Medial Prefrontal Activity Predicts Memory for Self

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The ability to remember the past depends on cognitive operations that are recruited when information is initially encountered. In the current experiment, we investigated neural processes that subserve the memorability of a fundamental class of social information: self-knowledge. Participants evaluated the extent to which a series of personality characteristics were self-descriptive. Brain activation was measured using event-related functional magnetic resonance imaging (fMRI) and contrasted based on: (i) whether each word was later remembered or forgotten; and (ii) whether or not each item was judged to be self-relevant. Results revealed that activity in medial prefrontal cortex predicted both subsequent memory performance and judgements of self-relevance. These findings extend current understanding of the nature and functioning of human memory.

Introduction

An intriguing aspect of memory function is why some events from the past spring easily to mind, while others are all too readily forgotten. But what is it that determines the memorial fate of one's prior experiences? The available psychological evidence points to the processing operations that are recruited during initial encoding as a critical determinant of subsequent memory. Generally speaking, items processed for their meaning (i.e. semantic processing) are more memorable than those that attract only superficial, surface-based processing (e.g. case judgements) (Craik and Lockhart, 1972; Craik and Tulving, 1975).

Exploring this issue further, neuroimaging investigations have sought to identify regions of the brain that are enlisted when memories are formed. This issue was initially addressed in studies using electrical scalp-recording techniques. When scalp potentials were recorded while participants memorized words, distinct neural signatures were observed for items that were later remembered relative to those that were forgotten (Fabiani *et al.*, 1986; Paller, 1990; Rugg, 1995). More recently, researchers have capitalized on advances in functional magnetic resonance imaging (fMRI) techniques to examine the same phenomenon but with enhanced spatial localization within the brain. In work of this kind, it has been shown that the level of activity in frontal and medial temporal brain regions can predict whether an item will later be remembered or forgotten (Brewer *et al.*, 1998; Wagner *et al.*, 1998b).

Reflecting the distributed nature of memory function, the neural correlates of memory formation appear to be related to the characteristics of the to-be-encoded material. Whereas the encoding of verbal information preferentially activates areas of left dorsal (near Brodmann's areas 6/44) and inferior (near Brodmann's areas 45/47) prefrontal cortex (Kapur *et al.*,

1994a,b; Demb *et al.*, 1995; Dolan and Fletcher, 1997; Brewer *et al.*, 1998; Kelley *et al.*, 1998; Wagner *et al.*, 1998b; Henson *et al.*, 1999; Kirchhoff *et al.*, 2000; Otten *et al.*, 2001; Otten and Rugg, 2001b), encoding of nonverbal, pictorial information is often associated with elevated levels of activation in homologous regions of right prefrontal cortex (Brewer *et al.*, 1998; Kelley *et al.*, 1998; Wagner *et al.*, 1998a; Kirchhoff *et al.*, 2000). Emotional intensity is yet another factor that impacts on the neural processes that support subsequent remembering, such that differential amygdala activation correlates with the memorability of emotional experiences (Cahill *et al.*, 1996; Hamann *et al.*, 1999; Canli *et al.*, 2000; Hamann, 2001). Taken together, these findings suggest that, depending on the characteristics of the to-be-encoded material, discrete brain regions support the memorability of prior experience.

In such a distributed neural architecture, it is likely that other cortical areas also contribute to memory formation, particularly if task demands are manipulated to encourage reliance on distinct processing operations. Take, for example, the central psychological topic of the self (James, 1890). Knowledge about the self is typically better remembered than other types of semantic information, prompting the assertion that the self may be a unique cognitive structure that possesses special mnemonic abilities (Rogers *et al.*, 1977; Maki and McCaul, 1985). Two separate effects appear to contribute to this memory facilitation. Tasks that permit self-referential processing promote better subsequent memory than tasks that encourage semantic processing; this task-dependent manipulation is robust and is typically referred to in the psychological literature as the self-reference effect in memory (Symons and Johnson, 1997). For example, Rogers *et al.* (1977) showed that trait adjectives that were processed with reference to the self (e.g. 'Does the word *honest* describe you?') were better recalled than comparable items that were processed only for their general meaning (e.g. 'Does the word *honest* mean the same as *trustworthy*?'). Additionally, the memory enhancement that accompanies self-referential processing is further modulated by the individual responses that are made to items. Items judged to be self-relevant are remembered better than items judged not to be relevant to self (Rogers *et al.*, 1977).

It has recently been suggested that distinct neural operations may subserve the functioning of the self-memory system (see Conway and Pleydell-Pearce, 2000). Although direct support has yet to be garnered for this viewpoint, suggestive evidence can be found in recent work that has investigated the neural substrates of self-referential mental activity and the retrieval of autobiographical memories. Areas of prefrontal cortex, particularly medial prefrontal cortex (MPFC), appear to be selectively engaged in tasks that involve self-referential processing operations (Craik *et al.*, 1999; Gusnard *et al.*, 2001;

Johnson *et al.*, 2002; Kelley *et al.*, 2002). But does this activity also contribute to memory formation? Is the memorability of self-knowledge supported by distinct neural operations? We used event-related fMRI to investigate this issue.

