

## Recognition memory for studied words is determined by cortical activation differences at encoding but not during retrieval

Michael W.L. Chee,<sup>a,\*</sup> Joshua O.S. Goh,<sup>a</sup> Yanhong Lim,<sup>a</sup> Steven Graham,<sup>a</sup> and Kerry Lee<sup>b</sup>

<sup>a</sup>Cognitive Neuroscience Laboratory, SingHealth Research Laboratories, Singapore, Singapore

<sup>b</sup>Psychological Studies, National Institute of Education, Nanyang Technological University, Singapore

Received 21 August 2003; revised 23 March 2004; accepted 23 March 2004

Available online 1 June 2004

In Memory of those who lost their lives to SARS in Singapore: March–May 2003

Prior work has shown that when responses to incidentally encoded words are sorted, subsequently remembered words elicit greater left prefrontal BOLD signal change relative to forgotten words. Similarly, low-frequency words elicit greater activation than high-frequency words in the same left prefrontal regions, contributing to their better subsequent memorability. This study examined the relative contribution of encoding and retrieval processes to the correct recognition of target words. A mixture of high- and low-frequency words was incidentally encoded. Scanning was performed at encoding as well as during retrieval. During *encoding*, greater activation in the left prefrontal and anterior cingulate regions predicted a higher proportion of hits for low-frequency words. However, data acquired *during recognition* showed that word frequency *did not* modulate activation in any of the areas tracking successful recognition. This result demonstrates that under some circumstances, the recognition of studied words is determined purely by processes that are active during encoding. In contrast to the finding for hits, activation associated with correctly rejected foils was modulated by word frequency, being higher for high-frequency words in the left lateral parietal and anterior prefrontal regions. These findings were replicated in two further experiments, one in which the number of test items at recognition was doubled and another where encoding strength for high-frequency words was varied (once vs. 10 times). These results indicate that word frequency modulates activity in the left lateral parietal and anterior prefrontal regions contingent on whether the item involved is correctly recognized as a target or a foil. This observation is consistent with a dual process account of episodic memory.

© 2004 Published by Elsevier Inc.

**Keywords:** Word frequency; Episodic memory; Recognition; Dual process models

### Introduction

Understanding the functional anatomy of successful memory encoding and retrieval using different tasks has been the goal of many brain imaging studies on memory (Maccotta et al., 2001; Rugg and Yonelinas, 2003; Rugg et al., 2002). In this study, we sought to characterize the neural correlates of successful episodic retrieval of verbal memories by studying neural activity both at encoding and during recognition using a within-subjects design.

During verbal encoding, tasks that engage semantic processing lead to higher rates of recognition compared to those that involve the processing of features like letter case (Demb et al., 1995), alphabet order (Otten et al., 2001), or the number of syllables in each word (Otten and Rugg, 2001). In each of these studies, semantic ('deep') processing resulted in encoding that was associated with relatively higher blood flow in the left prefrontal cortex. Interestingly, many studies of episodic memory using a variety of tasks and stimuli also show that apart from the effects of encoding strategy, events that elicit higher left prefrontal blood flow predict a higher probability of correct item recognition at test (Buckner et al., 2001; Henson et al., 1999; Kapur et al., 1994; Kirchoff et al., 2000; Otten and Rugg, 2001; Wagner et al., 1998). Significantly, these inferences have been based on the post hoc sorting of recognition judgments that did not involve scanning during item retrieval.

Word frequency is an index of our cumulative exposure to printed words and it affords us a means of studying the neural correlates of how stimulus manipulation modulates item memorability. Following encoding, low-frequency words are better recognized with fewer false alarms than high-frequency words. This 'mirror effect' (Glanzer and Adams, 1985) has been a subject of many studies seeking to explain why we remember (recognize) one class of items better than another.

We previously observed that making semantic judgments on low-frequency words elicited higher left prefrontal, anterior cingulate and left inferior temporal activation compared to high-frequency words (Chee et al., 2002, 2003). Critically, in showing that remembered low-frequency words were associated with greater left prefrontal activation than forgotten low-frequency words, we

\* Corresponding author. Cognitive Neuroscience Laboratory, SingHealth Research Laboratories, 7 Hospital Drive, #01-11, Singapore 169611, Singapore. Fax: +65-62524735.

E-mail address: mchee@pacific.net.sg (M.W.L. Chee).

Available online on ScienceDirect (www.sciencedirect.com.)

pointed out that word frequency and ‘successful encoding’ make separate contributions to subsequent recognition (Chee et al., 2003). We suggested that the greater BOLD signal change associated with low-frequency words as they are encoded relates to neural processes that enhance their subsequent recognition. However, it is not known whether additional neural processes operating at retrieval contribute to the superior recognition of low-frequency words.

The neural correlates of successful episodic recognition have been characterized using words (Donaldson et al., 2001; Henson et al., 1999; Konishi et al., 2000), word-pairs (McDermott et al., 1999), or objects (Ranganath et al., 2000). However, fewer studies have directly related cortical activation at encoding and retrieval in the same subjects. This point is important because episodic memory tasks elicit cortical activation that shows good intra-subject reproducibility but significant inter-individual variation in spatial location and extent (Miller et al., 2002). To date, we are aware of only one event-related fMRI study that combined the evaluation of episodic retrieval and encoding in the same subjects (Henson et al., 1999). During encoding, greater left prefrontal activation was associated with later recollected words compared to words subsequently rated as ‘familiar’. However, during recognition, activation in the same prefrontal voxels did not differentiate words that were recollected versus words that

were ‘familiar’. This observation illustrates how a determinant of recognition memory may influence cortical activation at encoding but not at recognition.

In this study, we used word frequency to manipulate cortical activation at encoding as previously described. We then evaluated activation during item recognition in the same subjects. We found that word frequency did not modulate activation during the recognition of studied words; instead, word frequency modulated activation for unstudied foils. These results support a dual process model of recognition memory and led us to perform two additional experiments to confirm the obtained results. The first additional experiment was intended to minimize the possibility that a small effect was missed because of lack of statistical power. The second additional experiment examined whether an alternative method of manipulating retrieval success would influence the effect of word frequency on unstudied foils.

