

Specific and Nonspecific Neural Activity during Selective Processing of Visual Representations in Working Memory

Hwamee Oh and Hoi-Chung Leung

Abstract

■ In this fMRI study, we investigated prefrontal cortex (PFC) and visual association regions during selective information processing. We recorded behavioral responses and neural activity during a delayed recognition task with a cue presented during the delay period. A specific cue (“Face” or “Scene”) was used to indicate which one of the two initially viewed pictures of a face and a scene would be tested at the end of a trial, whereas a nonspecific cue (“Both”) was used as control. As expected, the specific cues facilitated behavioral performance (faster response times) compared to the nonspecific cue. A postexperiment memory test showed that the items cued to remember were better recognized than those not cued. The fMRI results showed largely overlapped activations across the three cue conditions in

dorsolateral and ventrolateral PFC, dorsomedial PFC, posterior parietal cortex, ventral occipito-temporal cortex, dorsal striatum, and pulvinar nucleus. Among those regions, dorsomedial PFC and inferior occipital gyrus remained active during the entire postcue delay period. Differential activity was mainly found in the association cortices. In particular, the parahippocampal area and posterior superior parietal lobe showed significantly enhanced activity during the postcue period of the scene condition relative to the Face and Both conditions. No regions showed differentially greater responses to the face cue. Our findings suggest that a better representation of visual information in working memory may depend on enhancing the more specialized visual association areas or their interaction with PFC. ■

INTRODUCTION

Findings from animal and human investigations have shown that prefrontal cortex (PFC) has diverse functions in supporting the control of behavior from information processing to planning to decision making and response execution (Miller & Cohen, 2001; Fuster, 1989; Goldman-Rakic, 1987). A parallel line of experimental psychology research has formulated working memory as a cognitive construct that supports the maintenance and manipulation of information required by virtually all complex functions such as speech comprehension and reasoning (Baddeley & Hitch, 1974). The roles of prefrontal and visual association regions and their interactions during controlled information processing have been subjects of current interest and debate in the field of cognitive neuroscience (e.g., Miller & Cohen, 2001; Fuster, 1989; Goldman-Rakic, 1987).

The control of information processing must rely on the ability to select task-relevant information and ignore task-irrelevant information, which is important for the adaptive interaction between a person and the ever-changing environment. Neuroimaging and neuropsychological studies have examined the underlying neural substrates by apply-

ing a probe-familiarity manipulation in delayed recognition tasks (e.g., Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998). In particular, ventrolateral PFC has been implicated in resolving semantic competition among possible conceptual associates from long-term memory (Thompson-Schill, 2003; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997) and proactive interference caused by recently experienced probes/events (Nelson, Reuter-Lorenz, Sylvester, Jonides, & Smith, 2003; Zhang, Leung, & Johnson, 2003; D’Esposito, Postle, Jonides, & Smith, 1999). Others have further suggested that different parts of the frontal and posterior parietal cortices are involved in selecting and/or inhibiting verbal and spatial information that are no longer relevant in working memory (Leung & Zhang, 2004). However, because task-relevant and task-irrelevant stimuli in these studies were drawn from the same material type and were presented simultaneously, it is impossible to determine whether the interference was resolved by enhancing task-relevant information, suppressing task-irrelevant information or both.

More recent neuroimaging studies have investigated the cognitive control of information processing from the perspective of attentional modulation of perceptual and working memory processes. Some of these studies have made use of the functional specialization in visual processing of face and scene stimuli observed in the visual association regions such as lateral fusiform gyrus (FG;

commonly referred as FFA) (Kanwisher, McDermott, & Chun, 1997; Puce, Allison, Gore, & McCarthy, 1995) and parahippocampal gyrus (PHG, commonly referred to as PPA) (Aguirre, Zarahn, & D'Esposito, 1998; Epstein & Kanwisher, 1998), respectively. By presenting a cue before stimulus presentation, these studies showed that activity in FG and PHG was enhanced or reduced depending on the specific encoding requirement of face and scene stimuli compared to passive viewing (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005). Egnor and Hirsch (2005) also demonstrated heightened activity in FG to pictures of famous faces in the presence of distraction (an incongruent name) in a modified Stroop task. By showing that changes in activity of FG and PHG followed the cue instruction (e.g., switch to remembering face) during the delay period of a delayed recognition task, Lepsien and Nobre (2007) suggested that shifting attention between items in working memory may involve the top-down modulation of FG and PHG activity by PFC.

