

Recollective Qualities Modulate Hippocampal Activation During Autobiographical Memory Retrieval

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ABSTRACT: Recent neuroimaging studies report preferential hippocampal engagement during autobiographical memory (AM) retrieval. Although the basis of this preferential activation remains unclear, it may be related to the temporal specificity, recency, or recollective qualities of AMs, such as detail, emotionality, and personal significance. Typically, however, these variables are confounded, and thus we sought to investigate the contributions of each to hippocampal activation during AM retrieval. We conducted an event-related functional magnetic resonance imaging (fMRI) study in which participants retrieved temporally specific AMs and general, repeated AMs, and rated each for level of detail, emotion, or personal significance. These ratings, as well as the recency of AMs, were used in parametric modulation analyses to identify brain regions that correlated positively with ratings, independent of recency, and vice versa. Retrieval of AMs activated a number of regions, including the hippocampus. No differences in hippocampal activation were evident between specific and general AM retrieval, suggesting that temporal specificity, on its own, is not a key modulator of hippocampal activation. Activation of the left hippocampus during specific AM retrieval did vary with the level of detail, personal significance, and at a subthreshold level, emotionality, when the effect of recency was covaried out. Further, during general AM retrieval, all three recollective qualities modulated activity in the right hippocampus. Although the recency of specific AMs modulated hippocampal activation bilaterally, this effect dissipated in the left hippocampus when detail or emotionality was included as a covariate, and was no longer present in either hippocampus when personal significance was taken into account. Our results suggest that recollective qualities are important predictors of hippocampal engagement during AM retrieval independent of factors such as recency. These findings are consistent with theories of hippocampal function that emphasize its role in the recollection of multifaceted autobiographical experiences.
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INTRODUCTION

The hippocampus appears to be crucial for the retrieval of episodic memory, particularly autobiographical memory (AM), but what factors determine its involvement remain to be specified. Hippocampal damage can impair AM, even without disrupting other aspects of memory (Barr et al., 1990; McCarthy and Warrington, 1992; Nadel and Moscovitch, 1997; Fujii et al., 2000; Viskontas et al., 2000; Westmacott et al., 2001). Recent neuroimaging studies have reported a predominantly medial and left-lateralized network engaged during memory retrieval (Conway et al., 1999; Maguire and Mummery, 1999; Maguire et al., 2000, 2001b; Maguire and Frith, 2003b; Piefke et al., 2003) in which the hippocampus appears to be a key structure (Fink et al., 1996; Maguire and Mummery, 1999; Maguire et al., 2000, 2001b; Ryan et al., 2001; Maguire and Frith, 2003a,b; Piefke et al., 2003). Despite this converging evidence, it has yet to be determined what characteristics of AM actually drive this preferential hippocampal activation. In this study, we examined the influence of temporal specificity (i.e., whether the event is specific to one point in time or repeated over time), recency (i.e., the age of the AM) and recollective qualities of AM on hippocampal activation.

Research by Maguire and Mummery (1999) has indicated that temporal specificity of AM may be one factor that modulates hippocampal activation. These investigators found greater hippocampal activation during the retrieval of temporally specific event memories (e.g., my brother's wedding) in comparison to autobiographical facts (e.g., my brother's name is John). However, there may be aspects of AM other than temporal specificity, such as recollective experience, which is likely associated with AM and distinguishes it from autobiographical facts, which typically lack this characteristic. In the present study, we directly compared two types of recollective event memories that differed in degree of temporal specificity, enabling direct investigation of hippocampal modulation by this factor. Participants retrieved temporally specific events (e.g., breaking one's leg), and general, repeated events, which lack temporal specificity (e.g., repeated visits to the hospital to have one's leg examined; Conway, 1992, 1996, also termed "repsisodes"; Neisser, 1982). Although this distinction has been considered

theoretically important (Conway, 1992; 1996), no study has investigated the neural bases of general AM retrieval, nor differentiated this from that of specific AMs.

The recency of AMs is another factor that may drive hippocampal activation, although whether this is the case is still a matter of debate. Damage to the hippocampus can result in temporally graded memory loss (e.g., Scoville and Milner, 1957; Squire and Alvarez, 1995), with recent memories disproportionately affected relative to remote. This has formed the basis of the consolidation hypothesis (Squire, 1992), which asserts that the role of the hippocampus in memory retrieval is time-limited. However, hippocampal damage does not always result in a temporally graded amnesia; recent and remote AMs can be equally impaired (e.g., Tulving et al., 1988; Barr et al., 1990; McCarthy and Warrington, 1992; Viskontas et al., 2000). To account for this, Nadel and Moscovitch (1997) propose that contextually rich memories, such as AMs, remain dependent on the hippocampus during retrieval. Evidence from the neuroimaging literature relevant to this debate remains mixed, with some studies reporting increased hippocampal activation for retrieval of recent relative to remote AMs (Maguire and Frith, 2003a; Piefke et al., 2003), and others reporting no such difference (e.g., Conway et al., 1999; Maguire et al., 2001a; Ryan et al., 2001; Gilboa et al., 2002; Niki and Luo, 2002).

This discrepancy may be explained, in part, by other qualities of AMs, in particular those that contribute to recollection. For example, in Piefke et al.'s (2003) study, the recent events that were associated with a bilateral increase in hippocampal activation during retrieval relative to remote events were also rated by participants as being higher in re-experiencing, richness of details, and emotionality. Conversely, Ryan and colleagues (2001) report no significant differences in the level of detail, emotional arousal, or importance of recent and remote AMs, and also no difference in the level of hippocampal activity during retrieval. In another study, where the level of detail was held constant across recent and remote AMs, differential hippocampal activation was evident, but this was limited to the right hippocampus (Maguire and Frith, 2003b). Thus, these studies suggest that even if recency does influence the activity of the hippocampus, recollective qualities are also important, if not crucial, determinants of hippocampal activation.

