

Behavioral/Systems/Cognitive

Separating the Brain Regions Involved in Recollection and Familiarity in Recognition Memory

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The neural substrates of recognition memory retrieval were examined in a functional magnetic resonance imaging study designed to separate activity related to recollection from that related to continuous variations in familiarity. Across a variety of brain regions, the neural signature of recollection was found to be distinct from familiarity, demonstrating that recollection cannot be attributed to familiarity strength. In the prefrontal cortex, an anterior medial region was related to recollection, but lateral regions, including the anterior and dorsolateral prefrontal cortex, were related to familiarity. Along the lateral parietal cortex, two functionally distinct regions were also observed: a lateral parietal/temporal region related to recollection and a more superior parietal region involved in familiarity. Similarly, in medial parietal regions, the posterior cingulate was related to recollection, whereas the precuneus was related to familiarity. The hippocampus was related to recollection, but also exhibited an inverse relationship to familiarity-driven recognition confidence. The results indicate that recollection and familiarity rely on different networks of brain regions and provide insights into the functional roles of different regions involved in episodic recognition memory.

Key words: cingulate; hippocampus; imaging; memory; parietal; prefrontal; recognition; temporal

Introduction

Human neuroimaging studies have indicated that prefrontal, parietal, and medial temporal cortices are involved in recognition memory of prior episodes, but the functional roles that these regions play in recognition are widely debated. The aim of the current study was to determine the extent to which these regions are involved in recollection (i.e., the retrieval of qualitative information about a study event, such as where or when an item was encountered) and familiarity (i.e., assessments of continuous memory strength). Behavioral studies have indicated that these two types of recognition memory processes are functionally independent, but the extent and loci of their differential anatomical substrates is unclear (Yonelinas, 2002; Rugg and Yonelinas, 2003).

Previous neuroimaging studies have identified regions related to recollection and familiarity, either by contrasting recognition responses accompanied by reports of conscious remembering to those accompanied by reports of familiarity in the absence of recollection (cf. Tulving, 1985) or by contrasting recognized items for which subjects can correctly recognize where or when the item was studied (i.e., accurate source recognition) to those for which they fail to recollect source information (cf. Jacoby, 1991; Johnson et al., 1993). Results from studies using these

methods have suggested that several regions are selectively related to recollection, such as the left lateral prefrontal cortex, the left lateral and medial parietal cortices, and medial temporal lobe regions including the hippocampus, whereas other regions are selectively related to familiarity, such as an anterior temporal lobe region in or around the perirhinal cortex (Henson et al., 1999, 2000; Eldridge et al., 2000; Cansino et al., 2002; Henson et al., 2003) (but see Stark and Squire, 2001; Wheeler and Buckner, 2003).

Interpretation of these results, however, is complicated by the fact that whereas “remembered” items and those eliciting correct source judgments tend to be associated with high recognition confidence, those accepted on the basis of familiarity can be associated with a wide range of recognition confidence (e.g., Yonelinas, 2001). Thus, regions identified with recollection in these previous imaging studies may not be related to recollection per se, but may simply reflect areas that respond to increased familiarity confidence. For example, a brain region that increases its activity with familiarity confidence may be less active, on average, for familiarity-based responses than for remember responses, even if the region does not respond preferentially for recollected items. Thus, regions that appear to be related to recollection in previous studies may be more accurately characterized as responding to familiarity strength. To overcome this objection it is necessary to demonstrate that increases in familiarity confidence are associated with a pattern of neural activity that is qualitatively different from that revealed by the contrast between recollection and high confidence familiarity. This finding cannot be accommodated by the assumption that recollection simply lies

Received July 28, 2004; revised Feb. 4, 2005; accepted Feb. 4, 2005.

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DOI:10.1523/JNEUROSCI.5295-04.2005

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at the upper end of a continuum of memory strength or confidence.