However, whether the subdivisions of PFC play any specific role in selective information processing remains unclear. Johnson et al. (2005) have shown that lateral PFC is involved in refreshing visual information in working memory. They found that left middle frontal gyrus (MFG) and inferior frontal gyrus (IFG) were active in correspondence to refreshing words and pictures of people and places and that right anterior PFC was more active with refreshing pictures of people. These PFC areas were not reported in most of the working memory studies described above, although Gazzaley et al. (2007) recently examined the functional connectivity between dorsolateral PFC and visual association regions by applying beta-series correlation analysis on the data they previously reported in 2005. They found that activity in left MFG was positively correlated with activity in a seed region such as PHG and the degree of correlation significantly varied depending on the specific task (i.e., remembering scenes but ignoring faces vs. remembering faces but ignoring scenes).

Although there are different connotations associated with each finding, previous studies together suggest that information control in working memory is achieved by either selecting task-relevant items, inhibiting task-irrelevant items, or both, and is supported by a distributed network including prefrontal, temporal, and subcortical regions. Similar issues have been considered in behavioral research using the directed forgetting paradigm to examine the effect of cued remembering versus cued forgetting on memory retrieval (MacLeod, Dodd, Sheard, Wilson, & Bibi, 2003; Brown, 1954). The purpose of our study was to determine the involvement of prefrontal and visual association regions during selective information processing by examining brain activity in correspondence to specific versus nonspecific memory cues during a delayed recognition task. It was expected that if a region is involved in selective maintenance, its activity would be correspondingly greater to the relevant specific cue than to the nonspecific cue.

METHODS

Participants

Twelve healthy adults (6 women, age = 18–33 years, mean = 22.6 years) were recruited from the Stony Brook campus. All participants had no history of neurological disorder, psychiatric disorder, and drug abuse according to self-report and had normal or corrected-to-normal vision. Prior to participation, they gave informed consent that was reviewed and approved by the Institutional Review Board of the State University of New York at Stony Brook.

Visual Stimuli

Our stimulus database for this study consisted of 95 unique pictures of faces and 95 scenes. Face stimuli were adopted from Nimstim database (www.macbrain.org/resources.htm) and Nottingham face database from University of Sterling (<http://pics.psych.stir.ac.uk/>) under the permission of using them and images were cropped in order to eliminate most of the hair and some body parts (e.g., neck, ear) (see Figure 1). Scene stimuli, most of which were mountains and lakes, were either adopted from the digital library at UC-Berkeley (<http://calphotos.berkeley.edu/landscape/>) or downloaded from the Internet. All images were scaled into the same size (subtended visual angle of $3^\circ \times 4^\circ$), converted to black and white, and equalized for brightness. Pictures were not repeated during the main working memory task. Another set of eight pictures was used in the localizer task (see below). Since previous studies often only use a limited number of stimuli (usually less than 24), the level of attention and other cognitive demands may interfere with mnemonic processes (e.g., selective rehearsal). We therefore chose not to repeat the visual stimuli except for matched probes.

Working Memory Task

In order to study the specificity of brain activity to selective information processing in working memory, we used a delayed recognition task with a cue inserted during the delay period. The task included three conditions: remember face, remember scene, and remember both (Figure 1A). On each trial, a fixation point (a small green square) was first presented for 2.5 sec on a black background and it turned into red for 200 msec as a warning before stimulus presentation. After 300 msec, two pictures (a face and a scene) were presented sequentially, each for 800 msec, with a 200-msec ISI. After the disappearance of the second picture, a mask (black-and-white checkerboard) was displayed for 200 msec. After a delay of 2.5 sec, a cue word ("Face" or "Scene" or "Both") was presented in the center of the screen for 1 sec, indicating the picture category to be tested at the end of a 9.5-sec delay. Because all the cues were valid, the participants would only need to remember either the face or the scene image if they saw "Face"