Indeed, a number of studies indicate that the hippocampus is necessary for the recollection and re-experience of events (Eldridge et al., 2000; Maguire et al., 2001b; Moscovitch and McAndrews, 2002). In an interesting study, Maguire and colleagues (2001b) found that a patient with partial hippocampal damage showed increased activation in these regions for retrieval of AMs that he could re-experience in comparison to AMs he only knew about. Recollection was also found to be an important determinant of hippocampal activation in normal people (Eldridge et al., 2000). If hippocampal involvement is associated with the ability to re-experience events, it is likely that certain qualities of AM associated with re-experiencing, such as detail, emotionality, and personal significance, would modulate the level of hippocampal activation. Detail and emotionality have been described as important characteristics of AMs (Larsen, 1998; Moscovitch et al., 1999; Nadel et al., 2000; Levine et al., 2002; D'Argembeau et al., 2003), contributing to vividness and re-experiencing. Personal significance may also have

an important role in re-experiencing and auto-noetic consciousness, as highlighted by Wheeler and colleagues (1997). Thus, although a number of studies suggest that degree of hippocampal engagement may be correlated with different aspects of autobiographical re-experiencing, no one has investigated this directly.

We used event-related fMRI to elucidate the factors that modulate hippocampal activation during AM retrieval. Retrieval of specific AMs should be associated with greater hippocampal activation than retrieval of general AMs if temporal specificity is a key factor. Further, if recency is the more important determinant, then hippocampal activation should vary with the age of the AMs, even when recollective qualities are taken into account. If recollective qualities are crucial, the level of detail, emotionality, and personal significance should modulate activity in the hippocampus independent of AM recency.

MATERIALS AND METHODS

Participants

Fourteen healthy right-handed adults (seven male, seven female; mean age, 28 years; range, 20–40 years), with no prior history of neurological or psychiatric impairment, participated in this study. All participants gave written informed consent for the study, approved by the University Health Network Research Ethics Board.

Pre-Scan Interview

At least 48 h prior to scanning, each participant completed a 2-h pre-scan interview in which he or she produced 20 specific and 20 general AMs. Specific AMs were defined as events that happened only once, while general AMs were repeated events that had occurred at least 10 times. Only AMs that had not occurred within the past year were permitted. This was done to decrease the likelihood of general AMs cueing a specific exemplar (Conway 1992, 1996), which may have additional salience as the most recent repetition of that event. Further, it was ensured that any general AMs that cued specific instances were not included. A list of cues was provided to facilitate retrieval, but event memories were not limited to these cues. For each AM, participants dated the event (i.e., the number of years since a specific event, or the number of years since the last instance of a general event) and provided a brief "title" to be as a cue during scanning. Additionally, participants rated each AM on a five-point scale for the level of detail (i.e., vividness, ranging from "faint with few details" to "exceptionally clear with great detail recalled"), emotionality (i.e., the intensity of emotion the memory currently evokes for the participant, ranging from "detachment; no emotional experience" to "an intense emotional experience"), and personal significance (i.e., how self-defining the event was; ranging from "not significant; it made no difference to my life and/or how I think about myself" to "great personal significance, changing my life and/or how I view myself").

Scanning

Immediately prior to scanning, the AM and control tasks were explained to participants. They were shown the five-point rating

scales they would use in the scanner, and were presented with the AM titles they produced in their pre-scan interview to ensure that there was no confusion during scanning.

During scanning, all stimuli were presented in black text on a white background, and were back-projected onto a white screen viewed by the participants through a mirror incorporated into the head coil. SuperLab Pro 2.0 (Cedrus Corporation, San Pedro, CA) was used for the presentation and timing of stimuli. Each trial was 16 s, and consisted of the task presentation, rating, and rest. Participants completed two scanning sequences (each 10 min, 50 s) in a single session.

Autobiographical memory tasks

During each scanning sequence, the titles for 10 general and 10 specific AMs produced in the pre-scan interview were presented as retrieval cues (thus, 20 of each were presented over the two scanning sequences). Each AM title was presented visually for 6 s, and participants retrieved the relevant memory. This short time-window was also considered necessary to decrease the likelihood of a general event cueing specific instances of that general event (Conway, 1992, 1996). We considered this time-window to be sufficient for the following reasons. It has been determined electrophysiologically that the average time taken to retrieve specific AMs is 5 s (Conway et al., 2003). This finding is further supported by the ratings of participants in this study (see below), which indicated there was indeed sufficient time for recollection. A five-point rating scale (either detail, emotionality, or personal significance) was then presented visually for 4 s, during which participants rated the AM by lifting the finger of the right hand corresponding to their rating (thumb = one, etc.) A researcher present in the scanning room recorded each rating. In order to reduce the load on the participant and shorten the duration of the scan, only one dimension was rated for each AM. Further, the dimension rated remained the same over the duration of a scanning sequence, but differed between the two sequences. The rating tasks were included during scanning to enable later correlations with the ratings on the same dimension obtained within more extensive post-scan ratings. Such correlations were conducted to ensure post-scan ratings were indeed based on the AM retrieved in the scanner. A rest period of 6 s followed the rating task, during which a blank screen was presented and participants were instructed to focus on resting.

Control tasks

Twenty control task trials were randomly interspersed between the twenty AM task trials in each scanning sequence. Ten of these were sentence completion tasks (Ryan et al., 2001). Participants were presented visually with a sentence missing the last word (e.g., "The dog ate a _____"), and were instructed to complete the sentence with a word silently. This task provided a control task involving the retrieval of information, but from semantic memory rather than AM. Ten size discrimination tasks were also included in each scanning session to provide a similar control for visuospatial processing. The names of two objects were presented (e.g., "CD or coin") along with the word "Biggest" to cue participants to judge the larger of two items. Each control task was presented for

4 s followed by the presentation of a five-point rating scale for difficulty of task completion for 4 s. This rating was included as a control for the act of making a rating in the AM retrieval tasks. A rest period of 8 s followed.

