

Content-specificity of the neural correlates of recollection

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Abstract

It is widely assumed that episodic retrieval (recollection) involves reinstatement of cortical activity engaged during the processing of an episode when it was initially experienced. It follows from this assumption that the cortical correlates of recollection should differ with the content of what is recollected, and that retrieval of different content should be associated with activity in functionally distinct cortical regions. The present experiment investigated these predictions. Subjects ($N = 17$) studied a mixed list of words and pictures and were then presented with a test list comprised of words only. Test items were studied words, the names of studied pictures, and unstudied (new) words. Functional magnetic resonance images were acquired while the subjects made Remember/Know/New judgments to these test words. Independent of study material, studied items endorsed as Remembered elicited greater activity than correctly classified unstudied items in several regions, including left frontal, left lateral parietal, and posterior cingulate cortex. In addition, Remembered items elicited greater activity in the right hippocampus and parahippocampal gyrus than items accorded Know judgments, replicating previous findings. Analysis of content-specific effects demonstrated a regional double-dissociation within left fusiform cortex; recollected words elicited greater activity than recollected pictures in lateral fusiform, whereas the reverse effect was evident in an anterior fusiform region. The lateral and anterior fusiform areas correspond closely to areas held to be functionally specialized for the processing of visual words and pictures, respectively. Thus, the current findings support the cortical reinstatement hypothesis of episodic retrieval.

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1. Introduction

It is widely assumed that retrieval of an episodic memory (henceforth, ‘recollection’) involves reinstatement of cortical activity elicited when the episode was originally experienced (the ‘consensus view’ of episodic retrieval according to Rubin & Greenberg, 1998). For example, in the model of Norman and O’Reilly (2003) (see for similar proposals Alvarez & Squire, 1994; Rolls, 2000; Shastri, 2002; Wallenstein, Eichenbaum, & Hasselmo, 1998) recollection of a recently encoded episode occurs when a retrieval cue activates a hippocampally stored representation of the pattern of cortical activity that encoded the episode. Through reciprocal hippocampo-cortical connections, activation of this represen-

tation causes reinstatement of the pattern in the cortex, allowing access to encoded aspects of the episode. To the extent this and similar proposals are correct, it follows that cortical activity associated with successful recollection should be at least partially content-dependent; for example, retrieval of auditory versus visual memories should be associated with distinct, modality-dependent patterns of cortical activity. One way to assess this prediction is with functional neuroimaging, which permits the neural activity associated with the retrieval of memories that differ in content to be contrasted.

In light of the popularity of what might be termed the ‘reinstatement hypothesis’, it is perhaps surprising that only a relatively small number of neuroimaging studies have directly assessed whether, as predicted by the hypothesis, the neural correlates of recollection are content-sensitive. Four studies addressing this question employed blocked experimental designs. Nyberg, Habib, McIntosh, and Tulving

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(2000) used PET to demonstrate greater activity in what was referred to as ‘auditory-responsive cortex’ for recognition of words that had been paired at study with sounds, relative to recognition of words presented alone. Persson and Nyberg (2000) reported that encoding and retrieval of spatial information activated overlapping regions of bilateral parietal cortex. Nyberg et al. (2001) reported analogous effects in motor and somatosensory regions for retrieval of action instructions that had been associated at study with overt versus covert movement. And Vaidya, Zhao, Desmond, and Gabrieli (2002), employing fMRI, used visually presented test words to cue retrieval of pictures versus words and found greater activity in extrastriate visual cortex when pictures were retrieved. The findings from each of these studies are consistent with the proposal that retrieval-related neural activity has a content-specific component, but the limitations of blocked designs leave them open to alternative interpretations. For example, it is not possible to rule out the possibility that the findings reflect ‘set’- or ‘state’-related effects, rather than differences in the activity associated specifically with successful recollection (Rugg, 1998).

Other fMRI studies have employed event-related, randomized designs and investigated activity elicited specifically by test items giving rise to successful retrieval. Wheeler, Petersen, and Buckner (2000) (see also Wheeler & Buckner, 2003) had subjects study words in association with either a pictorial or an auditory referent. The test task required a judgment whether words had been paired at study with a picture or a sound. Relative to correctly recognized words that had been paired with pictures, those paired with sounds elicited greater activity in auditory association cortex, whereas the reverse contrast yielded greater activity in fusiform and occipito-parietal cortex. The findings demonstrate that retrieval of pictorial versus auditory information can be associated with elevated activity in different, modality-specific, cortical areas. The employment of multiple study exposures over a protracted period makes the relevance of these results to episodic memory (that is, memory for unique events) uncertain, however. A related criticism can be leveled at another recent study in which objects were paired at study with different odors (Gottfried, Smith, Rugg, & Dolan, 2004). At test, relative to new items, correctly recognized old objects elicited enhanced activity in primary olfactory (piriform) cortex. The authors interpreted this finding as evidence for reinstatement of the olfactory component of the test items’ encoding episode, that is, as support for the proposal that recollection is associated with cortical reinstatement. An alternative possibility, however, is that the effect reflects a non-episodic form of associative learning.