In an incidental memory-encoding task, brain activity was measured while participants judged the personal relevance of a series of personality characteristics. Afterwards, their memory for the items was assessed in a surprise memory test. By contrasting brain activation elicited by items that were subsequently remembered with those that were later forgotten, brain regions that predict successful recognition could be identified (Fig. 1). We also investigated whether brain activity could further predict which items were deemed to be self-descriptive by contrasting activation for traits judged to be self-relevant with activity for traits judged not to be relevant to self.

Materials and Methods

Subjects

Twenty-two participants between the ages of 18 and 31 (seven male, mean age = 20) were recruited from the local Dartmouth community. All participants were strongly right-handed as measured by the Edinburgh handedness inventory (Raczkowski *et al.*, 1974). Participants reported no significant abnormal neurological history and all had normal or corrected-to-normal visual acuity. Participants were either paid for their participation or received course credit. All participants gave informed consent in accordance with the guidelines set by the Committee for the Protection of Human Subjects at Dartmouth College.

Imaging Procedure

Imaging was performed on a 1.5 Tesla whole body scanner (General Electric Medical Systems Signa, Milwaukee, WI) with a standard head coil. Visual stimuli were generated using an Apple G3 Laptop computer running PsyScope software (Cohen *et al.*, 1993). Stimuli were projected to participants with an Epson (model ELP-7000) LCD projector onto a screen positioned at the head end of the bore. Participants viewed the screen through a mirror. A fiber-optic, light-sensitive key press interfaced with the PsyScope Button Box (New
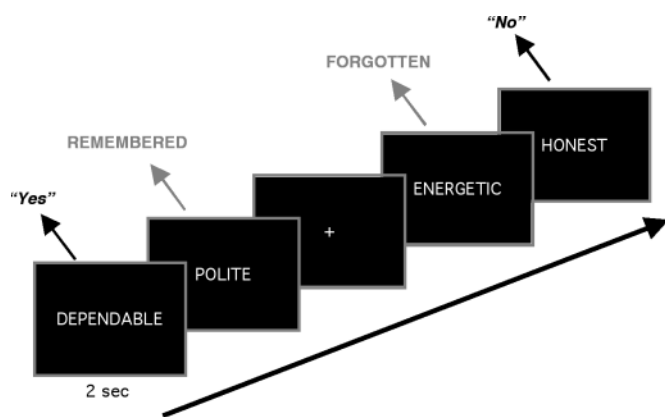

Figure 1. Participants were scanned while viewing trait adjectives and indicated (via a yes/no button press) whether the word was self-descriptive. Two separate analyses were performed. To identify brain regions that were sensitive to self-relevance, word trials were sorted based on how participants responded to each trait descriptor. In this analysis, 'yes' responses were contrasted with 'no' responses (black arrows). To identify brain regions that predicted subsequent memory performance, word trials were re-sorted based on a surprise memory test given outside the scanner. In this second analysis, word trials that were later remembered were contrasted with word trials that were later forgotten (gray arrows).

Micros, Dallas, TX) was used to record participants' behavioral performance. Cushions were used to minimize head movement.

Anatomical images were acquired using a high-resolution 3-D spoiled gradient recovery sequence (SPGR; 124 sagittal slices, T_E = 6 ms, T_R = 25 ms, flip angle = 25°, voxel size = 1 × 1 × 1.2 mm). Functional images were collected in runs using a gradient spin-echo echo-planar sequence sensitive to blood oxygen level-dependent (BOLD) contrast (T_2*) (T_R = 2000 ms, T_2* evolution time = 35 ms, flip angle = 90°, 3.75 × 3.75 mm in-plane resolution). During each functional run, 90 sets of axial images (20 slices; 5.5 mm slice thickness, 1 mm skip between slices) were acquired allowing complete brain coverage.

Behavioral Tasks

Participants were imaged during three functional runs while making judgements about trait adjectives—specifically, 'Does this adjective describe you?'. Participants indicated their responses via a left- or right-handed key press. Each trial lasted 2000 ms and consisted of a unique trait adjective (e.g. 'polite') presented for 750 ms followed by a central fixation (plus sign) for 1250 ms. All text was presented in Geneva font (white letters on a black background; letters subtended ~0.5° of visual angle). Prior to the first functional run, participants were given practice trials to familiarize them with the task. Practice continued until participants indicated they were comfortable with the task.

