J Neurophysiol 94: 813–820, 2005.
First published February 23, 2005; doi:10.1152/jn.01200.2004.

Distinct Roles for Lateral and Medial Anterior Prefrontal Cortex in Contextual Recollection

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Submitted 22 November 2004; accepted in final form 21 February 2005

Simons, Jon S., Sam J. Gilbert, Adrian M. Owen, Paul C. Fletcher, and Paul W. Burgess. Distinct roles for lateral and medial anterior prefrontal cortex in contextual recollection. *J Neurophysiol* 94: 813–820, 2005. First published February 23, 2005; doi:10.1152/jn.01200.2004. A key feature of human recollection is the ability to remember details of the context in which events were experienced, as well as details of the events themselves. Previous studies have implicated a number of regions of prefrontal cortex in contextual recollection, but the role of anterior prefrontal cortex has so far resisted detailed characterization. We used event-related functional MRI (fMRI) to contrast recollection of two forms of contextual information: *1*) decisions one had previously made about stimuli (task memory) and *2*) which of two temporally distinct lists those stimuli had been presented in (list memory). In addition, a retrieval cue manipulation permitted evaluation of the stage of the retrieval process in which the activated regions might be involved. The results indicated that anterior prefrontal cortex responded significantly more during recollection of task than list context details. Furthermore, activation profiles for lateral and medial aspects of anterior prefrontal cortex suggested differing roles in recollection. Lateral regions seem to be more involved in the early retrieval specification stages of recollection, with medial regions contributing to later stages (e.g., monitoring and verification).

INTRODUCTION

Our understanding of the role played by the human prefrontal cortex (PFC) in the recollection of previously experienced events has advanced considerably in recent years as a result of research using functional neuroimaging. One position on which a current consensus exists is that the functions subserved by two broad PFC regions, ventrolateral and dorsolateral PFC, include elaborative processing of retrieval cues and monitoring and verification of retrieved information, respectively (see Fletcher and Henson 2001; Simons and Spiers 2003 for recent reviews). However, characterization of the role in recollection played by another prominent prefrontal region, anterior PFC [broadly corresponding to Brodmann area (BA) 10], has typically resisted such general agreement (Ramnani and Owen 2004). This is despite activation in this region being reported in numerous studies that have involved the recollection of contextual details relating to past events (Dobbins and Wagner 2005; Dobbins et al. 2002; Kahn et al. 2004; Ranganath et al. 2000; Rugg et al. 1999). Perhaps one reason for the lack of consensus in identifying the role played by anterior PFC is that a number of equally well-conducted, ostensibly very similar context recollection studies failed to identify activation in this region (Henson et al. 1999; Nyberg et al. 1996; Suzuki et al. 2002).

In a recent study, Simons et al. (2005) investigated whether a distinction originating from several cognitive theories of memory might provide assistance with characterizing the involvement of anterior PFC in the control of recollection. According to these theories, it is possible to distinguish between recollection of contextual details that, at the time of an event occurring, were either derived from the external world (e.g., when and where the event happened) or generated internally (e.g., our thoughts and feelings about the event) (Burgess and Shallice 1996; Johnson et al. 1993; Schacter et al. 1998; Tulving 1983). Simons et al. (2005) explored whether anterior PFC might be sensitive to this distinction by contrasting recollection of participants' previous thoughts (e.g., remembering which of two study tasks were undertaken with stimuli) with recollection of a different type of context (e.g., which of two positions on a monitor screen stimuli were studied in). The results showed that activation in regions of anterior PFC was differentially modulated according to the nature of the contextual details retrieved, exhibiting significantly greater response during recollection of task than position details (Simons et al. 2005; see also Dobbins and Wagner 2005).

The aim of the present study was to investigate in more detail the involvement of anterior PFC in recollective memory. If the distinction between different types of context is to serve as a useful account of activation in this region, differential recruitment should also be evident when recollection of task is contrasted with memory for another kind of contextual detail, such as *when* a stimulus was previously presented. Accordingly, study phases in the present experiment comprised two temporally distinct lists of stimuli. As in our previous study (Simons et al. 2005), one of two study tasks was undertaken with each stimulus, with task order pseudo-randomized within each list. If anterior PFC is reliably sensitive to the retrieval of different kinds of contextual details, then significant differences in activation would be predicted when contrasting recollection of task versus list context details.

This study also attempted to ascertain the stage of the retrieval process to which anterior PFC might contribute: the specification of retrieval strategies before a retrieval search (a stage termed, retrieval orientation; Rugg and Wilding 2000), or the recovery and subsequent monitoring of stored information (Burgess and Shallice 1996). To study this issue, a test phase

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manipulation was employed whereby a recollection cue specifying the type of contextual detail to be retrieved on the upcoming trial was either followed by a previously studied target stimulus (in which case it would be expected that a retrieval search would be undertaken) or followed by a control stimulus which would not provoke the occurrence of a retrieval search. If anterior PFC is involved in preretrieval processes, activation would be expected both during trials in which both cue and target stimulus are presented, and during cue-only trials. On the other hand, if anterior PFC plays a role in retrieval search or postretrieval monitoring of recovered information, activation would not be predicted during trials in which target stimuli are not presented.

METHODS

Participants

Sixteen right-handed native speakers of English (6 males and 10 females), with normal or corrected-to-normal vision, took part in the experiment. The volunteers (mean age = 22.9 yr; range, 18–29 yr) were screened using a comprehensive medical questionnaire and informed consent was obtained in a manner approved by the Addenbrooke's NHS Trust Local Research Ethics Committee. Data from one additional participant was excluded from the analysis due to poor task performance.

Design and materials

The stimuli consisted of 80 words and 80 grayscale photographs of famous faces. Thirty-two of the words (e.g., jazz) and 32 of the faces (e.g., Audrey Hepburn) related to entertainment and 32 words (e.g., veto) and 32 faces (e.g., Thabo Mbeki) related to politics. Thus 64 words and 64 faces were used as target items in the study and test phases. In addition, eight living and eight nonliving concrete words and eight male and eight female famous faces drawn from fields other than entertainment or politics, were used as baseline items in the test phase. The words assigned to each experimental condition were matched as closely as possible for Kucera-Francis frequency, and the famous faces for gender and approximate time period of fame.

