

Prefrontal cortex hemispheric specialization for categorical and coordinate visual spatial memory

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Abstract

During visual spatial perception of multiple items, the left hemisphere has been shown to preferentially process categorical spatial relationships while the right hemisphere has been shown to preferentially process coordinate spatial relationships. We hypothesized that this hemispheric processing distinction would be reflected in the prefrontal cortex during categorical and coordinate visual spatial memory, and tested this hypothesis using functional magnetic resonance imaging (fMRI). During encoding, abstract shapes were presented in the left or right hemifield in addition to a dot at a variable distance from the shape (with some dots on the shape); participants were instructed to remember the position of each dot relative to the shape. During categorical memory retrieval, each shape was presented centrally and participants responded whether the previously corresponding dot was ‘on’ or ‘off’ of the shape. During coordinate memory retrieval, each shape was presented centrally and participants responded whether the previously corresponding dot was ‘near’ or ‘far’ from the shape (relative to a reference distance). Consistent with our hypothesis, a region in the left prefrontal cortex (BA10) was preferentially associated with categorical visual spatial memory and a region in the right prefrontal cortex (BA9/10) was preferentially associated with coordinate visual spatial memory. These results have direct implications for interpreting previous findings that the left prefrontal cortex is associated with source memory, as this cognitive process is categorical in nature, and the right prefrontal cortex is associated with item memory, as this process depends on the precise spatial relations among item features or components.

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1. Introduction

Visual spatial perception of an item (e.g., a face, an object, or an abstract shape) produces activity in both the ventral cortical processing stream – occipital and ventral temporal cortex – for item identification and the dorsal cortical processing stream – occipital and parietal cortex – for item spatial localization in non-human primates (Ungerleider & Mishkin, 1982; although there are between stream connections, see Felleman & Van Essen, 1991). In humans, neuroimaging evidence indicates that the ventral (‘what’) processing stream extends from occipital cortex to ventral temporal cortex and into ventral prefrontal cortex, while the dorsal (‘where’) processing stream extends from occipital cortex to parietal cortex (Haxby et al., 1991; Haxby et al., 1994; Köhler, Kapur, Moscovitch, Winocur, & Houle, 1995).

There has been a long-standing debate as to whether this dorsal–ventral visual spatial perceptual processing distinction also exists in the prefrontal cortex during working memory (given that this cognitive function has been associated with the prefrontal cortex; see Baddeley & Della Sala, 1996). There is now compelling evidence that the ventral prefrontal cortex is preferentially associated with item working memory and the dorsal prefrontal cortex is preferentially associated with spatial working memory (Belger et al., 1998; Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; Courtney, Ungerleider, Keil, & Haxby, 1996; Haxby, Petit, Ungerleider, & Courtney, 2000; Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000; Sala, Rämä, & Courtney, 2003). Although some researchers have failed to find differential item and spatial working memory effects in prefrontal cortex (D’Esposito et al., 1998; Owen et al., 1998; Postle, Berger, Taich, & D’Esposito, 2000; Postle & D’Esposito, 1999), such null results can occur due to a number of reasons (e.g., a lack of sensitivity or insufficient task demands). In illustration of this point, a reanalysis of Postle et al.’s (2000) functional magnetic resonance imaging (fMRI) data was con-

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ducted using event-related timecourse analysis, rather than the more typically used beta-weight analysis, and revealed spatial working memory specific activity in dorsal prefrontal cortex, supporting the dorsal–ventral prefrontal cortex working memory distinction (Slotnick, 2005). Thus, the significant findings affirm that the ventral and dorsal visual spatial perceptual processing streams extend into ventral and dorsal prefrontal cortex during item and spatial working memory.