A total of 540 unique adjectives were selected from a pool of normalized personality trait adjectives (Anderson, 1968). Words were divided into lists of 60 that were counterbalanced for word length, number of syllables, and valence (half of the words in each list were positive traits, the remaining half were negative traits). Across participants, lists were rotated such that each participant viewed only three of the lists during scanning. During each of the three functional runs, 60 word trials and 30 fixation trials were pseudo-randomly intermixed. Fixation trials consisted of a central fixation point presented on the screen for 2000 ms. These trials were included to introduce 'jitter' into the time series so that unique estimates of the hemodynamic responses for the trial types of interest could be computed (Ollinger *et al.*, 2001) (see Data Analysis below).

Following the three encoding runs, participants were given a surprise recognition memory test. Participants viewed all 180 trait adjectives that were previously presented during scanning along with 180 new trait adjectives. Words were presented individually in the center of the computer screen with self-paced timing. A fixation point (500 ms) preceded each word. Participants were asked to indicate via button press whether they remembered the word with high confidence, with low confidence, or whether they believed the word to be new.

Data Analysis

Functional MRI data were analyzed using Statistical Parametric Mapping software (SPM99, Wellcome Department of Cognitive Neurology, London, UK) (Friston *et al.*, 1995). For each functional run, data were preprocessed to remove sources of noise and artifact. Functional data were corrected for differences in acquisition time between slices for each whole-brain volume, realigned within and across runs to correct for head movement, and coregistered with each participant's anatomical data. Functional data were then transformed into a standard anatomical space (2 mm isotropic voxels) based on the ICBM 152 brain template (Montreal Neurological Institute) which approximates Talairach and Tournoux atlas space (Talairach and Tournoux, 1988). Normalized data were then spatially smoothed [6 mm full-width-at-half-maximum (FWHM)] using a Gaussian kernel. Analyses took place at two levels: formation of statistical images; and regional analysis of hemodynamic responses.

First, for each participant, general linear models, incorporating task effects [modeled with a canonical set of three functions: the hemodynamic response function, its temporal derivative, and its dispersion derivative (Friston *et al.*, 1998)], a mean for each functional run, and a linear trend for each functional run was used to compute parameter estimates (β) and *t*-contrast images (containing weighted parameter estimates) for each comparison at each voxel. These individual contrast images were then submitted to a second-level, random-effects analysis to create mean *t*-images (thresholded at *P* = 0.0001,

uncorrected; minimum cluster size = 20 mm^3). An automated peak-search algorithm identified the location of peak activations and deactivations based on z-value and cluster size. This analysis allowed several comparisons to be made. First, word trials could be compared with baseline to identify general task-related activations and deactivations. Second, parameter estimates for trials that were later remembered (high confidence hits) could be computed and contrasted with parameter estimates for trials that were later forgotten (low confidence hits and misses). Third, parameter estimates for words judged to be self-relevant could be computed and contrasted with parameter estimates for words judged not to be self-relevant. This was accomplished by computing a separate design matrix for each participant where trials were coded based on their yes/no responses during the self-reference task.

To obtain time courses for trial types in an unbiased manner, regions of interest (ROIs) were defined based on peaks identified in the mean t-image comparing all word trials to baseline. In this way, each trial type contributed equally to the generation of ROIs. All significant voxels ($P < 0.0001$) within 10 mm of a peak location were included in each region. For each participant, hemodynamic response functions (10 frames long) for each trial type were then estimated across each ROI using a finite impulse response formulation of the general linear model (Burock and Dale, 2000; Ollinger et al., 2001). The parameter estimates for this model (calculated using the least-squares solution to the general linear model) are estimates for the temporally evolving response magnitude at each of the 10 points in peristimulus time, selectively averaged across all occurrences of that peristimulus time interval. This approach has recently been implemented by Poldrack and colleagues as an add-on toolbox to the SPM analysis software (SPM ROI Toolbox, http://spm-toolbox.source-forge.net).

Results

Behavioral Data

Following the scanning session, participants were given a recognition memory test. For each word on the subsequent memory test, participants responded 'high confidence studied', 'low confidence studied', or 'new'. A repeated measures analysis of variance (ANOVA) examining effects of word type (old/new), recognition response (high confidence/low confidence/new), and the word type by recognition response interaction revealed a significant main effect of recognition response [$F(2,40) = 29.36$, $P < 0.0001$] and a significant interaction between word type and recognition response [$F(2,40) = 171.41$, $P < 0.0001$]. Planned comparisons showed that participants were able to discriminate old ($M = 72\%$) and new (22%) words when responding with high confidence [$F(1,21) = 198.98$, $P < 0.0001$], but were incorrect more often than they were correct when responding with low confidence [Old = 17%, New = 25%; $F(1,21) = 5.50$, $P < 0.05$]. The inability to discriminate old from new words when responding with low confidence likely reflects the adoption of a guessing strategy during the recognition task. Importantly, response latencies during the self-reference judgements did not differ for words that were later remembered with high confidence ($M = 1095$ ms), low confidence ($M = 1116$ ms), or those that were subsequently forgotten ($M = 1118$ ms) ($F < 1$, NS).

