

Direct Comparison of Episodic Encoding and Retrieval of Words: An Event-related fMRI Study

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Functional magnetic resonance imaging (fMRI) was used to compare directly episodic encoding and retrieval. During encoding, subjects studied visually presented words and reported via keypress whether each word represented a pleasant or unpleasant concept (intentional, deep encoding). During the retrieval phase, subjects indicated (via keypress) whether visually presented words had previously been studied. No reliable differences were found during the recognition phase for words that had been previously studied and those that had not been studied. Areas preferentially active during encoding (relative to retrieval) included left superior frontal cortex, medial frontal cortex, left superior temporal cortex, posterior cingulate, left parahippocampal gyrus, and left inferior frontal gyrus. Regions more active in retrieval than encoding included bilateral inferior parietal cortex, bilateral precuneus, right frontal polar cortex, right dorsolateral prefrontal cortex, and right inferior frontal/insular cortex.

INTRODUCTION

Episodic memory refers to the type of long-term memory that allows a person to recollect personally experienced events (Tulving, 1983). It encompasses both the initial acquisition of information (encoding) and the subsequent remembering of the previous experiences (retrieval). The recent advent of neuroimaging techniques, e.g. positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), has offered a new window through which to view episodic memory; we can now observe the living, awake brain as it encodes and later retrieves experiences. In the last decade, there has been a flurry of neuroimaging research designed to identify the neural substrates of episodic

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encoding and retrieval. Although the eventual goal is to understand the unique contributions of the individual structures contributing to encoding and retrieval, identification of the differences in activation patterns for the two processes is an important first step. It is this latter goal that is the primary focus of the present experiment.

Relatively little is known about the similarities and differences of the neural substrates underlying encoding and retrieval. The focus has generally been on two structures: hippocampus (and surrounding medial temporal regions) and frontal cortex. On the basis of lesion studies, we might expect the hippocampus and surrounding structures in the medial temporal lobe to contribute to encoding more than to retrieval; damage to these structures often renders one amnesic and unable to form lasting representations of newly encountered information. However, demonstrations of intact implicit memory in medial temporal amnesic patients (e.g. Warrington & Weiskrantz, 1968) could be taken as implicating medial temporal structures in conscious recollection (i.e. retrieval). Due to difficulties in attributing lesion-induced memory deficits to being encoding-or retrieval-based, as just demonstrated, the contribution of medial temporal structures to encoding and/or retrieval is unknown. Effects of frontal lobe damage have been reported to lead to memory disorders (Stuss et al., 1994), but this claim is controversial (Shimamura, Janowsky, & Squire, 1990). Lesion studies do not project a clear picture with respect to the role of frontal cortex in episodic memory.

On the basis of behavioural theories of memory (e.g. the encoding specificity principle, Tulving, 1983; transfer appropriate processing, Morris, Bransford, & Franks, 1977), we might expect the neural mechanisms in encoding and retrieval processes to overlap considerably (Roediger, Buckner, & McDermott, 1999). That is, retrieval will benefit to the extent that the cognitive operations performed reinstate those performed during encoding. Therefore, we might expect retrieval to involve a reactivation of processing areas used during encoding.

A complicating factor is that no single task captures the essence of encoding, and no single task captures the essence of retrieval. For example, both encoding and retrieval can be verbal or nonverbal, intentional or incidental. Further, encoding can be "deep" (meaning-based, Craik & Lockhart, 1972) or "shallow" (based on surface features); similarly, retrieval can be performed at a recollective level ("remembering" in Tulving's 1985 terminology) or a more heuristic level ("knowing"). Retrieval can be cued or noncued. Because all these variables interact behaviourally with encoding and retrieval they could be expected to differ somewhat in their neural substrates. In addition, encoding often involves a form of semantic retrieval, and episodic retrieval involves an element of encoding. Thus, no single study can definitively answer the question of how encoding and retrieval relate neurally.

Difficulties notwithstanding, the identification of structures differentially involved in encoding and retrieval has interested researchers and has both theoretical and clinical implications. However, direct, within-subject com-

parisons of the two tasks have been rarely reported (Fletcher et al., 1995b; Nyberg et al., 1996; Petrides et al., 1993; Shallice et al., 1994).

The present study was designed to compare encoding and retrieval of visually presented words. It builds on the existing studies in that it employs fMRI, which offers more observations per subject, and usually better spatial and temporal resolution than PET. In addition, fMRI permits the recognition test to closely approximate those typically given behaviourally. That is, old and new items can be randomly intermixed without sacrificing the ability to compare the two item types directly because selective averaging of trials is possible with fMRI (Dale & Buckner, 1997; Josephs, Turner, & Friston, 1997; Zarahn, Aguirre, & D'Esposito, 1997; for a review see Rosen, Buckner, & Dale, 1998). Following the scan, one can parse out certain types of trials (e.g. studied words) and compare them to others (e.g. nonstudied words). Designs that permit such analyses are typically called *event-related* designs. This type of design offers a significant methodological advance in that it minimises strategic differences that often plague blocked designs (in which a set, or block, of previously studied items occurs, followed by a block of nonstudied items).

In the present experiment, subjects studied (under intentional learning conditions) 64 words in four 295-second epochs (16 words per epoch, or 'run'). Trials were spaced 16.5 seconds apart to allow the haemodynamic response from a given trial to peak and return to baseline before the subsequent trial (Buckner et al., 1996b). These encoding runs were compared to four retrieval runs (yes/no recognition memory), which were procedurally identical, with the exception of task instructions.