In everyday life, visual spatial perception not only involves processing items in isolation, but is also engaged in processing the positions of items relative to one another. Kosslyn (1987) proposed that the left hemisphere is preferentially associated with between-item categorical processing (e.g., one item is ‘above’ or ‘below’ the other, a discrete judgment) and the right hemisphere is preferentially associated with between-item coordinate processing (e.g., one item is ‘near’ to or ‘far’ from the other, an analog judgment). These distinct types of processing can also refer to the relative positions of parts or features of a single item (for further elaboration, see Section 4). This left–right hemisphere categorical–coordinate visual spatial perceptual processing distinction has been convincingly supported in a number of subsequent behavioral studies (Banich & Federmeier, 1999; Bruyer, Scailquin, & Coibion, 1997; French & Painter, 1991; Hellige & Michimata, 1989; Koenig, Reiss, & Kosslyn, 1990; Kosslyn et al., 1989; Laeng & Peters, 1995; Laeng, Shah, & Kosslyn, 1999; Michimata, 1997; Niebauer & Christman, 1998; Okubo & Michimata, 2002; Sergent, 1991; Servos & Peters, 1990). Some investigators have taken failures to find such categorical and coordinate hemispheric laterality effects as contradictory evidence (Bruyer et al., 1997; Cowin & Hellige, 1994; Rybash & Hoyer, 1992; Sergent, 1991). However, direct support for Kosslyn’s hemispheric processing distinction has been confirmed with patients that had one hemisphere (usually followed by the other) temporarily deactivated by injection with sodium amobarbital – the left hemisphere was preferentially associated with categorical visual spatial processing and the right hemisphere was preferentially associated with coordinate visual spatial processing, but only under sufficiently demanding task conditions (which may provide some explanation of previous null findings; Slotnick, Moo, Tesoro, & Hart, 2001). Furthermore, evidence from patients with focal lesions (Laeng, 1994; Laeng, Carlesimo, Caltagirone, Capasso, & Miceli, 2002) and neuroimaging (Baciu et al., 1999) suggests that categorical and coordinate perceptual processing may be particularly reliant on the left and right parietal lobes, respectively, although there is neuroimaging evidence that this hemispheric distinction also occurs in the prefrontal cortex during perceptual processing (Kosslyn, Thompson, Gitelman, & Alpert, 1998) and spatial imagery (Trojano et al., 2002). The overall pattern of results can be taken as strong evidence that the left hemisphere is preferentially associated with categorical visual spatial perceptual processing and the right hemisphere is preferentially associated with coordinate visual spatial perceptual processing (see meta-analysis by Laeng, Chabris, & Kosslyn, 2003).

Similar to the ventral–dorsal prefrontal cortex distinction that has been associated with item and spatial working memory, we hypothesized that the left–right hemisphere prefrontal

cortex distinction would be manifested during categorical and coordinate visual spatial memory. In particular, we focused on the dorsolateral and anterior prefrontal cortex, as these regions have been associated with source memory and item memory (Cansino, Maquet, Dolan, & Rugg, 2002; Nyberg, McIntosh, Cabeza, Habib, & Houle, 1996; Rugg, Fletcher, Chua, & Dolan, 1999; Slotnick, Moo, Segal, & Hart, 2003). To anticipate the results, a region in left prefrontal cortex was associated with categorical visual spatial memory while a region in right prefrontal cortex was associated with coordinate visual spatial memory.

2. Methods

2.1. Participants

After providing informed consent, 11 right-handed participants took part in the imaging study, which had been approved by the Johns Hopkins University institutional review board. Due to excessive head movement in three participants (i.e. greater than 1 mm), eight participants were included in the analysis (age range 23–35 years, five females), which was sufficient to conduct the imaging analysis (Friston, Holmes, & Worsley, 1999). A follow-up behavioral study, approved by the Harvard University institutional review board, was also conducted with eight additional participants that had provided informed consent (age range 23–37 years, five females). All participants had normal or corrected-to-normal visual acuity.

2.2. Behavioral protocol

The behavioral protocol is illustrated in Fig. 1. In a blocked design, participants completed two categorical (A) and two coordinate memory (B) runs (in the order ABBA). Immediately before the MRI scanning session, participants were briefly trained to familiarize them with both tasks. During the encoding phase of both types of runs, following a 6 s instruction screen, six abstract shapes (spanning 5.7–7.1° of visual angle) were presented every 4 s with equal probability on the left or right half of the screen (with the nearest shape boundary ranging from 2.1° to 2.8° of visual angle, as measured horizontally, from the display center). In addition, each shape was paired with a dot 0.3° of visual angle in diameter that varied in distance from the shape from 0° to 1.1° or 1.7° to 3.3° of visual angle (where 0° distance indicates the dot was centered directly on the boundary that defined a shape, and the spatial gap in dot to shape distance was based on the coordinate retrieval reference distance of 1.4°, as will be discussed below). The encoding phase format and instructions were identical for both run types. Participants were instructed to remember the position of the dot relative to each shape by visually encoding the shape-dot pair precisely as it appeared on the display, rather than using verbal encoding strategies (all participants reported using visual encoding strategies, as instructed). We emphasize here that had participants used verbal encoding strategies, similar categorical and coordinate memory related activity would be predicted, while employment of visual encoding strategies would predict differential activity (as observed; see Section 3). Participants were not informed as to the type of subsequent retrieval run in an effort to enforce consistent encoding strategies. During the retrieval phase of both types of runs, following an 8 s instruction screen, the six shapes from the encoding phase (without the dots) were presented at the center of the screen every 6 s, each for a duration of 3 s. Central presentation precluded participants from remembering dot location based upon cues other than relative position to the associated shape (e.g., the use of the screen as a frame-of-reference; see Banich & Federmeier, 1999) that might have diminished or eliminated differential categorical and coordinate effects beyond the initial block (Koenig et al., 1990; Kosslyn et al., 1989; Laeng et al., 1999; Michimata, 1997). Shapes were never repeated. When presented with a shape, participants had been encouraged to retrieve a visual representation of the associated shape-dot pair (all participants reported doing so). It should again be noted that if participants simply retrieved verbal labels, similar categorical and coordinate memory related activity would be predicted; as differential activity was observed (see Section 3), this supported their use of visual spatial retrieval. During categorical memory runs, participants