Post-Scan Interview

Immediately following the scanning session, participants completed a 30-min post-scan interview. Participants retrospectively rated each AM for detail, emotionality, and personal significance, based on their retrieval in the scanner. This included a re-rating of the dimension previously rated in the scanner. Post-scan ratings were highly correlated with ratings obtained during the scan ($r = 0.80$), indicating they were in fact basing their ratings on the AM retrieved in the scanner. Additionally, participants also made three categorical judgments concerning the content of each AM retrieved: (1) whether the AM was primarily visual or verbal ("story-based"); (2) whether the AM was more active and dynamic or more static; and (3) whether the content of the AM was primarily about place (i.e., the location of the event) or objects (e.g., persons, inanimate objects). Lastly, participants reported whether they were able to retrieve the memory. One event (a general AM) from one participant was dropped from all analyses, due to a failure to retrieve the AM in the scanner.

Data Acquisition

Functional data were acquired on a 1.5-Tesla Signa MR System (GE Medical Systems, Milwaukee WI), using single-shot spiral acquisition (TE = 40 ms, TR = 2,000 ms, FOV = 220 mm). Slices were 5 mm thick, with a 1-mm gap, covering the entire brain. These were acquired in a coronal-oblique orientation, with each slice being perpendicular to the long axis of the hippocampus to avoid partial volumes of this structure. The first three frames were dropped to allow for signal equilibrium. To acquire anatomical images, a standard three-dimensional T₁-weighted sequence (FOV = 200) was used to generate 60 axial slices (2.2 mm thick).

Data Processing and Statistical Analyses

All preprocessing and analyses of imaging data were performed using SPM99 (Wellcome Department of Cognitive Neurology, London, UK). All functional images were co-registered to a structural image, realigned for motion correction, corrected for within-frame time of acquisition, spatially normalized and smoothed using a Gaussian kernel of 7.6-mm full-width half maximum. Data were high-pass filtered to account for low-frequency drifts and voxel time-series were temporally smoothed with a Gaussian filter (full-width half maximum 4 s). Each stimulus event was modeled by SPM99's canonical hemodynamic response function (applied at task onset) and the six head-movement parameters were included as confounds in an event-related, random-effects model with four conditions: specific AMs, general AMs, sentence completion and size comparison. The following contrasts were made: (1) AM retrieval (specific and general AMs) versus the two control tasks (sentence completion and size comparison); (2) retrieval of general versus specific AMs and vice versa; (3) specific AM retrieval versus

the two control tasks; and (4) general AM retrieval versus the two control tasks. A significance threshold of $P < 0.05$ (corrected), and a minimum extent threshold of 25 contiguously activated voxels ($2 \times 2 \times 2$ mm) were applied to these contrasts.

Further, two parametric modulation analyses were performed (specific and general AMs), with the age of memories used as covariates of interest (modeled linearly). Six parametric modulation analyses of the response to AM retrieval (specific and general) were conducted, with post-scan ratings on three dimensions used as covariates of interest (detail, emotionality, and personal significance; modeled linearly). As the first set of parametric analyses revealed that the age of specific AMs modulates hippocampal activation, we entered this as a covariate into the models for the specific AM parametric modulations. Each of these analyses therefore revealed the unique contribution of the recollective quality, as it was orthogonalized with respect to the rest of the design matrix, including the age of the AM. Additionally, we conducted the reverse contrasts and looked at the effect of age, independent of each of the recollective qualities. The significance threshold for parametric analyses was set at $P < 0.005$ (uncorrected) for parametric modulation analyses (Rombouts et al., 1999). An extent threshold of five contiguously activated voxels ($2 \times 2 \times 2$ mm) was also applied. For all analyses, Montreal Neurological Institute coordinates were converted to Talairach space, and regions of activations were localized in reference to a standard stereotaxic atlas (Talairach and Tournoux, 1988).

RESULTS

Behavioral Results

Ratings for the three dimensions were compared for specific and general events using the Mann-Whitney U-test. The differences were significant for amount of detail [specific ($M = 3.18$, $SD = 1.07$), general ($M = 2.84$, $SD = 0.88$), $U = 31412$, $P < 0.001$], emotionality [specific ($M = 2.58$, $SD = 1.00$), general ($M = 2.25$, $SD = 0.99$), $U = 31835$, $P < 0.001$] and personal significance [specific ($M = 2.63$, $SD = 1.13$), general ($M = 2.33$, $SD = 0.98$), $U = 33433$, $P < 0.01$]. The magnitude of the effect in each case was modest, ranging from 0.28 to 0.35 SD units (Cohen, 1988). Ratings for all three dimensions were moderately intercorrelated. Detail ratings were significantly correlated with those of emotionality [specific ($r = 0.537$, $P < 0.001$), general ($r = 0.424$, $P < 0.001$)] and personal significance [specific ($r = 0.462$, $P < 0.001$), general ($r = 0.384$, $P < 0.001$)]. Emotionality ratings were also significantly correlated with personal significance ratings [specific ($r = 0.580$, $P < 0.001$), general ($r = 0.664$, $P < 0.001$)].

To determine whether specific and general AMs differed with regard to the each of the three categorical judgments (visual/verbal, action/static, place/object), three chi-square tests were conducted. There was no significance difference between specific and general AMs in the frequency of visual and verbal categorizations [χ^2 (1, $N = 559$) = 1.81, $P = 0.178$] or active and static categorizations [χ^2 (1, $N = 559$) = 2.06, $P = 0.151$]. There was, however, a significant difference between specific and general AMs in the fre-

quency of place and object categorizations [χ^2 (1, $N = 559$) = 19.04, $P = < 0.001$], with more specific AMs classified as being object-focused, and more general AMs being classified as place-focused.