METHOD

Subjects

Eight subjects (three males, five females, mean age 22.3, ranging from 21 to 25 years) were recruited from the Washington University community in return for payment. All were right-handed, native speakers of English, had normal or corrected-to-normal vision, and reported no history of significant neurological problems. Subjects provided informed consent in accordance with the guidelines set by the Washington University Human Studies Committee.

Procedure and Materials

Scans were conducted on a Siemens 1.5 Tesla Vision System (Erlangen, Germany) with a standard circularly polarised head coil. A Power Macintosh computer (Apple, Cupertino, CA) and Psyscope software (Cohen et al., 1993) were used for display of visual stimuli. Subjects responded by pushing one of two keys on a fibre-optic light-sensitive keypress connected to a Psyscope Button Box (Carnegie Mellon University, Pittsburgh, PA). An LCD projector

(Sharp, model XGE850) projected stimuli onto a screen positioned at the head of the bore. Subjects viewed the screen via a mirror positioned on the head coil. A pillow was used to minimise head movement, and headphones dampened scanner noise and allowed for communication with subjects.

Structural images were acquired using the MPRAGE sequence with 2mm isotropic voxels (Mugler & Brookeman, 1990). Functional images were collected with an asymmetric spin-echo-planar sequence sensitive to blood oxygenation level-dependent (BOLD) contrast (TR = 2.364, 3.75×3.75 mm in-plane resolution). In each functional run, 125 sets of 16 contiguous, 8mm-thick axial images were acquired parallel to the anterior–posterior commissure plane; this procedure offered whole-brain coverage at a high signal-to-noise ratio (Conturo et al., 1996). Each run lasted approximately five minutes (2.364 seconds per whole-brain acquisition, with 125 such acquisitions per run). There were approximately three minutes between runs, during which time subjects were allowed to rest.

Both encoding and retrieval runs were event-related. Trials occurred every 16.5 seconds to allow the haemodynamic response to rise and return to baseline before the next trial commenced. Trials began on (or near) the onset of the TR (or repetition time, the time required for one whole-brain scan), which allowed seven complete whole-brain acquisitions to occur for each (16.5-second) trial. In all runs, words were presented for one second, followed by a blank screen for three seconds and then a fixation point (a plus sign) for 12.5 seconds (see Fig. 1). Subjects were instructed to respond either while the word was on the screen or during the immediately following blank screen. Subjects were told that during the fixation phase they should look at the fixation point while remaining still. In the encoding runs, subjects were instructed to press one of two keys with their right hand to indicate whether the concept represented by the word was more “pleasant” or “unpleasant”. They were also told to remember the words as well as possible for a later memory test. During the retrieval runs, subjects pressed one of two keys to indicate whether or not they had studied the word previously. Thus, there were visual, binary decision, and keypress components to both types of runs.

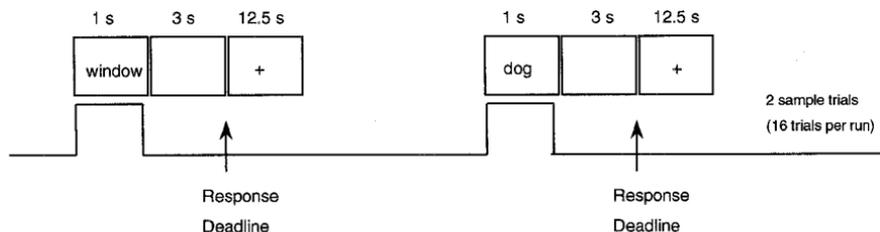


FIG. 1. Schematic depiction of two trials. Trials occurred every 16.5 seconds, and each run included 16 trials.

As demonstrated in Fig. 2, half of the subjects participated in four encoding runs (or sets of 16 trials) followed by six retrieval runs, and the other half received the reverse order (six retrieval, then four encoding runs).¹ Because encoding runs sometimes followed retrieval runs, there were two types of encoding task: those scanned and those unscanned but later tested during retrieval runs (see Fig. 2). Similarly, there were two types of retrieval task: those scanned and unscanned. This manipulation was implemented primarily to control for order effects manifested in signal drift in the scanner; further, they helped control for other order effects (e.g. subject fatigue). Although the specific procedure is complex, the essence is that all subjects participated in three study-test cycles, and we varied which of the study and test episodes were scanned.

As depicted in the top row of Fig. 2, subjects in the encoding-first condition performed four encoding runs (64 words, 16 words/run, half high-frequency and half low-frequency of occurrence in the English language).² Subjects were instructed to try to remember the words for a later memory test; they also had to determine whether each word referred to a concept that was more "pleasant" or "unpleasant" and to indicate their decision with a keypress. Thus, intentional

