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NeuroImage

NeuroImage 18 (2003) 827–836

www.elsevier.com/locate/ynimg

Feeling-of-knowing in episodic memory: an event-related fMRI study

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Received 8 May 2002; revised 30 October 2002; accepted 21 November 2002

Abstract

An individual may fail to recall an item from memory but still feel that it would be recognized on a later test, a retrieval state termed the "feeling-of-knowing" (FOK). In this study we used event-related fMRI and the FOK to examine both encoding- and retrieval-related factors that are associated with different levels of recall performance: successful retrieval of a previously studied item, retrieval failure accompanied by the FOK, and retrieval failure without any FOK. The results revealed one predominant pattern of retrieval-related activation: an intermediate level of activation for FOK—less than that associated with successful recall and greater than that associated with unsuccessful recall (frontal and left parietal cortices). Two further patterns were also observed: greater activation for both successful recall and FOK than for unsuccessful recall (left midlateral prefrontal cortex) and greater activation for successful recall than for both FOK and unsuccessful recall (left MTL). Analysis of encoding trials conditional upon subsequent retrieval success revealed a pattern of activation that appeared to predict subsequent recall, but which further analysis indicated to be a better predictor of subsequent recognition. These results provide evidence that the phenomenology of graded recall is represented neurally in frontal and parietal cortices, but that activation at encoding may not precipitate the different levels of recall experience.

Episodic memory is typically expressed by successful retrieval of a past experience or by failure to retrieve it. Recent studies using event-related functional magnetic resonance imaging (fMRI), which allows comparisons between successful and unsuccessful retrieval trials, have revealed brain regions associated with success and failure at episodic recognition (Buckner et al., 1998; Henson et al., 1999a, 1999b; Nyberg et al., 2000) and recall of sensory details of previously presented information (Wheeler et al., 2000). Here we report an event-related fMRI study of episodic recall that goes beyond the simple dichotomy between successful and unsuccessful performance.

Although neuroimaging studies have focused on the contrast between successful and unsuccessful performance, episodic retrieval is not always all-or-none. When recognition tests are used to assess memory for studied items, successful recognition can be expressed in two forms: remembering and knowing (Tulving, 1985). Recent studies have examined the neural correlates of recognition accompanied by specific recollection of episodic details ("remember") versus recognition accompanied by a general sense of familiarity ("know"; cf. Eldridge et al., 2000; Henson et al., 1999b). Activity in the prefrontal cortex and MTL regions differentiated between the two forms of recognition.

When recall is used to test episodic memory, people sometimes fail to retrieve previously encoded information, but express a feeling-of-knowing (FOK) that they could recognize the information on a later test (Hart, 1965; Nelson and Narens, 1980; Schacter, 1983). In the present study we examined FOK responses, in addition to successful and unsuccessful recall trials, to characterize the brain regions associated with differing levels of episodic recall. We recently used event-related fMRI to accomplish a similar objective within the domain of semantic memory. We identified prefrontal cortical regions associated with the "tip-of-

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doi:10.1016/S1063-8119(03)00014-4

the-tongue" state, in which people fail to retrieve a fact from semantic knowledge, but feel that they are on the verge of recovering it (Maril et al., 2001).

Cognitive studies of FOK have examined both the underlying mechanisms and the accuracy of judgments. Although there is debate over the mechanisms underlying FOK (e.g., Koriat, 1993; Metcalfe et al., 1993), the accuracy of FOK judgments in predicting later recall or recognition is usually above chance (Nelson, 1984; Schwartz, 1994). Evidence from neuropsychological studies suggests that prefrontal cortex may be important for FOK, with frontal lobe damaged patients showing impaired FOK accuracy after a long delay (Janowsky et al., 1989; Souchay et al., 2000). Damage to temporal lobe regions, by contrast, does not appear to affect FOK accuracy (Funnell et al., 1996; Prevey et al., 1991; Shimamura and Squire, 1986). Thus, the feeling-of-knowing seems to be a valid indicator of future successful recognition, and there is at least an initial suggestion that FOK accuracy may depend upon prefrontal cortex.

Theoretical and experimental work investigating cognitive mechanisms underlying FOK have largely focused on factors operating at retrieval that may be responsible for eliciting FOK; only a few studies have explored possible influences of encoding conditions on FOK responses (Lupker et al., 1991; Nelson et al., 1982; Schacter, 1983). At the level of brain systems, next to nothing is known regarding the contributions of encoding and retrieval influences to FOK responses. Although the neuropsychological data discussed earlier provide some clues regarding brain regions that are relevant to FOK, it is difficult, in patient studies, to determine whether memory impairments are occurring during the encoding or retrieval stages of memory.

Functional neuroimaging techniques allow the separate examination of blood flow differences during different stages of the memory process. Previous fMRI studies have reported activations at encoding that differed according to whether or not items were later successfully recalled (Fernandez et al., 1999a; Strange et al., 2002).

The present study utilized event-related fMRI to investigate neural regions associated with both encoding and retrieval that distinguish between successful recall, unsuccessful recall, and FOK. Participants were scanned during encoding and retrieval of word pairs. This design allows us to identify regions associated with different levels of recall success and to determine whether activation at encoding predicts subsequent graded recall performance. On the basis of the prior patient and neuroimaging studies noted above, we expected that differential patterns of activation within prefrontal cortex would be associated with different levels of episodic recall performance. We also expected to observe encoding activation predictive of subsequent memory in frontal and MTL regions; of special interest was the question of whether encoding activation would predict events that receive an FOK response at the recall stage.

Materials and methods

Participants

Participants were 17 right-handed, native speakers of English (10 men; ages 18–26 years), with normal or corrected-to-normal vision. Participants received $50 for participation. Informed consent was obtained in a manner approved by the Human Studies Committee of the Massachusetts General Hospital.

Stimuli and cognitive task

Stimuli consisted of 900 nouns selected from the "concrete" items used in an earlier event-related fMRI study (Wagner et al., 1998). Five lists of 180 items, matched for frequency and length, were used to create unrelated word pairs, such that the location of each word in a pair was counterbalanced across participants and each word was not consistently paired with the same word across study lists. Across two encoding scans, 180 word pairs were presented for 3 s, followed by 1 s of visual fixation. Additional periods of baseline fixation lasting between 2 and 8 s were interspersed between the experimental trials to optimize the efficiency of the design matrix (Dale, 1999). For experimental trials, subjects were instructed to form a mental image that included the two concepts represented by the words in each pair. They were asked to form as detailed an image as possible, trying to "see" colors, sizes, and the relative position of both items in the image. For each such trial, subjects were asked to indicate the quality of the image they managed to form, by pressing one of three response keys. The response options were: (1) successfully formed a good detailed image, (2) formed an image but one that was poor in details, or (3) not able to form an image at all or formed a poor one. Participants were not told there would be a subsequent memory test.

