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Attention-related activity during episodic memory retrieval: a cross-function fMRI study

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Abstract

In functional neuroimaging studies of episodic retrieval (ER), activations in prefrontal, parietal, anterior cingulate, and thalamic regions are typically attributed to episodic retrieval processes. However, these activations are also frequent during visual attention (VA) tasks, suggesting that their role in ER may reflect attentional rather than mnemonic processes. To investigate this possibility, we directly compared brain activity during ER and VA tasks using event-related fMRI. The ER task was a word recognition test with a retrieval mode component, and the VA task was a target detection task with a sustained attention component. The study yielded three main findings. First, a common fronto-parietal-cingulate-thalamic network was found for ER and VA, suggesting that the involvement of these regions during ER reflects general attentional processes. This idea is compatible with some of the interpretations proposed in the ER literature (e.g. postretrieval monitoring), which may be rephrased in terms of attentional processes. Second, several subregions were differentially involved in ER versus VA. For example, the frontopolar cortex and the precuneus were more activated for ER than for VA, possibly reflecting retrieval mode and processing of internally generated stimuli, respectively. Finally, the study yielded an unexpected finding: some medial temporal lobe regions were similarly activated for ER and VA. This finding suggests that the medial temporal lobes may be involved in indexing representations within the focus of consciousness, regardless of whether they are mnemonic or perceptual. Overall, the present results suggest that many of the activations attributed to specific cognitive processes, such as episodic memory, may actually reflect more general cognitive operations.

Keywords: Episodic retrieval; Visual attention; Functional MRI (fMRI); Prefrontal cortex; Parietal cortex; Hippocampus

1. Introduction

Episodic memory retrieval has been the focus of dozens of positron emission tomography (PET) and functional MRI (fMRI) studies. These studies have associated episodic retrieval (ER) with activations in a distributed network of brain areas, including prefrontal cortex (PFC), parietal, anterior cingulate, thalamic, precuneus, and medial temporal lobe (MTL) regions (for reviews, see [6,52]). In general, episodic memory researchers have attributed the involvement of these different regions to distinct aspects of ER. For example, right PFC activations have been attributed to the evaluation of recovered information (postretrieval monitoring: e.g. [28,50,51]), lateral parietal activations, to the processing of spatial aspects of the study episode [62], and anterior cingulate activations, to the initiation of retrieval operations [9].

These accounts illustrate the widespread practice in functional neuroimaging of interpreting activations only in terms of the particular cognitive function being investigated. Yet, when one reviews functional neuroimaging data across several cognitive functions, it is obvious that the same brain regions can be activated by different functions [11]. For example, many of the regions activated during ER tasks, including PFC, parietal, anterior cingulate, and thalamic regions, also tend to be activated during visual attention (VA) tasks (for reviews, see [25,29]). Moreover, these regions are generally assumed to be critical components of a brain network for attention [41,48]. Since ER tasks normally require attention, whereas attention tasks rarely require episodic memory, it is more parsimonious to assume that some of the PFC, parietal, anterior cingulate, and thalamic activations during ER reflect general attentional operations rather than specific mnemonic processes.

On the other hand, it is also possible that particular PFC and parietal subregions recruited by ER tasks are not the same ones recruited by VA tasks. For example, activations

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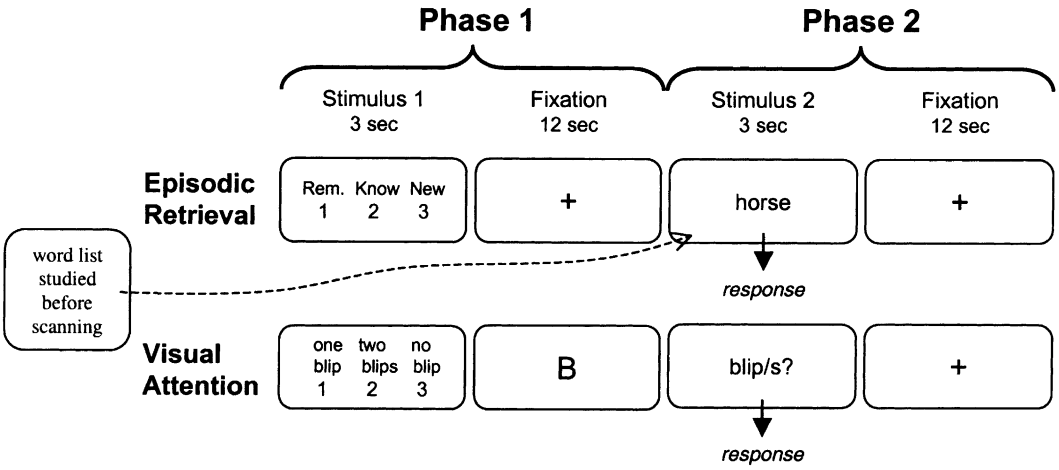

