episodic Memory*. Oxford Univ. Press, Oxford.
- Tulving, E., Kapur, S., Craik, F. I. M., Moscovitch, M., and Houle, S. 1994. Hemispheric encoding/retrieval asymmetry in episodic memory: Positron emission tomography findings. *Proc. Natl. Acad. Sci. USA* **91**: 2016–2020.
- Wagner, A. D., Desmond, J. E., Glover, G., and Gabrieli, J. D. E. 1998. Prefrontal cortex and recognition memory: Functional-MRI evidence for context-dependent retrieval processes. *Brain* **121**: 1985–2002.
- Zola, S. M., Squire, L. R., Teng, E., Stefanacci, L., Buffalo, E. A., and Clark, R. E. 2000. Impaired recognition memory in monkeys after damage limited to the hippocampal region. *J. Neurosci.* **20**: 451–463.