The age, or recency, of specific and general AMs (i.e., the number of years since a specific event, or the number of years since the last instance of a general event) was compared using an independent samples *t*-test. No significant difference was apparent [specific ($M = 10.23$, $SD = 7.78$, range = 1–36 years), general ($M = 10.24$, $SD = 7.13$, range = 1–36 years), $t = -0.024$, $P = 0.981$]. The age of general AMs did not correlate significantly with the detail ($r = -0.079$, $P = 0.187$), emotionality ($r = 0.005$, $P = 0.938$), or personal significance ($r = -0.031$, $P = 0.609$) ratings of these AMs. The age of specific AMs, however, was negatively correlated with all three ratings (detail, $r = -0.242$, $P < 0.001$; emotionality, $r = -0.189$, $P = 0.001$; personal significance, $r = -0.261$, $P < 0.001$), indicating that more recent specific AMs (i.e., those that occurred fewer years ago) were rated as higher in these recollective qualities.

AM Retrieval

To identify brain regions involved in the retrieval of AMs, we conducted a random effects *t*-test, comparing the blood oxygenation level-dependent (BOLD) signal associated with autobiographical memory retrieval (specific and general AMs) to that of the two control tasks (sentence completion and size comparison). As evident in Table 1 and Figure 1, this comparison demonstrated the activation of regions comprising the memory retrieval network reported by others (Conway et al., 1999; Maguire and Mummery, 1999; Maguire et al., 2000, 2001b; Piefke et al., 2003; $P < 0.05$, corrected for multiple comparisons). Activation of the medial frontal lobe, lateral temporal lobe, and angular gyrus was left-lateralized. In contrast, activation of thalamus, precuneus, posterior cingulate, and the medial temporal lobes (MTL), including the hippocampus and parahippocampal gyrus, was bilateral, although the MTL activation was more extensive in the left hemisphere.

Retrieval of Specific and General AMs

To investigate the effect of temporal specificity on neural activation, random-effects *t*-tests contrasting specific and general AM retrieval were performed. These revealed no significant differences in BOLD signal between the retrieval of these two types of event memory ($P < 0.05$, corrected) in any brain region, including the hippocampus. Employing a less conservative threshold ($P < 0.005$, uncorrected) failed to yield any significant differences in hippocampal activation, suggesting that the hippocampus was active in both conditions. To determine if this lack of difference reflected the activation of the hippocampus during the retrieval of both specific and general AMs, each AM type was compared to the control tasks. Extensive activation of the hippocampus was evident during the retrieval of both specific and general AMs ($P < 0.005$, uncorrected). Although our comparison of specific and general AMs at a less conservative threshold ($P < 0.005$, uncorrected) yielded no differences in hippocampal activation, it did reveal differential activation of other brain regions. The retrieval of specific

TABLE 1.

*Brain Regions Activated During AM Retrieval (Specific and General) Compared to Control Tasks (Sentence Completion and Size Discrimination)**

Brain region	Coordinates			Z-score
	x	y	z	
L Medial frontal lobe (BA 10)	-4	50	-4	5.08
L Cingulate (BA 31/23)	-8	-39	31	7.29
R Cingulate (BA 31)	4	-35	35	7.62
R Thalamus ^a	2	-13	10	5.69
L Hippocampus	-24	-22	-12	6.31
R Hippocampus	34	-26	-9	6.14
L Parahippocampal gyrus (BA 36)	-24	-35	-10	6.57
R Parahippocampal gyrus (BA 34)	16	-10	-11	5.74
R Parahippocampal gyrus (BA 36)	22	-32	-10	5.67
L Middle/inferior temporal gyrus (BA 21)	-59	-7	-16	6.51
L Posterior cingulate (BA 31)	-10	-53	19	7.40
R Posterior cingulate (BA 30)	6	-44	19	7.69
L Precuneus (BA 31)	-6	-57	32	7.47
L Precuneus (BA 19)	-40	-74	40	7.01
L Angular gyrus (BA 39)	-46	-65	34	7.09
L Medulla	-7	-43	-35	5.27

AM, autobiographical memory; BA, Brodmann area.
 *All activations are significant at $P < 0.05$ (corrected). For each region of activation, the coordinates of the maximally activated focus within each different structure are reported, as indicated by the highest Z-score.
^aAlthough the only local maximum for this structure was right-lateralized, this activation was bilateral.

AMs was associated with greater activation of right parahippocampal gyrus (Brodmann area [BA] 19), right anterior cingulate (BA 31), left superior temporal gyrus (BA 39), left precuneus (BA 31/7) and posterior cingulate (BA 31). The retrieval of general AMs was associated with increased activation of left parahippocampal (BA 36) and fusiform (BA 37) gyri.

Parametric Modulation by Recency of AMs

To determine whether the varying recency of specific and general AMs modulated hippocampal activation, we modeled the parametric modulation of the BOLD signal associated with each type of AM retrieval by the age of the AMs (i.e., the number of years since a specific event, or the number of years since the last instance of a general event) using a linear function. Based on the literature, we wanted to investigate whether hippocampal activation would increase with the recency of the AM. Thus, we conducted two parametric modulations (general and specific AMs) and tested the data for negative correlations (i.e., greater activation with the decreasing age of an AM). Activations within the MTL are presented in Table 2. During the retrieval of specific AMs, activity in the hippocampus bilaterally was negatively correlated with the age of the AMs retrieved (all MTL maxima were significant at $P \leq 0.003$, uncorrected; Fig. 2a). In contrast, the age of general AMs

did not modulate the activation of any MTL structure during retrieval ($P < 0.005$, uncorrected).

Parametric Modulation by Recollective Qualities of AMs

We wanted to investigate whether varying degrees of detail, emotionality, and personal significance were associated with fluctuations of hippocampal activation. Thus, we modeled the parametric modulation of BOLD signal associated with the retrieval of specific and general AMs by the rating of the memory on a particular dimension (detail, emotionality, and personal significance) using a linear function.

Specific AMs

For specific AMs, three parametric modulations were conducted: detail, emotionality, and personal significance. As the recency of AMs was found to modulate hippocampal activation during specific AM retrieval, recency was entered as a covariate into these analyses. Therefore, for each parametric modulation, two contrasts were made: (1) a contrast testing for positive correlations between the recollective quality and BOLD signal, with the AM age covaried out; and, (2) a contrast testing for negative correlations between AM age and BOLD signal, with the recollective quality covaried out. This second contrast enabled an additional investigation, of whether the parametric effect of recency was independent of the recollective qualities. Thus, the results of these six contrasts are presented, and the focus is limited to activations that extend into the MTL (Table 3).