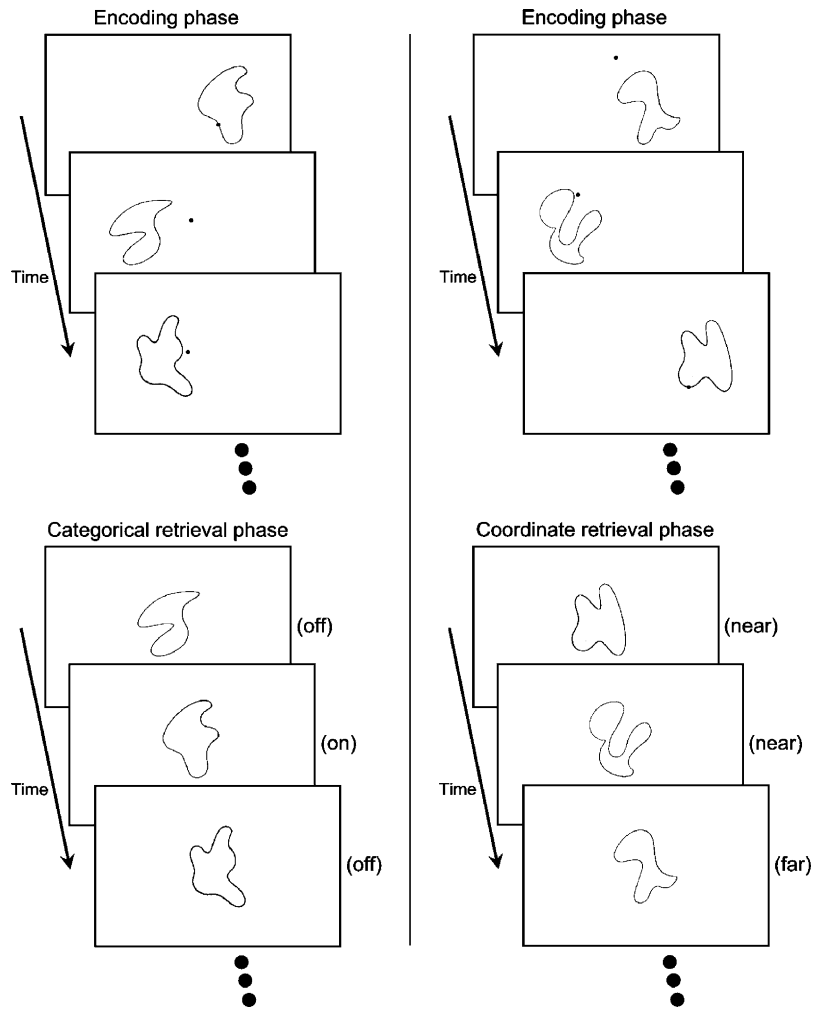


Fig. 1. Categorical and coordinate visual spatial memory tasks are illustrated to the left and right, respectively. During the encoding phase of both types of tasks, each shape was presented on the left or right side of the display along with a dot that was placed a variable distance from the shape (either 'on' the shape, 'near' to the shape, or 'far' from the shape). Participants were instructed to remember each shape and dot spatial configuration, but were not informed as to the type of subsequent retrieval task (to enforce consistent encoding processes). During the retrieval phase of both tasks, shapes were presented at the center (without the dots); participants responded whether the previously corresponding dot had been 'on' or 'off' of that shape in the categorical visual memory task, or responded whether the associated dot had been 'near' to or 'far' from that shape in the coordinate visual memory task (the coordinate task instructions included a line segment for use as a reference). Correct responses are shown to the right of each shape.