Fig. 1. Behavioral methods.

in left PFC tend to be more frequent during ER tasks than during VA tasks [11]. Also, frontopolar activations (e.g. Brodmann Area—BA 10) are among the most common during ER, but are rarely found during VA [11]. Beyond PFC, precuneus and MTL regions are often activated during ER but they are uncommon during VA [11]. However, these differences are suggested by cross-study comparisons (e.g. [11]), which are typically confounded with differences in stimuli, imaging methods, and significance thresholds. In order to clearly identify similarities and differences between the activation patterns for ER and VA, it is necessary to compare these two functions within-subjects and under similar conditions. Several functional neuroimaging studies have compared different cognitive functions within-subjects [4,7,35,43,44,49], but a direct comparison between episodic memory and attention has never been attempted. This was the goal of the present study.

The paradigm is summarized in Fig. 1. Subjects studied a list of words before scanning, and during scanning they randomly performed ER and VA trials. Each trial consisted of two phases. During the first phase of ER trials, participants generated the mental set of ER (retrieval mode, [61]), and during the second phase, they made a Remember/Know/New response to a word cue. During the first phase of VA trials, participants sustained attention to a symbol on the screen to determine if it blipped once, twice, or never during a 12 s interval, and during the second phase, they made the Once/Twice/Never response. Because only no-blip trials were included in the analyses, the memory component of the VA condition was minimal.

We made two predictions. First, we expected overlapping activations for ER and VA in PFC, parietal, anterior cingulate, and thalamic regions [11]. Given that sustained attention has been associated with a right lateralized fronto-parietal network (for reviews, see [17,54]), we expected overlaps to occur primarily in the right hemisphere. Second, we expected several regions to be more activated for ER than for VA, including left PFC, frontopolar, precuneus, and MTL regions [11].

2. Method

2.1. Subjects

The subjects were 20 young adults (13 males) Duke University students/staff, with a mean age of 22.6 years (S.D. = 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.

2.2. Behavioral methods

2.2.1. 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 4–6 letters in length, and of moderate frequency. Half of the words referred to living things and half to nonliving things.

2.2.2. 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 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 per 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 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 VA 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 letter string. 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 the 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 VA trials, the first stimulus was the instruction to perform the VA task, and the second stimulus was a response screen. Following the instruction screen, subjects had to stare continuously at the fixation symbol (a letter "B") in order to determine if it "blipped" (a brief disappearance) once, twice, or never during the 12 s interval. When the response screen was presented, subjects entered their response (once, twice, never). Only no-blip trials were included in the analyses.

Functional scanning consisted of 12 runs, and each run included 6 critical trials: 3 ER trials with studied words, and 3 VA trials with no blips. Additionally, each run contained several filler trials that were not included in the analyses: an average of 1.0 ER trial with new words, and 0.5 VA trials with blips. VA trials with blips functioned as "catch trials" and were not included in the analyses. There were also trials of a working memory task, whose results were reported in a previous publication [7]. Across the 12 runs, there were a total of 36 old-word ER trials and 36 no-blip VA trials. Only trials in which the word was correctly classified as part of the study list (ER trials) or in which the absence of blips was correctly noted (VA trials) were included in the analyses. With accuracy levels around 93–97%, subjects contributed about 34 trials to each condition.

2.3. fMRI Methods

2.3.1. 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 field of view (FOV), 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.

2.3.2. 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.

2.3.3. Image preprocessing

All image preprocessing and statistical analyses were performed using SPM99 (http://www.fil.ion.ucl.ac.uk/spm/). 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.

2.3.4. Statistical analyses

Statistical analyses were separately performed for Phase 1 and Phase 2. 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. Phase 1 and 2 were modeled by separate covariates. 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, to identify regions *similarly* involved in ER and VA we performed three steps: (a) compared each condition to the implicit baseline (each contrast: $P < 0.033$); (b) calculated the conjunction of the two activation maps (joint probability: $0.033 * 0.033 = P < 0.001$, e.g. [1]); (c) eliminated from the conjunction map those voxels that showed significant differences between conditions (see next sentence). Second, to identify brain regions *differentially* activated by ER and VA, the two conditions were directly compared to each other using a standard significance threshold ($t > 3.58$: $P < 0.001$). In both types of analyses, the risk of false positives was minimized by excluding activations with less than 20 contiguous voxels (e.g. [23]).