Following the two encoding scans, participants underwent two cued-recall scans in which memory for all 180 studied items was probed. Each 4-s trial consisted of presentation of the left word from each pair, with a question mark appearing in the right word's position. Participants were asked to press one of three keys depending on the retrieval outcome: they successfully recalled the missing word ("Know," K), they did not recall the missing word but felt that they would be able to recognize it if it were shown to them in a list among distractors ("Feeling-of-Knowing," FOK), or they did not recall the missing word and did not feel that they would be able to recognize it ("Don't know," DK). The order of presentation of stimuli in the cued-recall scans was pseudo-randomized, with the constraint that equal numbers of items from each encoding scan were represented in each cued-recall scan.

Following scanning, subjects were taken to another office where they were given a recognition test. Each trial in this test consisted of four word pairs, one of which was a studied pair. The remaining pairs had the same first word but were paired with extra-list distractors. Two-hundred forty such trials were presented, 180 of which contained a studied pair, and 60 of which contained only nonstudied pairs. For each trial, subjects were asked to press one of five keys. By pressing one of the first four keys, subjects indicated that the corresponding pair came from the study list. By pressing the fifth key, subjects indicated that none of the pairs had appeared on the study list.

Functional imaging

A 3-T Siemens Allegra system was used to acquire high-resolution T1-weighted anatomical images (MP-RAGE), and T2*-weighted gradient-echo echo-planar functional images (TR = 2000 ms, TE = 40 ms, 21 axial slices aligned parallel to the AC–PC plane, 5 mm thickness, 1 mm interslice skip, 200 mm FOV, 64 × 64 matrix, 240 volume acquisitions per run). Four additional volumes were collected and discarded at the beginning of each run to allow for T1 equilibration.

Preprocessing and data analysis

Data were preprocessed using SPM99 (Wellcome Department of Cognitive Neurology, London, UK). Images were first corrected for differences in slice acquisition timing by resampling all slices in time to match the first slice, followed by motion correction across all four runs (using sinc interpolation). Data were then spatially normalized to an EPI template based upon the MNI305 stereotactic space (Cocosco et al., 1997). Images were resampled into 3-mm cubic voxels and then spatially smoothed with an 8-mm FWHM isotropic Gaussian kernel. Statistical analysis was performed using the general linear model in SPM99.

Encoding and retrieval trials were sorted into bins depending on participants' responses in the cued-recall and recognition tests. Specifically, each trial was placed in one of three bins depending on the subject's response at the cued-recall stage (K, FOK, DK). These bins were then divided between items that were correctly answered at the recognition test stage (correct-K, correct-FOK, correct-DK) or incorrectly answered (incorrect-K, incorrect-FOK, incorrect-DK). There were too few trials categorized as incorrect-K or incorrect-FOK to permit meaningful analysis. The remaining correct-K, correct-FOK, correct-DK, and incorrect-DK trials were modeled using a canonical hemodynamic response. These effects were estimated using a subject-specific fixed-effects model, with session-specific effects and low-frequency signal components treated as confounds. Linear contrasts were used to obtain subject-specific estimates for each of the effects of interest. These estimates were entered into a second-level analysis treating participants as a random effect, using a one-sample t test against a contrast value of zero at each voxel. Statistical parametric maps were created for the contrast of task > fixation as well as the direct contrast of FOK > DK and were subsequently characterized using, at the voxel level, an uncorrected height threshold of $P < 0.001$ and, at the cluster level, an extent threshold of $P < 0.05$, corrected for the entire imaged volume. To further explore the nature of activation associated with each encoding/retrieval outcome condition, regions of interest (ROIs) were identified from clusters that survived the thresholding criteria. The hemodynamic responses were extracted from each ROI on a participant-by-participant basis and were subjected to subsequent repeated-measures analyses that included factors for condition (correct-K, correct-FOK, correct-DK, incorrect-DK) and peristimulus time (2–8 s).

Table 1
Mean (SD) number of responses given in each response type

	At cued recall		
	Don't know	FOK	Know
At recognition			
Correct	47 (21)	37 (11)	41 (21)
Incorrect	34 (20)	14 (12)	4 (3)

Results

Behavioral data

The distribution of trials across the six response types (see Materials and methods) is presented in Table 1. Almost half of the studied items (46%) were given a DK response during cued recall; the remainder of the responses were fairly evenly divided between FOK (29%) and K (25%). Accuracy during the subsequent recognition test differed significantly between the three cued-recall response types: accuracy was the highest for trials that had been previously given a K response (91%), intermediate for trials that had been given a FOK response (72%), and lowest for trials that had been given a DK response (58%). Thus, subjects' predictions at the time of recall regarding future recognition showed well-above-chance levels of accuracy. To confirm these observations statistically, we performed a gamma correlation, which provides a quantitative index of the strength of the relation between FOK predictions and subsequent recognition performance (Nelson, 1984). The mean gamma correlation was +0.44, which compares favorably with previous estimates of FOK accuracy reported in the behavioral literature (Metcalfe, 1996; Schwartz and Metcalfe, 1994). Median (SD) reaction times differed significantly across conditions [K, 1845 (343) ms; DK, 2077 (275) ms; FOK, 2220 (367) ms, $F(2,48) = 5.56$, $P < 0.01$]. Finally, we correlated the probability that an item was associated with K, FOK, and DK responses with established norms of concreteness and imageability (Kucera and Francis, 1967). For the subset of 806 words for which such norms exist, neither

Table 2
Cortical and medial temporal regions modulated by retrieval performance

	Retrieval			Encoding
	K > FOK > DK	K = FOK > DK	K > FOK = DK	K = FOK = cDK > iDK
Superior frontal/ACC	−6, 27, 39*			
Middle frontal	−51, 24, 30	−48, 39, 18*		
Inferior frontal	−36, 21, 9			−51, 27, 9
	−42, 18, 27			−48, 33, 15
	−42, 27, 18			−48, 39, 6
	−45, 30, 6			−45, 21, 9
	−30, 24, −6			−42, 24, 24
				−48, 18, 30
				−42, 9, 30
				42, −36, −24
Parietal cortex	−45, −54, 45*			
	−30, −60, 36			
	−30, −69, 51			
	−33, −48, 36			
MTL			−18, −33, −6	−36, −39, −24
				−33, −15, −27

Note. Regions of interest were defined from voxels that were activated in Task > fixation or the direct contrast of FOK > DK * and were further interrogated for differences between know (K), feeling-of-knowing (FOK), and don't know (DK) responses. The first three columns list the peak voxel in regions that demonstrated graded retrieval (K > FOK > DK), a subjective sense of memory for the target (K = FOK > DK), and actual retrieval success (K > FOK = DK). The rightmost column lists the peak voxel in regions that demonstrated successful encoding as measured by a subsequent recognition test. Coordinates are in MNI space.

concreteness nor imageability correlated with the probability of an item being associated with FOK or DK responses ($r = -0.05$ to -0.02, ns). A relatively weak correlation was observed between the probability of an item being associated with a K responses and both concreteness ($r(805) = 0.12, P < 0.01$) and imageability ($r(805) = 0.08, P < 0.05$). However, because none of the reported patterns of neuroimaging results were obtained in regions subserving visual imagery, this small correlation is unlikely to account for the pattern of results reported below.