**Methods**

*Experiment 1: episodic retrieval I*

Sixteen participants (11 women) aged 19 to 25 years gave informed consent for this experiment. All were neurologically

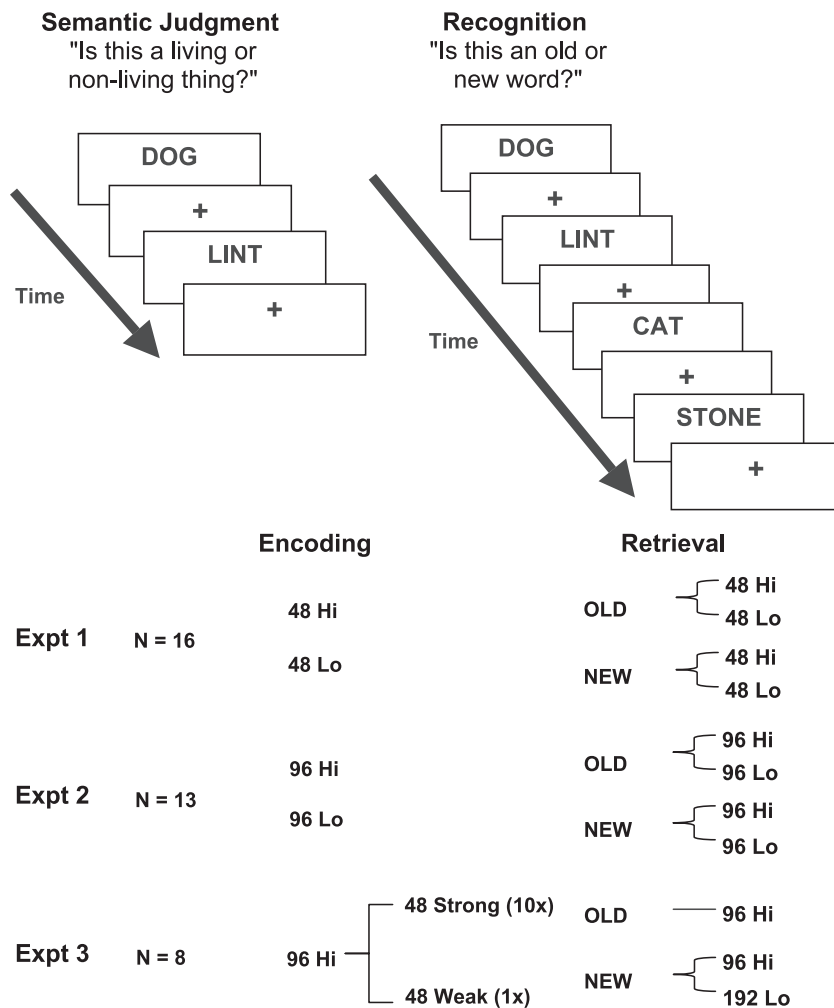


Fig. 1. Schematic showing details of the experimental task, stimuli used, and the number of subjects.

Table 1  
Mean accuracy and response times (standard deviations in parentheses) for Living/Non-Living judgment

Experiment	Condition	Proportion correct	Response time (ms)
1	HF	0.97 (0.02)	826 (88)
	LF	0.92 (0.04)	915 (132)
2	HF	0.96 (0.01)	807 (28)
	LF	0.91 (0.01)	908 (38)
3	HF	0.95 (0.01)	724 (31)

Data for Experiment 3 are reported for first presentations only.

normal, right-handed individuals who were selected from good performance in standardized English examinations described previously (Chee et al., 2001).

Three hundred and eighty-four words were obtained from the MRC Psycholinguistic Database ([http://www.psy.uwa.edu.au/MRCDatabase/uwa\\_mrc.htm](http://www.psy.uwa.edu.au/MRCDatabase/uwa_mrc.htm)) to create the stimuli used in this experiment. One hundred ninety-two words equally divided into four groups according to frequency (high and low) and animacy (living and non-living) were used during encoding. During episodic retrieval, 96 ‘old’ words and 96 ‘new’ words were presented for evaluation (Fig. 1). Target words were used as foils in some volunteers and vice-versa in others so as to counterbalance the words used at encoding and retrieval. High-frequency words had a median frequency of 50 per million words. Low-frequency words had a median frequency of 2 per million. All the words used were also matched for concreteness.

Volunteers underwent fMRI while incidentally encoding test words and 24 h later when recognition was tested. At encoding,

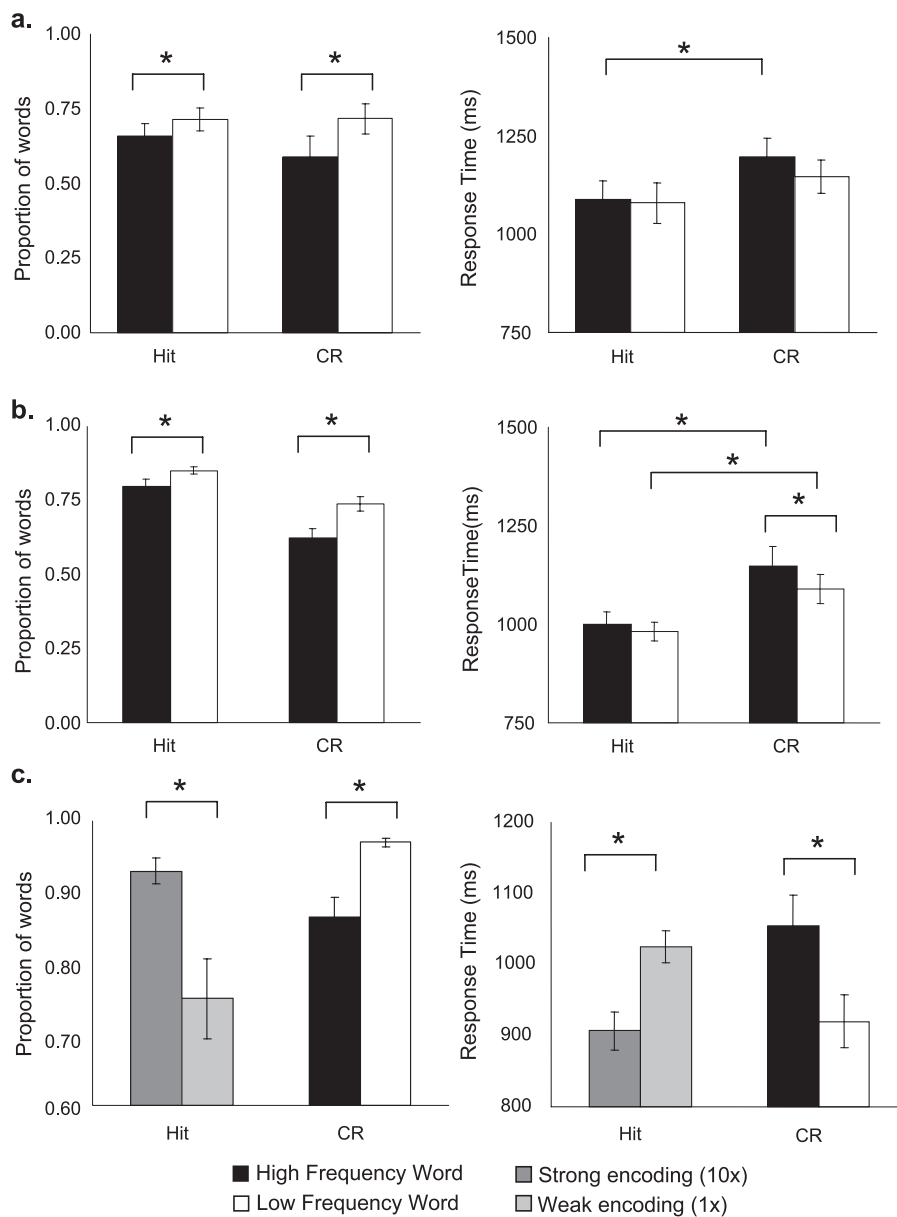


Fig. 2. Accuracy and response times during recognition for Hits and CRs during (a) Experiment 1 (Recognition I), (b) Experiment 2 (Recognition II), and (c) Experiment 3 (Encoding Strength) ( $P < 0.05$ ).