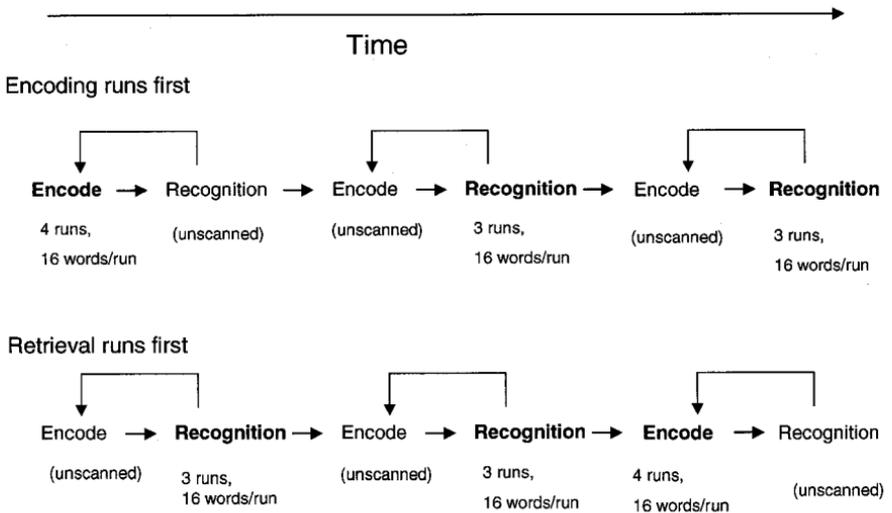


FIG. 2. Schematic depiction of the procedure for subjects receiving the encoding scans first, followed by retrieval scans (top row) and those scanned on the retrieval task first, followed by encoding scans (bottom row). Tasks in bold were those scanned; those in roman were not scanned.

¹To equate power in the two conditions, we analysed only four retrieval runs per subject for the purposes of this paper.

²High frequency was defined as greater than 50 occurrences per million words; low frequency was defined as fewer than 10 occurrences per million words (Kučera & Francis, 1967).

semantic encoding was examined. A short recognition test followed the encoding scans (30 words, half old, not scanned); the purpose of the test was to ensure the words had been encoded effectively. Subjects then studied another set of words (24 words in an unscanned encoding task). Half of the encoded words were high-frequency and half low-frequency. Further, half were assigned to a deep level of processing and half to a shallow level. The deep condition required subjects to mentally determine (on a scale of 1 to 7) how pleasant the concept was, and the shallow task required them to count the number of vowels in the word. The encoding task was followed by three runs of memory tests. Subjects were required to determine whether the visually presented word had been previously studied or not, and to indicate their judgement via keypress. (Half of the tested words had been studied previously.) This final cycle repeated (unscanned encoding phase, three scanned recognition runs) with a different set of words.

For the ‘‘retrieval runs first’’ condition, which is depicted in the bottom row of Fig. 2, subjects studied 24 words (unscanned). Again, half were high-frequency and half low-frequency; further, half occurred under deep encoding and half shallow. Subjects were then tested on those words, via a recognition memory test, which was scanned. The test required subjects to determine whether visually presented words had been studied in the preceding session and to register the response via keypress (see Fig. 1). Again, half of the tested words had been studied in the preceding encoding session. This study (unscanned)–test (scanned) cycle then repeated, as shown in Fig. 2. Finally, these subjects participated in the four encoding scans, followed by an unscanned memory test to ensure instructions had been followed.

In summary, as depicted in Fig. 2, subjects either participated in the encoding first condition ($n = 4$; scanned encoding, then unscanned recognition; unscanned encoding, then scanned recognition; unscanned encoding, then scanned recognition) or in the retrieval first condition ($n = 4$, unscanned encoding, then scanned recognition; unscanned encoding, then scanned recognition; scanned encoding, then unscanned recognition).

Data Analysis

Data for each subject were subjected to the standard processing stream used at Washington University, which includes movement-correction within and across runs using an automated procedure (Snyder, 1996), whole brain normalisation to a common mode of 1000 to allow for comparisons across subjects, and temporal interpolation to correct for offsets in the acquisition times of individual slices (see Ojemann et al., 1997 for an overview).

The data were analysed using an in-house implementation of the general linear model. We began by identifying regions active in separate condition types (e.g. encoding relative to fixation). Specifically, we cross-correlated the time-

course of the BOLD response to each condition at each voxel (with lagged gamma function with a delay of 2.83 seconds and a width of 2 seconds, Dale & Buckner, 1997). The resulting magnitudes were then used to compute *t*-statistics to determine those reliably different from .00 (Friston, Jezzard, & Turner, 1994; Worsley & Friston, 1995).

In addition, comparisons between conditions were computed by assigning appropriate weights to each condition. This approach allowed for direct comparisons to determine regions differentially active in one condition relative to another (i.e. encoding to retrieval; high to low-frequency words; and, within retrieval, previously studied words to previously nonstudied words). The contrast of primary interest was the comparison of encoding and retrieval.

The resulting statistical images were warped into standardised atlas space (Talairach & Tournoux, 1988) and averaged across subjects. The resulting composite images were then corrected for multiple comparisons (Ollinger, 1997) such that $P < .05$ where *P* refers to the probability of a single erroneous activation in the image volume; in addition, single-voxel regions were rejected. The correction method uses a region-size dependent threshold to guarantee that the experiment-wide Type I error is $< .05$; this method provides weak Type I control at the voxel level but strong control at the cluster level. An automated peak-search algorithm (Mintun, Fox, & Raichle, 1989) identified the location (in atlas coordinates) of peak activations on the basis of level of statistical significance and cluster size.

RESULTS AND DISCUSSION

Behavioural Results

Due to equipment failure (in the fibre-optic light source), we obtained behavioural data for only four of our subjects; we therefore report only proportions of hits and correct rejections (and their median RTs) here. For the unscanned recognition tests following the encoding runs, the hit rate was 1.0 (761ms) and the correct rejection rate .98 (875ms). For the retrieval runs, the hit rate was .86 (1029ms) and the correct rejection rate .83 (1234ms). From these data we can conclude that subjects effectively encoded and retrieved in all phases of the experiment.