The time-courses of fMRI activations were examined by manually drawing regions-of-interest 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 percent 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 Tailarach and Tournoux's (TT) brain space [59] using software available online (http://www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html).

3. Results

3.1. Behavioral data

Mean correct responses were 93.4% for ER and 97.2% for VA. A one-way ANOVA analysis indicated that this difference was nonsignificant ($F(1, 19) = 4.2$, $P > 0.05$). Most ER hits were Remember responses (76.9%). Mean reaction times (RTs) were 1711 ms for ER and 993 ms for VA. A one-way ANOVA indicated that this difference was significant ($F(1, 19) = 128.8$, $P < 0.01$). Thus, accuracy was similar for ER and VA tasks but RTs were slower for ER than for VA.

3.2. fMRI data

Table 1 and Fig. 2 show brain regions that were significantly activated during *both* ER and VA compared to baseline. Consistent with our prediction, overlapping activations were found in right PFC (BAs 9, 47, BA 6: Fig. 2B-D), dorsal parietal (BA 7, Fig. 2E), anterior cingulate (BA 32, Fig. 2A), and thalamic (Fig. 2F) regions. Unexpectedly, similar activations for ER and VA were also found in MTL regions bilaterally (Fig. 2G). Overlapping activations were also observed in basal ganglia (caudate, globus pallidus) and cerebellar regions. Consistent with the sensory and motor demands of the tasks compared to the fixation baseline, common activations were also found in visual and sensorimotor cortices. As illustrated by Fig. 2, the time-courses of common activations were very similar for ER and VA. This finding suggests that these regions performed similar functions during the two tasks.

Table 2 and Fig. 3 show brain regions that were differentially involved in ER or VA. Consistent with our predictions, left PFC (e.g. BA 45: Fig. 3B), frontopolar (BAs 10: Fig. 3A), and precuneus (e.g. medial BA 7: Fig. 3L) regions were more activated for ER than for VA. Other regions that were differentially involved in ER included posterior parietal (left > right, BA 40/39: Fig. 3C), left middle temporal (BA 21, Fig. 3D), and medial PFC (BA 8/32; Fig. 3J) regions. The posterior parietal region (BA 40/39) was more ventral

Table 1
Regions similarly activated by SA and ER tasks

Region	BA	Lat	Ph	*x*	*y*	*z*	T-SA	T-ER
A. Anterior cingulate Ctx.	32	M	2	4	27	30	5.7	4.9
B. Dorsolateral PFC	9	R	2	45	16	27	5.2	3.2
C. Ventrolateral PFC	47	R	2	45	18	−8	5.8	5.7
D. Dorsomedial PFC	6	R	1	26	0	66	3.9	4.8
	6	M	2	−4	−1	49	9.3	7.5
E. Dorsal parietal Ctx.	7	L	1	−30	−56	55	3.8	3.1
	7	R	1	26	−56	55	3.7	4.6
	7	L	2	−30	−52	48	3.4	2.7
F. Thalamus		R	1	15	−29	−2	4.4	3.7
		L	1	−15	−29	−2	4.8	3.0
		L	2	−11	−18	8	9.3	8.7
		M	2	8	−14	8	6.4	6.0
G. Medial temporal lobe (MTL)	L	1	−15	−29	−2	4.6	3.0	
		R	1	15	−33	−2	4.5	4.1
		L	2	−19	−29	−2	3.9	7.0
		R	2	19	−29	−5	2.1	4.5
Caudate		R	2	11	4	7	4.3	4.6
Globus pallidus		L	2	−11	4	3	3.7	4.8
Cerebellum		L	2	−30	−63	−19	6.8	7.3
		R	2	30	−51	−19	8.5	7.9
Occipital Ctx.	19	L	1	−33	−87	8	11.0	10.5
	19	L	2	−23	−81	−12	9.7	9.9
	18	R	2	34	−84	−5	11.8	10.0
	17	R	1	11	−80	7	9.3	12.2
Sensorimotor Ctx.	3	L	2	−41	−22	56	8.6	10.0
	4	L	2	−37	−19	56	7.9	7.7

Notes: capital letters correspond to letters in Fig. 2. BA: Brodmann Area; Ctx.: cortex; Lat: lateralization (L: left, R: right, M: medial); Ph.: phase; T: T score; *xyz*: coordinates form Talairach and Tournoux's (1988).