A second ANOVA examining subsequent memory performance as a function of participants' responses at encoding (self-relevant vs not self-relevant) revealed a main effect of recognition response [$F(2,40) = 163.67$, $P < 0.0001$] and an interaction between encoding judgement and recognition response [$F(2,40) = 18.59$, $P < 0.0001$]. Planned comparisons revealed that words judged to be self-relevant were more likely to be remembered with 'high confidence' than words judged not to

be self-relevant (78% and 67%, respectively, $F(1,21) = 23.55$, $P < 0.001$). Response latencies were significantly faster for words judged to be 'self-relevant' ($M = 1032$ ms) than for words judged not to be 'self-relevant' [$M = 1079$ ms] [$t(21) = 3.36$, $P < 0.005$].

fMRI Data

Figure 2 shows statistical activation maps for all self-reference trials relative to the baseline fixation task. Several brain regions exhibited increased activation relative to baseline, including bilateral regions of the striate and extrastriate visual cortex, the parahippocampal gyrus, the parietal cortex, dorsal PFC (near BA 6/44), and cerebellum. Activations were also noted in left ventral PFC (near BA 45/47), left motor cortex, left thalamus, left caudate nucleus, and anterior cingulate. Other brain regions exhibited decreases in activation relative to baseline, including MPFC (BA 10), the posterior cingulate (near precuneus), the right hippocampus, and bilateral regions in lateral temporal and parietal cortex.

Imaging data were then analyzed by sorting encoding trials in two ways. First, encoding trials were categorized based on whether the word was subsequently remembered or forgotten on the post-scan memory test. High confidence hits were classified as 'remembered'; low confidence hits and misses were collectively classified as 'forgotten' as behavioral analyses revealed that participants could not discriminate studied from new words when responding with low confidence. Indeed, participants were incorrect more often than they were correct when responding with low confidence. In a second analysis, encoding trials were separately categorized based on participants' responses during the self-reference task (i.e. whether they classified the item as 'self-relevant' or 'not self-relevant').

When encoding trials were contrasted based on subsequent memory performance (remembered > forgotten), differential activation was observed in MPFC, left anterior prefrontal cortex, and bilateral regions of the parahippocampal gyrus (Fig. 3). The reverse comparison (forgotten > remembered) revealed no significant activations. When encoding trials were contrasted based on whether participants judged a word to be
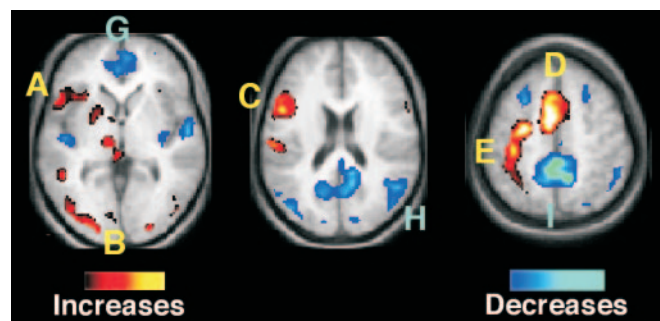

Figure 2. Whole brain statistical activation maps show general task-related activity in relation to baseline averaged across all 22 participants. Images are axial sections in the Talairach and Tournoux (1988) atlas space. Sections from left to right correspond to $z = -4$, $z = 24$ and $z = 44$. Colored pixels exceeded the statistical threshold and are superimposed on corresponding anatomy images. The left side of the image corresponds to the left side of the brain. Increases in activation (red color scale; areas labeled in yellow letters) were observed in the (A) left inferior frontal cortex, (B) extrastriate visual cortex, (C) left dorsal frontal cortex, (D) anterior cingulate, and (E) left motor cortex. Decreases in activation (blue color scale, areas labeled in blue letters) were noted in the (G) medial prefrontal cortex, (H) right parietal cortex, and (I) posterior cingulate.
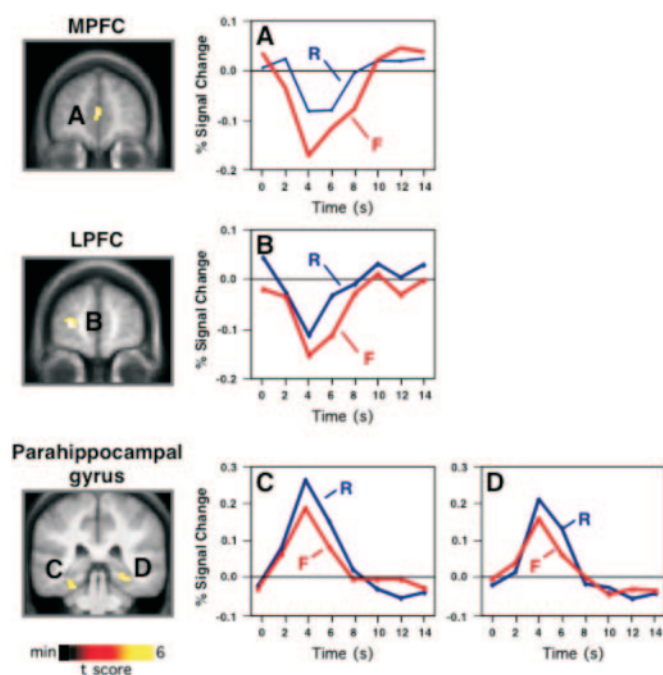
MPFC