There were 16 blocks in the experiment, which alternated between study and test phases (Fig. 1). Each study phase comprised two lists of eight items each. Participants undertook a semantic task with 50% of the items in each list (deciding whether each item related more to entertainment or politics) and a pleasantness task (deciding whether each item seemed pleasant or unpleasant) with the other 50% of items, with task order randomly distributed within each list. There were 28 trials in each test phase, 8 of which assessed memory for which task (entertainment/politics or pleasant/unpleasant) had been undertaken with items in the preceding study phase; 8 asked which of the two study lists (first or second) items had appeared in; 4 were baseline trials involving a nonrecollective judgment (living or nonliving judgment with words; male or female judgment with faces) to control for perceptual, decision, and motor demands; and 8 involved presentation of a retrieval cue without being followed by target item (cue-only trials) to investigate retrieval orientation effects. Four different versions of the paradigm were created, which systematically counterbalanced the task undertaken in the study phase (entertainment/politics or pleasant/unpleasant) and which of the two study lists items appeared in (first list or second list). Items were also counterbalanced in terms of the type of recollection that was cued during the test phase (memory for task or list), and within each phase item order was pseudo-randomized such that no more than three consecutive trials were of the same condition.

Procedure

Each study phase consisted of two lists of eight items each, with the beginning of each list signaled by a "List 1" or "List 2" marker. In each study trial, a cue appeared at the bottom of the screen, indicating the task that was to be carried out during that trial. After 1 s, the stimulus item (either a word or famous face) was presented in the center of the screen. If the cue was "1 = entertainment 2 = politics," participants were instructed to decide whether the stimulus item related more to entertainment or to politics and press the appropriate button on a buttonbox. If the cue was "1 = pleasant 2 = unpleasant," participants made a judgment as to whether the stimulus item seemed pleasant or unpleasant to them. They were given 3 s to make their judgment and were instructed to remember the task they carried out on

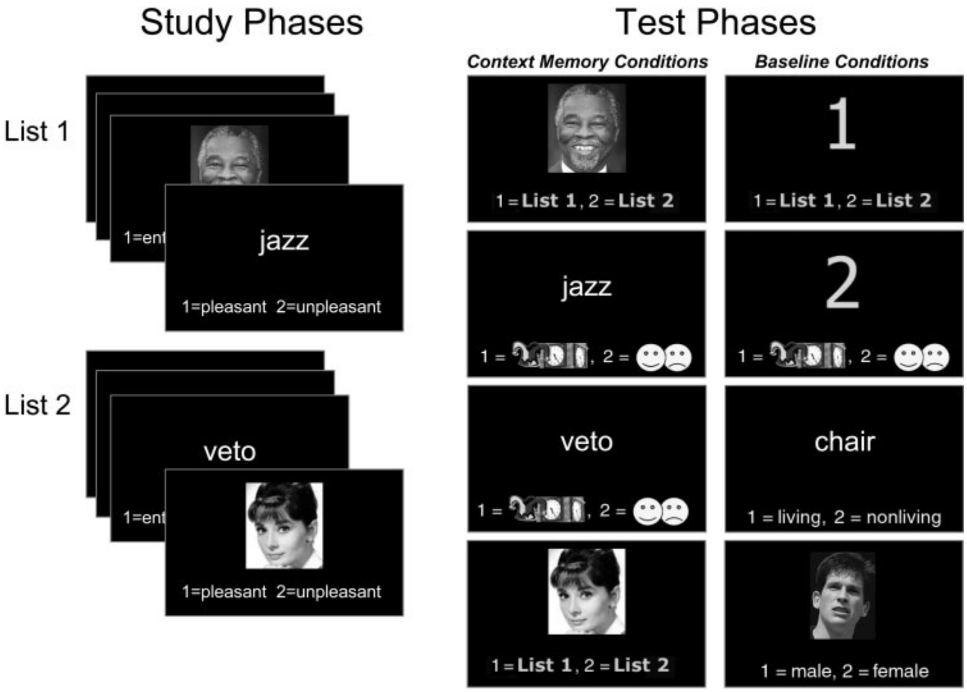

FIG. 1. Examples of the cues and stimuli used during study and test phases. In the study phase, two temporally distinct lists of items were presented. In each list, participants were pseudo-randomly cued to make entertainment/politics or pleasant/unpleasant judgments about either words or faces. In the test phase, participants were cued to make context memory or baseline decisions about stimuli. In context memory conditions, decisions required recollection of whether stimuli had been studied in list 1 or list 2 or whether the entertainment/politics or pleasant/unpleasant task had been undertaken. In baseline conditions, participants responded by pressing the 1 key or 2 key in the cue-only conditions (1st 2 panels) or made living/nonliving or male/female decisions in the semantic baseline conditions (final 2 panels).

the stimulus and whether it was in the first or second study list, for the following memory test phase.

In each test phase, trials began with a cue presented at the bottom of the display, indicating the type of recollective or baseline judgment that participants were to make during that trial. After 1 s, the stimulus item appeared in the center of the display. This was either a word or famous face presented during the preceding study phase in the recollection conditions, a nonstudied word or famous face in the baseline conditions, or a large "1" or "2" in the cue-only conditions. To reduce possible encoding specificity influences, the task memory cue consisted of graphical icons (Fig. 1). If the task memory cue was presented, participants were instructed to remember whether they had carried out the entertainment/politics task or the pleasant/unpleasant task on the stimulus item during the preceding study phase. If the list memory cue appeared, participants were asked to remember whether the stimulus item had been presented during the first or second study list. In the baseline conditions, participants were cued to decide whether the word specified a living or nonliving object, or whether the famous person was male or female. In the cue-only conditions, participants simply pressed the 1 or 2 button on the buttonbox depending on the number displayed in the center of the screen. In all conditions, participants had 3 s to make their response. Participants were instructed that they were likely to perform most successfully during the test phase if, when the retrieval cue was presented, they started to think about the type of memory specified by the cue, so that they would be ready and able to search their memory for the stimulus item as soon as it appeared.

To increase the efficiency of the event-related functional MRI (fMRI) design, the intertrial interval in both phases was jittered according to an exponential distribution (Henson 2004) between 480 and 1,080 ms, and additional fixation periods lasting 4 s were pseudo-randomly interspersed between trials. Participants were familiarized with the paradigm during practice sessions both before the experiment and inside the scanner.