We tested this hypothesis in the current study by differentiating between regions related to recollection and those sensitive to variations in familiarity strength in the absence of recollection. Subjects were scanned while they made recognition memory judgments about previously studied words and words that were new to the experiment. For each item, they indicated whether they could recollect qualitative information about the study event, or, if it was not recollected, they indicated how confident they were that the item was studied using a four-point confidence scale. Recollection-related regions were identified as those eliciting greater activity for remembered responses compared with confidently recognized but nonrecollected items (e.g., four responses). Familiarity-related regions were identified as those in which activation correlated with the confidence reports 1–4. This design allowed us to determine whether there were any regions that were selectively related to either recollection or variations in familiarity.

Materials and Methods

Subjects. Sixteen volunteers (nine men, seven women) with a mean age of 21 years (range, 19–33) gave informed consent to participate in the experiment. All volunteers reported themselves to be right handed and native English speaking, with no neurological and psychiatric histories. They were remunerated for their time at a rate of £7.50 per hour.

Experimental tasks and procedure. The procedures of the experiment were approved by the joint medical ethics committee of the National Hospital for Neurology and Neurosurgery and Institute of Neurology in London. The experiment proper consisted of one study phase and one test phase, both performed in the scanner. During the study phase, subjects saw a series of 150 critical words, presented one at a time. For each word, subjects had to decide whether the word denotes an abstract or concrete entity. Concrete entities were defined as anything that can be held or touched (e.g., “harp” vs “retain”). Subjects indicated their decision by depressing one of two buttons on a five-button response box as quickly as possible without sacrificing accuracy. The response box was custom built and shaped to allow the fingers of the right hand to rest comfortably on the buttons. Concrete/abstract decisions were given with the index and middle fingers, with responding finger counterbalanced across subjects. The study phase was administered in a single session of ~8 min.

Immediately after the study phase, subjects performed a recognition memory test. All 150 critical words seen at study were presented again, intermixed with 150 words not seen before in the experiment and 150 fixation-only trials (“null events”). For each word, subjects were asked to press one of the five buttons on the response box according to whether, and how, they remembered that word as having been presented in the study phase. If they were able to remember something specific about seeing the word at study (e.g., the key that was pressed, what they thought about when the word was presented, or what the word looked like on the screen), subjects were asked to give a response with their thumb [a remember (R) judgment]. If they could not recollect anything specific about experiencing the item, subjects were asked to use the remaining four buttons to rate their memory confidence in order of high to low confidence. The index finger was used when they were sure the item had been studied (we will refer to this as a “4” judgment), the middle finger was used when they thought the item had been studied but were not entirely sure (a “3” judgment), the ring finger was used when they thought the item had not been studied but were not entirely sure (a “2” judgment), and the little finger was used when they were sure the item had not been studied (a “1” judgment). Response assignment was kept constant across subjects, and both speed and accuracy were stressed. Subjects were encouraged to spread out their responses such that they used all response buttons. The test phase was divided into two equal sessions of ~12 min each. After the test phase, a 15 min structural scan was acquired.

Before entering the scanner, subjects received practice sessions for both the study (3 min) and test (8 min) phases to familiarize themselves with the concrete/abstract judgments and response requirements at test. For the first 16 words in the test phase, subjects were asked to explain why they pressed a particular button to ensure that they had understood the response instructions. After completion of the experiment, subjects were debriefed about the purpose of the study and paid for their time.

All stimuli were presented in central vision. They were projected onto a mirror in direct view of the reclining volunteer. Words were shown one at a time for 500 ms in a white uppercase Helvetica font on a black background. A fixation point (a plus sign) was continuously present on the screen other than when words were presented. Five hundred milliseconds before the onset of each word, the fixation point changed into a warning stimulus (an exclamation mark) that signaled that a word was about to be presented. At study, the time between successive word onsets was a constant 3150 ms. At test, the time between successive word onsets varied between 3150 and 12600 ms because of the insertion of null events. Words subtended approximate visual angles of 3–6° horizontally and 1° vertically. Stimulus presentation was realized using Cogent2000 software developed by the Cogent2000 team at the Wellcome Department of Imaging Neuroscience and Institute of Cognitive Neuroscience.