Imaging data

The fMRI data were analyzed to assess activation associated with the episodic encoding and retrieval tasks, as well as to assess how this activation differed depending on retrieval outcome as assessed by both cued recall and recognition (correct-K, correct-FOK, correct-DK, incorrect-DK). As noted above, the small number of trials in both incorrect-K and incorrect-FOK conditions precluded meaningful analysis of imaging data for these conditions.

Retrieval

Compared to baseline, activation associated with episodic retrieval was predominantly left lateralized and included regions in inferior prefrontal, superior parietal, posterior–inferior temporal cortices, and bilateral occipital cortices. These results, while somewhat inconsistent with older, mainly block-designed imaging studies (see Fletcher and Henson, 2001; Tulving et al., 1994), which were often characterized by right-lateralized activation patterns for episodic retrieval, are consistent with more recent event-related fMRI studies that also found left lateralized activation for episodic retrieval of words (e.g., Konishi et al., 2000; McDermott et al., 2000; Nolde et al., 1998).

Comparisons of the different retrieval conditions revealed a strikingly consistent pattern of activation within frontal and posterior regions. This pattern was characterized by a graded response in which K trials were associated with greater activation than FOK trials, which in turn were associated with greater activation than DK trials (Table 2, leftmost column). ROI analyses revealed that this effect was exhibited in multiple regions throughout the left prefrontal cortex (see Figs. 1a–c), as well as in the left parietal cortex (see Fig. 1d) and anterior cingulate cortex. Activation in these regions appeared to track the phenomenology of FOK, mirroring the subjective experience of an intermediate retrieval state between knowing and not knowing.

In addition to the extensive graded activation observed, activation in the left middle frontal cortex (Brodmann area 9) was modulated to the same extent by both K and FOK trials, with DK trials producing significantly less activation (Table 2, second column; Fig. 2a). Activation in this region would, therefore, appear to be correlated with the subjective feeling that the target item was known regardless of whether it could be successfully recalled.

A third retrieval related pattern was observed in the left medial temporal lobe (MTL) (Table 2, third column; Fig. 2b). Time series analysis indicated that K responses were associated with significantly more activation in this region than were FOK and DK responses. Thus, activation in this region was associated with successful retrieval of the target item only.

Encoding

Compared with baseline, activation associated with episodic encoding was also mainly left lateralized, including regions in the left prefrontal, left inferior–posterior temporal, left parietal, and bilateral occipital cortices. These results are largely consistent with prior neuroimaging studies of verbal encoding (e.g., Dolan and Fletcher, 1997; Kelley et al., 1998).

Encoding-related activation patterns that differentiated among the outcome of the subsequent retrieval process were first assessed using recall responses as a measure of retrieval. A contrast comparing the encoding of trials that were later recalled (K) to the encoding of trials that were later not successfully recalled (FOK and DK) revealed differential encoding activation in a left posterior parahippocampus/fusiform region (−33, −42, −18). No other regions survived threshold in this contrast.

Encoding-related activation was then assessed again, this time using responses from the recognition test to define successful retrieval. Thus, the critical contrast of interest here was successful recognition (correct-K, correct-FOK, and correct-DK) compared to forgotten or unrecognized trials (incorrect-DK). This comparison revealed the same posterior MTL region (Fig. 3a) that was observed in the subsequent recall analysis, as well as regions within the left prefrontal cortex (Figs. 3b and c), extending from the inferior to dorsal PFC (Table 2, rightmost column).

Analysis of the time series associated with each response type in these regions suggests that encoding activation was a better predictor of memory performance as measured by a recognition, rather than recall, probe. In all regions, including the posterior MTL regions that showed an apparent subsequent recall effect, trials that were subsequently successfully recognized, regardless of their status at the recall stage, elicited comparable activation at encoding; the only trial type that showed a significantly lower level of encoding-related activation was the unrecognized, incorrect-DK.

In light of studies suggesting that encoding activation should also be observed in the hippocampus—particularly, given the relational nature of our task, in anterior hippocampus—a hypothesis-driven search for activation in this structure was conducted with a less lenient threshold of $P = 0.005$, uncorrected (Otten et al., 2001; Strange et al., 2002). With this threshold, encoding activation was observed that differentially predicted successful recognition (but not recall) in the bilateral anterior hippocampus, parahippocampus, and right perirhinal regions (Fig. 4).

Discussion

This study represents the first event-related fMRI investigation of graded recall success in episodic memory, utilizing FOK in addition to the standard successful and unsuccessful retrieval outcomes.