Imaging acquisition and data analysis

A 3-T Bruker system was used to acquire echo-planar functional images (TR = 1,100 ms, TE = 27.5 ms, 21 interleaved axial slices oriented ~10° from the AC–PC transverse plane, 4 mm thickness, 1 mm interslice skip, 200 mm FOV, 64 × 64 matrix, 4 sessions each of 509 volume acquisitions). Twelve additional volumes were collected and discarded at the beginning of each session to allow for T1 equilibration. In addition, two magnetic field maps were acquired for each subject, which were used in the field map undistortion stage of preprocessing (see next paragraph).

Data were preprocessed and analyzed using SPM2 (Wellcome Department of Imaging Neuroscience, London, UK). Images were first corrected for differences in slice acquisition timing by resampling all slices in time to match the middle slice, followed by motion correction by realigning all images with respect to the first (using 4th-degree B-spline interpolation). The realigned images then underwent an undistortion procedure using the acquired magnetic field maps (Cusack et al. 2003), and a mean undistorted image was created. A mask image was specified using MRIcro software (Rorden and Brett 2000), which identified regions of residual signal dropout in the undistorted mean image. This mask image was used to weight the spatial normalization of the undistorted data (Brett et al. 2001b) to an EPI template in MNI stereotactic space (Cocosco et al. 1997). Normalized images were resampled into 3 mm cubic voxels and spatially smoothed with an 8 mm FWHM isotropic Gaussian kernel. The time series in each voxel were high-pass filtered to 1/128 Hz to remove low-frequency noise, corrected for temporal autocorrelation using an AR(1) + white noise model, and scaled to a grand mean of 100 across voxels and scans within each session.

Random effects statistical analysis was undertaken in two stages. In the first stage, 13 event types were defined for each session, consisting of four regressors for correct responses during the study phase (semantic and pleasantness task trials for words and faces) and eight regressors for correct responses during the test phase (recollection of task and list plus baseline for words and faces, as well as cue-only task and list memory trials). An additional "not applicable" regressor coded the incorrect response trials plus the few trials for which participants made no behavioral response and other events such as instructions and list markers. Fixation trials were modeled implicitly. Events for each of the regressors were modeled by convolving onset times with a canonical hemodynamic response function. Parameters for each regressor were estimated using a subject-specific model, with movement parameters in the three directions of motion and three degrees of rotation included as confounds, and covariates representing the mean session effects.

Linear contrasts were used to obtain subject-specific estimates for each of the effects of interest. These estimates were entered into the second stage of analysis treating subjects as a random effect, using one-way ANOVAs or one-sample *t*-tests across subjects. Because the primary experimental hypotheses concerned executive processes that could be expected to be engaged significantly regardless of the type of stimuli involved, contrasts of interest involved conjunctions between the independent words and faces contrasts, using nonsphericity correction (Friston et al. 2002). Statistical parametric maps of the conjunction contrasts were constructed using uncorrected height thresholds of $P < 0.001$. Activations that occurred within BA 10, our a priori region of interest, were reported if they exceeded the threshold of $P < 0.05$ corrected for multiple comparisons across voxels in this region (as defined by the Brodmann map supplied with MRIcro; Rorden and Brett 2000). Activations occurring outside BA 10 were only reported if they exceeded the threshold of $P < 0.05$ corrected for multiple comparisons across the entire brain. The peak locations of significant activations of ≥10 (except where specified) contiguous voxels were localized on an averaged structural scan, with approximate BAs estimated from the atlas of Talairach and Tournoux (1988), after adjusting coordinates to allow for differences between the MNI and Talairach templates (Brett et al. 2001a). To further explore the nature of the activation associated with recollection of task and list, mean percentage signal change magnitude relative to fixation was extracted from the subject-specific parameter estimates of activation peaks and subjected to repeated-measures analyses. The time-course of activation in BA 10 was analyzed using a finite impulse response model (Henson 2004) with bin size 2 s, normalized for overall regional variations in signal strength, using software made available by Northwestern Cognitive Brain Mapping Group (www.brain.northwestern.edu/cbmg).

RESULTS

Behavioral results

Accuracy and reaction time data for the study and test phases are displayed in Table 1. In the study phase, accuracy for the subjective pleasantness judgment task could obviously not be assessed, but such judgments were associated with longer reaction times than were semantic decisions [$t(15) = 5.8$, $P < 0.001$]. Turning to the test phase, participants were better at recollecting which task they had performed than which list an item was from [$t(15) = 6.6$, $P < 0.001$]. It should be noted that the fMRI analysis model included correct recollection trials only. Importantly, reaction times did not differ between recollection of task and list [$t(15) = 1.4$, not significant].

Neuroimaging results

Brain regions implicated in central domain-independent processes were characterized using group level conjunction con-

TABLE 1. *Accuracy and reaction time (ms) data, collapsed across stimulus type*

	Accuracy		Reaction Time	
	Mean	SD	Mean	SD
Study phase				
Semantic task	0.90	0.04	1,455	161
Pleasantness task	—	—	1,598	205
Test phase				
Recollection of task	0.86	0.06	1,666	251
Recollection of list	0.67	0.10	1,593	191

Accuracy could not be assessed for the subjective pleasantness judgment task.

trasts to identify areas of significant activation common to both word and face pairwise comparisons.

Study phase

When the two study tasks (semantic and pleasantness) were each contrasted against fixation, a number of similarities in the patterns of activation were observed, including regions such as the amygdala, thalamus, and fusiform cortex (Table 2). In addition, differences emerged, with activation in medial anterior, ventrolateral, and dorsolateral PFC during the pleasantness task, none of which were involved in the semantic task (activation was found in left ventrolateral PFC during the semantic task when the threshold was lowered to $P < 0.001$ uncorrected). When the two tasks were contrasted directly, a region centered in medial anterior PFC (−3, 51, 27; BA 10; $Z = 5.7$, 236 voxels) showed significantly greater activation during the pleasantness task than the semantic task, as did areas in ventrolateral (−30, 21, −21; BA 47; $Z = 5.3$, 22 voxels), dorsolateral (−24, 51, 30; BA 46; $Z = 5.4$, 11 voxels), and superior (0, 33, 54; BA 8; $Z = 5.5$, 31 voxels) PFC (Fig. 2). There were no significantly greater activations in the semantic compared with the pleasantness talk.