Stimulus lists were created from a pool of 921 words, selected pseudo-randomly from the Medical Research Council Psycholinguistics Database (http://www.psy.uwa.edu.au/mrcdatabase/uwa_mrc.htm) (Coltheart, 1981). Only words for which frequency, concreteness, and imageability ratings were available were considered. Words were selected to be between four and eight letters in length and to have a written frequency of 10–50 occurrences per million according to the Thorndike–Lorge (1944) L frequency count (mean frequency of selected words was 26; SD, 11). Within these constraints, words were allowed to have any concreteness and imageability rating as based on three merged sets of norms (Coltheart, 1981). Concreteness and imageability ratings in the word pool therefore represented a continuum, ranging from 214 to 646 (mean, 472; SD, 113) and from 218 to 667 (mean, 494; SD, 87) for concreteness and imageability, respectively.

For each subject, 300 words were selected at random from this pool to create a study list of 150 words and a test list of 300 words (150 old, 150 new). A total of 150 null events were interspersed pseudorandomly with the words in the test list, with the restriction that no more than three null events would occur in succession. Additional words were selected to act as filler items at the beginning of each scanning session (two for each session) and for the practice lists (109 in total).

Magnetic resonance imaging scanning. Scanning was performed at the Wellcome Department of Imaging Neuroscience (London, UK). Scanning took place during both the study and test phases, but only the results of the test phase are described here. A 1.5 T Siemens (Erlangen, Germany) Sonata scanner was used to acquire T1-weighted anatomical volume images and T2*-weighted echoplanar images (EPIs) (echo time, 40 ms) with blood oxygenation level-dependent (BOLD) contrast. Each EPI volume comprised 28 3-mm-thick axial slices separated by 1.5 mm, positioned to cover all but the most superior region of the brain and the cerebellum. Functional images were acquired during three sessions, corresponding with the study phase and the two parts of the test phase. The study phase comprised 195 volumes, and each part of the test phase comprised 290 volumes. Volumes were acquired continuously with an effective repetition time of 2.52 s/volume.

Data analysis. The data acquired during the test phase were analyzed using Statistical Parametric Mapping (Friston et al., 1995), version SPM2 (<http://www.fil.ion.ucl.ac.uk/spm/spm2.html>). The first five volumes in each session were discarded to allow for T1 equilibration effects. The remaining volumes were realigned to the first volume in the series and corrected for residual motion artifacts resulting from field inhomogeneities (Andersson et al., 2001). Volumes were then corrected for different slice acquisition times, normalized to a standard EPI template based on the Montreal Neurological Institute (MNI) reference brain in Talairach space, resliced to a voxel size of 3 × 3 mm, and smoothed with an isotropic 8 mm full-width half-maximum Gaussian kernel.

The volumes acquired during the two test sessions were treated as separate time series. For each series, the variance in BOLD signal was

decomposed with a set of regressors in a general linear model. Activity related to the presentation of each test item was modeled with a δ (stick) function representing stimulus onset, convolved with three hemodynamic response functions: a canonical hemodynamic response function and its temporal and dispersion derivatives (Friston et al., 1998). The temporal and dispersion derivatives did not add meaningful information and are not reported. Separate regressors were constructed for items receiving R, 4, 3, 2, and 1 judgments, regardless of their old/new status, filler items, and items not responded to. These regressors, together with a regressor representing the mean over scans, comprised the full model for each session. The data and model were high-pass filtered to a cut-off of 1/128 Hz.

Parameter estimates were estimated for events of interest using a general linear model. Nonsphericity of the error covariance was accommodated by an autoregressive (1) model, in which the temporal autocorrelation was estimated by pooling over suprathreshold voxels (Friston et al., 2002). The parameters for each covariate and the hyperparameters governing the error covariance were estimated using restricted maximum likelihood. Images were transformed into statistical parametric maps of the Z statistic. Effects of interest were estimated with across-subject one-sample *t* tests of linear contrasts of parameter estimates averaged across the two sessions per subject. Regions sensitive to recollection were identified by computing the difference between the parameter estimates for the regressors for remember versus high confidence familiarity (“4”) judgments. Regions sensitive to familiarity were identified by computing a linear contrast across the regressors associated with judgments 1–4. Subsequent analyses were also conducted in which a quadratic component was added, but this did not alter the pattern of results. Effects were thresholded at $p < 0.001$, uncorrected for multiple comparisons. Only activations involving contiguous clusters of at least five voxels are reported. Stereotactic coordinates are reported in Talairach space and correspond to the standard MNI normalized canonical brain (Cocosco et al., 1997).