were instructed to press the right button if the corresponding dot had been previously presented 'on' the shape (i.e. distance of 0° of visual angle) and the left button if the corresponding dot had been previously presented 'off' the shape (i.e. greater than 0° of visual angle). During coordinate memory runs, participants were instructed to press the right button if the corresponding dot was previously 'near' the shape (i.e. closer than the reference distance – a horizontal line 1.4° of visual angle in width presented at the center of the screen – shown in the instruction screen) and the left button if the corresponding dot had been previously presented 'far' from the shape (i.e. farther than the reference distance shown in the instruction screen). All responses were made with the middle and index fingers of the left hand (one hand was used to eliminate the potential confound between hand of response and contrast condition). The six dot-shape pairs during categorical runs consisted of 2 'on', 2 'near', and 2 'far' configurations, while the coordinate runs consisted of 1 'on', 2 'near', and 3 'far' configurations. These configurations aimed at balancing response type (which would push to increase 'on' configurations) and bias participants against a categorical encoding strategy (which would push to decrease 'on' configurations), to support the encoding of the actual spatial configuration of each shape and the corresponding dot.

The proximity of the dot to the reference distance (i.e. within 2° of visual angle) was designed to make the coordinate memory task relatively difficult in an effort to increase the associated neural effects, given that coordinate

visual spatial processing hemispheric effects have been shown to be greater during more difficult task conditions (Slotnick et al., 2001). Although pilot results indicated that six shapes per block consistently produced an intermediate level of memory performance for both types of task, avoiding floor and ceiling effects, the behavioral results corresponding to the imaging session were corrupted. As such, a follow-up behavioral study was conducted in a separate group of participants, and indirectly confirmed an intermediate and similar level of categorical memory performance (69 ± 6.3 S.E.) and coordinate memory performance (83 ± 5.0 S.E.) ($t = 1.82$, two-tailed t -test, n.s.). These results reflect the subjective experience of an intermediate level of memory reported by participants from the imaging study, and when considered in light of the significant neural effects reported below (as a general failure in memory would predict null findings) provide compelling evidence that the imaging results reflect activity associated with categorical and coordinate visual spatial memory.

2.3. Imaging acquisition

Imaging data was acquired on a 1.5 T Phillips ACS-NT scanner with a standard birdcage head coil. T2*-weighted functional images used an echo

planar imaging (EPI) sequence (TR = 1000 ms, TE = 50 ms, flip angle = 70°, field-of-view = 240 mm × 240 mm, acquisition matrix = 64 × 64, slices = 15 (no gap), slice orientation = axial-oblique parallel to the AC–PC line, slice thickness = 7 mm, i.e. 3.75 mm × 3.75 mm × 7 mm resolution). Although our choice of TR might be considered relatively short this value is not uncommon (e.g., Buračas & Boynton, 2002; Christoff, Ream, Geddes, & Gabrieli, 2003; Dale & Buckner, 1997; Kourtzi, Tolia, Altmann, Augath, & Logothetis, 2003; Zeng, Gatenby, Zhao, & Gore, 2004), and if anything would tend to decrease our signal strength; our robust findings (see Section 3) show that this was not a concern. In addition, our slices might be considered relatively thick but this value is also not uncommon (e.g., Poldrack et al., 2001; Ruge et al., 2005; Todd & Marois, 2004), and would tend to increase our signal strength. Of critical importance, this slice thickness is completely sufficient to localize neural activity to a given Brodmann area by gyrus/sulcus intersection (i.e., the spatial resolution necessary to conduct the present analysis, as is discussed below). T1-weighted anatomic images were acquired using with the same slice thickness and slice position/orientation as the functional images but with higher in-plane resolution (TR = 500 ms, TE = 15 ms, flip angle = 90°, field-of-view = 240 mm × 240 mm, acquisition matrix = 256 × 256, i.e. 0.9375 mm × 0.9375 mm × 7 mm resolution), and if time allowed – which it did for five of the eight participants – additional high-resolution T1-weighted images were acquired using a multiplanar rapidly acquired gradient echo sequence (MPRAGE, 12.4 min acquisition time, TR = 8.1 ms, TE = 3.7 ms, flip angle = 8°, field-of-view = 256 mm × 256 mm, acquisition matrix = 256 × 256, slices = 256 (no gap), slice thickness = 1 mm, i.e. 1 mm isotropic resolution).

2.4. Imaging analysis

Unless otherwise noted, all pre-processing and data analysis was conducted using SPM99 (Wellcome Department of Cognitive Neurology). Functional image pre-processing included slice-time correction, motion correction, concatenation of runs, and spatial normalization to Montreal Neurological Institute (MNI) space (which included re-sampling at 3 mm isotropic resolution). No spatial smoothing was conducted to maximize the spatial precision of the results. A high-pass temporal filter with a cutoff period of 100 s was used. For each participant, the highest resolution anatomic volume available was normalized to MNI space (an automated process which included re-sampling at 1 mm isotropic resolution), and these normalized images were then averaged to produce a group anatomic image that was used to precisely identify the anatomic loci corresponding to the group functional results. Note that although the anatomic images were not acquired with the same protocol for all participants, the anatomic location of critical landmarks (e.g., the superior and inferior frontal sulci) following normalization to a common space was consistent across participants, thus ensuring the group localization reflected that of individual participants. For visualization purposes only, the group functional results were projected onto a surface reconstruction of a representative individual participant (Slotnick, Schwarzbach, & Yantis, 2003).