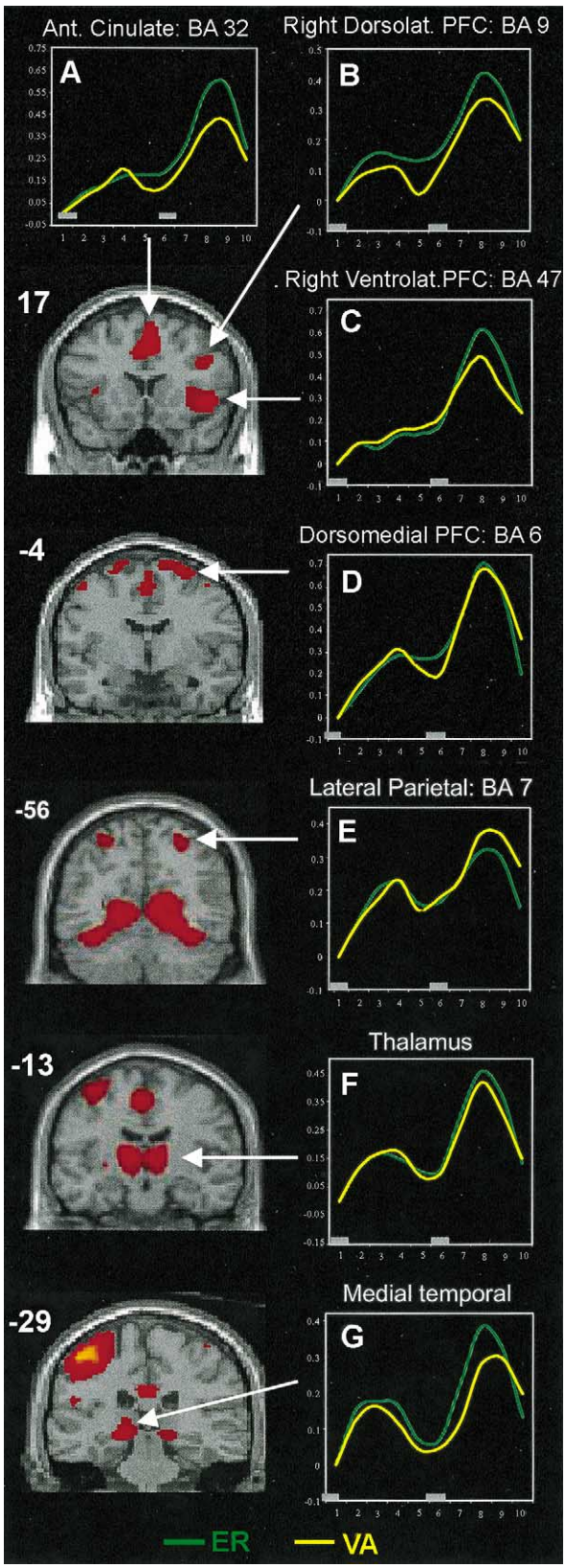

Fig. 2. Brain regions similarly activated during ER and VA and their corresponding activation time-courses. The numbers on the left indicate the *Y* coordinate of each coronal slice. In the plots, the *Y*-axis indicates percent signal change from the first image in the trial, and the *X*-axis, the image number within a trial (each image: 3 s). The white squares symbolize the presentation of a stimulus at the beginning of trial phase.