With one exception, a minimum of 14 trials were available for each judgment type (range, 14–119; mean, 60). One subject did not make any “1” judgments. Excluding this subject from the analyses did not alter the results in any important way, and we therefore report the results from the analyses incorporating all 16 subjects.

Results

Behavioral data

At study, abstract/concrete judgments were given with a mean reaction time of 1288 ms (SD, 179). The mean proportions of responses and reaction times for each judgment type during the recognition memory test are shown in Table 1. Accuracy was high, as indexed by the greater number of old than new items receiving remember or high confidence familiarity-based responses. Consistent with previous studies of recognition confidence, the response time distributions exhibited an inverted U-shape (Ratcliff and Murdock, 1976) whereby responses were slightly faster for the extreme categories (i.e., R and 1) than for the adjacent categories.

Table 1. Recognition memory performance

Word type	Recognition judgments				
	R	4	3	2	1
Proportion of responses					
Old	0.38 (0.18)	0.32 (0.13)	0.17 (0.08)	0.09 (0.06)	0.03 (0.03)
New	0.02 (0.19)	0.07 (0.07)	0.18 (0.09)	0.37 (0.11)	0.34 (0.18)
Mean reaction time (ms)					
Old	1346 (155)	1645 (325)	1803 (258)	1842 (251)	1808 (532) ¹
New	1499 (352) ²	1789 (370) ³	1784 (248)	1762 (270)	1601 (234) ⁴

Values are across-subject means (SD). ^{1–4}The mean reaction times for “1” judgments to old items, R judgments to new items, “4” judgments to new items, and “1” judgments to new items are based on 13, 11, 15, and 15 subjects, respectively. The remaining subjects did not make any such judgments.

Table 2. Brain regions showing significantly greater BOLD signal ($p < 0.001$) for remember responses than for high confidence familiarity responses

Region of activity	Left/right	BA	Number of voxels	MNI coordinates			Z value
				x	y	z	
Medial frontal gyrus	L	10	431	−6	54	−6	4.29
	R	10	30	9	63	21	3.75
Middle frontal gyrus	L	11	20	−30	39	−12	4.03
	R	11	8	24	30	−15	3.57
Precentral gyrus	R	6	5	63	3	27	3.93
Posterior cingulate	L	30	21	−3	−54	6	3.71
Cingulate gyrus	L	31	286	0	−45	30	4.54
Postcentral parietal gyrus	R	40	27	60	−24	15	3.77
	L	40	37	−54	−27	18	3.91
	L	5	14	−21	−42	63	4.1
	R	3	10	36	−36	60	4.14
Superior temporal gyrus	L	3	5	−45	−21	39	3.64
	R	3	7	54	−12	48	3.46
	L	22	151	−42	−54	15	4.58
	L	13	38	−54	−42	21	3.99
Middle temporal gyrus	L	22	9	−45	−3	−3	3.42
	R	39	5	54	−69	9	3.46
	R	22	9	57	−48	3	3.45
	L	37	17	−54	−63	0	4.03
Hippocampal formation	R	21	7	66	−39	−3	3.45
	L		69	−24	−21	−21	4.22
Parahippocampal gyrus	R		12	30	−21	−21	3.58
	L	19	39	−15	−51	−15	4.44
Lingual gyrus	R	19	7	15	−60	−15	3.63
Insula	L	13	20	−45	−6	12	4.43
Lentiform nucleus	R		11	18	−3	12	4.72

Imaging data

Remember versus high confidence recognition responses

Various regions exhibited greater event-related responses to remember than to high confidence recognition judgments (i.e., “4” responses), whereas no regions exhibited the opposite pattern (i.e., greater response for confident recognition than recollection). The maxima of all voxel clusters showing differential event-related responses to remember versus high confidence recognition judgments are presented in Table 2, and the most notable regions demonstrating these effects are illustrated in Figure 1. In general, the most robust effects were observed in the left hemisphere, which likely reflects the use of verbal materials, although in most cases, similar but weaker activity was observed in the right hemisphere.