To identify differential prefrontal cortex activity associated with categorical and coordinate visual spatial memory, a ‘power analysis’ was conducted that involved two stages: (1) general linear modeling (i.e. beta-weight analysis) was used to identify neural regions associated with either categorical or coordinate visual spatial memory and (2) event-related timecourses were extracted from beta-weight analysis defined prefrontal cortex regions-of-interest (ROIs) to assess differential activity associated with categorical and coordinate visual spatial memory (i.e. timecourse analysis). For a detailed discussion of beta-weight versus timecourse analysis, see Slotnick (2005). For the beta-weight analysis, on an individual participant basis, each of the six event types (encoding instructions, encoding, categorical retrieval instructions, categorical retrieval, coordinate retrieval instructions, coordinate retrieval) was modeled by convolving a canonical hemodynamic response function with a square-wave reflecting that events stimulus onsets and durations. Note that these models incorporate baseline activity by modeling no activity at the beginning of each run, an absolute measure of baseline, in addition to modeling no activity during the other event types, a relative measure of baseline (e.g., the activity associated with categorical retrieval is modeled as high during the respec-

time epochs, but otherwise a baseline level of no activity is modeled). These event type models, in an additional to a model of constant value (allowing for the elimination of nuisance changes in the mean level of activity across runs), were entered into a general linear model and fit to the functional activity timecourse on a voxel-by-voxel basis. This produced a magnitude associated with each event type (i.e. beta-weights), where positive values indicate the corresponding voxel activity was correlated with a given event type (i.e. the activity was greater than baseline). As such, voxels with categorical or coordinate visual spatial memory beta-weights that were consistently positive across participants (where between participant variability was used to estimate variance) defined regions of visual spatial memory related activity ($p < 0.001$). Correction for multiple comparisons to $p < 0.05$ was enforced using a voxel cluster extent threshold procedure (see Slotnick & Moo et al., 2003; Slotnick & Schacter, 2004). This procedure is based upon the fact that the probability of observing clusters of activity due to voxel-wise type I error (i.e. noise) systematically decreases with increasingly large cluster sizes (while signal is expected to be associated with large clusters of activity). As such, a cluster extent threshold can be determined to ensure an acceptable level of corrected cluster-wise type I error. Specifically, a Monte Carlo simulation with 1000 iterations was conducted using the acquisition matrix and number of slices in our study to model the acquisition/brain volume (64 × 64 × 15), where activity at each voxel was modeled with a normally distributed random number (mean = 0, variance = 1) and then spatial autocorrelation was implemented through convolution with a 4.5 mm full-width-half-maximum Gaussian kernel (Aguirre, Zarahn, & D’Esposito, 1997). An individual voxel threshold was then applied to achieve the assumed voxel-wise type I error rate ($p < 0.001$). Finally, the spatial extent of each cluster was computed, the number of clusters of each size in the acquisition volume was tallied, and the probability of observing a given cluster extent was computed across iterations. The cluster extent threshold was taken to be the cluster size at or above which the sum of probabilities were below the desired corrected level of significance ($p < 0.05$). In the present study, this translated to a minimum cluster extent threshold of 11 re-sampled voxels.

The above beta-weight analysis identified all activity associated with the categorical or coordinate visual spatial memory tasks, including that associated with visual and motor processing. However, as pointed out in the introduction, the hypothesis under investigation relates specifically to prefrontal cortex activity. As such, only prefrontal cortex activity (and one medial temporal lobe region, analyzed based on its general relevance to memory research) was subjected to event-related timecourse analysis. Each prefrontal cortex ROI was located at the center of each unique Brodmann area and gyrus/sulcus intersection. For each ROI, individual participant event-related activity timecourses (from 0 to 10 s after stimulus onset) were extracted from voxels within a sphere of 7 mm radius. Timecourses were baseline corrected such that activity from 0 to 2 s following stimulus onset had a mean of zero, and were corrected for linear drift. The magnitude of timecourse activity was taken as the average of activity at 5 and 6 s following stimulus onset, given that the expected maximum value was between these values (i.e. 5.3 s, based on convolution of a square-wave with 3 s duration and a canonical hemodynamic response function). For additional details on timecourse analysis, see Slotnick and Schacter (2004).