As noted in *Behavioral results*, the pleasantness task was associated with longer reaction times than the semantic task. It is unlikely, however, that time on task could be an adequate explanation for the greater medial BA 10 activation during the pleasantness task because there was no correlation between reaction time (in the pleasantness task minus the semantic task) and signal change (in the pleasantness vs. semantic task contrast) in this region across subjects [$r(16) = 0.22$, $P = 0.42$].

Test phase

The test phase analysis first sought to identify regions involved in recollection (i.e., not including the cue-only conditions), averaging across task and list memory, versus the baseline conditions. Significant activation was seen in this contrast in bilateral anterior PFC, ventrolateral and dorsolateral PFC, lateral parietal cortex, and precuneus (Table 3). Much of this network of regions was common to both task (Fig. 3*A*) and list (Fig. 3*B*) conditions, although inspection of Fig. 3, *A* and *B*, suggests increased levels of activation in a number of the relevant regions during task compared with list trials. This impression is borne out by the direct contrast between recollection of task and list, which revealed significantly greater activation during task memory in lateral and medial regions of left anterior PFC, as well as areas in left ventrolateral PFC and precuneus (Table 4; Fig. 3*C*).

The regions that differentiated between memory for task and list are very similar to those observed in the previous study that compared recollection of task and position (Simons et al. 2005). One other region that showed significantly greater activation for task versus position in that study was the left medial temporal lobe, centered on the hippocampus (−21, −30, −9). Activation in this region did not survive the whole brain–corrected threshold of $P < 0.05$ in the present experi-

TABLE 2. *Regions of significant activation in the contrasts between correct study phase trials (semantic task and pleasantness task) and fixation*

	Coordinates				
Brain Region	*x*	*y*	*z*	*Z*	Voxels
Semantic task > fixation					
Left amygdala (BA 34)	−27	0	−15	6.0	22
Left putamen	−18	−6	12	5.3	27
Left thalamus	−12	−10	−3	6.2	61
Cerebellum	0	−42	0	5.4	15
Left lateral occipital cortex (BA 19)	−45	−72	−15	5.9	16
Right lateral occipital cortex (BA 18)	18	−99	0	5.9	42
Pleasantness task > fixation					
Left medial anterior PFC (BA 10)	−3	54	27	6.4	274
Left dorsolateral PFC (BA 9)	−18	51	30	6.4	188
Left ventrolateral PFC (BA 47)	−33	27	−12	6.9	128
Right ventrolateral PFC (BA 47)	51	27	−3	6.2	84
Right supplementary motor area (BA 8)	3	24	51	6.3	71
Left caudate	−15	6	12	5.1	18
Left amygdala (BA 34)	−21	0	−15	6.3	121
Right thalamus	18	−10	6	5.3	19
Right posterior fusiform cortex (BA 19)	33	−66	−24	5.7	21
Left lateral occipital cortex (BA 18)	−12	−99	−9	6.2	121

Coordinates are in MNI atlas space (Cocosco et al. 1997), with brain regions and Brodmann areas (BA) estimated from the Talairach and Tournoux (1988) atlas. Activations in anterior prefrontal cortex (PFC) significant at $P < 0.05$ corrected for voxels in BA 10. All other activations significant at $P < 0.05$ corrected for voxels in whole brain.

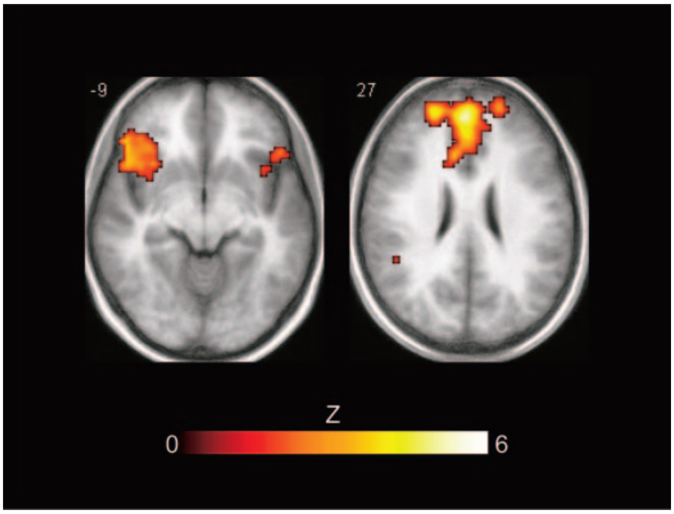

FIG. 2. Group functional activation maps, displayed on axial slices of an averaged structural image, of the study phase contrast between pleasantness and semantic judgments. Significant activation can be seen in medial anterior prefrontal cortex (PFC), in a very similar region to that observed by Gusnard et al. (2001), as well as in other PFC regions.

ment. At a threshold of $P < 0.05$ corrected for the voxels in an 8-mm sphere around the peak from the previous study, however, significant medial temporal lobe activation did emerge (−15, −27, −9; BA 30; $Z = 3.4$).

The next analysis examined whether any of the regions activated in the task versus list contrast might play a role in the specification of retrieval strategies (retrieval orientation). If this were the case, it would be expected that such regions would show significant activation both when retrieval cues were presented and retrieval searches undertaken and when cues were presented but no retrieval search occurred. To address this question, a conjunction analysis identified brain regions that exhibited activation common to both the task versus list recollection contrast and the task versus list cue-only contrast. As shown in Fig. 4, this analysis implicated left lateral anterior PFC (−33, 60, 0; BA 10; $Z = 4.4$, 5 voxels) as well as bilateral posterior fusiform cortex (−33, −78, −21; $Z = 5.1$, 7 voxels; 36, −75, −21; $Z = 5.7$, 36 voxels; both BA 19). At the lower threshold of $P < 0.001$ uncorrected, activation was also seen in ventrolateral PFC (−48, 27, 0; BA 47; $Z = 4.5$, 45 voxels) but not in dorsolateral PFC, even when the threshold was dropped further to $P < 0.01$. These results suggest that left lateral anterior PFC may be part of a network that includes ventrolateral PFC and fusiform cortex, which is involved in recollection at a stage of processing before the instigation of a retrieval search, exhibiting significant activation associated with the presentation of the retrieval cue regardless of whether or not a retrieval search takes place. Significant medial anterior PFC activation did not emerge in the conjunction contrast, even at the lowest threshold. This apparent difference in the response of lateral and medial anterior PFC to the cue-only conditions was reflected in a region by cue type interaction [$F(1,15) = 6.9$, $P < 0.05$].