The level of detail and personal significance modulated the activation of left and right MTL structures during retrieval when the recency of specific AMs was covaried out (all MTL maxima were significant at $P \leq 0.001$, uncorrected; Fig. 3). Specifically, the amount of detail positively correlated with activation of the left hippocampus and right amygdala, while the level of personal significance correlated with activation of the hippocampus bilaterally. Although the level of emotionality did not modulate MTL activation when recency was taken into account, the left hippocampus

TABLE 2.

*Medial Temporal Regions That Were Negatively Modulated by the Recency of AMs (in Years Since Encoding) of Retrieved AMs**

Brain region	Coordinates			Z-score
	x	y	z	
Specific AMs				
L Hippocampus	-22	-22	-9	2.97
R Hippocampus	22	-26	-5	2.95
	28	-28	-10	2.79

AM, autobiographical memory; BA, Brodmann area.
 *All maxima are significant at $P \leq 0.003$ (uncorrected). For each region of activation in the medial temporal lobe, the coordinates of the maximally activated focus within each different structure are reported.

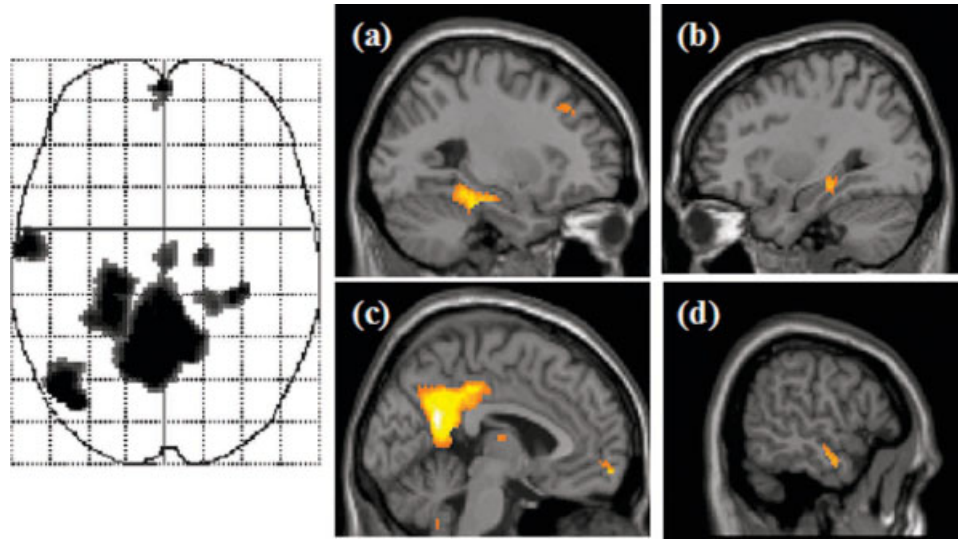


FIGURE 1. Activations associated with the retrieval of autobiographical memories (AMs) (specific and general) relative to the control tasks (sentence completion and size discrimination) ($P < 0.05$, corrected). a: Left hippocampus and parahippocampal gyrus. b: Right

hippocampus and parahippocampal gyrus. c: Cingulate, posterior cingulate, precuneus, thalamus, and left medial temporal lobe. d: Left lateral temporal lobe. As shown by the glass brain, these activations are predominantly medial and left-lateralized.

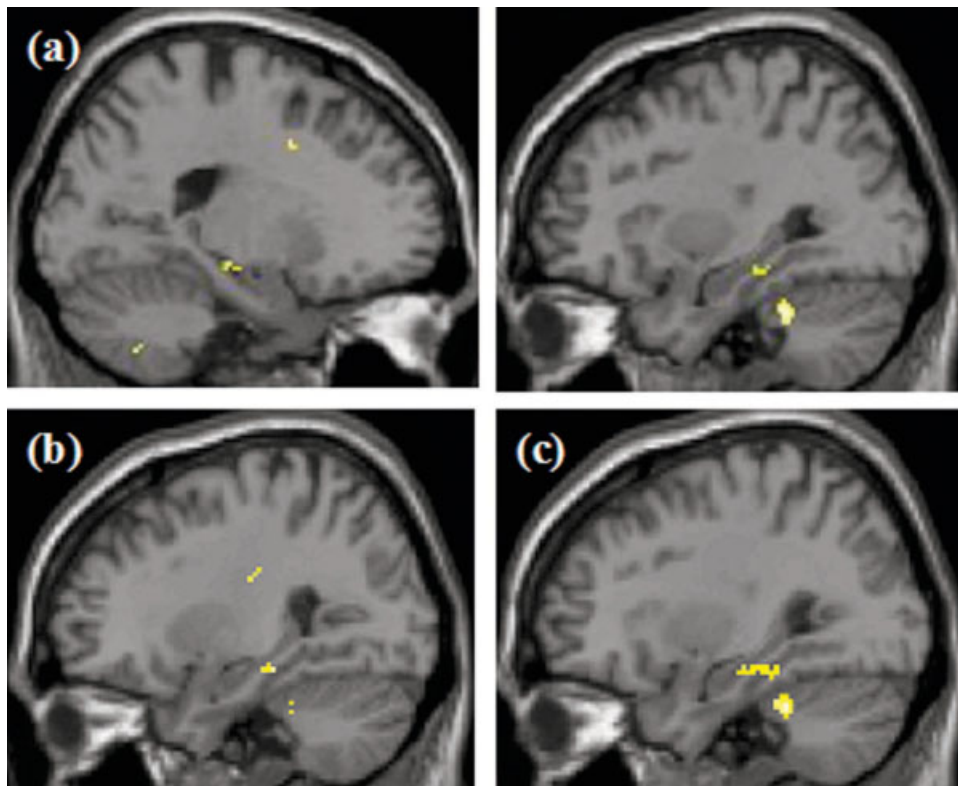


FIGURE 2. Regions of the medial temporal lobes that exhibited a parametric response to the recency of specific autobiographical memories (AMs) (a), and this parametric response after covarying out either the level of detail (b) or emotion (c). Note that when the level of

personal significance was entered as a covariate, the parametric effect of recency dissipated. In each case, activation increased with the decreasing age (increasing recency) of the AM.