Recollection-related activity was observed in the medial and lateral cortex. On the medial surface, recollection-related activity was observed in the anterior medial frontal cortex [Brodmann’s area (BA) 10/32] and in a separate region within the posterior cingulate (BA 31/30) (Fig. 1*a*). On the lateral surface, recollection-related activity was observed throughout the lateral parietal/temporal cortex (BA 40/39/22/21), including the central parietal gyrus, the posterior portion of the superior temporal gyrus, and the middle temporal gyrus (Fig. 1*c*). Recollection-related activity was also observed within

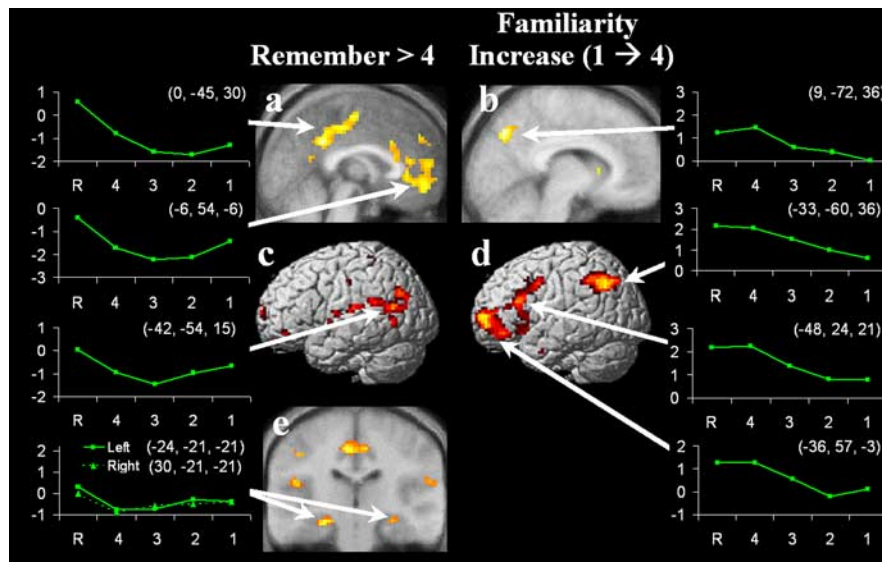


Figure 1. Regions showing greater activity for remember than for high confidence familiarity judgments (*a, c, e*) and those showing increasing activity related to increases in familiarity confidence (1→4 judgments) (*b, d*). Activities on the cross sections are rendered onto the normalized T1 anatomical images averaged across volunteers; those on the lateral surface are rendered onto the MNI normalized canonical brain (Cocosco et al., 1997). All activated clusters exceeded an uncorrected threshold of $p < 0.001$ and were at least five voxels in size. Parameter estimates at the maximum peak of each region (MNI coordinates as indicated) are plotted for each of the five possible response categories.

the medial temporal lobe, including the hippocampus bilaterally (Fig. 1*e*), and in a separate region in the left posterior parahippocampal cortex (data not shown).

The activity profiles for each of the recollection regions are presented in the leftmost panels of Figure 1. Figure 1 indicates that these regions responded more to the remembered than to the high confidence familiarity responses and that, with the exception of the hippocampus (discussed below), the regions did not consistently increase or decrease with familiarity confidence. However, an examination of the activity profiles for the regions identified with recollection suggests that in some cases, the items confidently identified as new (i.e., “1” judgments) elicited slightly higher levels of activity than the less-confident responses (i.e., “2” judgments). Although this may reflect noise (i.e., none of these differences were statistically significant), its consistency is noteworthy and suggests either that these regions are somewhat sensitive to extremely low levels of familiarity or that recollection may play a limited role in confidently rejected items (Rotello and Heit, 2000).