LPFC

Parahippocampal gyrus

min ■■■■■ 6
t score

Figure 3. Statistical activation maps reveal brain regions that demonstrate greater activity during self-judgements for words later remembered (R) relative to words later forgotten (F). Images are coronal sections averaged across participants. The left side of the image corresponds to the left side of the brain. Greater activation was observed in medial prefrontal cortex (MPFC) (A: 0, 50, 8; BA 10), left anterior prefrontal cortex (B: –24, 58, 1; BA 10), and bilateral regions of the parahippocampal gyrus (C: –26, –31, –16 and D: 27, –33, –8). Time courses were computed for each condition in an unbiased manner by generating ROIs from the combined statistical activation map comparing all word trials to baseline (Fig. 2). An automated algorithm identified all contiguous voxels within 10 mm of the peak that reached the significance level (P < 0.0001).
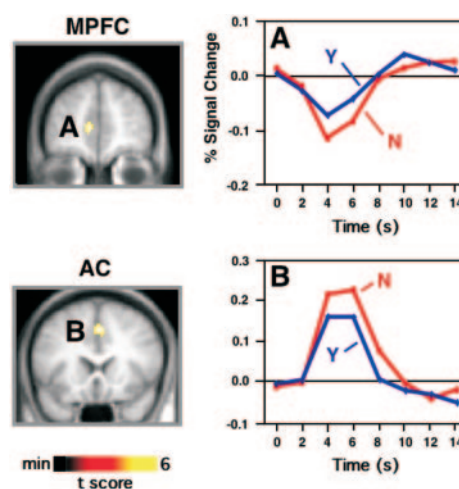

MPFC

AC

min ■■■■■ 6
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Figure 4. Statistical activation maps reveal brain regions that demonstrate differential activity dependent on whether trait adjectives were judged to be self-relevant (Y) or not (N). Images are coronal sections averaged across participants. The left side of the image corresponds to the left side of the brain. Traits judged to be self-relevant produced greater activation in MPFC (A: –9, 50, 0; BA 10) than did traits judged not to be self-relevant. The reverse pattern (N > Y) was observed in the anterior cingulate (B: 2, 19, 40; BA 32). Time courses were computed for each condition in an unbiased manner by generating ROIs from a combined statistical map comparing all word trials to baseline. An automated algorithm identified all contiguous voxels within 10 mm of the peak that reached the significance level (P < 0.0001).

Thus, Region 2 predicted subsequent memory and ratings of self-descriptiveness. The failure to observe a memory × rating interaction in either region indicated that the linkage between MPFC activity and subsequent memory performance was not driven only by trials in which the items were judged to be self-descriptive.

Discussion

The present study used event-related fMRI to investigate the neural basis of the self-reference effect in memory. A network of brain regions were active when participants were asked to evaluate whether personality traits were self-descriptive, replicating most of the regions observed in earlier work using a similar experimental paradigm (Kelley *et al.*, 2002). While some areas exhibited increased activation relative to the base-line control task, other brain areas, most notably MPFC, exhibited decreased activation relative to the resting baseline condition. Consistent with a broad literature on task-related BOLD decreases, responses in MPFC are almost always observed as decreases relative to low-level baseline conditions (Shulman *et al.*, 1997; Gusnard and Raichle, 2001; Raichle *et al.*, 2001). Further, resting metabolic activity in MPFC has been shown to be high at rest (Ingvar, 1979; Raichle *et al.*, 2001).

For a subset of these regions, the magnitude of activation differed as a function of the memorial fate of the words. When comparing subsequently remembered to forgotten words, differences were noted in MPFC, left anterior prefrontal cortex, and parahippocampal gyrus. Importantly, these results can not be attributed to time-on-task effects, as the response latencies during self-reference judgements did not differ as a function of whether words were later remembered or forgotten. The greater left parahippocampal activation for subsequently remembered words is consistent with results from earlier work that has examined memory formation for verbal experiences (Wagner *et al.*, 1998b). Importantly,

self-descriptive, significant differences were noted in an over-lapping region of MPFC (yes > no) and the anterior cingulate (no > yes) (Fig. 4). Thus, MPFC activity was linked to both subsequent memory and participants' responses at encoding.