Table 2
Brain regions differentially engaged by ER and VA tasks

Region	BA	Lat	Ph	*x*	*y*	*z*	*T*
ER > VA							
A. Anterior PFC	10	L	2	−19	63	11	7.6
B. Ventrolateral PFC	47	L	2	−45	43	−6	4.7
	45	L	2	−49	30	16	7.7
Dorsolateral PFC	9	L	2	−49	16	31	6.3
	9/46	L	2	−45	24	26	6.1
C. Posterior parietal ctx.	40	L	2	−49	−56	41	7.4
	39	L	1	−41	−71	31	5.3
	39	R	1	45	−68	27	6.4
D. Lateral temporal ctx.	21	L	2	−55	−40	−5	6.8
J. Medial frontal ctx.	8/32	M	2	−4	31	40	5.7
K. Retrosplenial ctx.	23/31	M	2	0	−31	33	10.0
L. Precuneus/cuneus	31	M	1	0	−68	25	6.9
	7	M	2	−4	−67	35	7.0
	18	M	2	−4	−90	18	5.9
Parahippocampal gyrus	27	L	2	−15	−40	2	4.1
Sensorimotor	4	L	1	−30	−19	64	4.5
	3	L	1	−34	−30	53	4.6
VA > ER							
E. Perisylvian/Insular ctx.	13	L	1	−41	8	−4	4.8
	13	L	2	−45	0	0	7.3
	13	R	2	41	4	0	8.3
	22	R	2	55	−4	4	9.0
	22	L	2	−49	0	0	7.7
F. Occipitotemporal ctx.	37	R	2	55	−54	−1	8.4
	19	L	2	−49	−72	7	6.5
	19	R	2	41	−76	14	4.6
	17	L	1	−15	−95	1	6.3
	19	R	1	38	−81	−5	5.6
G. Anterior parietal ctx.	40	R	2	52	−32	23	8.0
	40	L	2	−63	−28	25	7.6
	7	R	2	30	−48	54	5.9
H. Dorsolateral/ant. PFC	46/10	R	2	26	49	22	5.3
Ventrolateral PFC	44/45	R	2	45	37	2	4.3
Posterior PFC	6	R	1	49	0	7	6.0
	6	R	2	49	6	45	7.7
	6/44	R	2	55	8	10	7.9
	6	M	2	8	−5	56	6.7
	6	L	2	−59	5	14	7.8
I. Medial Parietal Ctx.	5	M	2	−8	−31	50	8.1
	7/5	L	2	−19	−45	57	4.9

Notes: Capital letters correspond to letters in Fig. 3. For abbreviations, see notes of Table 1.

than the dorsal parietal region (BA 7) showing similar activity for ER and VA, and the medial PFC region (BA 8/32) was more dorsal than the anterior cingulate region (BA 32) showing overlapping activity for ER and VA (compare activations to the star symbols in Fig. 3). An MTL region (left parahippocampal gyrus), more posterior than the one showing overlapping activations, was more activated during ER than VA (see Table 2). As indicated by the time-course plots in Fig. 3, most ER activations occurred during both phases, even if some of them were more pronounced during Phase 2. The medial frontal activation was specific to Phase 2, and the precuneus/cuneus activation was specific to Phase 1.

Regions that were more activated during VA than ER included Sylvian/insular, occipitotemporal, anterior parietal, PFC, and medial parietal regions. Sylvian/insular activations