Recognition confidence

Various regions were correlated with recognition confidence. Some areas increased their activity with confidence, whereas others demonstrated activity decreases (Table 3). As with the contrast identifying recollection-related activity, the most robust effects were observed in the left hemisphere, although in most cases similar, but weaker, activity was observed in the right hemisphere.

Regions in which response magnitude correlated positively with increasing recognition confidence included the medial parietal cortex (precuneus; BA 7) (Fig. 1*b*); the left anterior prefrontal cortex (BA 10), including the middle frontal gyrus; the left posterior prefrontal cortex (BA 45/47), including the inferior and middle frontal gyri; and the lateral parietal cortex (BA 39/40/7) (Fig. 1*d*). An examination of the activity profiles for each of these regions (Fig. 1, rightmost panels) shows that activity increased

gradually from confident new responses (i.e., 1) to confident old responses (i.e., 4), indicating that the identification of these regions in the regression analysis was not attributable to any one single outlying response category.

An examination of Figure 1 suggests that the regions related to increasing strength of familiarity were distinct from those related to recollection. To formally assess the extent of overlap, we inclusively masked the recollection-related activity (defined by $R > 4$) with those regions in which activity increased along with increasing familiarity, using a liberal $p < 0.01$ threshold for the familiarity mask. We found no overlap between the primary contrast and the mask. Similarly, we inclusively masked the familiarity-related activity with those regions associated with recollection, again using a liberal $p < 0.01$ threshold for the mask. In this case, there was only one small region (five voxels) of overlap in the left parietal cortex ($-33, -69, 36$; $Z = 3.87$). Thus, the voxels sensitive to recollection and to increasing levels of familiarity, which were identified in two independent contrasts, were almost completely nonoverlapping.

Several regions exhibited decreases in activity with increasing recognition confidence (i.e., lowest activity for the most confidently recognized items). The most notable of these regions was the same region of the hippocampus that was found to demonstrate recollection-related activity. The bottom left panel of Figure 1 presents the estimates of response magnitude for remember judgments and for each category of confidence judgment separately for the left and right hippocampus. Figure 1 shows a bilateral trend for activity to decline with increasing confidence that an item was old but to demonstrate a marked increase in activity for items endorsed as recollected.

Because previous studies have reported a region in the anterior parahippocampal gyrus (in the vicinity of the perirhinal cortex) that exhibited decreases in activity possibly related to familiarity (cf. Henson et al., 2003), we also examined this region in more detail. However, no such effects were apparent, even when the statistical threshold was lowered to $p < 0.01$.

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Discussion

In a test of recognition memory, brain regions associated with recollection were identified by contrasting the activity elicited by items endorsed as remembered to those elicited by items attracting high confidence familiarity responses. In contrast, regions associated with familiarity were identified as those for which activity correlated with recognition confidence for nonrecollected items. The results revealed that recollection and familiarity engaged distinct sets of brain regions. Recollection was associated with a network of regions, including the anterior medial prefrontal cortex, lateral parietal cortex, posterior cingulate, and hippocampus. In contrast, familiarity was related to a different set of regions, including the lateral prefrontal cortex, superior lateral parietal cortex, and precuneus. Crucially, the regions associated with recollection were almost completely distinct from those that responded to increases in familiarity confidence. In fact, the cor-

Table 3. Brain regions showing significant BOLD signal correlations ($p < 0.001$) with familiarity confidence