The behavioral results revealed that self-descriptive items were remembered better than their non-descriptive counter-parts (replicating Rogers *et al.*, 1977). An open question, there-fore, was whether the linkage between MPFC activity and subsequent memory was driven entirely by 'yes' responses at encoding. To explore this possibility, parameter estimates for subsequently remembered and forgotten words were calcu-lated separately for the 'yes' and 'no' responses. ANOVAs were then conducted on the two MPFC regions identified in the subsequent memory (Region 1: 0, 50, –8) and self-relevance (Region 2: –9, 50, 0) analyses. Each 2 × 2 ANOVA examined the main effects of subsequent memory performance (remem-bered/forgotten), self-relevance rating (yes/no), and the memory × rating interaction. In Region 1, results revealed a single main effect of subsequent memory [remembered > forgotten; $F(1,21) = 8.9$, $P < 0.01$]. The main effect of rating [$F[1,21] = 1.8$, $P = 0.2$] and the memory × rating interaction ($F < 1$) were not significant. As such, Region 1 predicted memory performance for both 'yes' and 'no' responses and was not modulated by the self-descriptiveness of the items. In Region 2, the ANOVA revealed both a main effect of subse-quent memory [remembered > forgotten; $F(1,21) = 5.2$, $P < 0.05$] and an effect of rating [yes > no; $F(1,21) = 4.7$, $P < 0.05$]. The memory × rating interaction was not significant ($F < 1$).

however, the current study also confirmed the involvement of frontal-polar regions, notably the MPFC and left anterior PFC, in the formation of memories. These findings are noteworthy as the additional recruitment of these frontal regions, particularly MPFC, may explain the general memory enhancement that is afforded to materials that trigger self-referential mental activity (Symons and Johnson, 1997). Although MPFC typically is deactivated by ongoing cognitive operations (Raichle *et al.*, 2001), its continued activity during self-relevant processing appears to contribute to this memory advantage.

What has been observed in the present study and others examining the neural correlates of subsequent remembering may be a general phenomenon underlying memory formation. To the extent that a task recruits brain regions involved in distinct processing operations, neural activity in those regions should predict subsequent memory performance. Thus, in much the same way that amygdala activation enhances the memorability of emotional information (Hamann *et al.*, 1999; Canli *et al.*, 2000; Erk *et al.*, 2003), and left and right prefrontal activation the memorability of verbal (Wagner *et al.*, 1998b; Henson *et al.*, 1999; Baker *et al.*, 2001; Buckner *et al.*, 2001; Davachi *et al.*, 2001; Otten *et al.*, 2001; Otten and Rugg, 2001a; Reber *et al.*, 2002; Strange *et al.*, 2002) and visual information (Brewer *et al.*, 1998; Kirchhoff *et al.*, 2000), memory for material pertaining to the self may be enhanced through the additional involvement of MPFC in the encoding experience. In this respect, MPFC would appear to be a critical component of the human memory system.

Corroborating this viewpoint, Figure 5 depicts regions of the brain that have been shown to support memory formation. Based on the extant literature on this topic (see Tables 1–4 in Fig. 6), Figure 5 clearly reveals the distributed nature of the neural operations that drive successful memory formation.
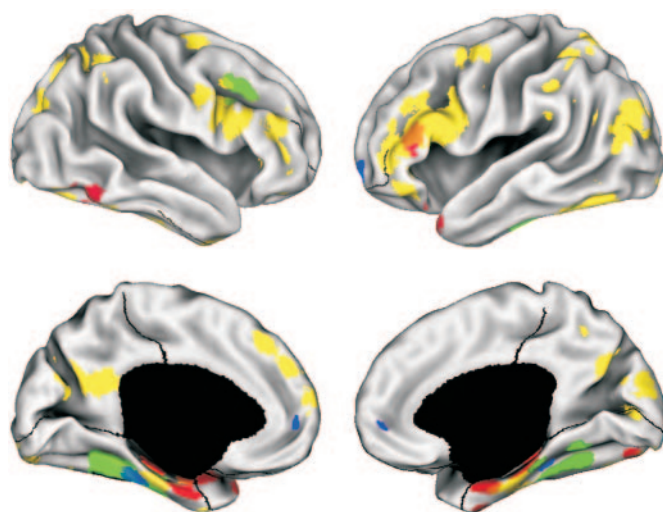

Figure 5. Brain regions engaged during human memory formation vary as a function of the to-be-remembered materials and task demands. Shown here are activations that predict subsequent memory performance from previously published reports (Tables 1–4 in Fig. 6) superimposed on inflated cortical renderings of the lateral (top) and medial (bottom) surfaces (Van Essen *et al.*, 2001). Activations are plotted as spherical regions (6 mm radius) centered on each peak reported in the tables. Activations are color-coded to depict regions that predict successful memory formation during verbal processing tasks (yellow; Table 1), visuo-spatial processing tasks (green; Table 2), emotional processing tasks (red; Table 3), and self-referential processing tasks (blue; Table 4).