Imaging Results

When compared directly, both encoding and retrieval revealed several distinct regions more active than the other (Plate 7; Tables 1 and 2). We consider first regions more active in encoding than retrieval (Plate 7, Panel A; Table 1). Three of these regions have been reported previously as being associated with encoding processes: posterior cingulate (Shallice et al., 1995); left parahippocampal gyrus (Dolan & Fletcher, 1997; Kelley et al., 1998); and left inferior

TABLE 1
Regions More Active in Encoding than Retrieval

<i>Location</i>		<i>Coordinates</i>			<i>Significance Level</i>	<i>BA</i>
		<i>x</i>	<i>y</i>	<i>z</i>	<i>z-score</i>	
Frontal	Superior	-15	33	52	4.02	8
		-5	55	22	4.09	9/10
		5	53	28	3.81	9
		-17	45	46	4.61	8
	Medial	-3	49	28	4.73	9
	Inferior	-1	55	14	3.84	10
Temporal	Superior	-41	25	-6	3.64	47
	Middle	-47	23	10	3.41	45
	Parahippocampal gyrus	-43	-57	20	3.96	39
Posterior Cingulate	Middle	-47	-61	14	3.94	39
	Parahippocampal gyrus	-19	-47	-4	3.76	19
Posterior Cingulate		-7	-53	6	4.03	30
		1	-61	14	3.6	30/23

Coordinates from the Talairach & Tournoux (1988) atlas; positive values refer to regions to the right of (x), anterior to (y), and superior to (z) the anterior commissure. The significance level for inclusion in the table was set to $P < .001$ (or $z = 3.3$). BA refers to approximate Brodmann area corresponding to atlas coordinates.

frontal cortex (in or near BA 45/47; Demb et al., 1995; Kapur et al., 1994; Nyberg, Cabeza, & Tulving, 1996). Three other regions found to be preferentially active in encoding have not been widely observed in other encoding studies: left superior frontal cortex (BA 8), medial frontal cortex, and left superior temporal cortex. Curiously, these three regions share another common feature: they seem to be de-activated in retrieval (see Fig. 3). We interpret these results cautiously, however, because the negative curves for retrieval do not follow the usual pattern for most negative curves. That is, typical curves for the BOLD signal (both positive and negative) have sharp onsets or offsets (as in the case for deactivations; Ojemann et al., 1998). That is, more typical negative curves would show sudden drops (much like a mirror reversal of the positive curves). Instead, the onset of these negative curves occurs more gradually.

Several regions were revealed as differentially active in retrieval relative to encoding (Plate 7, Panel B; Table 2). Timecourses for these regions can be seen in Fig. 4. The most robustly active regions were bilateral precuneus and bilateral inferior parietal cortex. In addition, right frontal polar cortex (specifically, anterior middle frontal gyrus, BA 10), right dorsolateral frontal cortex (BA 9/46), and right insular cortex (BA 45/47) were also more active in recognition memory than in encoding.