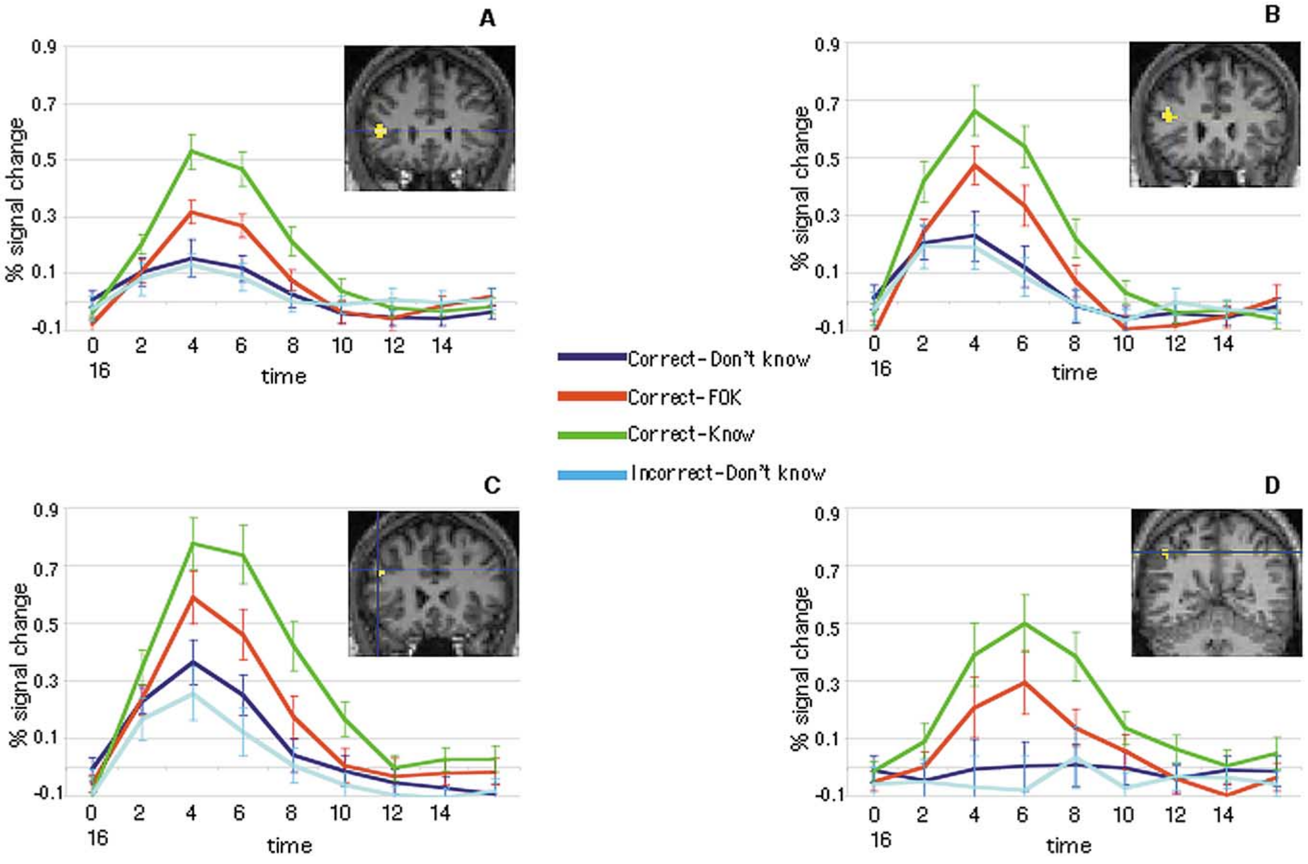
Activations at retrieval

An extensive pattern of retrieval-related activation was observed throughout the left inferior frontal gyrus: K trials were associated with significantly greater activation than were FOK trials, which in turn produced a significantly greater response than did DK trials. This pattern would seem, therefore, to mirror the behavioral manifestation of graded recall success and is consistent with findings from a recent fMRI study of FOK in semantic memory (Kikyo et al., 2002). A very similar pattern was also found in left superior posterior parietal cortex and anterior cingulate.

The intermediate level of activation associated with FOK can be interpreted in several different ways. First, it is possible that a response decision during the recall stage might be sensitive to the level of activation in frontal regions, such that even when the sought-after target item cannot be recalled, a response other than DK is available. A second interpretation is that the feeling that an item is available for retrieval might drive efforts to recall the item. If this were the case, however, to the extent that effort is reflected in reaction time, it might be expected that the RTs would follow the K > FOK > DK pattern. The behavioral data are not consistent with this hypothesis, because RTs associated with FOK responses were significantly longer than RTs associated with K and DK responses.

Fig. 1. Three frontal and one parietal regions demonstrated a graded recall success activation. Displayed are functionally defined ROIs and averaged event-related responses associated with each retrieval outcome. The examined ROIs are displayed on corresponding coronal slices. Activation associated with know responses was significantly greater than that associated with feeling-of-knowing responses, which was in turn significantly greater than that associated with don't know response in left inferior frontal cortex (A, ~BA 45/47;−45,30,6), left inferior/middle frontal cortex (B, ~BA 46;−42,27,18), left dorsal frontal cortex (C, ~BA46/9;−51,24,30) and left parietal cortex (D, ~BA 7;−45,−54,45). DK, don't know; K, know; FOK, feeling-of-knowing.

Fig. 2. Activation in left middle frontal cortex (A, ~BA; −48,39,18) was modulated to the same extent by both know and feeling-of-knowing trials. Know responses were associated with significantly higher activation than feeling-of-knowing and don't know responses in left MTL (B, −18,−33,−6). Displayed are functionally defined ROIs and the resultant averaged event-related responses. The examined ROIs are displayed on corresponding coronal slices.


A
B
C
D
0.9
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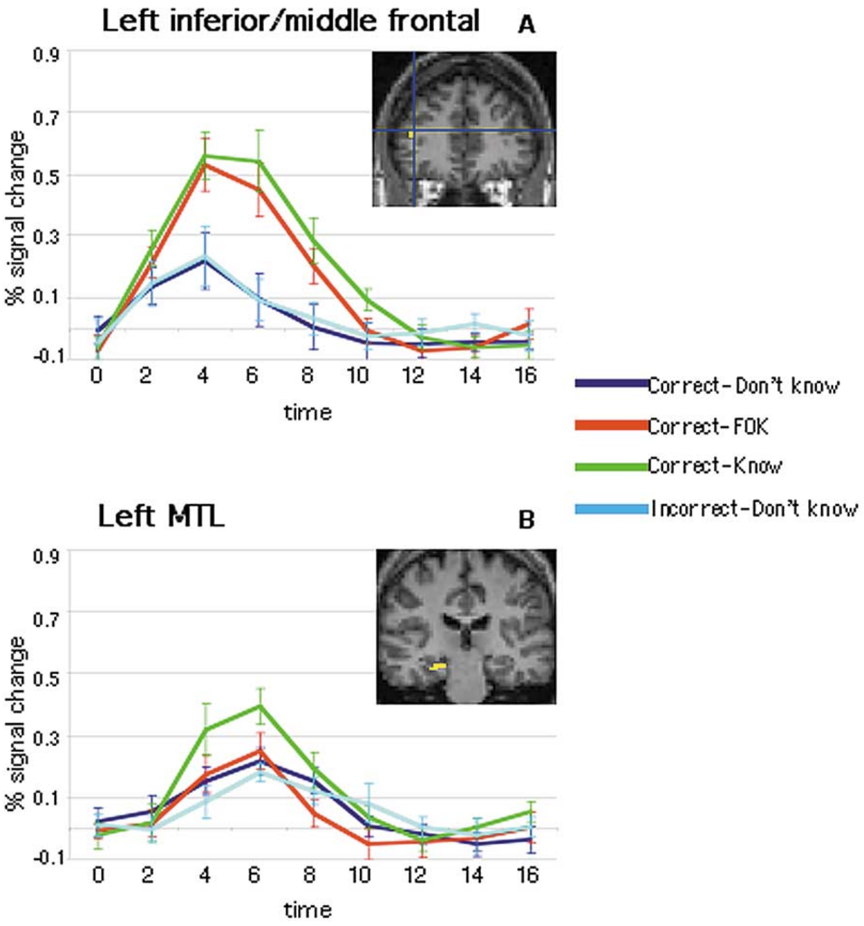
0 2 4 6 8 10 12 14
16
time
Correct-Don't know
Correct-FOK
Correct-Know
Incorrect-Don't know