Depending on the characteristics of the to-be-encoded material (i.e. visual, verbal, emotional) and the nature of the task at hand, discrete areas of the brain support the process of memory formation. In this respect, MPFC activity appears to be a critical component of memory formation when material is encountered in a task context that elicits self-reflection. As this cortical region has not emerged in previous work of this kind (see Fig. 5), self-referential mental activity likely entails more than elaborative semantic encoding; other component processes are also involved. One emerging possibility is that activity observed in MPFC indexes the metacognitive aspects of specific processing operations, notably the task of mentalizing about self (Johnson *et al.*, 2002). It is possible that these metacognitive operations, in turn, may enhance the formation of self-relevant memories. One task for future research will be to investigate this possibility. Notwithstanding the distributed nature of the human memory system, the commonality observed across studies investigating memory formation appears to be the participation of medial temporal brain regions in this task (see Tables 1–4 in Fig. 6). The function of these regions is likely to bind together the task-dependent processing outcomes of frontal and other cortical regions to form enduring memory traces (Moscovitch, 1992; Squire, 1992; Cohen and Eichenbaum, 1993).

The present results suggest further specificity in an overlapping region of MPFC for the task of self-referencing. Activity in this region of MPFC also predicts, on average, whether individuals will declare a trait to be self-descriptive. In contrast, non-descriptive characteristics are associated with increased activity in the anterior cingulate. This latter finding is interesting given the acknowledged role of the anterior cingulate in conflict monitoring (Botvinick *et al.*, 2001). To assess the descriptive accuracy of personality characteristics, people may compare the presented items with an activated conception or model of self (e.g. real or idealized self). Conflict will evidently arise when specific traits do not match this internal representation. As evidenced in the present investigation, these conflicts may be signaled by elevated levels of activity in the anterior cingulate. Thus, not only does the anterior cingulate monitor the extent to which ongoing behavior is concordant with one's current plans and objectives, but it may also evaluate the degree to which self is in conflict with environmental inputs. In so doing, the present findings demonstrate the importance of the anterior cingulate in pivotal aspects of social-cognitive functioning.

In summary, our results offer a neural substrate for the self-reference effect in memory and extend current understanding of the neural events that underlie memory formation. Rather than merely reflecting an enhanced contribution from brain regions typically engaged during elaborative semantic encoding (e.g. left inferior frontal cortex), a notion that would provide strong support for 'ordinary' theories of the self-reference effect (Klein and Kihlstrom, 1986; Greenwald and Banaji, 1989), the memorial advantage afforded to self-knowledge appears to depend on the additional recruitment of MPFC, at least in the task context considered herein. In this regard, self-referential processing appears to be functionally dissociable from general semantic processing, suggesting that the self-memory system may indeed evoke some distinct cognitive operations.