TABLE 3. *Medial Temporal Regions That Were Modulated by the Level of Detail, Emotionality, Personal Significance, and Recency (Covariates Specified) of Retrieved Specific AMs**

Brain region	Coordinates			Z-score
	x	y	z	
Detail (covariate: recency)				
L Hippocampus	-20	-37	0	3.49
R Amygdala	24	-6	-8	3.01
Personal significance (covariate: recency)				
L Hippocampus	-18	-12	-11	3.29
R Hippocampus	30	-35	5	3.01
Recency (covariate: detail)				
R Hippocampus	28	-28	-10	3.06
Recency (covariate: emotion)				
R Hippocampus	30	-20	-11	3.25

AM, autobiographical AM; BA, Brodmann area.
 *All maxima are significant at $P \leq 0.001$ (uncorrected). For each region of activation extending into the medial temporal lobe, the coordinates of the maximally activated focus within each different structure are reported.

and right uncus did show a subthreshold parametric response. The recency of specific AMs negatively correlated with activation of the right hippocampus when either the amount of detail or emotion was taken into account (Fig. 2b,c). However, when the level of personal significance was taken into account, the recency of specific AMs failed to modulate MTL activation.

General AMs

For general AMs, three parametric modulations were conducted: detail, emotionality, and personal significance. The recency of general AMs was not entered as a covariate into these analyses, because the recency of general AMs was not found to modulate MTL activation. Only activations that extend into the MTL are presented (Fig. 4 and Table 4). The activation of the right hippocampus positively correlated with the level of detail, emotionality, and personal significance of general AMs (all MTL maxima were significant at $P \leq 0.002$, uncorrected). Additionally, personal significance modulated the activation of the right parahippocampal gyrus.

DISCUSSION

AM Retrieval

We found activation of a predominantly medial and left-lateralized memory network during retrieval of AM. Consistent with other reports (Barr et al., 1990; McCarthy and Warrington, 1992; Fink et al., 1996; Nadel and Moscovitch, 1997; Maguire and Mummery, 1999; Eldridge et al., 2000; Fujii et al., 2000; Viskontas et al., 2000; Maguire et al., 2000, 2001b; Ryan et al., 2001;

Westmacott et al., 2001; Moscovitch and McAndrews, 2002; Maguire and Frith, 2003a,b; Piefke et al., 2003), our findings support the proposal that MTL structures are crucial to AM retrieval. There are mixed findings as to whether the MTL aspect of the memory retrieval network is bilateral (Fink et al., 1996; Ryan et al., 2001; Maguire and Frith, 2003a,b; Piefke et al., 2003) or left-lateralized (Maguire and Mummery 1999; Maguire et al., 2000, 2001b). In the present study, both the hippocampus and parahippocampal gyrus of the MTL were activated bilaterally, though more extensively on the left. In the contrast of all AMs to control tasks, a number of factors likely contribute to the bilaterality of MTL activation, including the type of AMs included in this contrast (i.e., general and specific), the level of recollective qualities and the recency of AMs. Our additional analyses have investigated the contributions of these variables to hippocampal activation during AM retrieval, and will be discussed further.

Temporal Specificity

To test the effect of temporal specificity, we compared the activation associated with the retrieval of specific AMs to that of general AMs. There were no significant differences in hippocampal activation between retrieval of these two types of memory, either at our initial threshold, or at a less conservative one. Although other investigators have suggested that temporal specificity may modulate hippocampal activation (Maguire and Mummery, 1999), their finding is based on the comparison of specific AMs to other types of memory, such as autobiographical facts, that typically lack any re-experiencing component. Our results indicate that the re-experience associated with AM retrieval, as well as the qualities of AM accompanying this re-experience, are more significant predictors of hippocampal activation than temporal specificity. It is possible, however, that both specific and general AMs have spatial specificity, which is thought to activate also the hippocampus (O’Keefe

TABLE 4. *Medial Temporal Regions That Were Modulated by the Level of Detail, Emotionality, and Personal Significance of Retrieved General AMs**

Brain region	Coordinates			Z-score
	x	y	z	
Detail				
R Hippocampus	34	-24	-6	2.87
Emotionality				
R Hippocampus	40	-29	-7	3.04
	30	-24	-9	2.81
Personal significance				
R Hippocampus	34	-26	-7	3.20
R Parahippocampal gyrus (BA 37)	34	-39	-8	3.00

AM, autobiographical memory; BA, Brodmann area.
 *All maxima are significant at $P \leq 0.002$ (uncorrected). For each region of activation in the medial temporal lobe, the coordinates of the maximally activated focus within each different structure are reported.