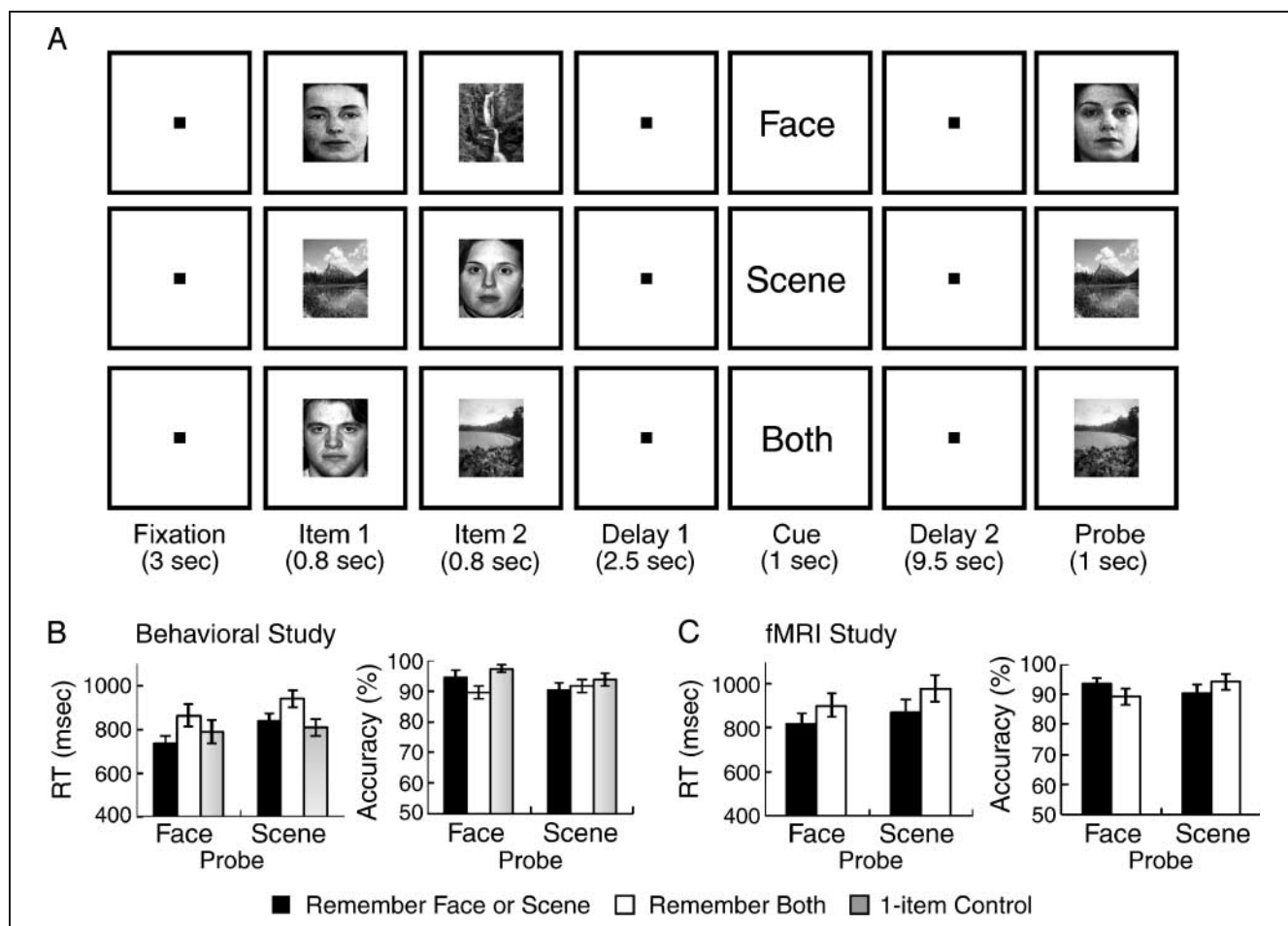


Figure 1. Selective maintenance paradigm and behavioral results. (A) A schematic diagram of the delayed recognition task. The three task conditions (remember face, remember scene, and remember both) differed only in the cue word displayed after the presentation of the two picture stimuli. The cues were “face,” “scene,” and “both,” indicating the participants to remember only the face, scene, or both pictures, respectively. All the probes were valid and pictures were not repeated except for the matched probes. For simplicity, the warning signal, ISI (200 msec), visual mask (black and white checkerboard), and ITI (8–14 sec) were not shown in the figure. (B) Behavioral results from the experiment conducted outside of the scanner. Bar graphs show the mean response time (\pm standard error of the mean [SEM]) and the mean accuracy (\pm SEM) for each task condition divided by the two probe types (face and scene). (C) Behavioral results from the fMRI experiment. Black bars = selection conditions (remember face or remember scene); white bars = remember both; gray bars = 1-item control.

(i.e., Remember Face) or “Scene” (i.e., Remember Scene), respectively. However, they were told to remember both images, if they saw “Both” (i.e., remember both). Either a new or a matched picture (50/50) was presented as a probe for the participants to make a response to indicate whether or not it was identical to the one they were supposed to remember. For Remember Both, half of the probes were faces and half were scenes. The intertrial interval (ITI) varied between 8 and 14 sec with a mean of 11 sec. The gender of face images, response type, and stimulus presentation order were counterbalanced across conditions and blocks.

We collected additional behavioral data from a separate group of subjects ($n = 12$, mean age = 19.5 years), outside of the magnet. Aside from the task conditions described above, we included two 1-item conditions where only one face or one scene was presented for the subjects to remember. The experimental procedure and param-

eters were the same as above, except the ITI was shortened to 2 sec.

Postexperiment Memory Test

To test whether the visual items cued to be selected in the main task were better remembered, as demonstrated in previous studies using the directed forgetting paradigm (MacLeod & Daniels, 2000; Macleod, 1989), we recruited yet another group of 12 subjects (7 women, mean age = 19.6) to perform a surprise postexperiment task in addition to the working memory task outside of the scanner. The postexperiment memory test included three types of pictures: 20 items that were previously cued to remember (“old-cued”), 20 items that were not cued to remember (“old-not cued”), and 20 new pictures (“new”). Half of the pictures were faces and half were scenes, with equal number of each type selected from