Encoding > Retrieval

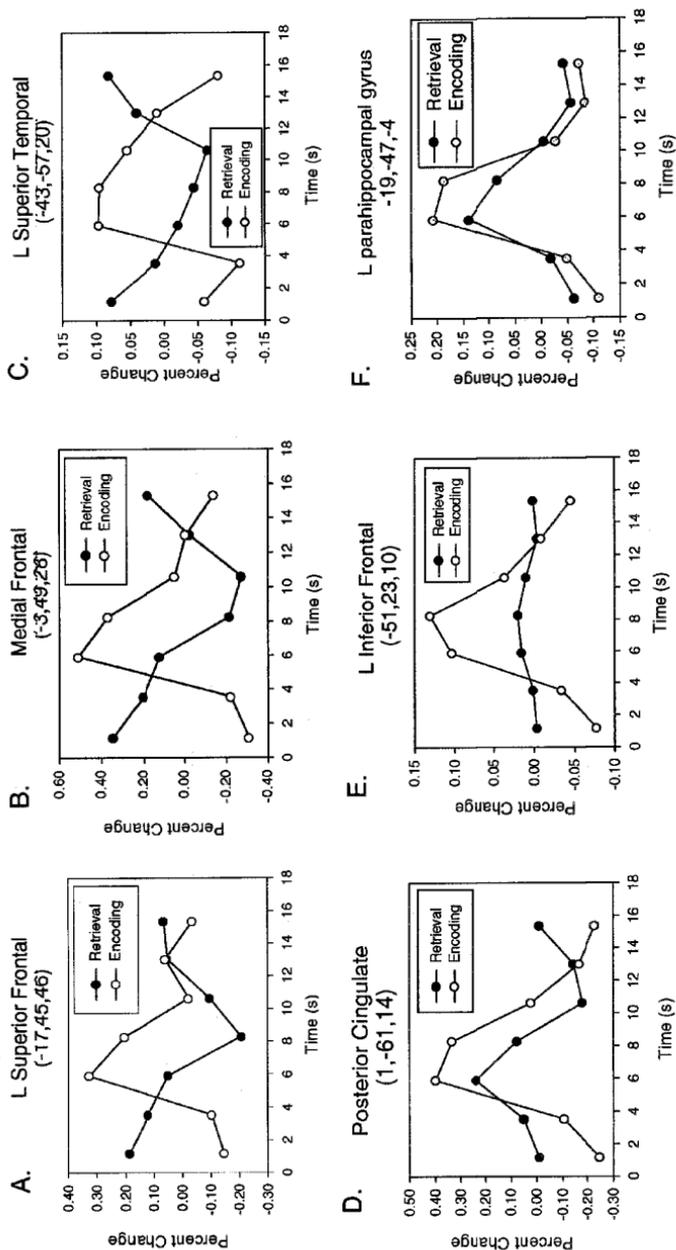


FIG. 3. Timecourses from selected peaks identified as more active in encoding than retrieval (see Plate 7, Panel A). Timecourses were obtained by defining a 15×15 mm square region around the peak point on a 3mm axial slice and averaging the timecourse data for only the voxels that reached significance within that region. Note that peaks are plotted as percent change in signal, but because the images have been normalised to a common value, positive-going curves tend to start below .00, whereas negative-going curves tend to start above .00. Because each whole-brain scan took 2.36 seconds, timepoints shown are the average timepoint for each of the seven scans within each trial (e.g. the first scan spanned from 0 to 2.36 seconds and is therefore plotted at 1.18 second). Note that the scale differs across graphs to highlight the response signal for each region. Alphabetic labels refer to the labels assigned in Plate 7.

TABLE 2
Regions More Active in Retrieval than Encoding

<i>Location</i>		<i>Coordinates</i>			<i>Significance Level</i>	<i>BA</i>	
		<i>x</i>	<i>y</i>	<i>z</i>	<i>z-score</i>		
Frontal	Middle	41	31	30	4.38	9/46	
		37	51	22	3.98	10	
	Inferior/insular	-41	49	4	3.72	10/46	
		31	21	2	3.4	45/47	
Parietal	Superior	-19	-73	38	4.09	19	
		31	-61	46	4.31	7	
	Inferior	-33	-55	40	5.72	40	
		37	-55	38	5.58	40	
		41	-47	56	4.42	40	
		53	-33	42	4.12	40	
		-45	-49	40	4	40	
		Medial/precuneus	-17	-67	48	3.52	7
			-7	-73	38	6.33	7/19
	9		-73	38	6.04	7/19	
	13		-67	30	5.39	7/31	
	Posterior Cingulate	-15	-69	28	4.95	31	
		15	-61	24	4.37	31	
5		-69	28	3.98	31		
-3		-29	24	3.97	23		

Coordinates from the Talairach & Tournoux (1988) atlas; positive values refer to regions to the right of (x), anterior to (y), and superior to (z) the anterior commissure. The significance level for inclusion in the table was set to $P < .001$ (or $z = 3.3$). BA refers to approximate Brodmann area corresponding to atlas coordinates.

The activations in precuneus and inferior parietal cortex are especially interesting; although they have been reported in the retrieval literature (Andreasen et al., 1995; Buckner et al., 1996a; Fletcher, Frith, & Rugg, 1997; Fletcher et al., 1995b; Shallice et al., 1994; see Cabeza & Nyberg, 1997 for a review), they have not been explored to any extent. Receiving much more attention has been right frontal polar cortex (BA 10, see Plate 7, Panel B; Andreasen et al., 1995; Buckner et al., 1996a, 1998a,b; Nyberg et al., 1995; Rugg et al., 1996; Schacter et al., 1997; Squire et al., 1992) and, to a lesser extent, a more superior region in right dorsolateral prefrontal cortex (BA 9/46), also seen in the present data in Plate 7, Panel B (Buckner et al., 1998a; Wagner et al., 1999).

An interesting finding with respect to the right frontal polar activations in retrieval tasks has been the observation that the onset of the activation is late compared to signals in other cortical regions (Buckner et al., 1998b; Schacter et