1


Left inferior/middle frontal
A
Left MTL
B
0.9
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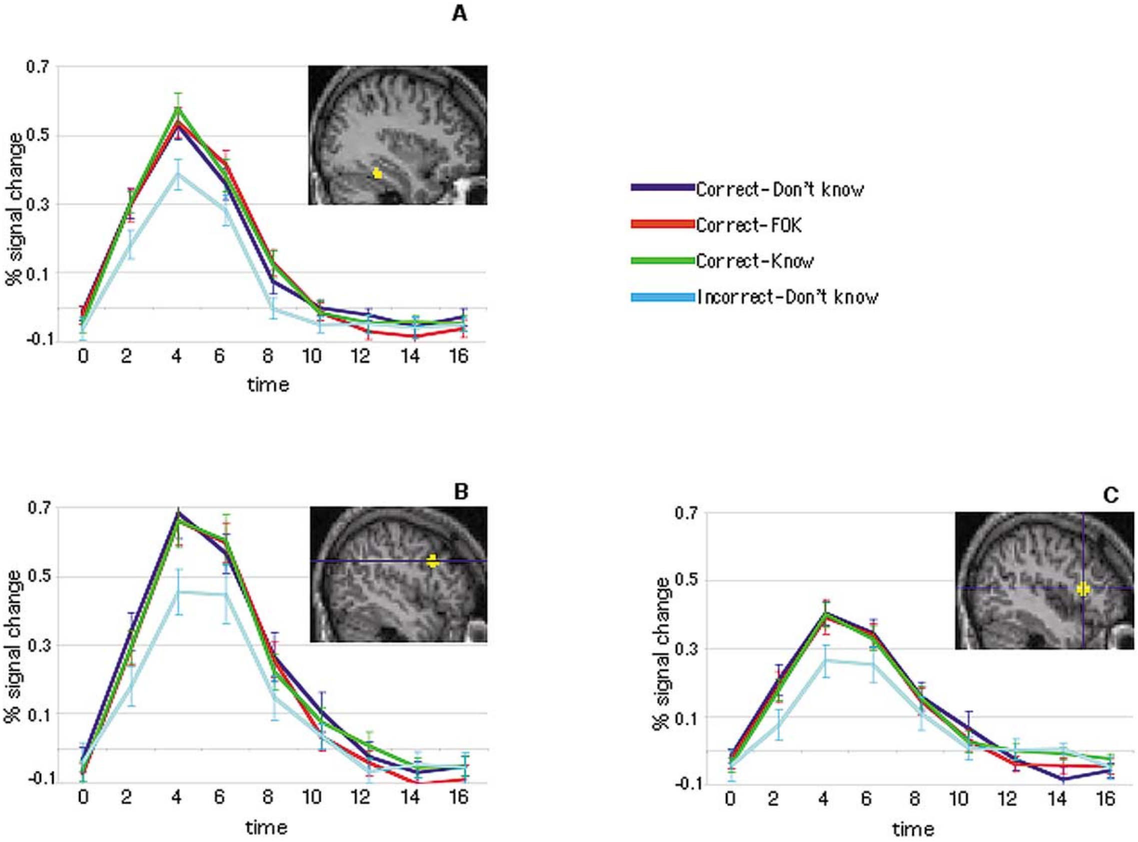
time
Correct-Don't know
Correct-FOK
Correct-Know
Incorrect-Don't know

2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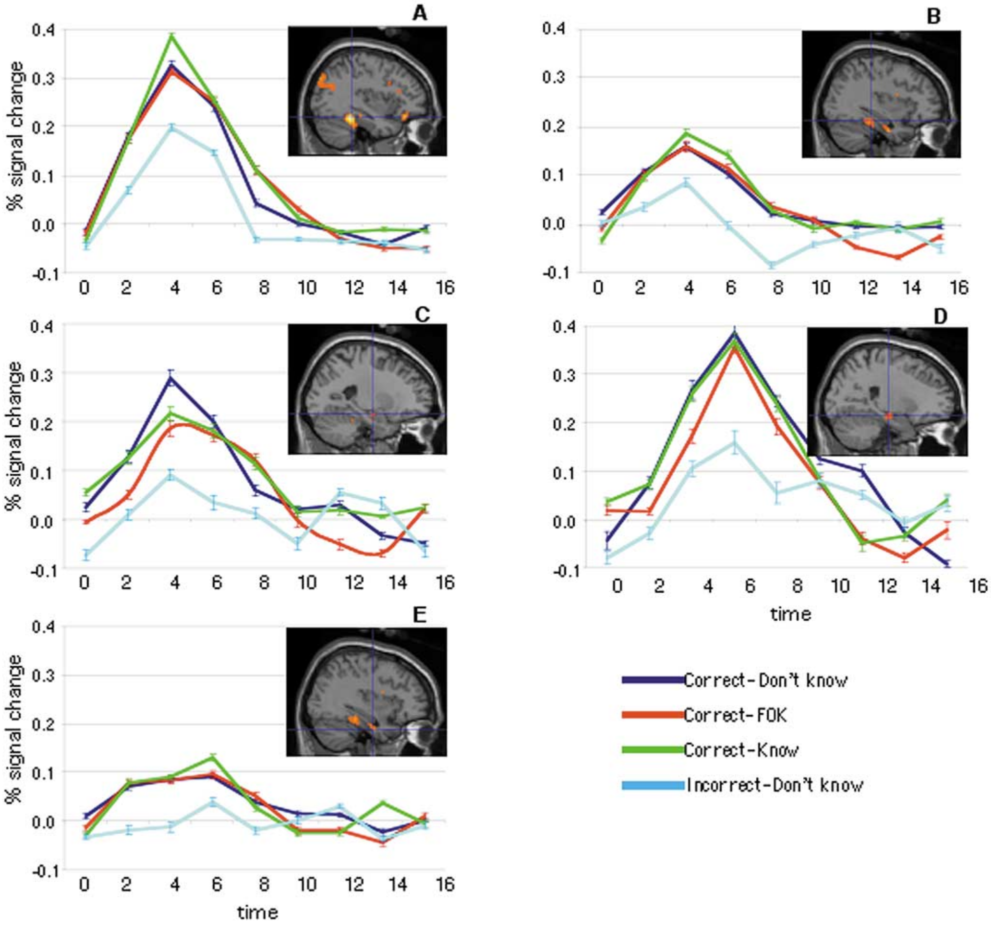
Correct-Don't know
Correct-FOK
Correct-Know
Incorrect-Don't know