TABLE 3. *Regions of significant activation in the contrast between correct context memory and baseline conditions, averaging over context type (memory for task and list)*

Brain Region	Coordinates *x*	*y*	*z*	Z	Voxels
Left lateral anterior PFC (BA 10)	−30	60	0	4.9	29
Right lateral anterior PFC (BA 10)	39	57	3	6.0	47
Left ventrolateral PFC (BA 45)	−42	30	27	5.6	30
Left dorsolateral PFC (BA 9)	−33	12	48	5.9	36
Right lateral parietal cortex (BA 40)	33	−54	39	5.6	59
Left lateral parietal cortex (BA 7)	−33	−57	51	5.7	71
Precuneus (BA 7)	0	−69	42	6.4	150

Coordinates are in MNI atlas space (Cocosco et al. 1997), with brain regions and Brodmann areas (BA) estimated from the Talairach and Tournoux (1988) atlas. Activations in anterior prefrontal cortex (PFC) significant at $P < 0.05$ corrected for voxels in BA 10. All other activations significant at $P < 0.05$ corrected for voxels in whole brain.

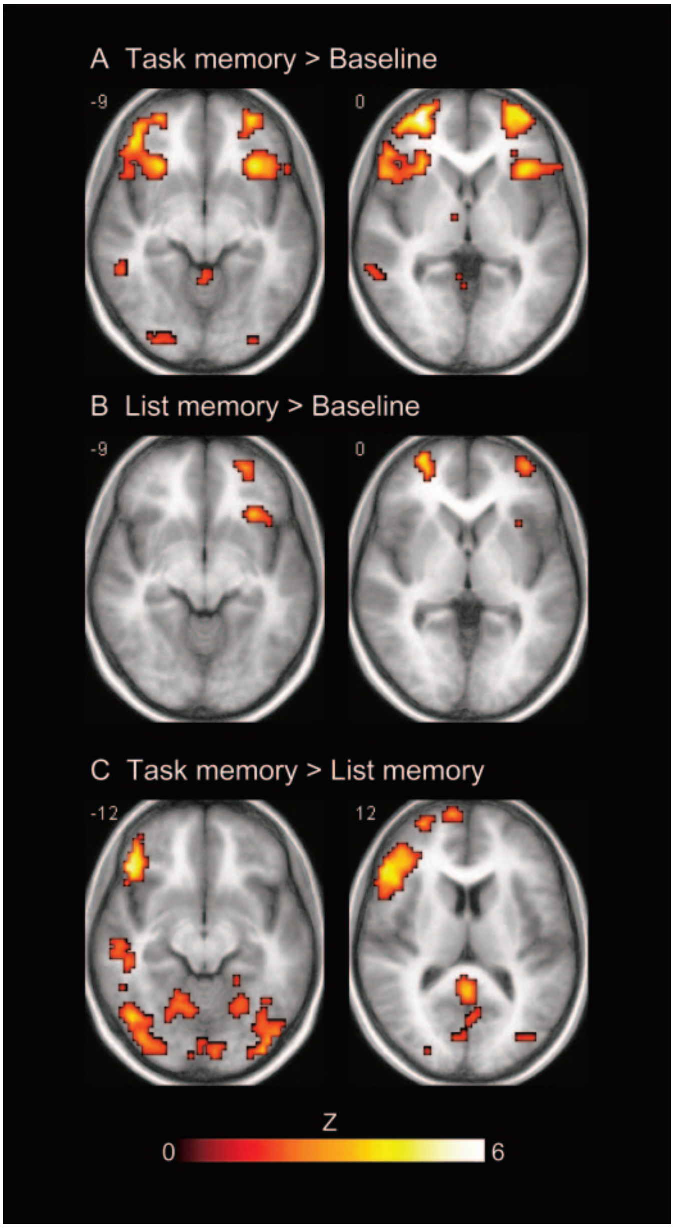

FIG. 3. Regions associated with contextual recollection in the test phase. Significant activation during recollection of (*A*) task and (*B*) list seen in similar regions of bilateral anterior PFC, ventrolateral PFC/insula, dorsolateral PFC, lateral parietal cortex, and precuneus. *C*: contrasting task and list recollection directly revealed significant activation in lateral and medial regions of left anterior PFC, left ventrolateral PFC, and precuneus.

TABLE 4. *Regions exhibiting significantly greater activation for recollection of task than list (correct trials in each condition only)*

Brain Region	Coordinates *x*	*y*	*z*	Z	Voxels
Left medial anterior PFC (BA 10)	−12	66	12	4.3	90
Left lateral anterior PFC (BA 10)	−30	60	12	4.5	23
Left ventrolateral PFC (BA 45)	−45	30	18	6.1	141
Left ventrolateral PFC (BA 47)	−48	30	−12	5.7	36
Supplementary motor area (BA 8)	0	21	54	5.5	15
Precuneus (BA 7)	−3	−69	36	5.9	53
Right posterior fusiform cortex (BA 19)	36	−75	−27	5.1	13

Coordinates are in MNI atlas space (Cocosco et al. 1997), with brain regions and Brodmann areas (BA) estimated from the Talairach and Tournoux (1988) atlas. Activations in anterior prefrontal cortex (PFC) significant at $P < 0.05$ corrected for voxels in BA 10. All other activations significant at $P < 0.05$ corrected for voxels in whole brain.