Two recent event-related fMRI studies employed test procedures allowing recognized items to be segregated according to whether they were recollected rather than judged old solely on the basis of a sense of familiarity (Kahn, Davachi, & Wagner, 2004; Wheeler & Buckner, 2004). It has been argued that familiarity-driven recognition is qualitatively distinct from recollection in that it does not depend on the hippocam-

pus (e.g. Brown & Aggleton, 2001, but see for an opposing view Squire, Stark, & Clark, 2004) and, presumably, therefore does not depend upon hippocampally mediated cortical reinstatement. Thus, the finding that cortical reinstatement effects are associated specifically with recollection would rule out the possibility that the effects are correlates of a non-episodic form of memory such as familiarity or implicit associative learning. This in turn would offer strong support for the reinstatement hypothesis of episodic retrieval.

In the study of Wheeler and Buckner (2004), subjects studied a series of concrete words, most of which were paired with a picture denoting the same object. At test, subjects made ‘Remember/Know/New’ judgments (Tulving, 1985) to a mixture of studied and unstudied words. Relative to both new items and old items recognized on the basis of familiarity (‘Know’ judgments), recollected words (those endorsed as ‘Remembered’) elicited greater activity in a left anterior fusiform region. This region overlapped with an area of fusiform cortex that had been demonstrated previously to be selectively activated by pictures (Maccota & Buckner, 2002). Kahn et al. (2004) required subjects to study words in the context of two intermixed encoding tasks that required either visual imagery or phonological processing. The authors operationalized recollection-related activity in the contrast between items that were recognized and assigned to their correct encoding context (imagery versus phonology) relative to items that were correctly recognized but assigned to the incorrect context. Recollected items from the imagery task elicited relatively greater activity in a posterior parahippocampal region, whereas recollection of items that had been encoded phonologically was associated with elevated activity in a frontal premotor region. These two regions overlapped with sites that demonstrated differential activation across the two encoding tasks.

The findings from these two studies suggest that successful recollection of different classes of information is associated with activity in cortical regions that play a selective role in the online processing of the same information. Whereas the findings of Wheeler and Buckner (2004) can be questioned on the grounds that they constitute only a single dissociation (leaving open the possibility that recollection of non-pictorial memories might have activated the same fusiform region), this criticism does not apply to the findings of Kahn et al. (2004). The double-dissociation demonstrated in that study constitutes what is arguably the strongest single finding to date in support of the proposal that the neural correlates of recollection have a content-specific component.

The aim of the present study was to build on the findings of Wheeler and Buckner (2004) by demonstrating a double-dissociation between activity associated with recollection of two classes of study material whose online processing is associated with selective activity in two distinct regions of fusiform cortex. In showing that material-specific recollection is associated with activation of regions known to be selectively active during online processing of the same material, this finding would add strong support to the cortical reinstatement

ment hypothesis of episodic retrieval. To accomplish this aim, we employed a study list comprising a mixture of pictures and words, and subsequently tested recognition memory for these items using the Remember/Know/New procedure. Test items were words only, and the ‘old’ items corresponding to studied words and studied pictures were randomly intermixed. Thus, subjects were unable to predict whether a particular test item would elicit recollection of a word or a picture, ruling out the possibility of a confounding of recollection effects with effects due to material-dependent differences in cue processing or task set (cf. Robb & Rugg, 2002). We predicted that relative to recollection of words, picture recollection should be associated with enhanced activity in the same anterior fusiform region that was identified by Wheeler and Buckner (2004). We further predicted that word recollection would activate the left lateral fusiform region referred to as the ‘visual word form area’ (McCandliss, Cohen, & Dehaene, 2003), a region that has been demonstrated in numerous studies to show selective activation for visual words and which should, therefore, be active during retrieval of episodic memories of these items.

2. Methods

2.1. Subjects

Seventeen right-handed subjects participated in the experiment (five males; age range, 18–30 years). They were recruited from the University of California, Irvine (UCI), community and were compensated for their time. All subjects gave informed consent prior to participation in the study, which was approved by the UCI Institutional Review Board.

2.2. Materials

Critical items were drawn from a pool of 150 pairs of color pictures of objects and their corresponding names (3–13 letters long; mean length = 5.5; mean written frequency = 21.9 counts per million; Kucera & Francis, 1967). The study lists comprised 50 names and 50 pictures (none of which corresponded to the name items). The associated test lists were comprised of names only. Fifty of these were studied names (*old words*), 50 corresponded to the studied pictures (*old pictures*), and 50 were unstudied (*new words*). Items (i.e. pictures or their names) were rotated across conditions to form three study-test sets. Thus, across every three subjects, each item appeared once in each condition. The beginning and end of each study list were buffered with two additional filler items (one picture and one name). The ordering of study items (pictures versus words) and test items (old words, old pictures, and new words) was randomly determined for each subject. A separate pool of 30 item pairs was employed to construct practice study and test lists.

Items were displayed with VisuaStim (Northridge, CA, USA) XGA MRI compatible headmounted display goggles

with a field of view of 30° visual angle and a resolution of 640 pixels × 480 pixels. Study items were displayed at the center of the visual field against a gray frame that subtended 9° × 9° visual angle. The maximum visual angle subtended by a picture was 6° × 6.5°. Words were presented in black upper case Helvetica font. The maximum visual angle subtended by any word was 8° × 1.5°. During the test phase, words were presented at the same size and in the same font as at study, but in white letters against a uniform black background.