Region of activity	Left/right	BA	Number of voxels	MNI coordinates			Z value
				x	y	z	
Increasing with familiarity (1→4)							
Anterior middle frontal gyrus	L	10	129	−36	57	−3	4.3
Inferior/middle frontal gyrus	L	45	110	−48	24	21	4.58
Medial frontal gyrus	L	6	21	−6	30	42	3.75
Angular gyrus	L	39	200	−33	−60	36	4.54
Inferior parietal lobule	R	40	20	39	−51	36	3.85
Superior parietal lobule	R	7	10	36	−66	48	3.59
Precuneus	R	7	190	9	−72	36	6.85
Cingulate gyrus	L	23	22	−6	−24	24	4.38
Insula	L	13	10	−33	15	−6	3.69
Caudate	R		6	9	15	3	3.5
Lentiform nucleus	R		8	21	15	6	3.4
Decreasing with familiarity (4→1)							
Middle frontal gyrus	R	8	6	27	9	39	3.91
Medial frontal gyrus	R	11	5	6	51	−12	3.3
Anterior cingulate	R	32	5	3	30	−9	3.46
Cingulate gyrus	R	24	15	6	0	39	3.88
Cuneus	L	18	8	−9	−96	6	3.31
Inferior temporal gyrus	L	37	7	−48	−69	0	3.47
Hippocampal formation	L		9	−18	−18	−21	3.77
Insula	L	13	12	−45	−27	18	3.65
Cerebellum	L		18	30	−51	−30	3.82

tical regions related to these two types of recognition judgments were almost completely nonoverlapping.

Consistent with many previous recognition studies, we found that prefrontal, parietal, and medial temporal cortices were involved in recognition memory. However, the current results indicated that within these general brain regions, distinct subregions were functionally specialized for recollection or familiarity. For example, one of the more surprising results of the current study was that the left lateral prefrontal cortex (including anterior and posterior regions) was related to familiarity confidence, whereas the anterior medial prefrontal cortex was related to recollection. This is a striking finding in light of previous suggestions that the left lateral prefrontal cortex might be particularly important for recollection (for review, see Nolde et al., 1998; Rugg and Henson, 2002; Yonelinas, 2002). Although previous studies have observed greater activity in the left lateral prefrontal cortex for remembered than for nonremembered items (Henson et al., 1999; Eldridge et al., 2000), the current results indicate that such findings arose not because of recollection per se but because this region responds to increases in familiarity confidence.

Two functionally distinct lateral parietal regions were also identified in the current study: an inferior region related to recollection and a more superior region related to familiarity confidence. The finding that there were two functionally distinct memory regions in the lateral parietal cortex is consistent with two recent recognition studies. First, Herron et al. (2004) showed that the inferior lateral parietal cortex was sensitive to recognition success (old vs new status), whereas a more superior region was sensitive to the ratio between old and new items in the test list, rather than just whether the item was old or new. Similarly, Wheeler and Buckner (2004) found a lateral parietal region related specifically to remember responses, whereas a slightly more superior region responded to both remember and know responses.

The medial parietal cortex also contained two functionally distinct regions of activity: an inferior region responding to recollection (i.e., the posterior cingulate) and a more superior region responding to familiarity confidence (i.e., the precuneus). Poste-

rior cingulate activity relating selectively to recollection has now been reported in several studies (Henson et al., 1999; Eldridge et al., 2000; Wheeler and Buckner, 2004). Precuneus activity appears less consistently, but Henson et al. (1999) reported a region close to that observed in the current study that was more active for know than for remember responses.

Within the medial temporal lobe, there was no evidence for functionally distinct subregions. Consistent with several previous imaging studies, recollection was associated with increases in activity in the hippocampus and posterior parahippocampal gyrus (Eldridge et al., 2000; Cansino et al., 2002; Wheeler and Buckner, 2004). However, in contrast to other studies (Henson et al., 2003) [for similar findings during memory encoding, see Davachi et al. (2003) and Ranganath et al. (2004)], we did not find any region in the vicinity of the perirhinal cortex that responded to decreases in familiarity. This may reflect a type II error, perhaps because of the vulnerability of this region to magnetic susceptibility artifact. Importantly, however, in the current study the hippocampus showed no evidence of an increase in activity with increasing familiarity (in fact, it showed a significant trend in the reverse direction), indicating that its sensitivity to recollection is not simply an exaggeration of a sensitivity to familiarity strength or confidence. Although the inverse relationship between hippocampal activity and familiarity strength may suggest that this region plays a role in familiarity, a variety of other evidence argues against this possibility. For example, the observed pattern of results is consistent with several previous neuroimaging studies that have indicated that the hippocampus is involved in encoding and novelty detection, and thus tends to be more active for new items than for familiar items (Tulving et al., 1994; Rugg et al., 1997; Yonelinas et al., 2001; Stark and Okado, 2003). Moreover, a variety of human patient and animal lesion studies have indicated that the hippocampus is not necessary for familiarity-based recognition judgments (Eichenbaum et al., 1994; Aggleton and Brown, 1999; Yonelinas et al., 2002; Fortin et al., 2004) (but see Manns et al., 2003).