3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% signal change
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0.1
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time
0 2 4 6 8 10 12 14 16
Correct-Don't know
Correct-FOK
Correct-Know
Incorrect-Don't know

4

Turning to possible sources of FOK, cognitive theories suggest that partial familiarity with the cue and/or partial access to the sought-after target may be responsible for the phenomenological experience of FOK (see Koriat and Levy-Sadot, 2001; Metcalfe, 1996). According to the first view, the intermediate level of activation associated with the FOK responses may reflect recognition of the previously studied cue word. If the experience of FOK was mediated by cue recognition, however, we might expect to see similar patterns of encoding-related activation to those reported in previous subsequent memory studies (e.g. Wagner et al., 1998), such as greater activity at encoding in left prefrontal and MTL regions for subsequently recognized than forgotten items (or cues in our study). Analysis of encoding data in the present experiment (see below) is not consistent with this idea, because no such pattern in the encoding activation was observed.

It may be more plausible to suggest that FOK-related activation reflects partial access to the sought-after target item. Behavioral data in support of this hypothesis include the results of Schacter and Worling (1985), who found that when participants gave FOK responses, they could produce more information about the items they were unable to recall than when they did not provide FOK responses. According to this view, the prefrontal and parietal activation observed in the present study could reflect the bringing on line of stored information and its manipulation and evaluation. It is conceivable that the phenomenological experience of more information being available for K trials than for FOK trials, and for FOK trials than for DK trials, might be associated with the amount and/or quality of information held and manipulated in working memory during the recall process. This idea is consistent with the extensive literature implicating prefrontal and parietal regions in such working memory processes (for a recent review, see Fletcher and Henson, 2001).

In contrast to the graded response in the left inferior frontal gyrus, a different pattern of retrieval-related activation was observed in the left middle frontal cortex, where both K and FOK trials were associated with significantly greater activation than DK trials, which themselves did not differ from baseline. This region would seem to modulate the subjective experience of knowing that an item is available for retrieval, irrespective of whether it can be subsequently recalled. This result echoes that of Henson and colleagues (1999b), who used the “remember/know” paradigm (Tulving, 1985), in which subjects make old/new recognition judgments to indicate whether they specifically recollect encountering items on an earlier study list (“remember”) or whether items just seem familiar (“know”). Henson et al. (1999b) reported activation in a left middle frontal region close to that observed in the present experiment, which responded similarly during “remember” and “know” judgments and significantly less during “don’t know” judgments. Therefore, both studies have documented activation in this region to be associated with a feeling that the target item is present in memory, regardless of whether it is consciously recollected. This comparison between findings should be regarded cautiously because there is currently no cognitive theory that incorporates both “intermediate” retrieval states. Nevertheless, the fact that such a consistent result emerges from experiments concerning both recall and recognition is striking and suggests that activation in the left middle frontal region may be independent of the particular memory process (i.e., recall vs. recognition) that is executed.

Selective activation for successfully retrieved items was observed in left parahippocampal cortex. Previous imaging work has linked this region with processes involved in conscious recollection (Eldridge et al., 2000; Schacter et al., 1996; Yonelinas et al., 2001). For example, Schacter et al. (1996) found activation in left MTL in a condition that yielded high levels of successful explicit retrieval compared with a condition that yielded lower levels of successful explicit memory and also compared to implicit memory. Similarly, when comparing activations relating to recollection- and familiarity-based memory, Yonelinas et al. (2001) recently observed greater activation in hippocampal and parahippocampal regions for associative memory (recollection-based) than for item (familiarity-based) recognition. Our data are consistent with the results of these studies, implicating the left parahippocampal cortex in conscious recall.

Activations at encoding

A pattern of encoding-related activation that differentiated, at our a priori threshold, between subsequently recalled and not recalled items was observed in a region of left posterior parahippocampal gyrus/fusiform cortex. This region was activated significantly in a contrast between trials later successfully recalled and those subjects failed to successfully recall. When the significance threshold was lowered to $P < 0.005$ uncorrected, in line with previous studies (e.g., Strange et al., 2002), additional regions in the bilateral anterior hippocampus, the parahippocampal cortex, and the

Fig. 3. Encoding activation associated with correct recognition at $P < 0.001$ threshold was observed in the left posterior MTL (A, −36,−39,−24), left prefrontal cortex (B, dorsal,−48,18,30; C, inferior; −45,21,9). Displayed are functionally defined ROIs and the resultant averaged event-related responses. The examined ROIs are displayed on corresponding sagittal slices.

Fig. 4. Additional MTL regions whose encoding activation was predictive of successful recognition were observed at a lower threshold—$P < 0.005$: bilateral posterior MTL (left, A, −36,−39,−18; right, B, 36,−33,−18), bilateral anterior hippocampus (left, C, −24,−12,−12; right, D, 24,−18,−15), and right perirhinal cortex region (E, 36,−9,−33). Displayed are functionally defined ROIs and the resultant averaged event-related responses. The examined ROIs are displayed on corresponding sagittal slices.

right perirhinal cortex area showed significant activation. Several previous studies reported encoding activations in similar regions that were predictive of subsequent recall performance (Alkire et al., 1998; Fernandez et al., 1998, 1999b), although comparison with these studies is complicated by the different methodologies used, such as blocked-design fMRI and recording from hippocampal electrodes in patients with temporal lobe epilepsy.

One recent study that used event-related fMRI methodology also reported encoding-related activation in medial temporal lobe regions that was predictive of subsequent recall success (Strange et al., 2002). In the present study, an advantage of measuring retrieval using both recall and recognition tests was the ability to categorize encoding trials for analysis on the basis of different factors operating at retrieval. When our encoding data were reanalyzed using subsequent recognition success as the criterion for retrieval, similar medial temporal lobe regions as in the subsequent recall analysis were activated, with the left prefrontal cortex additionally showing significant activation. Analysis of the time series data indicated that the encoding activation was a better predictor of recognition than recall performance.