2.3. Procedure

Instructions and practice were given outside the scanner. For the study phase, subjects were instructed to signal via a button-press whether each picture or a name denoted a living or a non-living thing. For the test task, the requirement was to signal via a button-press whether a test item corresponded to a name or picture that was recollected from the study phase (*Remember*), whether the item was familiar but unrecollected (*Know*), or whether it had not appeared at study (*New*). The Remember/Know distinction was explained using standard instructions (e.g. Rajaram, 1993) supplemented by examples. To ensure the distinction was comprehended, upon completion of the practice test list, each subject was re-presented with an item for which they had made a Remember response and one for which they had made a Know response and asked to describe the basis for the responses. Speed and accuracy of responding were given equal emphasis in the test task instructions.

Prior to the experiment proper each subject was positioned in the scanner and a structural scan was obtained. The study list was then presented, during which no scanning took place. The test task, during which fMRI data were obtained, followed approximately 5 min after the end of the study task. Study items were presented for 1500 ms. Presentation was self-paced, each item appearing 500 ms after the response to its predecessor. A central fixation cross was present during the inter-item intervals. Animacy decisions were signaled via button presses with the index and middle fingers of the right hand. Test items were presented for 500 ms with a stimulus onset asynchrony (excluding null trials, see below) of 3400 ms. A central fixation cross was continuously present during the inter-item interval. A series of 50 ‘null’ trials, during which the fixation cross remained on the screen instead of an item appearing and no response was required, was randomly interspersed within the list to permit efficient estimation of event-related responses with respect to baseline (Josephs & Henson, 1999). Responses were signaled by depressing a button with the index (Remember), middle (Know), or ring finger (New) of the right hand.

2.4. fMRI scanning parameters

A 1.5 T Philips Eclipse MR (Philips Medical Systems, Bothell, WA, USA) scanner was used to acquire 32 T2*-

weighted gradient-echo echo planar images (64×92 matrix, $2.6 \text{ mm} \times 3.9 \text{ mm}$ pixels, $\text{TE} = 37 \text{ ms}$) per volume with blood oxygenation level dependent (BOLD) contrast. EPIs comprised 3 mm-thick axial slices with a 1 mm interslice gap, acquired in a descending interleaved order. Scanning involved one session of 251 volumes with a repetition time (TR) of 2800 ms. The first five volumes were discarded to allow equilibration to occur. A T1-weighted structural scan (256×256 matrix, 1 mm^3 voxels) was also obtained for each subject.

2.5. Data analysis

Analyses were performed with Statistical Parametric Mapping (SPM2; Wellcome Department of Cognitive Neurology, London, UK, www.fil.ion.ucl.ac.uk) implemented in MATLAB 6 (The Mathworks Inc., USA). All volumes were spatially realigned to the first volume, and timecourses were temporally realigned to the middle slice in time. Resulting volumes were normalized to a standard EPI template based on the MNI reference brain in Talairach space and resampled to 2 mm^3 voxels. Normalized images were smoothed with an 8 mm FWHM Gaussian kernel. The timeseries in each voxel were highpass-filtered to 1/128 Hz to remove low-frequency noise and scaled within-session to a grand mean of 100 across both voxels and scans.

Statistical analysis was performed in two stages of a mixed effects model. In the first stage, neural activity was modeled by a delta function (impulse event) at stimulus onset. The ensuing BOLD response was modeled by convolving these neural functions with two hemodynamic response functions (HRFs). One function (the ‘early’ function) was a ‘canonical’ HRF (Friston et al., 1998). A second (late) function was modeled by the canonical HRF shifted one TR (2.8 s) later in time, and was included to capture possible delayed responses. The convolution was performed in high-resolution time space, and downsampled at the midpoint of each scan to form covariates in a General Linear Model (GLM). The covariates for the late function were orthogonalized with respect to those for the early function, thereby attributing any shared variance to the ‘early’ response. Unlike in some previous studies (e.g. Rugg, Henson, & Robb, 2003), results from the late HRF did not add to those from the early HRF in a theoretically meaningful way, and are not reported.

Nine event-types were defined, consisting of Remember, Know, and miss responses for pictures and words as well as Remember false alarms, Know false alarms, and correct rejection (new) responses. Additionally, six covariates capturing residual movement-related artifacts (the three rigid-body translations and three rotations determined from the realignment stage), and a single covariate representing the mean (constant) over scans were included. Parameter estimates were estimated for events of interest using a General Linear Model. Non-sphericity of the error covariance was accommodated by an AR(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 (ReML).

Second-stage analyses utilized linear contrasts of the parameter estimates for each subject, treating subjects as a random effect. Parameters estimates were submitted to one-sample *t*-tests across subjects for each contrast of interest. This was done separately for early and late HRFs. Contrasts showing significant effects at a threshold of $p < 0.001$, uncorrected for multiple comparisons, and extending over a minimum of five voxels were localized on the across-subject mean normalized MRIs. Stereotactic coordinates are reported in Talairach space and correspond to the standard MNI brain (Cocosco, Kollokian, Kwan, & Evans, 1997). These coordinates bear an approximate match to the atlas of Talairach and Tournoux (1988).

3. Results

3.1. Behavioral performance

Behavioral performance for all 17 subjects is summarized in Table 1. Overall recognition accuracy (proportion of old items endorsed as either Remembered or Known) did not differ significantly according to type of study material (0.79 versus 0.77 for words and pictures, respectively). As is evident from the table, there was a strong tendency to endorse recognized items as ‘Remembered’ regardless of whether they had been studied as words or as pictures. Neither the proportion of Remember responses nor the latency to make such responses differed according to material ($t_{16} = 1.6$ and $t_{16} \leq 1$, respectively). Due to the low rate of Know responding (seven subjects endorsed fewer than 10% of old items as Known), a formal analysis of these responses was not conducted.