In each ROI, the existence of differential activity associated with categorical and coordinate visual spatial memory was assessed using a paired two-tailed *t*-test (i.e. using between participant variability to estimate variance). Follow-up assessments to determine whether activity associated with categorical or coordinate visual spatial memory was positive in magnitude – which was predicted if this activity reflected increases in neural processing (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001) – were conducted using one-tailed *t*-tests. Hemispheric asymmetry in categorical and coordinate visual spatial memory was tested using a within participant ANOVA, as indicated by a significant condition × hemisphere interaction. Joint probabilities were computed using a Fisher test, where $\chi^2 = -2 \ln(p_1 p_2)$, p_1 and p_2 are the two individual probabilities, and there are four degrees of freedom (Fisher, 1973). Gender differences were assessed using a weighted mixed ANOVA (with condition as a within participant factor and gender as a between participant factor), by assessing whether there was a significant condition × gender interaction for left and right hemisphere ROIs. For all statistical tests, *p*-values < 0.10 were considered marginally significant and *p*-values < 0.05 were considered significant.

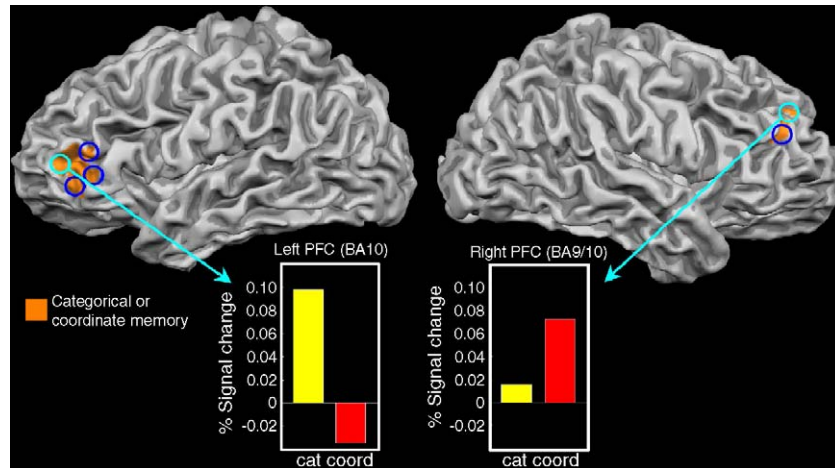


Fig. 2. Prefrontal cortex activity associated with categorical or coordinate visual spatial memory retrieval is shown in orange, projected onto the cortical surface reconstruction of a representative participant. Gyri are colored light gray and sulci are colored dark gray. Lateral views of the left and right hemispheres are illustrated to the left and right, respectively (superior toward the top and frontal poles toward the sides). Circles (in blue and cyan) demarcate the six prefrontal cortex regions-of-interest (ROIs). Differential activity was associated with categorical and coordinate visual memory in one left prefrontal cortex ROI (middle frontal gyrus, BA10) and one right prefrontal cortex ROI (middle frontal gyrus, BA9/10) marked by cyan circles, as revealed by the event-related activity designated by the cyan arrows. In the left prefrontal cortex (PFC) ROI, categorical (cat) memory related activity was significantly greater than coordinate (coord) memory related activity, while the opposite pattern of activity was observed in the right prefrontal cortex ROI. These results support the hypothesis that categorical and coordinate visual spatial memory are associated with activity in the left and right prefrontal cortex, respectively.

3. Results

The power analysis revealed activity in regions associated with visual spatial perceptual processing, including striate and extrastriate occipital cortex (right BA17, bilateral BA18 and BA19) extending into temporal cortex (bilateral BA37, left BA20 and BA21) and parietal cortex (left BA7 and bilateral BA40). Activity was also observed in regions associated with motor response (BA6 including the supplementary motor area and bilateral premotor cortex, BA24, and the right caudate; see Picard & Strick, 2001), eye movements (bilateral BA6, the frontal eye fields; see Paus, 1996), and in left insular cortex (BA13), a region that has been associated with a number of cognitive processes. A final non-prefrontal cortex region of activity was observed in the right parahippocampal cortex (BA36) within the medial temporal lobe, a finding which warrants further evaluation given that the medial temporal lobe has been shown to be critical for explicit memory retrieval (Schacter & Wagner, 1999). The right parahippocampal cortex (BA36) activity was located at $x = 15$, $y = -4$, $z = -12$ (Talairach coordinates), with both categorical and coordinate visual spatial memory activating this region to the same degree (categorical memory $t = 2.09$, $p < 0.05$, coordinate memory $t = 3.21$, $p < 0.01$, differential activity $t < 1$). This common right medial temporal lobe activity will be discussed in further detail below.