Encoding activations in similar areas predictive of subsequent recognition memory have been observed in numerous studies (Brewer et al., 1998; Otten et al., 2001; Wagner et al., 1998). For example, in the study by Wagner et al. (1998), subjects semantically encoded words and were later given a surprise recognition test in which they attempted to distinguish between previously encountered words and new words. Encoding activation in the left inferior frontal and left posterior MTL regions was found to predict subsequent successful recognition, as also demonstrated in the present study.

One region that differentiated between successful and unsuccessful recognition in the present experiment but was not reported previously is the left dorsal frontal cortex (Fig. 4). A possible explanation is that the encoding task used in the present study required subjects to encode two stimuli on each trial and to form a mental image that incorporated both concepts into one picture. It has been suggested that when selection of relevant features and organization of different items held in working memory are required to perform an encoding task, dorsal frontal regions are recruited (Fletcher and Henson, 2001).

In the recent fMRI study by Strange et al. (2002), which used intentional encoding of short lists of single words, the authors found encoding activation in different regions of MTL that predicted subsequent retrieval from different positions in the lists. Posterior MTL activation predicted successful recall of words in initial positions on the list, whereas activation in the region of perirhinal cortex predicted recall for words in all list locations. In trying to account for the posterior MTL activation found in previous subsequent memory studies for items from nonprimacy list positions (e.g., Brewer et al., 1998; Kirchhoff et al., 2000; Wagner et al., 1998), Strange et al. (2002) discussed the possibility that the structure of the lists in these studies—which included long interstimulus intervals of null events—rendered items immediately following such intervals as "situationally novel, capable of evoking an orienting response" (p. 527). Since the present study used similarly structured study lists, with baseline fixation events of varying duration intermixed with the word stimuli, we examined whether this explanation could apply to the posterior MTL region we observed.

An additional analysis was conducted, in which all words that immediately followed fixation at encoding were designated and analyzed separately from words that followed another word trial. To allow for a sufficient number of trials in each such bin to permit meaningful analysis, we examined only the items that were given a DK response at recall. These items were divided into correctly recognized versus forgotten (as before), and each such group was divided again into "primacy-like" trials, that is, immediately following fixation at study, and "non-primacy-like" trials. Behaviorally, the primacy-like items had no retrieval advantage over the non-primacy-like items.

All imaging data analysis involving this division failed to show a different pattern of activation for the two trial types—those that immediately followed fixation and those that did not. Specifically, subsequent recognition effects were observed when comparing remembered and forgotten items that did not follow fixation; the same pattern was observed when analysis was restricted only to those items that immediately followed fixation. No interaction between list location and activation pattern was found.

To conclude, several regions within the left frontal and parietal cortex showed retrieval-related activation that mirrors the phenomenology of graded recall success. Encoding-related activation patterns that differentiated between the outcome of the subsequent retrieval process were demonstrated to be attributable to processes operating at recognition. Our results thus indicate that study of FOK can provide useful insights into the nature of contributions made by specific brain regions to episodic recall. They also raise questions about the relative contributions of encoding and retrieval processes to the genesis of FOK that will require study in future research.

References

Alkire, M.T., Haier, R.J., Fallon, J.H., Cahill, L., 1998. Hippocampal, but not amygdala, activity at encoding correlates with long-term, free recall of nonemotional information. Proc. Natl. Acad. Sci. USA 95 (24), 14506–14510.

Brewer, J.B., Zhao, Z., Desmond, J.E., Glover, G.H., Gabrieli, J.D., 1998. Making memories: brain activity that predicts how well visual experience will be remembered. Science 281 (5380), 1185–1187.

Buckner, R.L., Koutstaal, W., Schacter, D.L., Dale, A.M., Rotte, M., 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 (3), 163–175.

Cocosco, C.A., Kollokian, V., Kwan, R.K.S., Evans, A.C., 1997. Brainweb: online interface to a 3D MRI simulated brain database. NeuroImage 5, 425.

Dale, A.M., 1999. Optimal experimental design for event-related fMRI. Hum. Brain Mapp. 8, 109–114.

Dolan, R.J., Fletcher, P.C., 1997. Dissociating prefrontal and hippocampal function in episodic memory encoding. Nature 388, 582–585.

Eldridge, L.L., Knowlton, B.T., Furmanski, C.S., Bookheimer, S.Y., Emgel, S.A., 2000. Remembering episodes: a selective role for the hippocampus during retrieval. Nat. Neurosci. 3, 1149–1152.

Fernandez, G., Brewer, J.B., Zhao, Z., Glover, G.H., Gabrieli, J.D.E., 1999a. Level of sustained entorhinal activity at study correlates with subsequent cued-recall performance: a functional magnetic resonance imaging study with high acquisition rate. Hippocampus 9, 35–44.

Fernandez, G., Effern, A., Grunwald, T., Pezer, N., Lehnertz, K., Dumpelmann, M., Van Roost, D., Elger, C.E., 1999b. Real-time tracking of memory formation in the human rhinal cortex and hippocampus. Science 285, 1582–1585.

Fernandez, G., Weyerts, H., Schrader-Bolsche, M., Tendolkar, I., Smid, H.G.O.M., Tempelmann, C., Hinrichs, H., Scheich, H., Elger, C.E., Mangun, G.R., Heinze, H.-J., 1998. Successful verbal encoding into episodic memory engages the posterior hippocampus: a parametrically analyzed functional magnetic resonance study. J. Neurosci. 18, 1841–1847.

Fletcher, P.C., Henson, R.N.A., 2001. Frontal lobes and human memory: insights from functional neuroimaging. Brain 124, 849–881.

Funnell, M., Metcalfe, J., Tsapkani, K., 1996. In the mind but not on the tongue: feeling of knowing in an anomic patient, in: Reder, L.M. (Ed.), Implicit Memory and Metacognition. Erlbaum, Hillsdale (NJ), pp. 171–194.

Hart, J.T., 1965. Memory and the feeling-of-knowing experience. J. Educ. Psychol. 56, 208–216.

Henson, R.N., Shallice, T., Dolan, R.J., 1999a. Right prefrontal cortex and episodic memory retrieval: a functional MRI test of the monitoring hypothesis. Brain 122, 1367–1381.

Henson, R.N.A., Rugg, M.D., Shallice, T., Josephs, O., Dolan, R.J., 1999b. Recollection and familiarity in recognition memory: an event-related functional magnetic resonance imaging study. J. Neurosci. 19, 3962–3972.