3.2. fMRI data

fMRI analysis was directed toward identifying voxels where (i) activity elicited by recollected items exceeded that for new items regardless of study material, and (ii) recollection-related activity differed in a material-dependent fashion. To accomplish the first goal, the contrast between recollected items (regardless of material) versus correctly rejected new items, thresholded at $p < 0.001$, was exclusively masked by the (non-directional) *F* contrast between the two classes of recollected item (recollected pictures versus recollected words thresholded at $p < 0.05$; note that the more liberal the mask threshold, the more conservative is the masking procedure). This procedure identified voxels where recollected items elicited greater activity than correct rejections, but where the recollection effects did not differ (at the chosen mask threshold) in magnitude according to study material.

Material-specific recollection effects were identified by contrasts between the two classes of recollected item. For the purposes of assessing the directional hypotheses in respect

Table 1

Percent accuracy and RT (ms) by condition and item type; FA, false alarm

Words			Pictures			New		
Remember	Know	Miss	Remember	Know	Miss	Remember FA	Know FA	Correct rejection
55.9	22.6	21.5	62.5	14.1	23.4	6.7	14.7	78.6
1357	1845	1754	1366	1867	1773	1204	2000	1629

of the two regions of the fusiform cortex predicted a priori to demonstrate material-specific effects, voxels were thresholded at $p < 0.001$, with a cluster extent of >4 contiguous voxels. The significance of activated voxels within an 8 mm radius of the expected loci of the two effects was evaluated using correction for multiple comparisons within a small volume (Worsley et al., 1996; 8 mm is approximately 1.5 S.D.s around the mean co-ordinates of the word-sensitive lateral fusiform region ('visual word form area') as defined by Cohen et al., 2002). The coordinates for this region were -42 , -57 , and -15 . The coordinates for the picture-sensitive anterior fusiform region, -25 , -37 , and -26 , were obtained from Wheeler and Buckner (2004); Wheeler and Buckner originally reported their findings with respect to the atlas of Talairach and Tournoux (1988). They are reported here in MNI co-ordinates using the non-linear conversion routine authored by M. Brett (available at www.mrc-cbu.cam.ac.uk/imaging/common/mnispace.shtml). Since other material-specific effects were unpredicted, they were thresholded in each directional contrast at $p < 0.0005$ so as to give a two-sided uncorrected threshold of $p < 0.001$, again with a cluster extent >4 .

One subject gave only six Remember responses to studied words, too few to permit reliable estimate of the associated fMRI response. For this reason, the principal fMRI analyses described below are based on data from the other 16 subjects.

3.3. fMRI effects common to word and picture retrieval

Regions where recollected items elicited greater activity than new items independent of study material are illustrated in Fig. 1, and listed in Table 2. The regions included several that have been consistently identified in previous event-related fMRI studies of the neural correlates of successful retrieval (Rugg & Henson, 2002), notably posterior cingulate, and medial and lateral parietal cortex. One region absent from Fig. 1

and Table 2 is left anterior prefrontal cortex, despite the fact that this region has also been consistently identified in previous studies. Lowering the threshold of the present analysis to $p < 0.005$ revealed an extensive effect in this region (114 voxels) with a peak that closely corresponded to the loci of previously described effects (-36 , 58 , and 6 ; cf. -31 , 51 , and 8 in Konishi, Wheeler, Donaldson, & Buckner, 2000).

A second region absent from Table 2 is the medial temporal lobe. The hippocampus and adjacent cortex have been reported to demonstrate recollection-related activity in two prior studies employing the Remember/Know procedure (Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Wheeler & Buckner, 2004). The failure to identify enhanced medial temporal activity in the present case may be a consequence of the employment of new items as the 'baseline'. New items elicit significant encoding-related activity in the medial temporal lobe, and this may have been sufficient to mask activity associated with successful recollection (Stark & Okado, 2003). In light of this possibility, a contrast was performed between recognized items endorsed as Remembered versus those endorsed as Known. Under the criterion of at least 10 trials to estimate activity associated with Know responses, 13 subjects contributed data to this contrast when trials were collapsed across study material. The contrast identified greater activity for Remember relative to Know items in the right posterior hippocampus and adjacent parahippocampal cortex (peak voxel: 32 , -36 , and -10 ; $Z = 4.30$; see Fig. 2). As would be expected from the data presented in Fig. 2, in both the hippocampus and parahippocampal gyrus, the new item activity was significantly greater than the activity elicited by old items assigned Know judgments ($t_{12} = 2.52$, $p < 0.05$, and $t_{12} = 2.95$, $p < 0.025$, respectively). At a reduced threshold enhanced activity for Remember versus Know responses was also observed in a more anterior right hippocampal region (peak voxel: 30 , -16 , and -18 ; $Z = 2.93$, $p < 0.002$).