the remember face and remember scene conditions. The pictures were presented consecutively in a random order and counterbalanced across subjects. Subjects made old/new judgment to each picture, indicating whether or not they have seen the picture during the main task. Accuracy was emphasized, thus each picture remained on the screen until a response was made.

Localizer Task

The localizer task was used to determine brain regions that show greater responses to faces in comparison to scenes, and vice versa. It was in 1-back task format, where one determines whether or not the current stimulus matches the last stimulus. Our task had eight alternating blocks (4 face blocks and 4 scene blocks). Each task block was 16 sec long and they were separated by a 16-sec fixation period. Within each task block, eight visual images were sequentially presented, each for 800 msec, with a 1.2-sec ISI.

General Experimental Procedure

Visual stimuli were presented using Inquisit 1.33 (Millisecond Software LLC, Seattle, WA, USA). The participants practiced the working memory task (about 20 min) and localizer task (about 10 min) before the fMRI session. During the scanning session, they performed five runs of the main working memory task and then one run of the localizer task. Overall, there were 20 trials for each cue condition in the main working memory task.

Participants made responses by pressing a button on the button box using their index fingers. The left/right hand-button designation for the yes/no responses was counterbalanced across participants. Response times and accuracy data were recorded during scanning.

fMRI Data Acquisition

Whole-brain images were acquired using a Philips 3-Tesla Achieva System (Cleveland, OH). High-resolution anatomical images were acquired with a T1-weighted three-dimensional turbo field echo sequence (repetition time [TR] = 9.9 msec; echo time [TE] = 4.6 msec; flip angle [FA] = 25°; field of view [FOV] = 256 × 256 mm). A T1-weighted in-plane anatomical volume of 24 axial-oblique slices, parallel to the anterior commissure–posterior commissure (AC–PC), was acquired (TR = 300 msec, TE = 5 msec, FA = 60°, FOV = 220 × 220 mm, matrix size = 256 × 256, slice thickness = 5 mm). For the main task, volumes of functional images were acquired using a T2*-weighted EPI sequence (TR = 1.5 sec; TE = 30 msec; flip angle = 80°, FOV = 220 × 220 mm). Each functional volume consisted of 24 axial slices in the same orientation as the in-plane images. For the localizer task, the same functional scanning parameters were used, except that the TR was 2 sec. Four dummy volumes were acquired at the be-

ginning of each functional run to allow the MR signal to reach equilibrium and these images were later discarded from the dataset before image processing and analysis.