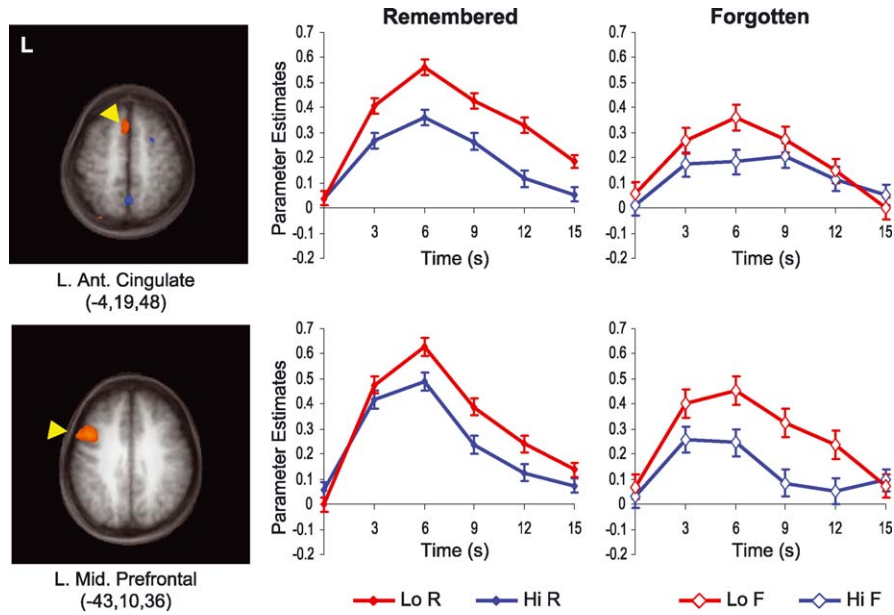


Fig. 3. Axial slices showing areas with greater BOLD signal for subsequently remembered (R) compared to subsequently forgotten (F) words ( $P < 0.001$  uncorrected).

participants decided if the presented word referred to a living or non-living entity and responded by pressing one of two buttons. Each stimulus appeared for 2 s with stimulus onset asynchronies (SOA: the time interval between the onset of successive stimuli) of 3, 6, or 9 s. Multiple SOAs were used to generate enough equations to solve for each predictor during the analysis of functional data (Miezin et al., 2000). Following a response, the stimulus was replaced by a fixation crosshair until the next stimulus appeared. There were six encoding runs whose order was counterbalanced across subjects. Each encoding run involved 84 functional scans.

During recognition participants decided whether each presented word was old (seen previously during encoding) or new and

responded accordingly. Stimuli were presented in three runs, each involving the acquisition of 148 functional scans. Other experimental parameters pertaining to stimulus presentation timings were identical to those used during encoding.

*Imaging protocol*

The fMRI experiments were performed in a 3.0-T Allegra scanner (Siemens, Erlangen, Germany). A blipped gradient-echo EPI sequence was used for the functional imaging with TR of 3000 ms, FOV  $19.2 \times 19.2$  cm,  $64 \times 64$  matrix. Thirty-two oblique axial slices approximately parallel to the AC-PC line and 3-mm

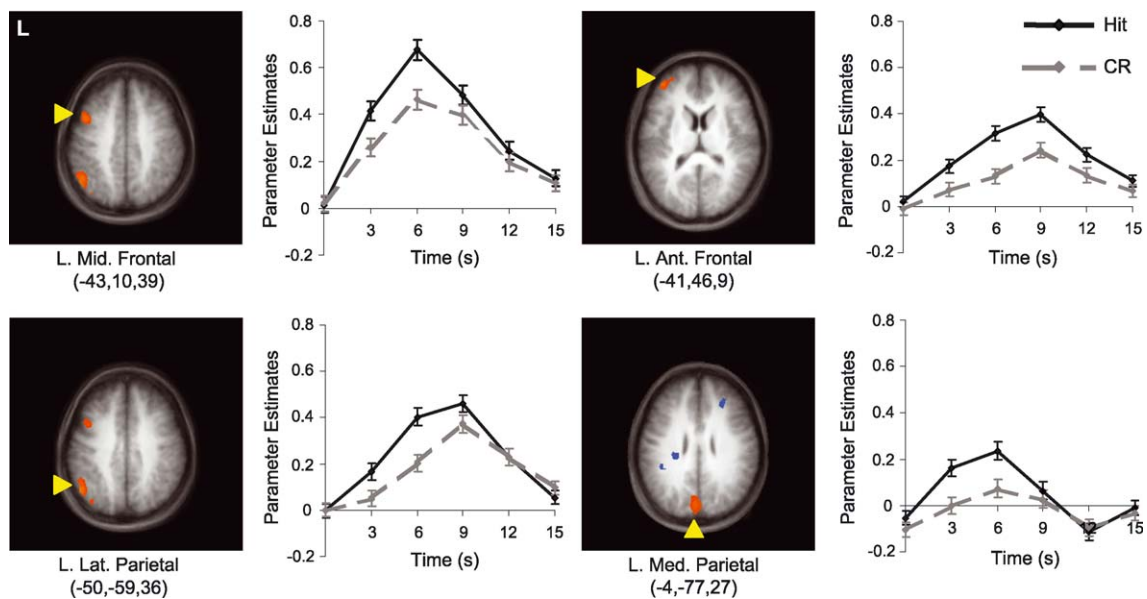


Fig. 4. Axial slices showing areas that tracked retrieval success, that is, areas that showed a greater BOLD signal response to Hits than to CR in Experiment 1 ( $P < 0.001$  uncorrected).