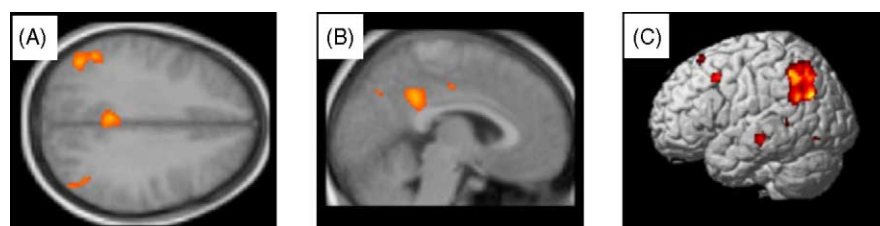


Fig. 1. Regions where activity elicited by recollected items exceeded activity elicited by new words independently of study material. (A) Axial section ($z = 32$) of normalized T1-weighted structural MRIs averaged across subjects. (B) Sagittal section of same images ($x = -4$). (C) Surface rendering of recollection effects on the left hemisphere of a canonical brain. In each case, the statistical threshold is $p < 0.001$, uncorrected for multiple comparisons.

Table 2
Peak loci of old/new effects common to remembering words and pictures

<i>x, y, z</i>	<i>Z</i>	No. of voxels	Region	Approximate Brodmann area
–12, 26, 58	3.67	30	Left superior frontal gyrus	6
–44, 14, 42	3.93	65	Left middle frontal gyrus	9
–30, 14, 46	3.93	12	Left superior frontal sulcus	8
–2, –16, 42	3.55	32	Left cingulate gyrus	24
–60, –24, –10	4.13	69	Left superior temporal sulcus	21
–64, –46, 6	3.31	7	Left superior temporal gyrus	22
–50, –56, 26	5.90	950	Left inferior parietal	39/40
–4, –72, 38	3.47	11	Precuneus	7
–42, –74, –10	3.35	6	Left inferior occipital gyrus	19
10, –8, 0	3.45	8	Right thalamus	7
4, –26, 68	3.58	17	Medial frontal gyrus	
–4, –42, 32	4.29	318	Posterior cingulate gyrus	6
66, –6, –22	3.60	8	Right inferior temporal gyrus	31
58, –24, –16	4.11	65	Right middle temporal gyrus	21
52, –52, 44	3.85	128	Right inferior parietal	21

3.4. Material-specific fMRI effects

Regions defined a priori: As is illustrated in Fig. 3, activity associated with word recollection exceeded the activity elicited during picture recollection in lateral fusiform cortex (peak voxel: –36, –62, and –12; $Z = 3.43$; six suprathreshold voxels). The effect survived the small volume correction procedure described above ($p < 0.05$). As is also illustrated in Fig. 3, activity in this region elicited by recollected pictures and new items was of similar magnitude. Among the regions exhibiting relatively greater activity for recollected pictures was a cluster of 128 suprathreshold voxels in the left anterior fusiform area (peak: –24, –42, and –20; $Z = 4.06$), which is also illustrated in Fig. 3. This effect survived small volume correction ($p < 0.05$) with respect to the anterior fusiform area

identified by Wheeler and Buckner (2004). Fig. 3 shows that recollected words and new items elicited comparable levels of activity in this region.

The above analyses identified the two regions predicted to demonstrate a regional dissociation between word and picture recollection effects. To confirm this dissociation, peak parameter estimates of the magnitude of the activity elicited by recollected words and pictures were subjected to repeated measures ANOVA with factors of material (word versus picture) and region (lateral versus anterior fusiform). As would be expected in light of Fig. 3, the ANOVA revealed a highly significant interaction between these two factors ($F(1, 15) = 62.10$, $p < 0.0001$).

Whereas the foregoing analyses demonstrate a double dissociation in the recollection effects exhibited by the lateral

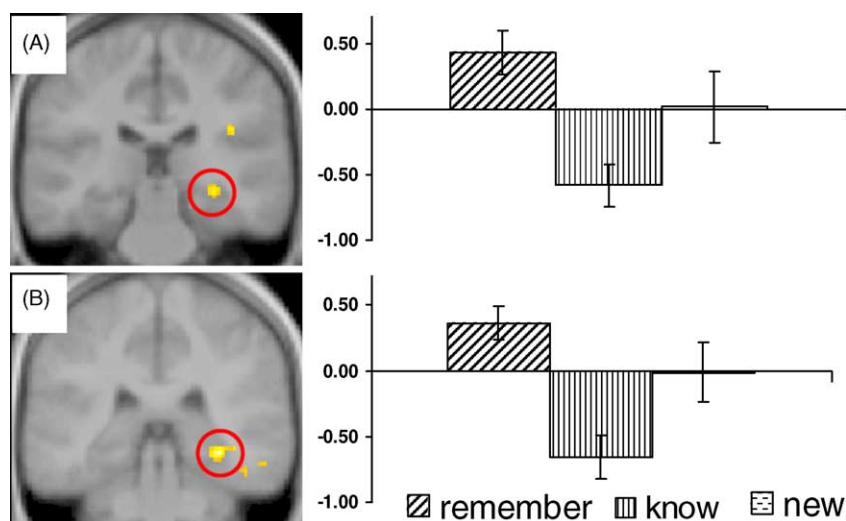


Fig. 2. Right hippocampal (A; $y = -30$) and parahippocampal regions (B; $y = -36$) where activity elicited by recollected items exceeded the activity elicited by old items receiving a 'know' judgment. Effects are thresholded at $p < 0.001$ uncorrected and superimposed on the across-subject mean of normalized T1-weighted structural MRIs. Adjacent histograms indicate mean (with standard error) parameter estimates ($N = 13$) from the two regions (hippocampus: 30, –30, and –9; parahippocampal gyrus: 32, –36, and –10) for activity elicited by recollected items, old items endorsed as 'known', and new items. The y-axis is in arbitrary units relative to baseline (i.e. residual activity after fit of the GLM).