TABLE 1: Regions predicting subsequent memory during verbal processing

STUDY	REGION	x	y	z
Baker et al, 2001				
abstract/concrete	L Inferior frontal gyrus	-45	5	26
	L Inferior frontal gyrus	-53	19	22
	L Inferior frontal gyrus	-45	39	6
	L Fusiform gyrus	-41	-73	-16
	R Inferior/middle frontal gyrus	45	35	20
	R inferior frontal/precentral gyrus	51	7	32
	R Fusiform gyrus	21	-87	-10
case judgments	L Inferior frontal gyrus	-47	31	18
	L Fusiform gyrus	-37	-69	-8
	R Inferior frontal/precentral gyrus	49	1	24
Buckner et al, 2001				
episodic retrieval as	L Medial prefrontal cortex	-9	63	18
encoding	L vInferior frontal gyrus	-43	33	6
	L pInferior frontal gyrus	-49	23	24
	L Prefrontal cortex	-41	-1	52
	L Frontal cortex	-39	-1	30
	L pInferior frontal gyrus	-47	9	22
	L Parietal/occipital	-35	-63	24
	L Parietal/occipital	-43	-75	18
	L Parietal/occipital	-37	-79	30
	Precuneus	-5	-63	26
	Cingulate gyrus	-7	-49	26
	L Occipital/temporal	-47	-63	-8
	R Parietal/occipital	29	-75	32
Davachi et al, 2001				
rote rehearsal	L Inferior frontal gyrus	-39	9	30
	L Inferior frontal gyrus	-45	30	-9
	L Superior parietal	-24	-57	45
	R Superior parietal	40	-63	45
Henson et al, 1999				
lexical decision	L Inferior frontal gyrus	-45	24	-6
	L Middle frontal gyrus	-57	18	27
	L Precuneus	-27	-60	60
	R Parahippocampal gyrus	18	-15	-24
	R Precuneus	2	-69	33
Otten & Rugg, 2001				
animacy judgments	L Medial frontal gyrus	-3	48	33
	L Inferior frontal gyrus	-51	18	15
syllable judgments	L Intraparietal sulcus	-39	-45	51
	L Fusiform gyrus	-42	-48	-15
	L Superior occipital gyrus	-24	-75	33
	L Cuneus	-27	-84	24
	R Inferior frontal gyrus	36	36	3
	R Intraparietal sulcus	39	-45	45
	R Fusiform gyrus	48	-48	-21
Otten et al, 2001				
animacy	L Inferior frontal gyrus	-36	36	9
	L Superior frontal gyrus	-3	36	45
	L Inferior frontal gyrus	-51	27	18
	L Inferior frontal gyrus	-51	12	21
	L Hippocampus	-27	-15	-12
	L Hippocampus	-30	-42	0
	L Fusiform/inferior temporal gyrus	-48	-54	-18
	L Lateral parietal cortex	-45	-39	33
	L Occipital cortex	-18	-93	-6
	R Inferior frontal gyrus	33	36	-9
	R Inferior frontal gyrus	39	27	9
	R Inferior frontal gyrus	57	12	21
	R Superior frontal gyrus	27	-3	57
	R Inferior temporal gyrus	33	3	-45
	R Subcentral gyrus	48	-6	18
	R Lateral occipital cortex	12	-87	24
	R Calcarine cortex	18	-81	12
Reber et al, 2001				
intentional encoding	L Inferior frontal gyrus	-58	10	21
('remember' & 'forget' cues)	L Parahippocampal/pHippocampus	-30	-34	-12
	R Superior parietal cortex	29	-61	46
Strange et al, 2002				
rote rehearsal	L Perirhinal cortex	-30	-4	-36
	L Hippocampus	-22	-26	-16
	R Parahippocampal cortex	36	-24	-24
	R Fusiform gyrus	38	-68	-14
Wagner et al, 1998				
abstract/concrete	L Inferior frontal gyrus	-50	9	34
	L Inferior frontal gyrus	-50	25	12
	L Frontal operculum	-31	22	6
	L Parahippocampal gyrus	-31	-46	-12
	L Fusiform/inferior temporal gyrus	-43	-55	29

TABLE 2: Regions predicting subsequent memory during visual processing

STUDY	REGION	x	y	z
Brewer et al, 1998				
indoor/outdoor	L Parahippocampal cortex	-34	-29	-18
	L Parahippocampal cortex	-33	-34	-13
	L Parahippocampal cortex	-27	-40	-9
	L Parahippocampal cortex	-29	-46	-6
	R Inferior Frontal cortex	40	15	32
	R Parahippocampal cortex	22	-35	-15
	R Parahippocampal cortex	24	-48	-8
Kirchhoff et al, 2000				
indoor/outdoor	L Parahippocampal gyrus	-28	-37	-9
	R Parahippocampal gyrus	31	-24	-6
	Hippocampus	28	-30	-6

TABLE 3: Regions predicting subsequent memory during emotional processing

STUDY	REGION	x	y	z
Canli et al, 2000				
emotionally intense scenes	L Amygdala	-20	-10	-14
Erk et al. 2003				
all emotional scenes	L Inferior frontal gyrus	-51	27	15
neutral scenes	L Inferior frontal gyrus	-42	21	-21
positive scenes	Parahippocampal gyrus	24	-9	-36
	Parahippocampal gyrus	33	-33	-27
negative scenes	Amygdala	18	-6	-9
Hamann et al, 1999				
pleasant pictures	L Amygdala	-21	-4	-10
	L Hippocampus	21	-19	-7
	R Amygdala	19	-9	-10
aversive pictures	L Amygdala/periamygdaloid cortex	-13	-7	-18
	L Parahippocampal gyrus	-15	-9	-22
	L Hippocampus	-33	-27	-9
	R Amygdala	17	-7	-18
	R Parahippocampal gyrus	16	-7	-22
	R Hippocampus	24	-22	-6
interesting pictures	R Hippocampus	34	-30	-3

TABLE 4: Regions predicting subsequent memory during self-referential processing

STUDY	REGION	x	y	z
Macrae et al				
trait judgments	L Anterior prefrontal cortex	-24	58	1
	Medial prefrontal cortex	0	50	8
	L Parahippocampal gyrus	-26	-31	-16
	R Parahippocampal gyrus	27	-33	-8

Figure 6. Regions predicting subsequent memory during processing. Table 1, verbal processing; Table 2, visual processing; Table 3, emotional processing; Table 4, self-referential processing.

Notes

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