Apropos the hypothesis under investigation, six ROIs were identified in the prefrontal cortex (Fig. 2 and Table 1). Of these six prefrontal cortex ROIs, differential activity associated with categorical and coordinate visual spatial memory was observed in the left middle frontal gyrus (BA10; $t = 3.46$, $p < 0.05$) and the right middle frontal gyrus (BA9/10; $t = 2.82$, $p < 0.05$), with no differential activity in the remaining four ROIs (three t -values < 1 , one t -value = 1.24, all p -values > 0.20). Furthermore,

categorical but not coordinate visual spatial memory evoked left middle frontal gyrus ROI (BA10) activity that was positive in magnitude (categorical $t = 1.97$, $p < 0.05$; coordinate $t < 1$) while coordinate but not categorical visual spatial memory evoked right middle frontal gyrus ROI (BA9/10) activity that was positive in magnitude (coordinate $t = 2.77$, $p < 0.05$; categorical $t < 1$), indicating that these cognitive processes were associated with increases in neural activity (Logothetis et al., 2001). The left and right prefrontal cortex hemispheric specialization for categorical and coordinate visual spatial memory was confirmed by a significant condition \times hemisphere interaction ($F(1, 7) = 16.26$, $MS_{\text{error}} = 0.0044$, $p < 0.01$). Of importance, the differential activity in left and right prefrontal cortex survived correction for multiple comparisons (post-hoc Bonferroni corrected in left prefrontal cortex, $p < 0.05$, right prefrontal cortex, $p < 0.10$, and joint $p < 0.01$; one-tailed paired t -tests), as did the condition \times hemisphere interaction (Bonferroni corrected $p < 0.05$). These differential prefrontal cortex effects were highly consistent, as every single participant evinced greater categorical than coordinate visual spatial memory related activity in

Table 1
Prefrontal cortex regions-of-interest (ROIs) associated with categorical or coordinate visual spatial memory

Region	BA	x	y	z
Left middle frontal gyrus	10	-45	55	3
Left inferior frontal gyrus	10	-48	43	-7
Left middle frontal gyrus	46	-48	38	6
Left inferior frontal gyrus	46	-50	38	-2
Right middle frontal gyrus	9/10	33	45	31
Right middle frontal gyrus	46	50	41	12

BA refers to Brodmann area and coordinates (x , y , z) are reported in Talairach space.

the left prefrontal cortex and evinced greater coordinate than categorical visual spatial memory related activity in the right prefrontal cortex. In addition, there was no effect of gender in either of the differential prefrontal cortex ROIs, as indicated by non-significant condition \times gender interactions (left hemisphere ROI, $F(1, 6) < 1$; right hemisphere ROI, $F(1, 6) < 1$).

4. Discussion

In direct support of our hypothesis, we observed a double dissociation with regard to visual spatial memory related activity in prefrontal cortex – a region in left prefrontal cortex (BA10) was associated with categorical visual spatial memory and a region in right prefrontal cortex (BA9/10) was associated with coordinate visual spatial memory. Furthermore, a right parahippocampal gyrus region (BA36) was identified that was associated with both types of visual spatial memory. The latter finding is consistent with previous results associating the right parahippocampal gyrus with visual spatial memory (in neuropsychology, Bohbot et al., 1998; see also, Kopelman, Stanhope, & Kingsley, 1997; in neuroimaging, Johnsrude, Owen, Crane, Milner, & Evans, 1999; unpublished results from Slotnick & Moo et al., 2003, where accurate spatial source memory versus correct rejection was associated with activity in the right parahippocampal gyrus (BA36) at Talairach coordinates $x = 30, y = -15, z = -24$). Given that the parahippocampal cortex has been associated with perceptual processing of visual context (Bar & Aminoff, 2003; Epstein & Kanwisher, 1998), sensory/contextual activity within this region may reflect the process of visual memory construction (Slotnick, 2004).