Retrieval > Encoding

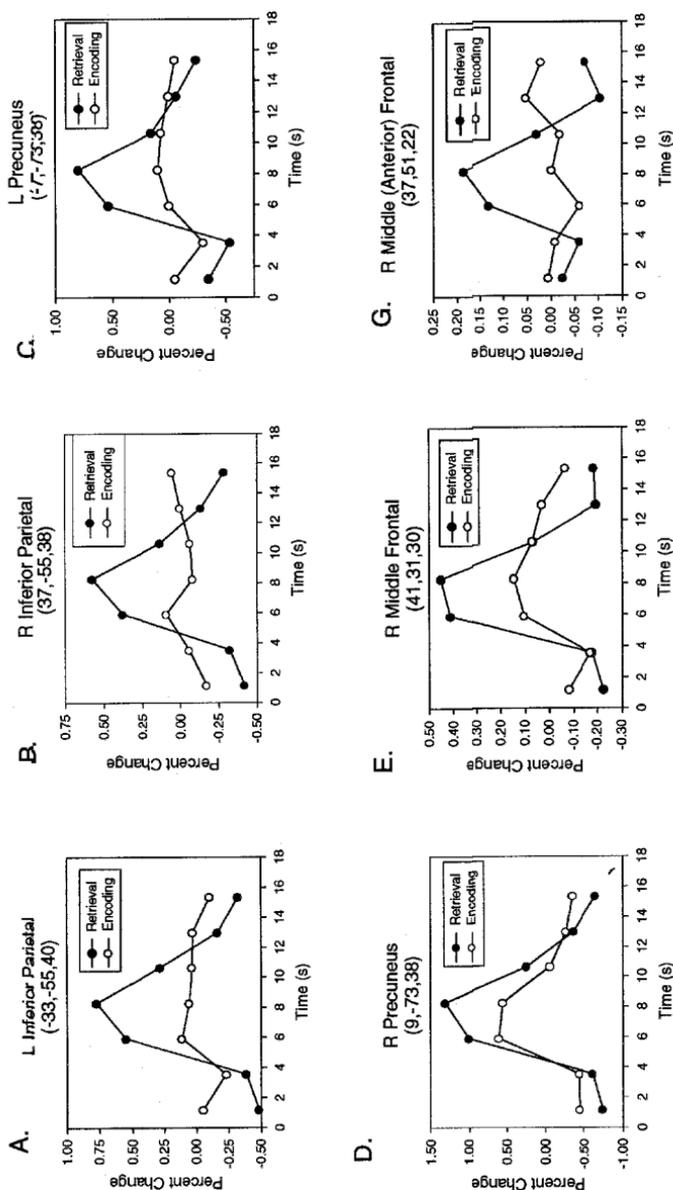


FIG. 4. Timecourses from selected peaks identified as more active in retrieval than encoding (see Plate 7, Panel B). Timecourses were obtained by defining a 15×15 mm square region around the peak point on a 3mm axial slice and averaging the timecourse data for only the voxels that reached significance within that region. Note that peaks are plotted as percent change in signal, but because the images have been normalised to a common value, positive-going curves tend to start below .00, whereas negative-going curves tend to start above .00. Because each whole-brain scan took 2.36 seconds, timepoints shown are the average timepoint for each of the seven scans within each trial (e.g. the first scan spanned from 0 to 2.36 seconds and is therefore plotted at 1.18 second). Note that the scale differs across graphs to highlight the response signal for each region. Alphabetic labels refer to the labels assigned in Plate 7.

al., 1997). The late onset, however, was not observed in the present study (as shown in the curve in Fig. 4); in addition, we examined statistical activation images with gamma functions lagged at longer delays (3.83 and 5.83 seconds) and did not observe responses in this region. The reason for the discrepancy between our study and the two similar studies, which also employed event-related fMRI to examine verbal recognition memory, is unclear. Nevertheless, our frontal polar timecourse appears similar in nature to those in other regions.

Although substantial differences between encoding and retrieval were observed, a number of striking similarities were also observed (see Plate 8). When compared to the low-level baseline (i.e. fixating on a cross-hair), encoding and retrieval shared many activations in common (Plate 8). These similarities occurred in part by design so that differences between encoding and retrieval could be attributed to high-level cognitive processes and not motor or perceptual differences in the tasks. In this respect, many of the similarities speak to the reliability of the data. On another level, however, some similarities may be attributable to similarities in higher-level processing (e.g. posterior inferior frontal gyrus, insular responses, thalamus contralateral to the motor response). In sum, a visual comparison between encoding (relative to fixation) and retrieval (relative to fixation) demonstrates similar activation patterns.

A direct comparison of high- and low-frequency words (collapsing across the encoding/retrieval factor) revealed no reliable differences in activations. Similarly, a direct comparison of types of words on the retrieval test (i.e. "old" or previously studied words and "new" or nonstudied words) yielded no reliable activations. Schacter et al. (1997) and Buckner et al. (1998b) have conducted very similar comparisons and also did not observe differences as a function of hits and correct rejections (although see Friston et al., 1998). It now appears as though previously reported differences between old and new items, which were observed in blocked designs, may have been a product of the design (Buckner et al., 1998b). In blocked designs, many trials of the same type (e.g. old words) typically occur in immediate succession; thus, clusters of old words would be compared to clusters of new words. However, this type of design can lead to strategic differences on the part of the subject, which could account for differences in activation patterns for old and new words. That is, if subjects detect (consciously or not) that there is a pattern in the test sequence, their strategies for making the old/new judgement could change (Wagner et al., 1998). With event-related designs, strategic differences are minimised because the sequencing of words (with respect to prior study status) can occur in a random order, so subjects cannot predict or detect patterns in the testing sequence. The current data add to two previous reports using event-related fMRI that demonstrate equivalent activations for old and new items. This null effect, however, is likely not to be the true state of events; rather, subtle phenomenological differences such as these may not yet be detectable with current methodology. Another possibility is that when subjects attempt to

recollect whether an item occurred previously, they think back to the list and retrieve some studied items (but not the item in question). Thus, they produce a correct rejection, but it is not the case that the retrieval attempt was wholly unsuccessful: some list words were accurately retrieved. This scenario could also explain the lack of old/new differences in recognition memory.

GENERAL DISCUSSION

The data reported here highlight both similarities and differences between intentional encoding and subsequent retrieval of visually presented words. The similarities are evident if one inspects the encoding activations relative to fixation and the retrieval activations relative to fixation. Differences between encoding and retrieval emerged when a direct comparison was performed. Areas more active in encoding than retrieval included left parahippocampal gyrus, posterior cingulate, left inferior frontal cortex, left superior frontal cortex, medial frontal cortex, and left superior temporal cortex. Regions more active in retrieval than encoding included bilateral precuneus, bilateral inferior parietal cortex, right frontal polar, right dorsolateral, and right insular cortex.