To examine further the possibility that lateral and medial anterior PFC may be involved at different stages of the retrieval process, the time-course of activation in the two regions was examined using a finite impulse response model (see *Procedures*). It can be seen in Fig. 5 that the response associated with recollection in lateral anterior PFC peaked significantly earlier (by $\sim$4 s) than the response in medial anterior PFC [$t(15) = 2.7$, $P < 0.05$]. To ensure that this latency difference did not merely reflect possible differences in vasculature between regions, (Henson 2004), for example the time-course associated with the baseline conditions was also examined. There was no difference in latency between lateral and medial anterior PFC for the baseline conditions [$t(15) < 1$]. This suggests that the regional latency effect was specific to recollection, a conclusion supported by a significant region by condition (recollection vs. baseline) interaction [$F(1,15) = 7.1$, $P < 0.05$].

A final analysis considered whether any of the anterior PFC activations observed in the task versus list contrast could be attributable to level of memory performance, given that task recollection was associated with significantly better behavioral accuracy than list recollection. However, this was shown to be an unlikely explanation. First, only correct recollection trials were included in the fMRI analysis. Second, correlational analysis revealed that there was no correspondence between accuracy (in the task condition minus the list condition) and signal change (in the task vs. list contrast) in anterior PFC across subjects [$r(16) = -0.2$, $P = 0.5$].

DISCUSSION

This experiment used event-related fMRI to show that, during a context recollection task, anterior PFC is differentially engaged by the requirement to recollect different kinds of contextual detail, such as the task previously carried out with stimuli or which of two temporally distinct lists those stimuli appeared in. Moreover, the results suggest that the role played by at least the lateral aspect of this anterior prefrontal region is in the control processes necessary for the specification of retrieval, rather than in postretrieval monitoring or verification (i.e., the descriptor rather than editing or mediator processes according to the framework of Burgess and Shallice 1996). Indeed, lateral anterior PFC activation was associated with readiness for a task memory judgment compared with a list memory judgment, irrespective of whether retrieval searches were actually undertaken. This suggests that in recollection, recruitment of this region reflects a very early stage of retrieval orientation (Rugg and Wilding 2000) or specification (Burgess and Shallice 1996) before the commencement of a retrieval search. In contrast, medial anterior PFC was activated when target stimuli were presented during the recollection of previous judgments about stimuli, and time-course data revealed that signal in this region peaked significantly later in the recollection process that did the response in lateral anterior PFC. Medial anterior PFC was also activated during the study phase, associated significantly more with pleasantness than semantic judgments about stimuli. These results suggest that anterior PFC plays an important role in recollection but that this role may be just one example of a more general information processing capacity. We have proposed a model of anterior PFC function that characterizes this capacity in terms of the biasing of attention between internally generated thoughts and stimulus-oriented perceptions (Burgess et al. 2005).

Turning first, however, to the finding of significantly greater activation in anterior PFC during the recollection of previous decisions made about a stimulus versus recollecting which of two lists the stimulus occurred in, this both confirms and expands on the results of Simons et al. (2005), who observed greater anterior PFC activation associated with task compared with position recollection. Cognitive models of contextual memory (e.g., Johnson et al. 1993; Schacter et al. 1998) make the distinction between contextual details that were internally generated (e.g., our thoughts and feelings about an event) or externally derived (e.g., where and when the event occurred). This replication of the results from our previous fMRI experiment using a different paradigm and involving different participants confirms that the processing supported by anterior PFC is sensitive to this context distinction. Consistent with this view, a survey of the literature reveals that activation of anterior PFC has been more reliably observed during experiments involving recollection of task (Burgess et al. 2001; Dobbins et al. 2002; Kahn et al. 2004; Rugg et al. 1999) than

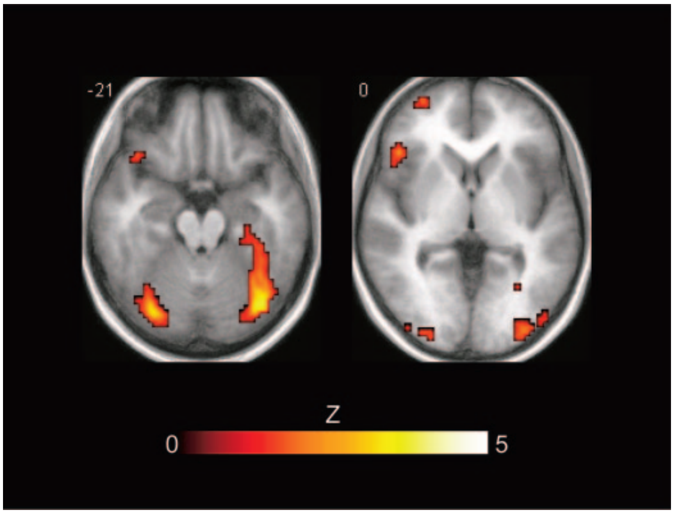

FIG. 4. Regions common to both context recollection and cue-only conditions included left lateral anterior and ventrolateral PFC and bilateral posterior fusiform cortex. These regions may play a role in retrieval orientation processes.

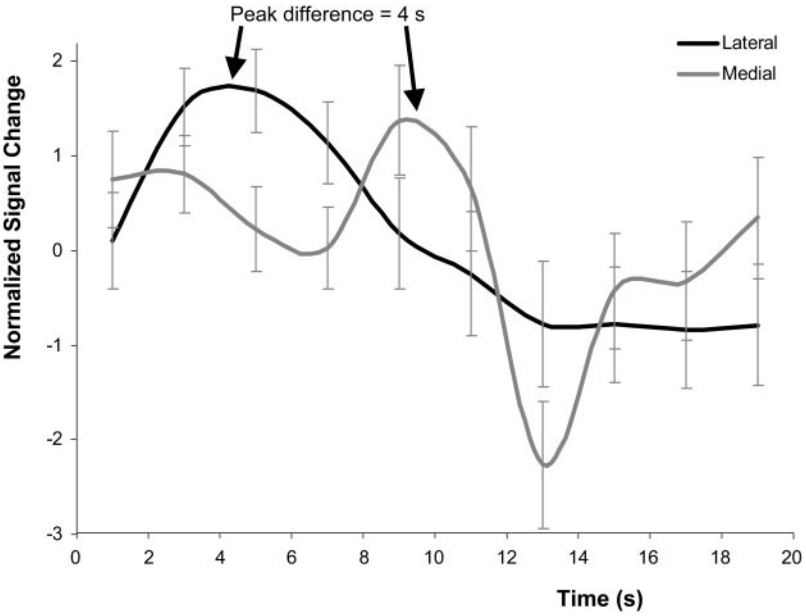

FIG. 5. Time-course analysis suggesting that lateral (in black) and medial (in gray) anterior PFC are involved in temporally distinct stages of the recollection process. Error bars denote SE.

either position or list[1] (Henson et al. 1999; Nyberg et al. 1996; Suzuki et al. 2002).