The current results demonstrate the importance of treating familiarity as a continuous rather than a dichotomous variable in

neuroimaging studies of recognition. These results are consistent with behavioral results that show that although recollection tends to be associated with the highest confidence recognition responses, only a subset of familiarity-based responses are associated with this high level of recognition confidence (Yonelinas, 2001). Based on the current experiment, however, we cannot rule out the possibility that the remembered items were associated with higher recognition confidence than high confidence familiarity-based responses, because we did not measure the confidence of the recollected items. Indeed, the remember responses were made ~300 ms faster than the high confidence familiarity responses, as might be expected if the remember responses were more confident. On the basis of these findings, one might argue for a type of strength account in which both recollection and familiarity regions respond positively to increases in memory strength (indexed here by level of confidence that an item was studied), but the recollection regions are only sensitive to very high levels of strength, whereas the familiarity regions are only responsive to lower levels of strength. However, regions such as the hippocampus did not exhibit a monotonic increase in activity with increasing memory confidence, but rather exhibited a U-shaped function, such that activity that was greater for R than for “4” responses but then reversed direction and began to increase as recognition confidence decreased. Trends of the same type were seen in several other recollection-sensitive regions (Fig. 1). Thus, the strength explanation cannot account for these results without recourse to additional *post hoc* assumptions.

In sum, the current study identifies two distinct memory-retrieval networks, each including anterior and posterior brain regions. As of yet, one can only speculate about the mnemonic functions supported by each of these regions. Within the recollection network, we suggest that the hippocampus plays a critical role in retrieving associations between the target item and aspects of the initial encoding event. We propose that the lateral parietal region and the posterior parahippocampal region reflect orientation to, or processing of, the content of such retrieved associations. For example, these regions may be involved in processing spatial-temporal context (Aguirre et al., 1996; Epstein and Kanwisher, 1998) or the specific perceptual, phonological, or semantic processes (Jonides et al., 1998; Ravizza et al., 2004) that were engaged when the item was originally studied. Although the anterior medial frontal and posterior cingulate cortices may also be involved in representing the content of recollection, we suggest that they may be better characterized as signaling that recollective information has been retrieved (thereby initiating further frontally mediated assessment; see below) or in some preliminary monitoring and evaluating of the recollected information.

The regions identified in the familiarity network (i.e., the lateral prefrontal cortex, superior lateral parietal cortex, and precuneus) could reflect functions specific to familiarity. However, we propose that they are more likely to be involved in a general executive control system that is involved in both familiarity and recollection. Support for the claim that these regions are not specific to familiarity derives from the following observations: (1) these regions were as active for remembered as for highly familiar items, (2) the lateral prefrontal cortex and superior lateral parietal cortex can reverse their activity (i.e., new→old) when new items are rarer than old items (Herron et al., 2004), and (3) similar prefrontal and parietal regions have been implicated in a variety of attention and working memory tasks (Jonides et al., 1998; Wojciulik and Kanwisher, 1999; Duncan and Owen, 2000). Thus, these regions may play a postretrieval monitoring role for both recollection and familiarity. They may also play a role in the

initiation or focusing of memory-retrieval processes by interacting with regions within the temporal lobe to directly support the computation of familiarity or recollection signals.

To conclude, the present study reveals that the neural correlates of recollection are markedly different from those related to familiarity confidence and highlights the importance of assessing variations in familiarity confidence when examining recognition memory. These findings offer no support for the proposal that recollection-based recognition merely reflects higher levels of memory strength or confidence than those typical of familiarity-driven recognition. Instead, the results add to the evidence that recollection and familiarity are supported by qualitatively distinct cognitive and neural processes.

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