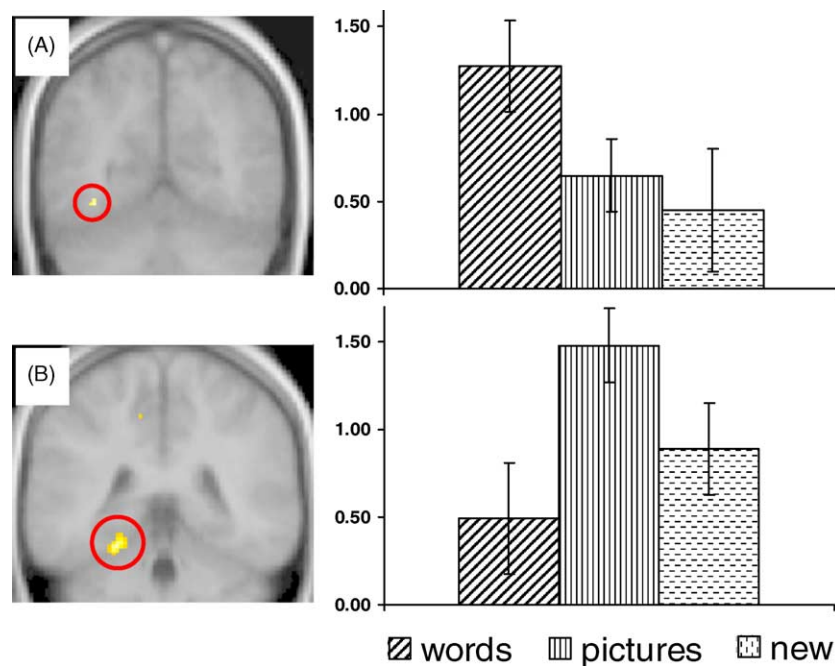


Fig. 3. (A) Lateral fusiform region ($y = -62$) where activity elicited by recollected words exceeded activity elicited by recollected pictures ($p < 0.001$, uncorrected). The adjacent histogram indicates the mean (with standard error) of the parameter estimates from the peak voxel for the activity elicited by these two classes of item, along with the estimate for the activity elicited by new items. The y-axis is in arbitrary units relative to baseline. (B) Anterior fusiform region ($y = -42$) where activity was greater for recollected pictures than recollected words. Adjacent histogram indicates the parameter estimates from the peak voxel for these items, along with the estimate for new item activity.

and anterior fusiform regions, they leave open the possibility that these effects are not selective for recollection, and might instead be exhibited by studied items regardless of whether they were recollected. There were too few Know responses to permit reliable material-specific estimates of the activity elicited by this class of trials. It was possible, however, to generate estimates of the activity elicited by the combination of Know and Miss trials according to material. Adopting the criterion that estimates of these responses should be based on 10 or more trials, data were available from 11 subjects for words and 10 subjects for pictures. The relevant parameter

estimates are illustrated in Fig. 4. Despite the lack of power in these contrasts, activity elicited by recollected items significantly exceeded the activity elicited by the other classes of old item ($t_{10} = 3.69$, $p < 0.005$, and $t_9 = 2.43$, $p < 0.05$, for words and pictures, respectively). These analyses indicate that the fusiform effects elicited by recollected items are not elicited by old items generally.

Other regions demonstrating dissociable recollection effects: Table 3 lists regions other than the fusiform where recollected items elicited material-specific effects. In light of its consistent association with retrieval success effects in simi-

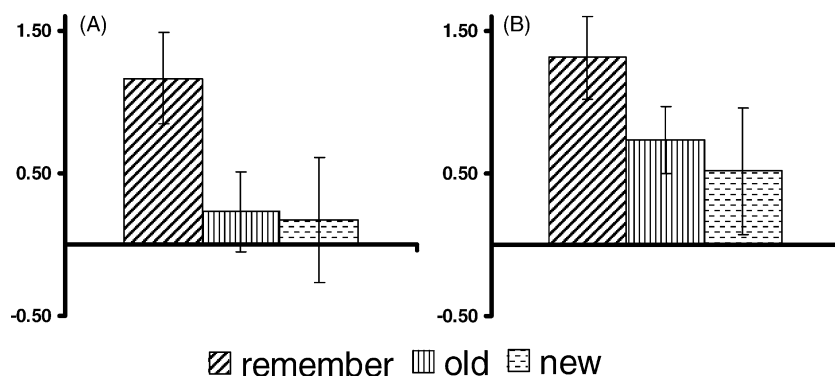


Fig. 4. (A) Histogram of mean ($N = 11$) parameter estimates (with standard error) from the peak voxel of the lateral fusiform region (-36 , -62 , and -12) for recollected words, along with estimates for 'old' (see text) and new items. The y-axis is in arbitrary units relative to baseline. (B) Mean parameter estimates ($N = 10$) from the peak voxel of the anterior fusiform region (-24 , -42 , and -20) for recollected pictures and for old and new test items.