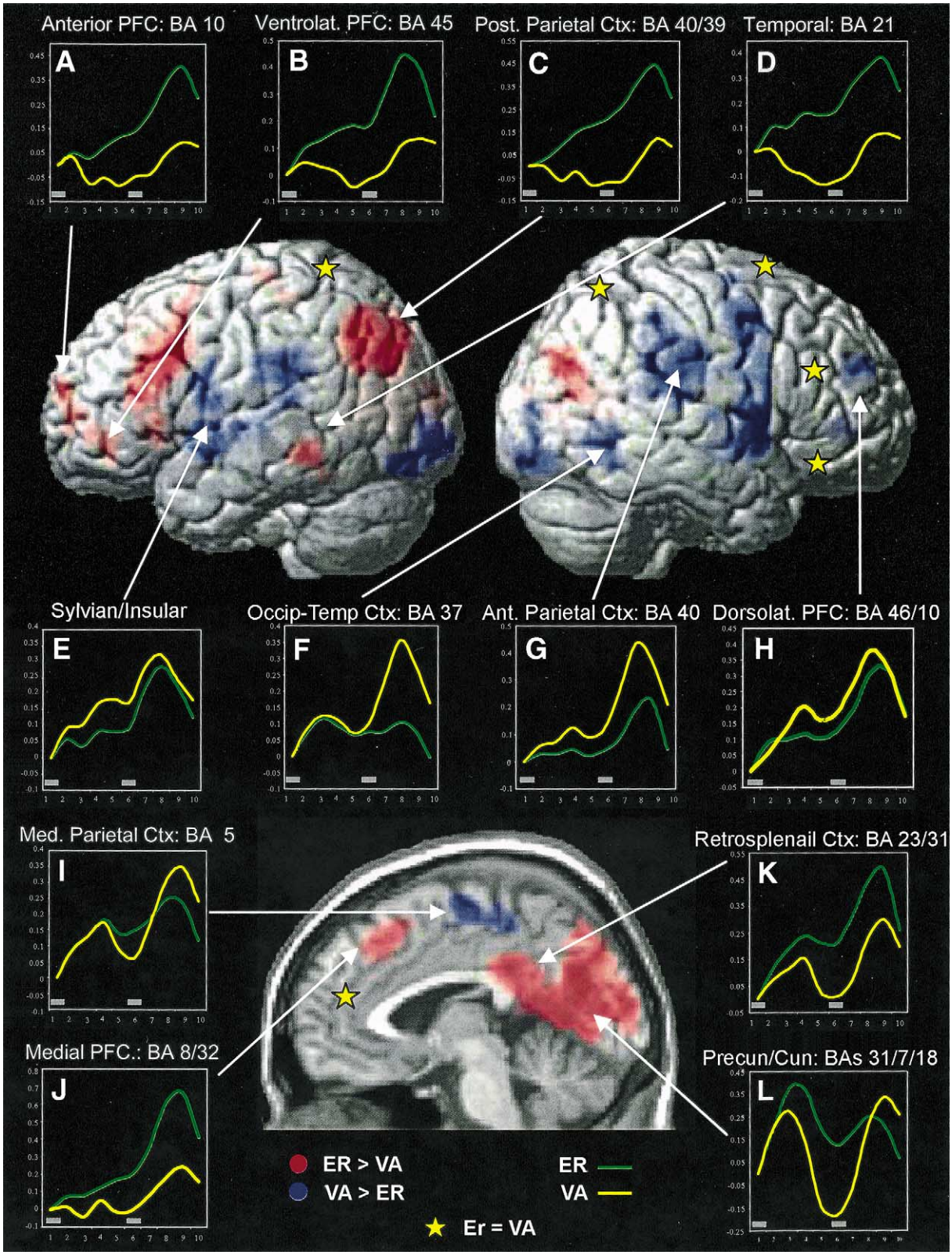

Fig. 3. Brain regions differentially involved in ER or VA, and their corresponding activation time-courses. The top brain images show activations projected to the lateral cortical surface of a 3D rendered template. The bottom brain image shows midline activations on a normalized sagittal slice. In the plots, the *Y*-axis indicates percent signal change from the first image in the trial, and *X*-axis indicates the image number within a trial (each image: 3 s). For comparison, the yellow stars indicate the approximate location of the overlapping cortical activations shown in Fig. 2A–E. The white squares symbolize the presentation of a stimulus at the beginning of trial phase.

were bilateral (BAs 13, 22, Fig. 3E) and extended over the superior temporal gyrus (BA 22). Occipital activations were bilateral and medial, and in the right hemisphere they extended into the posterior temporal cortex (BA 37, Fig. 3F). Anterior parietal activations were bilateral (BA 40, Fig. 3G), and more ventral than those common for the two tasks (BA 7). PFC activations included right dorsolateral (BA 46/10, Fig. 3H), right ventrolateral (BA 44/45), and bilateral posterior (BA 6) regions. The right dorsolateral region showing greater activity for VA than for ER was more anterior than the one similarly activated for the two tasks (compare activation with star symbol in Fig. 3). Finally, VA was associated with an anterior medial parietal region (BA 5, Fig. 3I). As indicated by the activation time-courses in Fig. 3, some Sylvian/insular and PFC regions showed differences during both phases, whereas occipito-temporal, lateral and medial parietal activations occurred primarily during Phase 2.

4. Discussion

The results were generally consistent with our predictions. First, we found overlapping activations during ER and VA in PFC, parietal, anterior cingulate, and thalamic regions (see Fig. 2A-F). Second, left PFC, frontopolar, and precuneus regions were more activated during ER than for VA (see Fig 3A, B, and L). Finally, the study yielded an unexpected finding: an MTL region was similarly activated during ER and VA (see Fig. 2G). Below, we discuss (i) the common fronto-parietal-cingulate-thalamic network, (ii) the regions differentially involved in ER and VA, and (ii) the activation overlap in MTL.