Curiously, right frontal polar cortex has received the most attention as a "retrieval" area, and there has been a controversy about its function in retrieval (Buckner et al., 1998a,b; Kapur et al., 1995; Nyberg et al., 1995; Rugg et al., 1996; Schacter et al., 1997). In addition, activations in this region during retrieval tasks have played a large role in the development of a widely known heuristic regarding the role of frontal cortex in episodic memory encoding and retrieval, which has been labelled Hemispheric Encoding/Retrieval Asymmetry (HERA) (Tulving et al., 1994; Nyberg, Cabeza, & Tulving, 1996). The claim is that left frontal areas are differentially involved in encoding, whereas right frontal areas are differentially involved in retrieval. Initially, HERA was intended to describe verbal episodic memory (Tulving et al., 1994), but it was later extended to episodic memory in general (whether verbal or nonverbal, Nyberg, Cabeza, & Tulving, 1996). To the extent that our data speak to this claim, there is some support for HERA. Verbal encoding activated left inferior and superior frontal gyri more than did retrieval; verbal retrieval activated right dorsolateral prefrontal regions (BA 9/46) and an anterior region of middle frontal gyrus (BA 10, R > L) in our study. However, our data suggest that frontal cortex may not be the most profitable area on which to focus when describing differences between encoding and retrieval (at least in the verbal domain). Intentional encoding and recognition memory also differ robustly in distinct regions of parietal cortex (i.e. bilateral precuneus and lateral inferior parietal regions).

Activations very similar to our parietal activations are often found in studies of working memory and have been attributed to verbal working memory (Jonides et al., 1997) and more specifically to phonological processing (Jonides et al., 1998). Fiez et al. (1996) surveyed the working memory literature and

found the mean activation site across studies to be $-33, -47, 37$ and $36, -48, 41$, coordinates that fall very close to the foci in the current experiment (i.e. $-33, -55, 40$ and $37, -55, 38$ for left and right inferior parietal regions, respectively). It is not obvious, however, why phonological processing in retrieval should exceed that in encoding. Perhaps gist-or dual process-based theories of recognition memory (e.g. Reyna & Brainerd, 1995) might predict this pattern. That is, some theories of recognition memory hold that the task can, in some instances, be performed on a quick, automatic basis (e.g. whether the word "seems familiar"). These low-level familiarity judgements could be, in part, based on phonology. However, lateral inferior parietal activations have been reported in free recall (Andreasen et al., 1995), which would seem to rule out any gist-based accounts for the present activations because free recall is not thought to have a gist-like component, and instead to be almost wholly recollective. Admittedly, though, once words are successfully retrieved in free recall, they are most certainly processed phonologically. Therefore, although the source of the activation in retrieval is not obvious, the similarity in the region often attributed to phonological processing and our own activations in recognition memory is striking.

The more medial activations in precuneus are also interesting. A similar region (but about 15mm anterior to the activations in the present study) has been implicated in imaginal processing (Fletcher et al., 1995a). It would be a stretch to argue that imaginal processing should be greater in recognition memory than encoding. Nevertheless, there is some similarity in activated regions.

We should note that the activations in precuneus and inferior parietal cortex are distinct from other regions in the same general area, which have been found to be de-activated in retrieval tasks (e.g. Buckner et al., 1996a, 1998a). That is, in addition to the region of medial parietal cortex that is activated in retrieval, there is also a region de-activated; this de-activated region is slightly anterior to the activated region. In addition, the lateral inferior parietal activations occur near a more-lateral region that is de-activated.

One interesting null result is that the posterior and dorsal extent of the left inferior frontal gyrus (BA 6/44) was activated to an equivalent extent in encoding and retrieval. (This region is superior to the inferior frontal region observed to be preferentially active in encoding in the present study.) This equivalence is noteworthy because Kelley et al. (1998) found this region to be more active in intentional encoding of verbal materials, which led to a high level of performance on a recognition memory test, than incidental encoding of the same materials, which led to a low level of later recognition. Thus, one interpretation of their finding would be that this region of dorsal inferior frontal cortex is specifically involved in verbal episodic memory encoding (e.g. that it is the process of encoding, or maybe the intention to encode that activates this region). Further evidence for this claim can be found in Wagner et al. (1998b), who showed level-of-processing effects (Craik & Lockhart, 1972) in this same

region, and, further, showed that greater activation in this region was predictive of later retrieval success. The current study suggests that it is neither encoding *per se* nor intent to encode that leads to activation here, but rather that active verbal processing in general elicits activation of dorsal inferior frontal cortex (see McDermott et al., in press).

In conclusion, our direct comparison of verbal episodic encoding and retrieval revealed many similarities and some differences between the two processes. Other similar comparisons, using different types of study and test materials, will be necessary to reveal the extent to which our results generalise across domains (e.g. verbal/nonverbal). Consistencies across studies will lead us to a better understanding of brain mechanisms underlying episodic encoding and retrieval. Our results highlight the importance of parietal cortex in episodic recognition of verbal materials; further comparisons will be necessary to establish the extent to which this observation generalises across different types of encoding and retrieval tasks.