Table 3
Peak loci of regions showing material-specific effects not predicted a priori

<i>x, y, z</i>	<i>Z</i>	No. of voxels	Region	Approximate Brodmann[area
Words > pictures				
−34, 22, 30	3.42	9	Left middle frontal gyrus	9
2, −68, 40	3.78	44	Precuneus	7
50, 24, 40	3.84	13	Right middle frontal gyrus	8
30, 20, −4	3.66	20	Right insula	47
Pictures > words				
−32, −14, 18	4.21	17	Left insula	13
−32, −34, −20	3.23	5	Left fusiform gyrus	20
−14, −66, 26	4.25	54	Left precuneus	31
−12, −72, −16	3.42	21	Left lingual gyrus	18
−4, −8, 50	3.58	35	Cingulate gyrus	24
−4, −2, −16	4.38	53	Hypothalamus	
42, 12, −24	3.69	32	Right superior temporal gyrus	38
10, −12, 20	4.43	38	Right thalamus	
30, −54, −34	3.94	24	Right cerebellum	
18, −62, 26	3.49	8	Right precuneus	31

lar previous studies (Rugg & Henson, 2002), the dissociation between two nearby regions of the precuneus (−13, −66, and 24 versus 2, −68, and 40) is of particular interest (Fig. 5).

4. Discussion

4.1. Behavioral performance

Neither the overall hit rate nor the proportion of items accorded ‘Remember’ judgments varied according to type of study material, and nor were there any differences in the response times associated with recollection of the two classes of material. These null findings likely reflect the opposing influences of the ‘picture superiority effect’, which would act to enhance memory for pictures relative to words, and transfer appropriate processing effects, which would act in the opposite direction (cf. Stenberg, Radeborg, & Hedman, 1995). Whatever the explanation, the findings indicate that the material-dependent differences in neural activity discussed below are unconfounded with performance factors.

4.2. Material-dependent recollection effects

Recollected words and pictures gave rise to a double dissociation in the activity they elicited in left mid-lateral and

left anterior fusiform cortex, respectively. These two cortical regions correspond closely to those identified as responding selectively to visual words and pictures in prior studies. The finding that recollection of pictures is associated with left anterior fusiform activity is a direct replication of the result reported by Wheeler and Buckner (2004) (see also Vaidya, Zhao, Desmond, & Gabrieli, 2002). The present data extend that result in two significant ways. First, the data indicate that the recollection-related anterior fusiform activity described by Wheeler and Buckner is selective (relative to words) for pictorial information, and therefore is unlikely to be general correlate of successful recollection. Second, the present findings demonstrate that analogous effects can be found for a different class of study material, words, in another functionally specialized fusiform region. This latter result is important both because it generalizes the previous findings for pictures and because it demonstrates that the absence of word recollection effects in the anterior fusiform does not merely reflect a tendency for these items to elicit weaker effects than pictures.

For the reasons noted in Section 1, the reinstatement hypothesis of episodic retrieval predicts that enhanced activity in content-specific cortical regions should be confined to items which are successfully recollected. In the study of

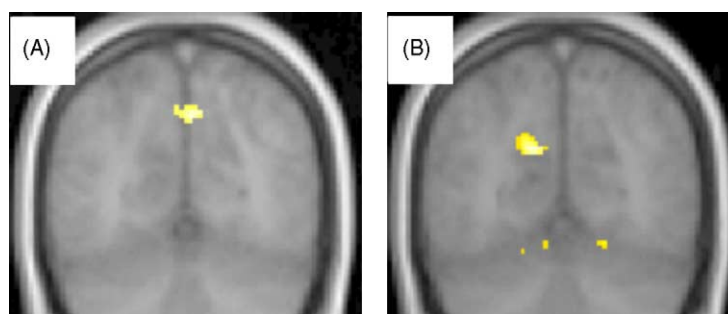


Fig. 5. Precuneus regions where activity elicited by recollected words exceeded that for recollected pictures (A; $y = -68$), and vice-versa (B; $y = -66$). Effects thresholded at $p < 0.001$ uncorrected, superimposed on the across-subject mean of normalized T1-weighted structural MRIs.

Wheeler and Buckner (2004), this prediction was fulfilled by the demonstration that anterior fusiform activity was not elicited by recognized items endorsed as familiar but unrecollected (Know judgments). Analogously, in Kahn et al. (2004), reinstatement effects were absent when recognized items attracted an incorrect source judgment, indicative of a failure to recollect the study task in which the item had been encoded. In the present experiment, subjects endorsed too few items as 'Known' to permit a direct comparison between correctly recognized items according to whether or not they were recollected. In the subjects with sufficient trial numbers, however, it was possible to characterize the neural activity elicited by the combination of study items that were endorsed as Known or incorrectly judged new (misses). There was no sign of enhanced activity, relative to correctly rejected new items, in either the lateral or anterior fusiform, and in both cases, activity elicited by recollected items significantly exceeded that elicited by the other classes of old items. These observations suggest that the two cortical regions were indeed selectively sensitive to recollection. A caveat to this conclusion arises from the fact that the non-recollected items comprised a mixture of those that attracted correct recognition judgments and those that did not. Conceivably, these latter items might have elicited 'repetition suppression effects' (Henson, 2003) rather than an enhancement of activity, by virtue of being primed but unrecognized (cf. Henson, Shallice, Gorno-Tempini, & Dolan, 2002). Such effects would act to cancel any enhancement of activity that might have been associated with recognized items. This possibility cannot be ruled out definitively on the basis of the present data, but it is worth noting that in the small number of subjects in whom the analyses were possible (eight in each case), there was no evidence of smaller responses for misses than correctly rejected new words in either fusiform region.