4.1. Common fronto-parietal-cingulate-thalamic network for ER and VA

As illustrated by Fig. 2, ER and VA shared a network of regions that included right PFC, lateral parietal, anterior cingulate, and thalamic regions. As noted in the Introduction, although these regions tend to be frequently activated during both ER and VA [11], it was uncertain if the activations for ER and VA would actually overlap. The present study provides clear evidence not only that they overlap, but also they show very similar time-courses (see Fig. 2). The fact that these regions were similarly activated during an ER task and during a VA task with no episodic memory component suggests that the involvement of these regions during ER is not related to specific memory processes but to general attentional operations.

Actually, some of the memory-related interpretations proposed in ER studies can be easily rephrased in terms of simpler attentional processes. For example, the role of right dorsolateral PFC in ER has been attributed to the evaluation of the retrieval output, or postretrieval monitoring [28]. This idea is supported by evidence that activity in this region tends to be greater in ER conditions in which confident responses cannot be easily made and additional monitoring is required [26,27]. Since monitoring involves continuous attention to the retrieval output, and sustained attention has been associated with right PFC activations (e.g. [3,15,16,37,46,47]), right PFC activations during ER may be described in terms of sustained attention processes.

A basic role in attention processes would also account well for the involvement of lateral parietal, thalamic, and anterior cingulate regions in ER. During ER tasks, lateral parietal activity tends to be greater when information is successfully retrieved from long-term memory (e.g. [12,27,31,33]). Although these parietal activations during ER have been attributed to episodic memory processes (e.g. retrieval success), they may reflect attentional shifts [32] elicited by the successful recovery of information [52]. For example, it is possible that when the memory search is successful, the focus of attention shifts from the processing of the retrieval cue to the processing of the information recovered. Likewise, the thalamus may play a role in orienting of attention [48] during retrieval. Finally, anterior cingulate activations during ER may reflect the involvement of attentional processes during target detection [48]. This idea could explain why anterior cingulate activity during ER tends be greater for recall than for recognition tasks [9,10] because the former involves detecting a target among several candidate responses.

Since both ER and VA tasks required attentional processes whereas only the ER task required mnemonic processes, it is parsimonious to attribute overlapping activations to attentional processes. However, it is also possible that overlapping activations reflected a different type of process shared by ER and VA tasks. For example, these tasks shared not only attentional processes but also simple sensorimotor operations. Although it is unlikely that simple sensorimotor operations can account for all overlapping activations, further research is required to investigate this alternative interpretation.

4.2. Differences in activation between ER and VA

Before discussing differences in activation between ER and VA tasks, two caveats are in order. First, given that the two tasks differed in RTs, there is a chance that some differences in activation reflect differences in task difficulty. To investigate this possibility, we correlated the fMRI signal in the regions that were more activated for ER than for VA with RTs during ER. If ER activations reflected ER difficulty, then one would expect significant correlations between these activations and RTs during ER, but none of the correlations was significant (all $P > 0.1$). Second, since the ER and SA tasks were not matched in all possible respects, differences in activation should be interpreted with caution. For example, even though visual and verbal aspects of the stimuli were matched (see Fig. 1), subjects retrieved words during the ER task but stared at a fixation letter during the VA task. Thus, the ER task was probably more dependent on verbal processing and the VA task, in visual processing.

Also, the distribution of cognitive demands across the two phases of the trials was not identical for the ER and VA, and this precludes a simple interpretation of differences in the timing of activations across tasks. Therefore, the differential activations discussed in this section should be considered preliminary results that require replication and clarification from future studies.

Consistent with our predictions, activity in left PFC and frontopolar regions was greater for ER than for VA. The differential involvement of left PFC in ER (e.g. Fig. 3A and B) was accompanied by a differential involvement of right PFC in VA (e.g. Fig. 3H). This hemispheric asymmetry is consistent with our recent proposal [10] that left PFC is involved in semantically-guided information production [8,24] whereas right PFC is involved in monitoring and verification [28,51,55]. Thus, left PFC activations during ER may reflect greater verbal/semantic demands in the ER task, and right PFC activations during VA may reflect greater sustained attention demands in the VA task. The verbal/semantic component of the ER task could also account for left temporal activations during ER (see Fig. 3D). As for frontopolar activity during ER (BA 10; see Fig. 3A), this activation developed during Phase 1, consistent with several studies that associated frontopolar activity during ER with retrieval mode (e.g. [7,9,19,36,45]).