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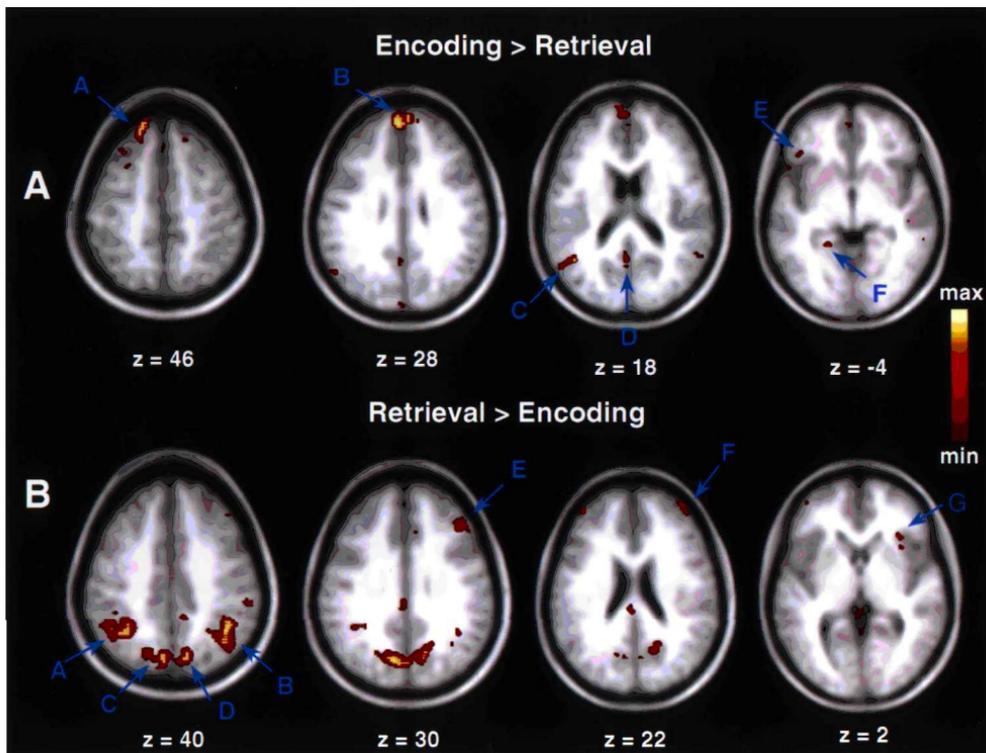


PLATE 7. Regions differentially active in encoding and retrieval. Coloured pixels exceeded the statistical threshold and were superimposed on the corresponding anatomical images (averaged for eight subjects, and warped into atlas space). The colour scale represents the significance level for activations from red (lowest) to yellow (highest). The left side of the images correspond to the left side of the brain. Panel A. Regions more active in encoding than retrieval. Peak activations included left superior frontal cortex (A); medial frontal cortex (B); left superior temporal cortex (C); posterior cingulate (D); left inferior frontal cortex (E); and left parahippocampal gyrus (F). Panel B. Regions more active in retrieval than encoding. Peak activations included bilateral inferior parietal cortex (A, B); bilateral precuneus (C, D); right dorsolateral prefrontal cortex (E); right frontal polar cortex (F); and right inferior frontal/insular cortex (G).

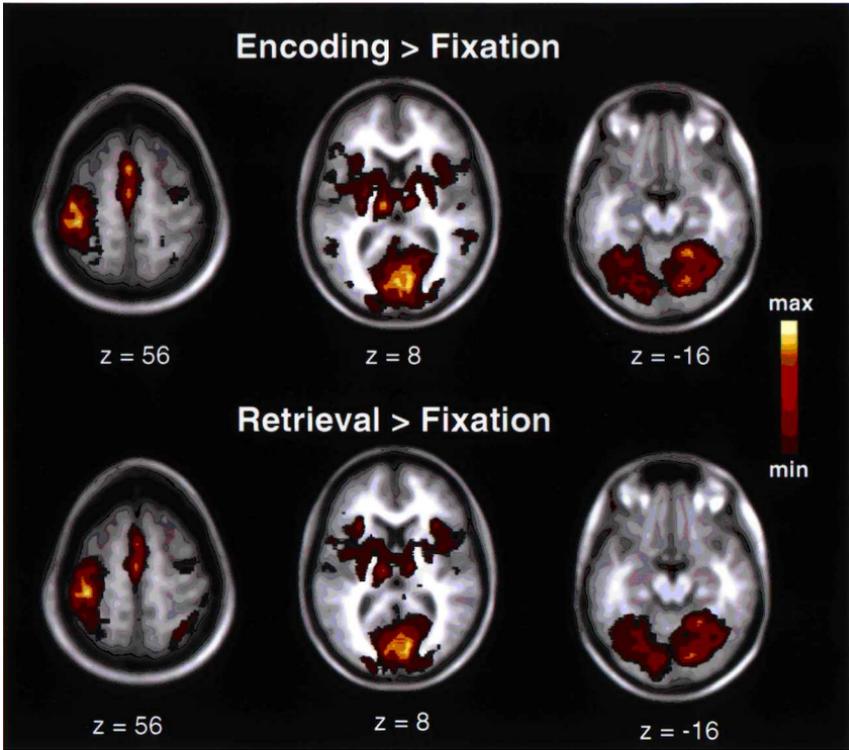


PLATE 8. Similarity of activation observed in encoding and retrieval runs can be seen in these slices. The most superior slice ($z = 56$) demonstrates SMA and motor cortex. The middle slice ($z = 8$) shows activations in bilateral frontal opercula, bilateral thalamus (L>R), bilateral putamen, and visual cortex. The most inferior slice shows cerebellar activation.