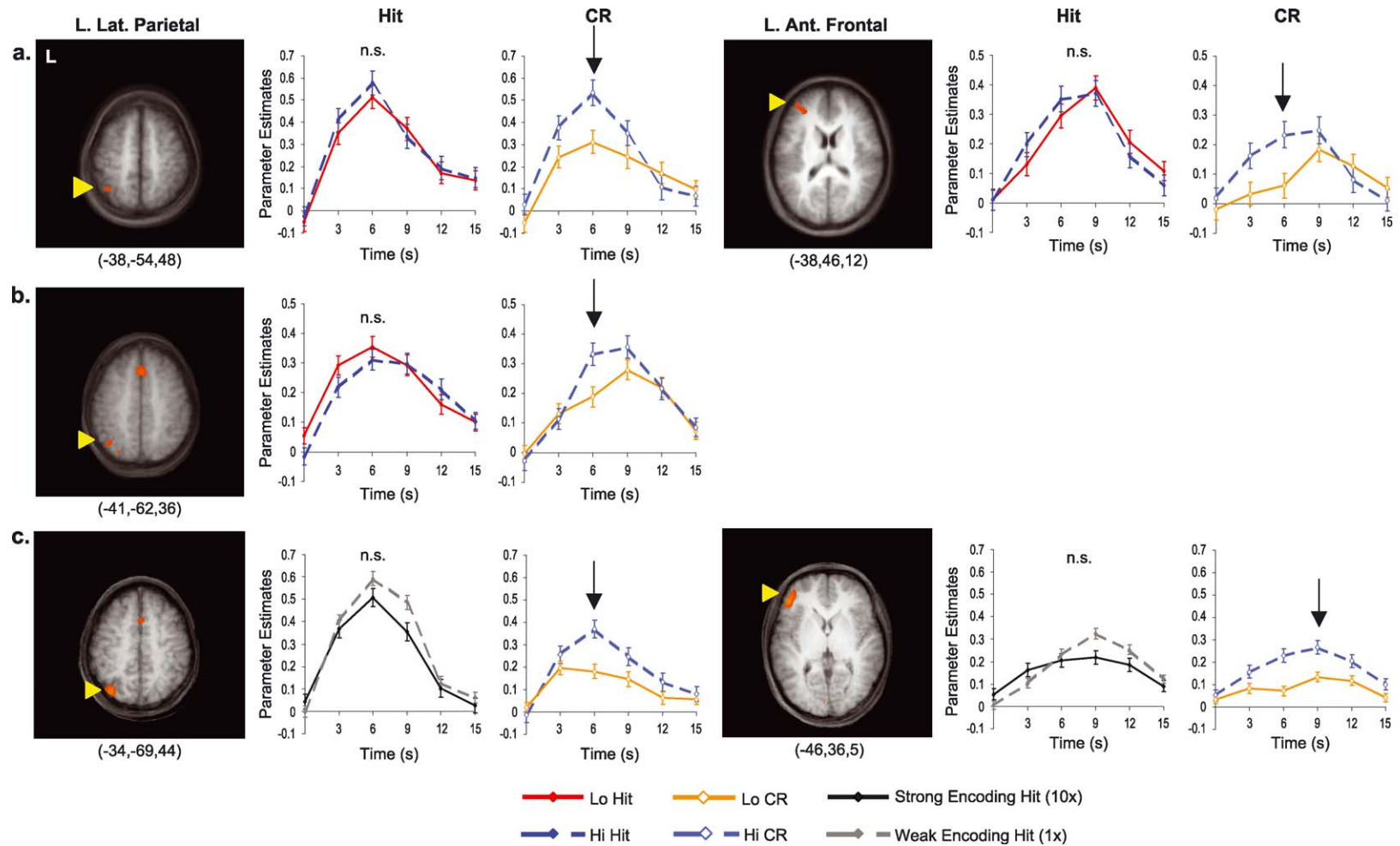


Fig. 5. Axial slices showing areas with greater BOLD signal response to Hi CR than to Lo CR for (a) Experiment 1 (Recognition I), (b) Experiment 2 (Recognition II), and (c) Experiment 3 (Encoding Strength). Arrows show the time point at which significant differences between conditions were revealed ( $P < 0.005$  uncorrected for illustration purposes).



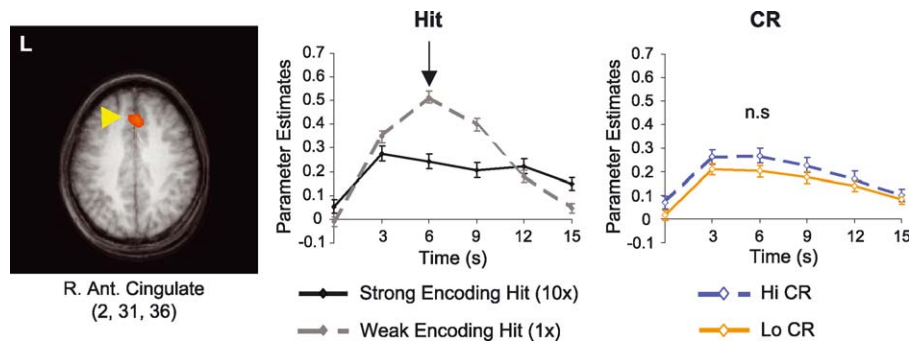


Fig. 6. Axial slice showing greater BOLD signal in the anterior cingulate for hits following weak encoding. Arrow shows that time point at which significant differences between conditions were revealed. ( $P < 0.001$  uncorrected).

thick (0.3-mm gap) were acquired. High-resolution coplanar T2 anatomical images were also obtained. For the purpose of image display in Talairach space, a further high-resolution anatomical reference image was acquired using a 3D-MPRAGE sequence. A bite-bar was used to reduce head motion. Stimuli were projected onto a screen at the back of the magnet while participants viewed the screen using a mirror.

#### Data analysis

Recognition responses were classified as high (Hi) and low (Lo) frequency: Hits (correctly identifying an old word), Misses (incorrectly identifying an old word as new), False Alarms (FA; incorrectly identifying a new word as old), or Correct Rejections (CR; correctly identifying a new word).

The methods used for analysis have been described previously (Chee et al., 2003). Briefly, functional images were analyzed using Brain Voyager 2000 ver 4.9 (Brain Innovation, Maastricht, Holland). Gaussian filtering was applied, in the spatial domain. A smoothing kernel of 8 mm FWHM was used in the computation of group-level activation maps. A fixed effects analysis was used owing to a software–hardware limitation. Reservations regarding data veracity might perhaps be assuaged by the reproducibility of the primary findings in all three experiments involving a total of 37 volunteers.

Voxel-by-voxel statistical analysis was performed using general linear model (GLM). Two GLMs were computed for the encoding data. This was to examine if we would replicate our previous findings (Chee et al., 2003) that suggested that word frequency and subsequent memorability had dissociable contributions to prefrontal BOLD signal change. One GLM considered word frequency as the explanatory variable (Hi and Lo) and the other considered both word frequency and subsequent memory (Subsequently Remembered (R) and Forgotten (F)) as explanatory variables. Two GLMs were also computed for the recognition data. In one GLM, the explanatory variables were recognition responses: Hits, Misses, FA, and CR. This GLM was to evaluate if the results of present study would replicate those obtained by Konishi et al. (2000). In a second GLM, the interaction between word frequency and recognition was of interest and events were sorted by word frequency for each of the four recognition response types.