Janowsky, J.S., Shimamura, A.P., Squire, L.R., 1989. Memory and metamemory: comparisons between patients with frontal lobe lesions and amnesic patients. J. Exp. Psychol. Learn. Mem. Cogn. 17, 3–11.

Kelley, W.M., Miezin, F.M., McDermott, K.B., Buckner, R.L., Raichle, M.E., Cohen, N.J., Ollinger, J.M., Akbudak, E., Conturo, T.E., Snyder, A.Z., Petersen, S.E., 1998. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding. Neuron 20 (5), 927–936.

Kikyo, H., Ohki, K., Miyashita, Y., 2002. Neural correlates for feeling-of-knowing: an fMRI parametric analysis. Neuron 36, 177–186.

Kirchhoff, B.A., Wagner, A.D., Maril, A., Stern, C.E., 2000. Prefrontal-temporal circuitry for episodic encoding and subsequent memory. J. Neurosci. 20, 6173–6180.

Konishi, S., Wheeler, M.E., Donaldson, D.I., Buckner, R.L., 2000. Neural correlates of episodic retrieval success. NeuroImage 12, 276–286.

Koriat, A., 1993. How do we know that we know? The accessibility account of the feeling of knowing. Psychol. Rev. 100, 609–639.

Koriat, A., Levy-Sadot, R., 2001. The combined contributions of the cue-familiarity and accessibility heuristics to feeling of knowing. J. Exp. Psychol. Learn. Mem. Cogn. 27, 34–53.

Kucera, H., Francis, W.N., 1967. Computational Analysis of Present-Day American English. Brown University Press, Providence (RI).

Lupker, S.J., Harblok, J.L., Patrick, A.S., 1991. Memory for things forgotten. J. Exp. Psychol. Learn. Mem. Cogn. 17, 897–907.

Maril, A., Wagner, A.D., Schacter, D.L., 2001. On the tip of the tongue: an event-related fMRI study of semantic retrieval failure and cognitive conflict. Neuron 31, 653–660.

McDermott, K.B., Jones, T.C., Petersen, S.E., Lageman, S.K., Roediger, H.L., 2000. Retrieval success is accompanied by enhanced activation in anterior prefrontal cortex during recognition memory: an event-related fMRI study. J. Cogn. Neurosci. 12, 965–976.

Metcalfe, J., 1996. Metacognitive processes, in: Bjork, E.L.B.a.R.A. (Ed.), Memory. Academic Press, San Diego, pp. 383–411.

Metcalfe, J., Schwartz, B.L., Joaquim, S.G., 1993. The cue-familiarity heuristic in metacognition. J. Exp. Psychol. Learn. Mem. Cogn. 19, 851–861.

Nelson, T.O., 1984. A comparisons of current measures of the accuracy of feeling-of-knowing predictions. Psychol. Bull. 95, 109–133.

Nelson, T.O., Leonesio, R.J., Shimamura, A.P., Landwehr, R.F., Narens, L., 1982. Overlearning and the feeling of knowing. J. Exp. Psychol. Learn. Mem. Cogn. 8, 279–288.

Nelson, T.O., Narens, L., 1980. Norms of 300 general-information questions: accuracy of recall, latency of recall, and feeling of knowing ratings. J. Verbal Learn. Verbal Behav. 19, 338–368.

Nolde, S.F., Johnson, M.K., D'Esposito, M., 1998. Left prefrontal activation during episodic remembering: an event-related fMRI study. NeuroReport 9, 3509–3514.

Nyberg, L., Persson, J., Habib, R., Tulving, E., McIntosh, A.R., Cabeza, R., Houle, S., 2000. Large scale neurocognitive networks underlying episodic memory. J. Cogn. Neurosci. 12 (1), 163–173.

Otten, L.J., Henson, R.N.A., Rugg, M.D., 2001. Depth of processing effects on neural correlates of memory encoding. Brain 124, 399–412.

Prevey, M.L., Delaney, R.C., Mattson, R.H., Tice, D.M., 1991. Feeling of knowing in temporal lobe epilepsy: monitoring knowledge inaccessible to conscious recall. Cortex 27, 81–92.

Schacter, D.L., 1983. Feeling of knowing in episodic memory. J. Exp. Psychol. Learn. Mem. Cogn. 9, 39–54.

Schacter, D.L., Alpert, N.M., Savage, C.R., Rauch, S.L., Albert, M.S., 1996. Conscious recollection and the human hippocampal formation: evidence from positron emission tomography. Proc. Nat. Acad. Sci. USA 93, 321–325.

Schacter, D.L., Worling, J.R., 1985. Attribute information and the feeling of knowing. Can. J. Psychol. 39, 467–475.

Schwartz, B.L., 1994. Sources of information in metamemory: judgments of learning and feeling of knowing. Psychonom. Bull. Rev. 1, 357–375.

Schwartz, B.L., Metcalfe, J., 1994. Methodological problems and pitfalls in the study of human metacognition, in: Metcalfe, J., Shimamura, A.P. (Eds.), Metacognition: Knowing about Knowing. MIT Press, Cambridge (MA), pp. 93–114.

Shimamura, A.P., Squire, L.R., 1986. Memory and metamemory: a study of the feeling-of-knowing phenomenon in amnesic patients. J. Exp. Psychol. Learn. Mem. Cogn. 12, 452–460.

Souchay, C., Isingrini, M., Espagnet, L., 2000. Aging, episodic memory feeling-of-knowing, and frontal functioning. Neuropsychology 14, 299–309.

Strange, B.A., Otten, L.J., Josephs, O., Rugg, M.D., Dolan, R.J., 2002. Dissociable human perirhinal, hippocampal and parahippocampal roles during verbal encoding. J. Neurosci. 22, 523–528.

Tulving, E., 1985. Memory and consciousness. Can. Psychol. 26, 1–12.

Tulving, E., Kapur, S., Craik, F.I.M., Moscovitch, M., 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., Schacter, D.L., Rotte, M., Koutstaal, W., Maril, A., Dale, A.M., Rosen, B.R., Buckner, R.L., 1998. Building memories: remembering and forgetting of verbal experiences as predicted by brain activity. Science 281 (5380), 1188–1191.

Wheeler, M.E., Petersen, S.E., Buckner, R.L., 2000. Memory's echo: vivid remembering reactivates sensory-specific cortex. Proc. Natl. Acad. Sci. USA 97, 11125–11129.

Yonelinas, A.P., Hopfinger, J.B., Buonocore, M.H., Kroll, N.E., Beynes, K., 2001. Hippocampal, parahippocampal, and occipito-temporal contributions to associative and item recognition memory: an fMRI study. Neuroreport 12, 359–363.