The present findings add to the evidence supporting the reinstatement hypothesis of episodic retrieval. It is important to note, however, that because these and similar findings do not demonstrate that regionally selective cortical activity is *necessary* for content-specific recollection, they do not offer unequivocal support for the hypothesis. For example, on the basis of the present results, it remains possible that material-dependent enhancement of fusiform activity is a *consequence* of successful recollection, reflecting processing 'downstream' of retrieval such as maintenance of recollected information in visual working memory. One way to address this issue would be to investigate whether dysfunction of a functionally specialized cortical region such as the left lateral fusiform is associated with a content-selective impairment of recollection. This will require studies along similar lines to those reviewed by Rubin and Greenberg (1998). Based on their review of the literature, these authors argued that damage to posterior cortex sufficient to cause global disruption of visual imagery leads to a material-non-specific, temporally ungraded retrograde amnesia, reflecting the predominant role of visual information in autobiographical memory. Accord-

ing to the present findings, circumscribed lesions that give rise to more selective visual processing deficits should be associated with correspondingly selective retrograde memory impairments.

A number of regions other than the two fusiform areas discussed above also demonstrated material-specific retrieval effects (Table 3). These regions were unpredicted, and whereas some of them lend themselves relatively easily to interpretation (for example, the right lingual region that exhibited relatively greater activity for pictures), the majority do not. One region that is of particular interest, however, is the precuneus. The precuneus has been implicated in episodic retrieval since the earliest PET studies (e.g. Tulving et al., 1994), but the functional significance of retrieval-related activity in this area has remained obscure. One early proposal linked this region to visual imagery (Fletcher et al., 1995), arguing that its activation during retrieval reflected the importance to recollection of internally generated visually based information (cf. Rubin & Greenberg, 1998). Other studies however have revealed functional dissociations within this region suggestive of multiple roles during retrieval (e.g. Buckner, Raichle, Miezin, & Petersen, 1996). Recently, Lundstrom et al. (2003) reported dissociations within the precuneus according to whether subjects were recollecting pictorial information that they had imagined paired with a study word versus pictorial information that was actually presented. Whereas retrieval of imagined information was associated with enhanced activity in a relatively superior region (−18, −66, and 40), retrieval of viewed information was associated with enhancement in a more inferior locus (−10, −68, and 26). These loci correspond roughly to those identified in the present case for the retrieval of words (2, −68, and 40) versus pictures (−14, −66, and 26). Together, these two sets of findings add weight to previous evidence of functional dissociations within the precuneus. A speculative possibility is that the findings indicate an inferior/superior dissociation between retrieval or representation of visual versus more abstract forms of information.

4.3. Material-independent recollection effects

In addition to the material-dependent effects discussed above, several regions were found to demonstrate enhanced activity for recollected relative to new items independent of study material (Fig. 1; Table 2). Among these regions were lateral parietal cortex, posterior cingulate, and, at a reduced threshold, left anterior prefrontal cortex. All of these regions have been reported to demonstrate greater activity for correctly recognized versus correctly rejected items in previous studies of recognition memory (Rugg & Henson, 2002) and some regions, notably inferior lateral parietal and posterior cingulate cortex, have been associated specifically with successful recollection (Yonelinas, Otten, & Rugg, 2004). It will be of interest to determine whether these regions reflect processes associated with successful recollection regardless of content, or whether, as appears to be the case for

the precuneus, recollection-related activity in these regions is content-sensitive. For example, the present finding that lateral parietal and posterior cingulate activity did not vary with study material may reflect the fact that these regions operate on information encoded at a level of representation shared by words and pictures (e.g. semantic information), rather than that the regions are content-insensitive. Studies employing a wider variety of study materials and encoding tasks will be required to resolve this issue.

Despite the lack of power, the contrast between activity elicited by old items accorded Remember versus Know judgments revealed activity in the right posterior medial temporal lobe, including, so far as can be ascertained, both the hippocampus and adjacent parahippocampal cortex (Fig. 2). Thus, the present findings converge with previous results (Cansino, Maquet, Dolan, & Rugg, 2002; Dobbins, Kroll, Tulving, Knight, & Gazzaniga, 2003; Eldridge et al., 2000; Kahn et al., 2004; Wheeler & Buckner, 2004; Yonelinas et al., 2004) in suggesting that the hippocampus and adjacent medial temporal cortex respond preferentially to items recognized on the basis of recollection rather than familiarity. The present finding that new items elicit greater medial temporal activity than do old items recognized in the absence of recollection also accords well with other results (Rugg & Yonelinas, 2003; Yonelinas et al., 2004; see also Stark & Okado, 2003). The implications of such findings for the role of the hippocampal region in recognition memory are discussed elsewhere (Rugg & Yonelinas, 2003; see also Squire et al., 2004).

4.4. Concluding comments

The present study identified a material-dependent (words versus pictures) double dissociation in recollection-related activity between two fusiform regions previously shown to respond differentially during on-line processing of the same stimulus classes. The findings thus join other functional neuroimaging data in supporting the proposal that successful episodic retrieval involves engagement of cortical regions recruited at the time the episode was initially encoded. Whether such engagement is necessary for successful recollection remains to be established.

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