A set of six finite-impulse-response (FIR) predictors was used to model the hemodynamic response for each explanatory variable. There was one predictor for each scan starting from stimulus onset covering a total of 15 s. No prior assumptions were made concerning response onset latency, peak, or waveform. The pa-

parameter estimate of signal change for each region-of-interest (ROI) was obtained from the third predictor (6 s from stimulus onset) for each condition. We also examined signal change at the fourth predictor (9 s) but the results reported pertain to those obtained from the third predictor only. A statistical threshold of  $P < 0.001$  (uncorrected) and a cluster size of  $>8$  contiguous voxels was used to create activation maps. ROI-based analysis of activation magnitude was performed on voxels jointly active in the conditions of interest ( $P < 0.001$  (uncorrected) except for the case of the left anterior frontal region where the map display threshold was  $P < 0.005$ ). Each ROI included significantly activated voxels within a bounding cube of edge 15 mm surrounding the activation peak for that ROI.

#### Experiment 2: episodic retrieval II

While Experiment 1 replicated some aspects of previous work on episodic memory, such as differences in activation between Hits and Correct Rejections, it did not reveal an imaging correlate of the mirror effect in recognition (Glanzer and Adams, 1985). To exclude an inadequate number of test items as an underlying reason for this null finding, 96 ‘old’ and 96 ‘new’ words were added to the list of words to be recognized in Experiment 2 (Fig. 1). A total of 384 words were presented in six experimental runs. The trade-off was that more words increased the likelihood of semantic interference. Thirteen participants (7 women, aged 19 to 31 years) who had similar demographic characteristics as the participants in Experiment 1 were recruited for this experiment. The imaging analysis methodology was identical to that used in Experiment 1.

#### Experiment 3: encoding strength

This experiment was performed as an additional check for the null finding observed for Hits in the prior experiments. It also served to evaluate the generalizability of the results from Experiment 1 by using an alternative means of manipulating recognition performance at retrieval. High-frequency words presented 10 times ( $10\times$ ) were expected to generate more hits than those presented once ( $1\times$ ). However, if hit and correct rejection decisions are made on different bases (see Discussion for elaboration), we would expect the effect of word frequency on activation associated with CR to remain intact with this manipulation.

Eight participants (6 women, aged 19 to 34 years) were recruited. The encoding task consisted of only high-frequency words. 48 words were presented once (Weak) and 48 words were

repeated 10 times (Strong) (Fig. 1). Volunteers performed incidental encoding as with the prior two experiments. Recognition was tested 30 min after encoding was completed. The test set of high- and low-frequency words was identical to that used in Experiment 2. The imaging analysis methodology was identical to that used in Experiment 1.

## Results

### Experiment 1: episodic retrieval I

Living/non-living judgments for high-frequency words yielded more accurate [ $t(15) = 6.05$ ,  $P < 0.001$ ] and faster responses [ $t(15) = -5.24$ ,  $P < 0.001$ ] than low-frequency words (Table 1). There was no difference in response time between subsequently recognized words and subsequently forgotten words. At recognition, low-frequency words were associated with a higher proportion of Hits [ $t(15) = 2.47$ ,  $P < 0.05$ ] and CRs [ $t(15) = 5.16$ ,  $P < 0.01$ ]

Table 2

Talairach coordinates of activation peaks for Experiment 1 (Recognition I) (\* $P < 0.005$  uncorrected)

Experiment 1: encoding					
Brain region	Brodmann's area	x	y	z	t value
<i>Lo &gt; Hi</i>					
Left anterior cingulate	32	-7	9	48	7.65
Left middle frontal gyrus	6/44	-46	4	29	6.28
Right middle frontal gyrus	6/44	46	7	33	5.98
Left inferior temporal gyrus	37	-46	-62	-10	5.42
Left lateral parietal region	7	-28	-60	43	4.55
Left middle occipital cortex	18	-19	-91	-3	3.84
Right middle occipital cortex	18	15	-89	-3	4.85
Left fusiform gyrus	18/19	-25	-78	-16	4.28
<i>Remembered &gt; Forgotten</i>					
Left anterior cingulate	8/32	-4	19	48	4.53
Left middle frontal gyrus	44	-43	10	36	5.63
Left inferior frontal gyrus	47	-49	22	-3	3.68
Left lateral parietal region	7	-28	-74	41	3.87
Left inferior temporal gyrus	20	-55	-41	-9	4.34
Experiment 1: recognition I					
Brain region	Brodmann's area	x	y	z	t value
<i>Hit &gt; CR</i>					
Left middle frontal gyrus	44	-43	10	39	4.56
Left inferior frontal gyrus	45	-37	19	18	4.09
Left anterior frontal gyrus	10	-41	46	9	4.71
Left lateral parietal region	40	-50	-59	36	4.90
Right lateral parietal region	40	37	-63	42	3.61
Left medial parietal region	7/19	-4	-77	27	4.31
Left insula	13	-32	19	5	3.65
Left thalamus		-10	-3	7	3.99
<i>Hi CR &gt; Lo CR</i>					
Left anterior frontal region	10	-38	46	12	2.96*
Right anterior frontal region	10	28	55	12	2.98*
Left lateral parietal region	40	-38	-54	48	3.37
Left medial parietal region	7	-7	-77	45	3.00*
Right fusiform gyrus	19	32	-71	-6	3.32

Table 3

Talairach coordinates of activation peaks for Experiments 2 (Recognition II) and 3 (Encoding Strength) (\* $P < 0.005$  uncorrected)

Experiment 2: recognition II					
Brain region	Brodmann's area	x	y	z	t value
<i>Hit &gt; CR</i>					
Left anterior frontal region	10	-34	43	15	4.19
Left lateral parietal region	39	-43	-65	33	3.52
Left medial parietal region	7/19	-10	-71	27	4.33
<i>Hi CR &gt; Lo CR</i>					
Left lateral parietal region	7/40	-41	-62	36	3.32
Left medial parietal region	7/19	-7	-77	24	5.04
Right anterior cingulate	45	2	22	45	3.77
Experiment 3: encoding strength					
Brain region	Brodmann's Area	x	y	z	t value
<i>1 Hit &gt; 10 Hit</i>					
Right anterior cingulate	32	2	31	36	4.86
<i>Hi CR &gt; Lo CR</i>					
Left anterior frontal region	10	-46	37	6	5.32
Left middle frontal gyrus	44	-43	19	33	4.32
Left lateral parietal region	40	-35	-68	42	4.60
Left medial parietal region	7/19	-9	-86	30	3.12*
Right anterior cingulate	32	5	13	42	3.61

than high-frequency words (Fig. 2a). There was no difference in response times for Hits [ $t(15) = 0.321$ , n.s.] although there was a trend towards for faster CR responses for low-frequency compared to high-frequency words [ $t(15) = 1.43$ ,  $P < 0.1$ ]. In addition, CRs elicited slower responses than Hits for high [ $t(15) = 2.74$ ,  $P < 0.01$ ] but not for low [ $t(15) = 1.35$ ,  $P < 0.1$ ] frequency words. The mean probability of Hits = 0.69; the probability of False Alarms = 0.23; recognition rate [p(Hit) - p(FA)] = 0.46. Mean response times collapsed across word frequency were: Hit = 1083 ms, Miss = 1186 ms, FA = 1210 ms, CR = 1171 ms.