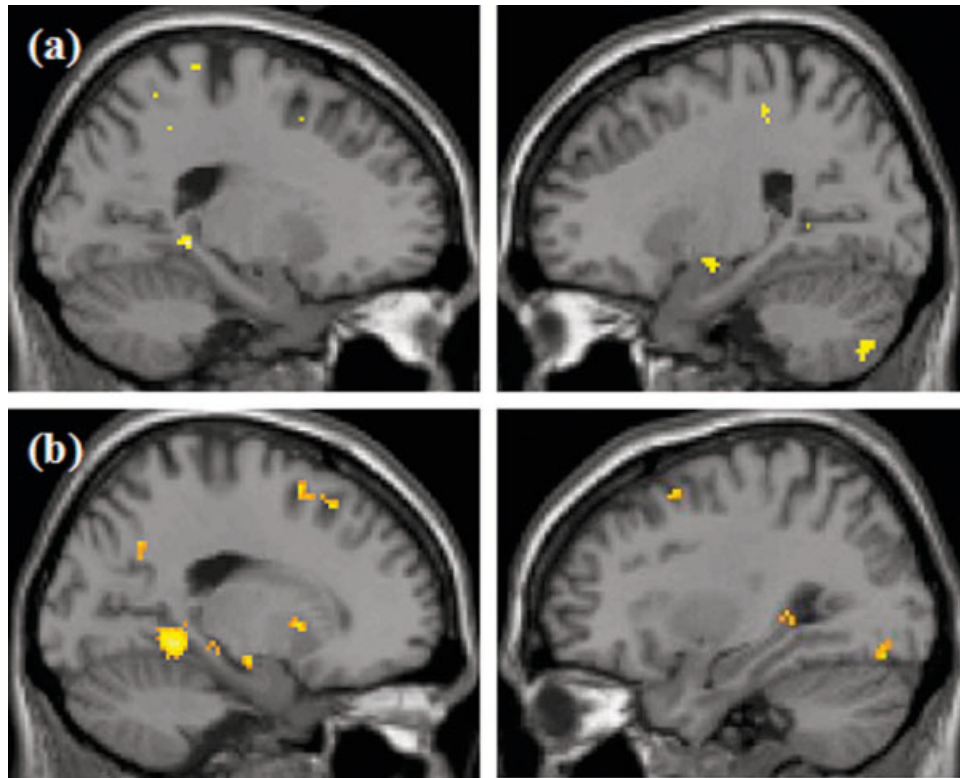


FIGURE 3. Medial temporal structures exhibiting parametric responses to the level of detail (a: left hippocampus, right amygdala) and personal significance (b: left and right hippocampus) during spe-

cific autobiographical memory (AM) retrieval ($P < 0.005$, uncorrected). In each case, the recency of AMs was entered as a covariate, and the activation increased with increasing levels of these qualities.

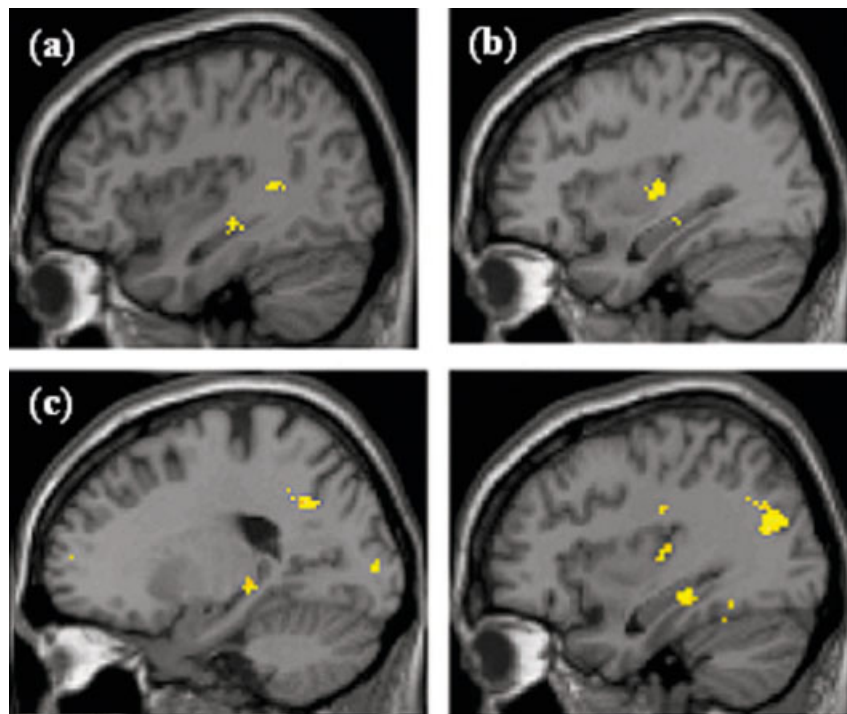


FIGURE 4. Regions of the right medial temporal lobe showing parametric responses to the level of detail (a: hippocampus), emotionality (b: hippocampus), and personal significance (c: hippocampus

[left] and parahippocampal gyrus [right]) during general autobiographical memory (AM) retrieval ($P < 0.005$, uncorrected). In each case, activation increased with the increasing level of these qualities.

and Nadel, 1978). If this is the case, this may have obscured any difference between specific and general AMs.

Recollective Qualities of AMs

While our results did not support the hypothesis that the temporal specificity of AMs correlates with hippocampal activation during retrieval, our parametric modulation analyses suggested that recollective qualities of specific and general AMs contributing to re-experiencing are important. It is interesting to note that these analyses did reveal some differences in patterns of hippocampal activity between specific and general AMs not demonstrated by univariate contrasts.

With regard to specific AMs, the retrieval of more detail correlated with increased left hippocampal activation, while the level of personal significance modulated hippocampal activity bilaterally, independent of the recency of AMs. The retrieval of AMs with greater emotionality, on the other hand, was also associated with an increase in left hippocampal activity, albeit subthreshold. Thus, it appears that the recollection of specific AMs may contribute consistently to the engagement of the left hippocampus. In contrast, all three recollective qualities of general AMs correlated with activity in the right hippocampus.

This difference in laterality may be related to a difference in the content of specific and general AMs: significantly more specific AMs were categorized as being focused on objects (e.g., people, inanimate objects), while more general AMs were categorized as place-focused. This is consistent with the findings of a study investigating the place and person contexts of episodic memories (Burgess et al., 2001), in which the right hippocampus was associated with place context (although at a subthreshold level), while the left hippocampus was activated during contextual retrieval, irrespective of whether this pertained to place or person. One can also speculate that specific memories rely more heavily on sequential processing of episodes within the event than do general AMs, resulting in a stronger dependence in the left hemisphere (e.g., Ehrle et al., 2001; Fortin et al., 2002), although our data do not compel this interpretation.