The present differential prefrontal cortex results associated with visual spatial memory retrieval are consistent with previous studies showing differential hemispheric activity associated with visual spatial perception (Baciu et al., 1999; Kosslyn et al., 1998; Laeng, 1994; Laeng et al., 2002; Slotnick et al., 2001). This is not surprising, given the extensive history of behavioral research relating memorial encoding and retrieval (Roediger, Gallo, & Geraci, 2002; Tulving & Thomson, 1973) and similar prefrontal cortex activity associated with both of these cognitive processes (for a detailed review, see Fletcher & Henson, 2001). Based on these similarities, it could be asked whether our differential prefrontal cortex results are due to differences in the process of retrieval per se, or rather differences in perceptual or decision processes. As the stimuli were well matched across conditions (see Section 2), perceptual differences can be ruled out as an explanation. However, encoding and imagery tasks have been associated with differential categorical and coordinate activity in the left and right prefrontal cortex, respectively (BA46, BA47 in Kosslyn et al., 1998; BA9/44 in Trojano et al., 2002). This might be taken to suggest that differential decision processes – which presumably would activate similar prefrontal regions regardless of the task (encoding, imagery, or retrieval) – may underlie our memory retrieval results. Although this is a viable possibility, it is important to consider that the differential prefrontal cortex activations in the previous studies were posterior to those found in the present study (i.e., BA10, BA9/10), which would argue against the notion that the differential pre-

frontal cortex activations observed in the previous and present studies reflect task independent decision processes. Nonetheless, as is typically done in the field of memory, we have defined retrieval as a unitary cognitive process (that includes retrieval content in addition to decision processes such as post-retrieval monitoring; for a review, see Slotnick & Schacter, *in press*); as such, our results can be considered as retrieval related differential prefrontal cortex activity.

Our prefrontal cortex results shed light on previous observations regarding prefrontal cortex hemispheric asymmetries during long-term memory (i.e. source memory and item memory). Evidence from previous studies that have investigated both source memory and item memory indicates that the left prefrontal cortex is associated with source memory retrieval, while the right prefrontal cortex is associated with item memory retrieval (Cansino et al., 2002; Nyberg et al., 1996; Rugg et al., 1999; Slotnick & Moo et al., 2003; see also, Buckner, 1996; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994).

The present results are particularly relevant to previous spatial source memory findings, given that spatial source memory paradigms can be considered directly analogous to our categorical visual spatial memory task. More specifically, participants in spatial source memory paradigms are presented with studied items and make a categorical response as to the previously studied spatial location (e.g., ‘on the left side of the display’ or ‘on the right side of the display’). As such, it is perhaps not surprising that the left prefrontal cortex has been associated with this cognitive function. However, source memory for non-spatial attributes (e.g., color, object size, gender of speaker) has also been associated with left prefrontal cortex (Dobbins, Foley, Schacter, & Wagner, 2002; Fan, Snodgrass, & Bilder, 2003; Lundstrom et al., 2003; Ranganath, Johnson, & D’Esposito, 2000). These findings suggest that the left prefrontal cortex may be associated with both spatial and non-spatial categorical memory. This reformulation underscores the fact that source memory paradigms in general require categorical processing.

To extend our item memory findings, coordinate visual spatial processing is considered on a single item basis, rather than between items, with reference to spatial relationships between parts or features of an item (e.g., the spatial relations among parts of an imaged object during shift transformations, Kosslyn, 1987; the relative position of the hands on a clock, Michimata, 1997; the precise position of an eye on a face, Cooper & Wojan, 2000). Of particular relevance, Laeng and colleagues have shown the right hemisphere is preferentially associated with conventional object processing (while the left hemisphere is preferentially associated with contorted object processing; behavioral evidence, Laeng et al., 1999; neuropsychological evidence, Laeng et al., 2002). Moreover, the right hemisphere (Marsolek, 1995, 1999) and in particular the right fusiform cortex (Garoff, Slotnick, & Schacter, 2005; Koutstaal et al., 2001) has been associated with specific visual memory, which can be taken to reflect within-item coordinate based visual spatial processing. Therefore, item memory may be associated with the right prefrontal cortex because of the associated within item specific/coordinate visual spatial feature processing.

5. Conclusion

In the present study, the left prefrontal cortex has been associated with categorical visual spatial memory and the right prefrontal cortex has been associated with coordinate visual spatial memory. The left prefrontal cortex categorical memory finding provides a direct explanation for source memory related activity in this region given the categorical nature of the associated decisions, and the right prefrontal cortex coordinate memory finding suggest item memory related activity in this region may be due to within-item coordinate visual spatial processing. To our knowledge, this is the first time that source memory related activity in left prefrontal cortex has been directly linked to categorical visual spatial processing and also the first time that item memory related activity in the right prefrontal cortex has been directly linked to coordinate visual spatial processing. The prefrontal cortex categorical and coordinate visual spatial memory hemispheric processing distinction parallels the prefrontal cortex item and spatial working memory ventral–dorsal processing distinction, in that both extend the same processing distinctions associated with visual spatial perception to the domain of visual spatial memory. Taken together, the present results and previous working memory results provide convergent evidence that visual memory related activity in the prefrontal cortex can reflect the same functional–anatomic segregation that has been classically associated with visual perception related activity in more posterior regions.

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