At encoding, the word frequency and subsequent memory effects were similar to those reported previously (Chee et al., 2003); (Fig. 3, Table 2). During recognition, Hits were associated with higher BOLD signal than CRs in the left middle frontal (BA 44), inferior frontal (BA 45), anterior frontal (BA 10) regions, medial parietal (BA 7/19), insula, bilateral lateral parietal (BA 40/39), and both thalami (Fig. 4, Table 2), replicating previous findings (Buckner et al., 1998a,b; Konishi et al., 2000; Wheeler and Buckner, 2003). High-frequency CRs were associated with higher BOLD signal in the left lateral parietal (BA 40), anterior frontal (BA 10) (Fig. 5a), and medial parietal (BA 7) regions (Table 2). Word frequency did not differentiate activation for Hits in any region even at lax thresholds.

### Experiment 2: episodic retrieval II

Behavioral and imaging data were similar to Experiment 1 (Table 1; Fig. 2). Low-frequency words were associated with a higher proportion of Hits [ $t(12) = 3.12$ ,  $P < 0.01$ ] and CR [ $t(12) = 5.73$ ,  $P < 0.001$ ] relative to high-frequency words (Fig. 2b). There was no difference in response time for Hits between high- and low-frequency words [ $t(12) = 1.06$ , n.s.], while CR responses for high-

frequency words took longer than for low-frequency words [ $t(12) = 3.38, P < 0.01$ ]. The mean probability of Hits = 0.77; the probability of False Alarms = 0.42; recognition rate [ $p(\text{Hit}) - p(\text{FA})$ ] = 0.35. Mean response times collapsed across word frequency were: Hit = 992 ms, Miss = 1147 ms, FA = 1150 ms, CR = 1145 ms.

Hits were associated with higher BOLD signal than CRs in the left lateral parietal (BA 39), medial parietal (BA 7/19) and anterior frontal regions (BA 10) (Table 3). High-frequency CRs were associated with higher BOLD signal than low-frequency CRs in the left lateral parietal (BA 7/40), and medial parietal (BA 7/19) regions (Fig. 5b; Table 3). No differences in activation were observed between high- and low-frequency Hits.

### Experiment 3: encoding strength

Words that were encoded 10× were recognized more accurately [ $t(7) = 4.42, P < 0.01$ ] and faster [ $t(7) = 6.02, P < 0.01$ ] than words that were encoded once (Fig. 2c; see Table 1 for living non-living judgment performance). There were significantly more CR responses for low-frequency than for high-frequency words [ $t(7) = 5.73, P < 0.01$ ]. Low-frequency CR responses were significantly faster than high-frequency CR responses [ $t(7) = 5.39, P < 0.01$ ].

Words that were encoded once were associated with greater BOLD signal in the right anterior cingulate (BA 32) (Fig. 6, Table 3) and at a very lax threshold ( $P < 0.01$ ), the left prefrontal region (see Wheeler and Buckner, 2003). High-frequency CRs were associated with greater BOLD signal than low-frequency CRs in the left anterior frontal (BA 10), lateral parietal (BA 40), medial parietal (BA 7/19), and middle frontal (BA 44) regions (Fig. 5c; Table 3).

## Discussion

We found that during encoding, greater activation in the left prefrontal and anterior cingulate regions predicted a higher proportion of hits for low-frequency words. However, scanning during recognition showed that word frequency *did not* modulate activation in any of the regions that tracked successful recognition. This suggests that the higher hit rate for low-frequency targets was due to differences in neural activity at encoding, without any apparent contribution from processes occurring during recognition. Neither word frequency nor strength of encoding modulated activation for hits in areas that tracked retrieval success, indicating that these areas were insensitive to how well encoded the recognized item was. Two areas among those tracking retrieval success, the left lateral parietal and anterior prefrontal regions were sensitive to the global familiarity of foils. Finally, the anterior cingulate tracked retrieval effort for words that differed in encoding strength.

### Dual process accounts of recognition

Recognition of studied items can occur via a general feeling of *familiarity* (alternatively termed ‘knowing’) and a more specific, higher ‘quality’ *recollection* (also termed ‘remembering’) that carries with it contextual information about the encoding episode (Tulving, 1985). These two modes of recognition memory can broadly be discussed under two theoretical frameworks: Single and Dual process models. In single process models, recognition is

based on a single dimension of memory strength for test items (Donaldson, 1996) whereby familiar items have a weaker ‘trace strength’ than recollected items. It would be difficult for such a model to explain why cortical activation at recognition is modulated by word frequency for Correct Rejections but not Hits (Reder et al., 2000). Dual process models (Mandler, 1980) posit that familiarity and recollection judgments are qualitatively different processes (Brown and Aggleton, 2001). They also argue that hits and correct rejections are driven by different cognitive processes (Reder et al., 2000). Dual process models are supported by behavioral, electrophysiological (for a review, see Rugg and Yonelinas, 2003), functional imaging (Henson et al., 1999) data as well as by the effects of short-acting benzodiazepines (Mintzer, 2003) on recognition memory.

The imaging findings of the present study can be explained within the framework of a dual process model of episodic memory by hypothesizing that the basis for making Correct Rejection and Hit judgments is different. Specifically, we propose that Correct Rejections in the context of the present experiment are predominantly based on familiarity judgments (Arndt and Reder, 2002). These judgments correlate with activation that is differentiated by word frequency. We further propose that without applying a strong bias, most Hits are judged from recollection (Gardiner et al., 2002); also see Chee et al., 2003; Henson et al., 1999). Such recollection engenders relatively higher word frequency and encoding strength independent activation in a subset of regions that track successful recognition.

### Word frequency and correct rejection judgments

Greater left lateral parietal (and medial parietal) activation for Hits relative to correctly rejected new items has emerged as a consistent finding across imaging studies on episodic memory and is thought to reflect the successful retrieval of a memory (Daselaar et al., 2003; Konishi et al., 2000; McDermott et al., 2000; Wheeler and Buckner, 2003).

The present results suggest that the parietal region may additionally index our experience with *unstudied* items. If we accept word frequency as indicative of pre-experimental exposure to a word (Reder et al., 2002), it follows that high-frequency foils should engender a greater sense of familiarity than low-frequency foils as a result of a higher level of pre-experimental exposure. As such, one could expect that they would engender greater parietal activation than less familiar low-frequency words. An alternative interpretation is that the greater activation merely reflects the point that high-frequency foils take longer to reject as ‘old’ because of their greater global familiarity. While correct rejection of high-frequency words did take longer, it is unlikely that the modulation of activation in this area is due to time-on-task since compared to Hits, Correct Rejections took *longer* but were associated with *less* activation.