Additionally, this laterality effect may be related to some contribution of recency to right hippocampal activation during general AM retrieval, considering our finding that recency correlates with activity in the right hippocampus. We found that recency of general AMs did not modulate hippocampal engagement, and thus we did not enter age of AMs as a covariate for the parametric modulations by recollective qualities of general AMs. It is possible, however, that using the number of years since the last instance of a general event as a measure of recency obscures any effect of recency by not capturing the full range of ages from which the general AMs come. Regardless, our findings overall show that hippocampal activity correlates with recollective qualities of AMs, even when recency is accounted for. This is consistent with the idea that the hippocampus likely reintegrates the various aspects or details of an AM during retrieval (Eichenbaum, 2001), which it helped bind into a memory trace during encoding (Moscovitch, 1989, 1992, 1995).

In addition to hippocampal activation, engagement of the anterior MTL was modulated by recollective qualities of specific AMs. The right amygdala showed increased activation when retrieving specific AMs high in detail. Why this is the case remains unclear particularly as this structure was not modulated by emotionality. We did find, however, that the emotionality of specific AMs modulated activity in the right uncus, though at a subthreshold level. The lack of correlation between amygdala activation and emotional intensity is not inconsistent with the literature. Its activation is associated typically with strong negative emotions (e.g., fear conditioning; Büchel and Dolan, 2000), and participants did not disclose such AMs in this study. Further, even when the neural correlates of emotional memory have been investigated within the context of AMs, amygdala activation has not been found consistently (Fink et al., 1996; Maguire and Frith, 2003a; Piefke et al., 2003).

Recency of AMs

When recollective qualities were not taken into account, we found a bilateral modulation of hippocampal activity by the recency of specific AMs. It is likely that this recency effect is related to recollection, considering that AMs were rated as higher in detail, emotionality, and personal significance. Thus, this result is consistent with the finding of Piefke and colleagues (2003), who also report that the retrieval of highly recollective recent AMs is associated with increased hippocampal activation bilaterally relative to less recollective remote AMs.

When we entered either detail, emotionality, or personal significance into the parametric analysis as a covariate, the effect of recency on hippocampal engagement was greatly reduced. This was particularly evident for left hippocampal activation, which was no longer modulated by recency when any of the three recollective qualities were taken into account. A similar finding is reported by Gilboa and colleagues (2002), who found that an effect of recency in the left hippocampus dissipated when recent and remote AMs were equated for detail. The right hippocampus still exhibited a parametric effect in response to recency when either detail or emotionality was covaried out. This is concordant with the recent finding of a correlation between right hippocampal activity and recency in AMs which are equated for richness of detail (Maguire and Frith, 2003a). This pattern of results suggests that the retrieval of AMs may remain continually dependent on the left hippocampus (Nadel and Moscovitch, 1997), while dependence on the right hippocampus appears to be time-limited, lending support to consolidation theories (Squire and Alvarez, 1995).

However, the effect of the recency of specific AMs on hippocampal activation was no longer evident when the level of personal significance was taken into account. This indicates that the personal significance of specific AMs is an important predictor of hippocampal activation regardless of recency, and suggests that the effect of recency may actually have more to do with the personal significance of the AMs. This finding is consistent with Maguire and Mummery's (1999) report of preferential activation of the hippocampus by personally relevant AMs. Personal significance is thought to have an important role in re-experiencing by enabling

mental time-travel of the self, described by Wheeler and colleagues (1997) as being essential for auto-noetic consciousness and the re-experiencing of AMs. Our findings are consistent with theories emphasizing the role of the hippocampus in retrieving memories of multifaceted autobiographical experiences (Nadel and Moscovitch, 1997), rather than those focusing on the age of the memory (Squire and Alvarez, 1995).

Overall, our data suggest that the recollective qualities of AMs are important predictors of hippocampal activation during AM retrieval, independent of other factors such as recency. Unfortunately, we were unable to tease apart the unique contributions of each of these qualities to hippocampal engagement, due to some overlap, as indicated by moderate correlations between the recollective ratings. Moreover, the three recollective qualities we investigated do not constitute an exhaustive list of factors likely contributing to autobiographical re-experience. Further studies should be designed with the aim of isolating and manipulating such factors to explore fully their contributions to the preferential activation of the hippocampus during AM retrieval.

A general limitation of this and other functional imaging studies of hippocampal engagement during memory retrieval tasks is the difficulty in distinguishing the role of retrieval from re-encoding processes. It is always possible that the AMs retrieved are also re-encoded, thus activating the hippocampus as well. The tasks we used to control for retrieval processes (sentence completion and size discrimination) also may have controlled for incidental encoding processes (Maguire, 2001; Ryan et al., 2001). Ryan and colleagues report that participants did incidentally encode information from this sentence completion task. However, tasks that involve more complex encoding, such as imagined events (e.g., Gilboa et al., 2002), would certainly provide a better control for re-encoding, but also pose some difficulties, such as uncontrolled retrieval of autobiographical information. Another possible methodological concern is that individuals may have been retrieving specific AMs associated with the pre-scan interview or other retrieval episodes, rather than the original general and specific events. Unfortunately, we do not have information regarding how often these AMs were retrieved since the original event occurred. However, we believe this to be unlikely for two reasons. Most importantly, we have found differences between general and specific AMs with regard to recollective qualities, and in particular with recency, making it likely that participants were in fact retrieving specific and general episodes rather than only specific pre-scan events. Second, the different effects that recency had on specific and general AMs suggests that subjects could not have been recovering memories of the same date (pre-scan interview) but likely were retrieving memories of the original experiences encoded at various ages.

In summary, our findings help elucidate which characteristics of AM preferentially engage the hippocampus during retrieval. It is apparent that the qualities contributing to re-experiencing, such as detail, emotionality, and personal significance are the important modulators. Further, we have shown that the level of recollective qualities modulate hippocampal activity independent of AM recency. These findings bring us a step closer to understanding the role of the hippocampus not only in

AM retrieval, but also more generally in memory processing as an integrator of various types of information which support rich and contextualized recollections.

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