Other brain regions showed a similar pattern to the lateral anterior PFC region identified here. Most notable of these was left ventrolateral PFC, consistent with suggestions that this region is involved in cue specification and elaboration (Dobbins et al. 2002). The same was found in bilateral posterior fusiform cortex, which has been linked with perceptual and object recognition processes (Malach et al. 1995; Simons et al. 2003). These results are what might be expected if retrieval orientation encompasses the transformation of the presented cue from a perceptual representation into task parameters that orient attention toward particular contextual details. The relevant contextual details may relate to the study task carried out with stimuli or to which of two study lists the stimuli were encountered in, depending on the nature of the recollection cue presented.

The idea that anterior PFC might be involved in retrieval orientation is supported by evidence from studies using event-related potentials (ERPs). For example, Ranganath and Paller (2000) reported recollection effects over frontal sites that occurred as early as 200 ms after stimulus onset. Of even more relevance to the present question, Herron and Wilding (2004) recently showed, using a paradigm similar to that employed by Simons et al. (2005), that a frontopolar site exhibited differential ERPs for task versus position recollection that occurred when the retrieval cue was presented, before the onset of the stimulus. It is difficult, for a number of technical reasons, to isolate the precise location of ERP generators in the brain. With the superior spatial resolution of fMRI, it seems on the basis of these results that lateral anterior PFC may be among the sources of the reported early frontally distributed ERP effects, indicating a role in the control processes that guide the retrieval of context information.

The pattern of medial anterior PFC activation observed during the study phase replicates that reported by Gusnard et al. (2001), who contrasted pleasantness judgments with a semantic indoor versus outdoor decision. The close similarity between the peaks (−3, 51, 27 in the present data; −3, 53, 24 from Gusnard et al.) is striking. At first sight, this seems consistent with the view that the internal nature of the representations involved in task performance is important for determining the differential recruitment of this medial anterior region (Gusnard et al. 2001). Such a view is given added foundation by the involvement of a similar region during the test phase of the present experiment in differentiating between recollection of task (likely to involve retrieval of internally generated processing operations engaged in thinking about study task judgments and making appropriate responses) and list (less likely to require information relating to the thoughts engaged during the previous study phase) (Johnson et al. 1993; see also Simons et al. 2005).

However, the finding that medial anterior PFC activation was associated with a relatively late stage of the recollection process when target stimuli were presented suggests it is also possible that it was the presence of these external stimuli that may have determined involvement of the region, perhaps fulfilling a role in the generation of criteria for successful retrieval, against which recovered contextual information could be compared. In this way, medial anterior PFC activation in this paradigm could be hypothesized to reflect stimulus-oriented processing of retrieved internally generated information. Further experimentation is clearly required to investigate these contrasting possibilities. One way in which they could be tested would be by examining the activation associated with recollecting contextual details about stimuli that, in the test phase, are being imagined by participants rather than being presented externally. If less medial anterior PFC activation is observed in that situation, an account of the region solely in terms of processing internally generated information may not be sufficient.

This latter possibility receives support from other recent findings that stimulus-oriented processing may be important in deter-

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[1] Note that the list memory category does not include experiments that involved decisions about temporal positioning of a stimulus *within* a list (e.g., Cabeza et al. 1997; Dobbins et al. 2003), on the basis of evidence that such recency judgments are based largely on assessments of stimulus familiarity rather than recollection (Hintzman 2003), and may be associated with different patterns of neural activation than discriminations *between* lists (Dobbins et al. 2003; Suzuki et al. 2002).

mining the involvement of medial anterior PFC (e.g., Gilbert et al. 2005; Janata et al. 2002; Small et al. 2003). For example, Gilbert et al. (2005) observed activation in this region that was greater when participants were performing a task on the basis of externally presented stimuli (e.g., navigating around the edge of a presented complex shape) than when they were performing the same task in their heads (i.e., imagining the now-absent complex shape and continuing to navigate around its edge). In this way, anterior PFC may act as a gateway, biasing attention between internally generated thoughts and externally derived perceptions (Burgess et al. 2005). These data are also broadly consistent with a recent analysis (Ramnani and Owen 2004) that suggests that "coordination of information processing. . . is an important aspect of aPFC function." In fact, the present data extend this view by showing that this coordination may be between internally generated and externally derived information and by indicating a functional distinction between lateral and medial regions of anterior PFC.

In conclusion, this experiment showed that anterior PFC is differentially engaged during different stages of the retrieval of contextual information. Lateral anterior PFC seems to be recruited during initial specification stages, regardless of whether target stimuli are presented on which a retrieval search might be based. Medial anterior PFC, conversely, seems to play a role at a later stage of recollection, its involvement determined by the presence of external target stimuli. One possible characterization is that the processes supported by anterior PFC operate to bias attention between the externally presented target stimuli and retrieval of the internally generated thoughts that were previously provoked by them.

ACKNOWLEDGMENTS

We are grateful to the staff of the Wolfson Brain Imaging Centre for scanning assistance.

GRANTS

This work was supported by Wellcome Trust Grant 061171 to P. W. Burgess.

REFERENCES

Brett M, Christoff K, Cusack R, and Lancaster J. Using the Talairach atlas with the MNI template. *NeuroImage* 13: S85, 2001a.

Brett M, Leff AP, Rorden C, and Ashburner J. Spatial normalization of brain images with focal lesions using cost function masking. *NeuroImage* 14: 486–500, 2001b.

Burgess N, Maguire EA, Spiers HJ, and O'Keefe J. A temporoparietal and prefrontal network for retrieving the spatial context of lifelike events. *NeuroImage* 14: 439–453, 2001.

Burgess PW and Shallice T. Confabulation and the control of recollection. *Memory* 4: 359–411, 1996.

Burgess PW, Simons JS, Dumontheil I, and Gilbert SJ. The gateway hypothesis of rostral prefrontal cortex (area 10) function. In: *Measuring the Mind: Speed, Control and Age,* edited by Duncan J, McLeod P, and Phillips L. Oxford: Oxford University Press, 2005, p. 215–246.