High-frequency Correct Rejections were also associated with greater activation than low-frequency Correct Rejections in the left anterior frontal region, although this was less consistently reproduced. Prior studies suggest that anterior frontal activation during episodic retrieval may be related to the engagement of a cognitive state focused on retrieving past experience (retrieval mode) (Kapur et al., 1995; Nyberg et al., 1995; Rugg et al., 1999), the retrieval of source information (Ranganath et al., 2000; Rugg et al., 1999), and the indexing of retrieval success (Buckner et al., 1998a; Habib and Lepage, 1999; Henson et al., 1999; Konishi et al., 2000). Our



results suggest that the left anterior frontal region may be involved in successful retrieval, tracking the pattern of activation in the left lateral parietal region. The BOLD response curves for this ROI revealed that the peak of activation occurred relatively late (9 s rather than 6 s) and may reflect post-retrieval monitoring of retrieved items as previously suggested (Buckner et al., 1998a; Schacter et al., 1997). Lateralization of activation in this region appears to be dependent on the task and experimental design. Compared to block designs, event-related designs examining recognition have tended to produce left lateralized activation (Buckner et al., 1998a,b; Henson et al., 1999; Konishi et al., 2000).

#### *Word frequency and Hit judgments*

Dual process accounts of recognition posit that studied (old) low-frequency words have an advantage at recognition compared to high-frequency words as a greater proportion of them are recognized from recollection as opposed to familiarity (Reider et al., 2000, 2002). One might expect reduced activation to be associated with low-frequency Hits because of the reduced retrieval effort that they might be expected to engage at retrieval given the additional activation they elicited at encoding. However, the present data show that successfully recognized target words elicit activation at retrieval that was not differentiated by word frequency.

This null finding with respect to target words is unlikely to be spurious given that it was replicated in three experiments involving a total of 37 volunteers. Further, the effects of three previously documented determinants of cortical activation: word frequency, subsequent memory and retrieval success were also replicated. Examination of the behavioral data shows that response times to low- and high-frequency Hits were similar. These results suggest that processes taking place during or after encoding minimize differences in the retrieval of episodic information about the studied words. We postulate that the more elaborate processing received by low-frequency words at encoding, indexed by greater left prefrontal activation, results in a higher probability of their having appropriate contextual information encoded so as to form a ‘higher quality’ recollection. We further propose that at retrieval, recovery of the appropriate ‘spatio-temporal’ context of studied words (Henson et al., 1999) is sufficient for their successful recognition. Further information is not used for the purpose of recognition, and is therefore neither reflected in behavioral nor imaging findings.

We are unable to comment about the role of medial temporal structures differentiating the ‘quality’ of recollection (Aggleton and Brown, 1999; Brown and Aggleton, 2001) as these structures were not visualized in our experiments (see Chee et al., 2003 for a discussion as to why). This aside, it should be noted that an alternative explanation for the null finding is that encoding processes taking place in the frontal lobe organize inputs into the medial temporal region and that the latter plays a more important role in retrieving episodic memories (Henson et al., 1999).

#### *Imaging correlates of retrieval success*

The present results add to the consensus that a consistent set of areas track retrieval success (Buckner et al., 1998a,b; Herron et al., 2004; Konishi et al., 2000; Wheeler and Buckner, 2003). However, different subsets of these regions show sensitivity or insensitivity to particular determinants of retrieval success (Henson et al., 1999, 2004; Wheeler and Buckner, 2003). Frontal areas (prefrontal and/

or anterior cingulate) are sensitive to the amount of controlled processing required (Wheeler and Buckner, 2003) or the probability of target detection (Herron et al., 2004), whereas the parietal region appears to be insensitive to either manipulation. Our data are congruent with a previous result (Wheeler and Buckner, 2003); these authors highlighted the left prefrontal region but their tables and figures showed that the anterior cingulate was also involved) in showing that whereas the anterior cingulate shows sensitivity to manipulation of encoding strength (10× vs. 1× presentation), the parietal region is insensitive to this manipulation.

#### *Caveat*

Our findings relate to recognition and not free recall (the latter being difficult to implement using fMRI). High-frequency words have been shown to be associated with better recall performance when high- and low-frequency words were presented in separate lists (Watkins et al., 2000). However, when low- and high-frequency words in a mixed list were presented for the same amount of time, and when a distractor task was introduced to prevent post-stimulus processing, low-frequency words were better recalled (Gregg et al., 1980).

#### *Conclusions*

Our experiments show that the effect of word frequency on brain activation at encoding and recognition differs. Whereas word frequency modulates left prefrontal and anterior cingulate activation at encoding, it does not do so during recognition. This result demonstrates that under some circumstances, subsequent memory can be determined purely by encoding processes. In contrast to null effects observed with studied words, the word frequency of correctly identified foils modulates left parietal and anterior prefrontal activation. This result shows that a subset of areas tracking retrieval success shows activity modulation that is contingent on whether the item involved is correctly recognized as a target or a foil. This dissociation in activity modulation is consistent with dual process models of episodic memory.

#### **Acknowledgments**

This work was supported by NMRC 2000/0477, BMRC 014 and The Shaw Foundation. We are deeply grateful to the two reviewers for their thoughtful comments.

#### **References**

- Aggleton, J.P., Brown, M.W., 1999. Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *Behav. Brain Sci.* 22, 425–444 (discussion 444–489).
- Arndt, J., Reider, L.M., 2002. Word frequency and receiver operating characteristic curves in recognition memory: evidence for a dual-process interpretation. *J. Exp. Psychol. Learn. Mem. Cogn.* 28, 830–842.
- Brown, M.W., Aggleton, J.P., 2001. Recognition memory: what are the roles of the perirhinal cortex and hippocampus? *Nat. Rev., Neurosci.* 2, 51–61.
- Buckner, R.L., Koutstaal, W., Schacter, D.L., Wagner, A.D., Rosen, B.R., 1998a. Functional-anatomic study of episodic retrieval using fMRI. I. Retrieval effort versus retrieval success. *NeuroImage* 7, 151–162.