Also consistent with our predictions, the precuneus and neighboring regions (e.g. Fig. 3K-L) were more activated during ER than during VA. Although these regions are among the most typical activations in functional neuroimaging studies of ER (e.g. [11,52]), their role in ER is still unclear. Precuneus activity during ER was originally attributed to imagery processes [21,22] but subsequent studies found that this area is activated during ER regardless of imagery [5,34]. Activity in the precuneus and neighboring areas tend to be greater when retrieval is successful [12,30], suggesting that these regions are involved in processing recovered information. Thus, one may speculate that whereas lateral parietal regions are involved in orienting attention to both external and internal stimuli (see Fig. 2E), medial parieto-occipital regions are involved in orienting attention to internally generated stimuli (see Fig. 3L).

4.3. Overlap of ER and VA activity in MTL

The finding of overlapping activity in MTL was unexpected because MTL has been strongly associated with episodic memory processes (for a review, see [57]) but not with attention processes. Thus, we predicted that MTL regions would be more activated for ER than for VA. Although a left posterior parahippocampal region was differentially involved in ER (see Table 2), a more anterior MTL region showed a very similar pattern of activation for ER and for VA (see Fig. 2G). MTL regions have been associated with other cognitive functions besides ER. For example, we recently found that MTL regions were similarly activated for ER and for working memory [7]. Since MTL is assumed to keep an index of memory representations [2,18,39], we speculated that these indexes are involved not only in recovering stored long-term memory traces but also in maintaining transient working memory representations ([7], see also [49]). However, the present results suggest that the representations accessed by MTL are not necessarily mnemonic representations. Since only no-blip trials were computed for the VA task, the memory demands of this task were minimal or null; participants just stared at the fixation symbol waiting for a blip.

Thus, activity in some MTL regions seems to reflect indexing of representations in the focus of consciousness, regardless of whether these representations originate in long-term memory, working memory, or the senses. This idea is consistent with Moscovitch's proposal that MTL is a module specialized in automatically registering the conscious experience [42]. Also, this idea is consistent with evidence that MTL activity during ER differs for old items associated with different forms of consciousness (remembering versus knowing: [20]) but is similar for old and new items associated with similar forms of consciousness (veridical versus illusory recognition: [12,56]).

The hypothesis that activity in some MTL regions reflects indexing of conscious representations entails some problems but these problems seem more apparent than real. First, the indexing hypothesis suggests that MTL activations should be found in almost every cognitive task, but this is not the case. A possible explanation is that MTL regions are activated during both target and control tasks, and hence, they are subtracted out in many neuroimaging studies. In the present study, for example, if we had used VA as a control task, we would have missed the MTL activations. Second, the indexing hypothesis suggests that MTL lesions should impair conscious processing in general, but they do not. Although MTL lesions are associated with episodic memory deficits (for a review, see [58]), they do not usually disrupt working memory, attention, or other conscious processing tasks. This is not a real problem because the hypothesis is that MTL indexes the contents of consciousness not that it produces them. This point was clear in Moscovitch's original proposal [42]. Finally, the indexing hypothesis seems inconsistent with reports that MTL lesions can impair forms of nonconscious (implicit) memory, such as trace conditioning (e.g. [60]), perceptual learning [13], and memory-guided eye movements [53]. However, recent evidence indicates that trace conditioning is not truly implicit [14,40] and that perceptual learning is not really impaired by hippocampal lesions [38]. In sum, the hypothesis that MTL is involved in indexing conscious representation is not incompatible with available data and ideas about MTL function.

5. Conclusions

The present study yielded three main findings. First, consistent with previous functional neuroimaging evidence, the

study identified a fronto-parietal-cingulate-thalamic network common to ER and VA. This finding suggests that many of the right-lateralized PFC and parietal activations frequently found during ER reflect general attentional processes rather than specific mnemonic operations. Second, several subregions were differentially involved in ER versus VA. For example, left PFC was more activated for ER than for VA, possibly reflecting semantically-guided information production, whereas right PFC was more activated for VA than for ER, possibly reflecting monitoring processes. Frontopolar cortex was differentially involved in ER, possibly reflecting retrieval mode. The precuneus and neighboring regions were more activated for ER than for VA, suggesting that these areas are involved in processing internally generated information. Finally, the study yielded an unexpected finding: some MTL regions were similarly activated during ER and during VA. This overlap suggests that some MTL regions are involved in processing information within the focus of consciousness. Overall, the present results suggest that many of the activations attributed to specific cognitive processes, such as ER operations, may actually reflect more general cognitive operations. Thus, to understand the role of different brain regions in cognitive processes, it is critical to compare brain activity across functions directly and within-subjects, as in the present study.

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