Cabeza R, Mangels J, Nyberg L, Habib R, Houle S, McIntosh AR, and Tulving E. Brain regions differentially involved in remembering what and when: a PET study. *Neuron* 19: 863–870, 1997.

Cocosco CA, Kollokian V, Kwan RKS, and Evans AC. Brainweb: online interface to a 3D MRI simulated brain database. *NeuroImage* 5:425, 1997.

Cusack R, Brett M, and Osswald K. An evaluation of the use of magnetic field maps to undistort echo-planar images. *NeuroImage* 18: 127–142, 2003.

Dobbins IG, Foley H, Schacter DL, and Wagner AD. Executive control during episodic retrieval: Multiple prefrontal processes subserve source memory. *Neuron* 35: 989–996, 2002.

Dobbins IG, Rice HJ, Wagner AD, and Schacter DL. Memory orientation and success: Separable neurocognitive components underlying episodic recognition. *Neuropsychologia* 41: 318–333, 2003.

Dobbins IG and Wagner AD. Domain-general and domain-sensitive prefrontal mechanisms for recollecting events and detecting novelty. *Cereb Cortex* In press.

Fletcher PC and Henson RNA. Frontal lobes and human memory: insights from functional neuroimaging. *Brain* 124: 849–881, 2001.

Friston KJ, Glaser DE, Henson RNA, Kiebel S, Phillips C, and Ashburner J. Classical and Bayesian inference in neuroimaging: applications. *NeuroImage* 16: 484–512, 2002.

Gilbert SJ, Frith CD, and Burgess P W. Involvement of rostral prefrontal cortex in selection between stimulus-oriented and stimulus-independent thought. *Eur J Neurosci* 21: 1423–1431, 2005.

Gusnard DA, Akbudak E, Shulman GL, and Raichle ME. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc Natl Acad Sci USA* 98: 4259–4264, 2001.

Henson RNA. Analysis of fMRI timeseries: linear time-invariant models, event-related fMRI and optimal experimental design. In: *Human Brain Function,* edited by Frackowiak RSJ, Friston KJ, Frith CD, Dolan RJ, and Price CJ. London: Elsevier, 2004, p. 793–822.

Henson RNA, Shallice T, and Dolan RJ. Right prefrontal cortex and episodic memory retrieval: a functional MRI test of the monitoring hypothesis. *Brain* 122: 1367–1381, 1999.

Herron JE and Wilding EL. An electrophysiological dissociation of retrieval mode and retrieval orientation. *NeuroImage* 22 1554–1562, 2004.

Hintzman DL. Judgments of recency and their relation to recognition memory. *Mem Cogn* 31: 26–34, 2003.

Janata P, Birk JL, Van Horn JD, Leman M, Tillmann B, and Bharucha JJ. The cortical topography of tonal structures underlying Western music. *Science* 298: 2167–2170, 2002.

Johnson MK, Hashtroudi S, and Lindsay DS. Source monitoring. *Psychol Bull* 114, 3–28, 1993.

Kahn I, Davachi L, and Wagner AD. Functional-neuroanatomic correlates of recollection: implications for models of recognition memory. *J Neurosci* 24: 4172–4180, 2004.

Malach R, Reppas JB, Benson R, Kwong KK, Jiang H, Kennedy WA, Ledden PJ, Brady TJ, Rosen BR, and Tootell RBH. Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proc Natl Acad Sci USA* 92: 8135–8139, 1995.

Nyberg L, McIntosh AR, Cabeza R, Habib R, Houle S, and Tulving E. General and specific brain regions involved in encoding and retrieval of events: what, where, and when. *Proc Natl Acad Sci USA* 93: 11280–11285, 1996.

Ramnani N and Owen AM. Anterior prefrontal cortex: insights into function from anatomy and neuroimaging. *Nat Rev Neurosci* 5: 184–194, 2004.

Ranganath C, Johnson MK, and D'Esposito M. Left anterior prefrontal activation increases with demands to recall specific perceptual information. *J Neurosci* 20: RC108, 2000.

Ranganath C and Paller KA. Neural correlates of memory retrieval and evaluation. *Cogn Brain Res* 9: 209–222, 2000.

Rorden C and Brett M. Stereotaxic display of brain lesions. *Behav Neurol* 12: 191–200, 2000.

Rugg MD, Fletcher PC, Chua PML, and Dolan RJ. The role of the prefrontal cortex in recognition memory and memory for source: an fMRI study. *NeuroImage* 10: 520–529, 1999.

Rugg MD and Wilding EL. Retrieval processing and episodic memory. *Trends Cogn Sci* 4: 108–115, 2000.

Schacter DL, Norman KA, and Koutstaal W. The cognitive neuroscience of constructive memory. *Annu Rev Psychol* 49: 289–318, 1998.

Simons JS, Koutstaal W, Prince S, Wagner AD, and Schacter DL. Neural mechanisms of visual object priming: evidence for perceptual and semantic distinctions in fusiform cortex. *NeuroImage* 19: 613–626, 2003.

Simons JS, Owen AM, Fletcher PC, and Burgess PW. Anterior prefrontal cortex and the recollection of contextual information. *Neuropsychologia* 43, 2005.

Simons JS and Spiers HJ. Prefrontal and medial temporal lobe interactions in long-term memory. *Nat Rev Neurosci* 4: 637–648, 2003.

Small DM, Gitelman DR, Gregory MD, Nobre AC, Parrish TB, and Mesulam MM. The posterior cingulate and medial prefrontal cortex mediate the anticipatory allocation of spatial attention. *NeuroImage* 18: 633–641, 2003.

Suzuki M, Fujii T, Tsukiura T, Okuda J, Umetsu A, Nagasaka T, Mugikura S, Yanagawa I, Takahashi S, and Yamadori A. Neural basis of temporal context memory: a functional MRI study. *NeuroImage* 17: 1790–1796, 2002.

Talairach J and Tournoux P. *Co-Planar Stereotaxic Atlas of the Human Brain.* Stuttgart, Germany: Thieme, 1988.

Tulving E. *Elements of Episodic Memory.* Oxford, UK: Clarendon Press, 1983.