- Buckner, R.L., Koutstaal, W., Schacter, D.L., Dale, A.M., Rotte, M., Rosen, B.R., 1998b. Functional-anatomic study of episodic retrieval. II. Selective averaging of event-related fMRI trials to test the retrieval success hypothesis. *NeuroImage* 7, 163–175.
- Buckner, R.L., Wheeler, M.E., Sheridan, M.A., 2001. Encoding processes during retrieval tasks. *J. Cogn. Neurosci.* 13, 406–415.
- Chee, M.W., Hon, N., Lee, H.L., Soon, C.S., 2001. Relative language proficiency modulates BOLD signal change when bilinguals perform semantic judgments. *NeuroImage* 13, 1155–1163.
- Chee, M.W., Hon, N.H., Caplan, D., Lee, H.L., Goh, J., 2002. Frequency of concrete words modulates prefrontal activation during semantic judgments. *NeuroImage* 16, 259–268.
- Chee, M.W., Westphal, C., Goh, J., Graham, S., Song, A.W., 2003. Word frequency and subsequent memory effects studied using event-related fMRI. *NeuroImage* 20, 1042–1051.
- Daselaar, S.M., Veltman, D.J., Rombouts, S.A., Raaijmakers, J.G., Jonker, C., 2003. Neuroanatomical correlates of episodic encoding and retrieval in young and elderly subjects. *Brain* 126, 43–56.
- Demb, J.B., Desmond, J.E., Wagner, A.D., Vaidya, C.J., Glover, G.H., Gabrieli, J.D., 1995. Semantic encoding and retrieval in the left inferior prefrontal cortex: a functional MRI study of task difficulty and process specificity. *J. Neurosci.* 15, 5870–5878.
- Donaldson, W., 1996. The role of decision processes in remembering and knowing. *Mem. Cogn.* 24, 523–533.
- Donaldson, D.I., Petersen, S.E., Ollinger, J.M., Buckner, R.L., 2001. Dissociating state and item components of recognition memory using fMRI. *NeuroImage* 13, 129–142.
- Gardiner, J.M., Ramponi, C., Richardson-Klavehn, A., 2002. Recognition memory and decision processes: a meta-analysis of remember, know, and guess responses. *Memory* 10, 83–98.
- Glanzer, M., Adams, J.K., 1985. The mirror effect in recognition memory. *Mem. Cogn.* 13, 8–20.
- Gregg, V.H., Montgomery, D., Castano, D., 1980. Recall of common and uncommon words from single and mixed lists. *J. Verbal Learn Verbal Behav.* 19, 240–245.
- Habib, R., Lepage, M., 1999. Novelty assessment in the brain. In: Tulving, E. (Ed.), *Memory, Consciousness and the Brain*. Psychology Press, Philadelphia, pp. 265–277.
- Henson, R.N., Rugg, M.D., Shallice, T., Josephs, O., Dolan, R.J., 1999. Recollection and familiarity in recognition memory: an event-related functional magnetic resonance imaging study. *J. Neurosci.* 19, 3962–3972.
- Herron, J.E., Henson, R.N., Rugg, M.D., 2004. Probability effects on the neural correlates of retrieval success: an fMRI study. *NeuroImage* 21, 302–310.
- Kapur, S., Craik, F.I., Tulving, E., Wilson, A.A., Houle, S., Brown, G.M., 1994. Neuroanatomical correlates of encoding in episodic memory: levels of processing effect. *Proc. Natl. Acad. Sci. U. S. A.* 91, 2008–2011.
- Kapur, S., Craik, F.I., Jones, C., Brown, G.M., Houle, S., Tulving, E., 1995. Functional role of the prefrontal cortex in retrieval of memories: a PET study. *NeuroReport* 6, 1880–1884.
- 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.
- Maccotta, L., Zacks, J.M., Buckner, R.L., 2001. Rapid self-paced event-related functional MRI: feasibility and implications of stimulus- versus response-locked timing. *NeuroImage* 14, 1105–1121.
- Mandler, G., 1980. Recognizing: the judgment of previous occurrence. *Psychol. Rev.* 87, 252–271.
- McDermott, K.B., Ojemann, J.G., Petersen, S.E., Ollinger, J.M., Snyder, A.Z., Akbudak, E., Conturo, T.E., Raichle, M.E., 1999. Direct comparison of episodic encoding and retrieval of words: an event-related fMRI study. *Memory* 7, 661–678.
- McDermott, K.B., Jones, T.C., Petersen, S.E., Lageman, S.K., Roediger III, 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.
- Miezin, F.M., Maccotta, L., Ollinger, J.M., Petersen, S.E., Buckner, R.L., 2000. Characterizing the hemodynamic response: effects of presentation rate, sampling procedure, and the possibility of ordering brain activity based on relative timing. *NeuroImage* 11, 735–759.
- Miller, M.B., Van Horn, J.D., Wolford, G.L., Handy, T.C., Valsangkar-Smyth, M., Inati, S., Grafton, S., Gazzaniga, M.S., 2002. Extensive individual differences in brain activations associated with episodic retrieval are reliable over time. *J. Cogn. Neurosci.* 14, 1200–1214.
- Mintzer, M.Z., 2003. Triazolam-induced amnesia and the word-frequency effect in recognition memory: support for a dual process account. *J. Mem. Lang.* 48, 596–602.
- Nyberg, L., Tulving, E., Habib, R., Nilsson, L.G., Kapur, S., Houle, S., Cabeza, R., McIntosh, A.R., 1995. Functional brain maps of retrieval mode and recovery of episodic information. *NeuroReport* 7, 249–252.
- Otten, L.J., Rugg, M.D., 2001. Task-dependency of the neural correlates of episodic encoding as measured by fMRI. *Cereb. Cortex* 11, 1150–1160.
- Otten, L.J., Henson, R.N., Rugg, M.D., 2001. Depth of processing effects on neural correlates of memory encoding: relationship between findings from across- and within-task comparisons. *Brain* 124, 399–412.
- Ranganath, C., Johnson, M.K., D'Esposito, M., 2000. Left anterior prefrontal activation increases with demands to recall specific perceptual information. *J. Neurosci.* 20, RC108.
- Reder, L.M., Nhouyvanisvong, A., Schunn, C.D., Ayers, M.S., Angstadt, P., Hiraki, K., 2000. A mechanistic account of the mirror effect for word frequency: a computational model of remember-know judgments in a continuous recognition paradigm. *J. Exper. Psychol., Learn., Mem., Cogn.* 26, 294–320.
- Reder, L.M., Angstadt, P., Cary, M., Erickson, M.A., Ayers, M.S., 2002. A reexamination of stimulus-frequency effects in recognition: two mirrors for low- and high-frequency pseudowords. *J. Exper. Psychol., Learn., Mem., Cogn.* 28, 138–152.
- Rugg, M.D., Yonelinas, A.P., 2003. Human recognition memory: a cognitive neuroscience perspective. *Trends Cogn. Sci.* 7, 313–319.
- Rugg, M.D., Fletcher, P.C., Chua, P.M., Dolan, R.J., 1999. The role of the prefrontal cortex in recognition memory and memory for source: an fMRI study. *NeuroImage* 10, 520–529.
- Rugg, M.D., Otten, L.J., Henson, R.N., 2002. The neural basis of episodic memory: evidence from functional neuroimaging. *Philos. Trans. R Soc. Lond., B Biol. Sci.* 357, 1097–1110.
- Schacter, D.L., Buckner, R.L., Koutstaal, W., Dale, A.M., Rosen, B.R., 1997. Late onset of anterior prefrontal activity during true and false recognition: an event-related fMRI study. *NeuroImage* 6, 259–269.
- Tulving, E., 1985. Memory and consciousness. *Can. Psychol.* 26, 1–12.
- 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, 1188–1191.
- Watkins, M.J., LeCompte, D.C., Kim, K., 2000. Role of study strategy in recall of mixed lists of common and rare words. *J. Exp. Psychol. Learn. Mem. Cogn.* 26, 239–245.
- Wheeler, M.E., Buckner, R.L., 2003. Functional dissociation among components of remembering: control, perceived oldness, and content. *J. Neurosci.* 23, 3869–3880.