Image Processing and Analysis

All preprocessing and statistical analyses were conducted using SPM2 (Wellcome Department of Cognitive Neurology, London, UK). Functional images were corrected for differences in slice timing. Head motion was corrected using a six-parameter rigid-body correction to realign each image to the first volume of the middle run. The in-plane and high-resolution images were segmented into gray and white matter and coregistered with the mean functional image. Images were then normalized to the MNI gray matter template brain using a 12-parameter affine registration followed by nonlinear transformations (Friston et al., 1995). Lastly, images were smoothed with a Gaussian kernel of 8 mm at a full width at half maximum.

We used the General Linear Model (GLM) to construct a design matrix for each individual dataset. We defined the onset times of stimulus presentation, cue, mid-delay, and probe as events for each cue condition in the working memory task. Mid-delay event is defined as the middle of the postcue delay period, following the same procedure used in previous studies of delay-related activity (Postle, Zarahn, & D'Esposito, 2000). Each event vector was convolved with a canonical hemodynamic response function and entered as a regressor in the GLM for analysis. For each individual, estimated parameters of the regressors (beta weights) were calculated for each voxel using the GLM and were used in the *t* tests to assess the main effects of task events and the differences between the task conditions (e.g., remember face vs. remember both). For group analysis, treating subjects as a random effect, a one-sample *t* test was applied to assess the effects of interest using the corresponding contrast image from each individual.

We also conducted regions of interest (ROI) analysis to examine cortical activity during the working memory task. ROIs were defined as spheres (radius = 5 mm) centered on the peak coordinates of the activation clusters obtained from the group composite maps. We used the MarsBar Matlab toolbox (Brett, Anton, Valabregue, & Poline, 2002) (<http://marsbar.sourceforge.net>) to extract data from each individual. Time courses were calculated by averaging signal from all the correct trials of each condition across subjects. The percent signal change for each time point was calculated relative to fixation baseline, which was the average of the first two volumes of a trial.

A separate GLM was constructed for each individual using data from the localizer task. Epochs of each 1-back task (face or scene) were modeled with a boxcar function and convolved with a canonical hemodynamic response function. Activation clusters showing preferential responses to face and scene stimuli were individually identified, and subject-specific face and scene ROIs were defined using the following steps. To define the face ROIs

of an individual, we used the face–scene contrast at a low threshold ($p < .1$, uncorrected) and used small-volume correction to identify activation peaks in both hemispheres in the FG masks. Anatomical masks were constructed from AAL (WFU_PickAtlas by Advanced Neuroscience Imaging Research Lab, Winston-Salem, NC; www.fmri.wfubmc.edu/download.htm). We then defined a spherical ROI centered in the individual’s peak coordinates with a 5-mm radius. For two subjects, their peak coordinates were two standard deviations away from the mean coordinates of the group so we used the mean coordinates in replacement of the originally identified ones. Scene-related ROIs were defined following the same procedures, except that we identified the peak activations using the scene–face contrast with an anatomical mask of PHG in both hemispheres. The peak coordinates identified for the scene-related activations of each subject were all within one standard deviation from the mean.

RESULTS

Behavioral Results

Both response time and accuracy data were analyzed by repeated measures analyses of variance (ANOVAs) and post hoc paired t tests. The results are summarized in Figure 1B and C. Data points three standard deviations away from the mean were not included in the response time analysis (less than 1% of total trials). For the behavioral data collected outside of the magnet (Figure 1B), average response times for Remember Face (736.8 msec) and Remember Scene (837.2 msec) were faster compared to Remember Both (overall mean = 901.9 msec; face probe = 863.29 msec; scene probe = 940.56 msec) [$F(1, 11) = 57.39, p < .001$] but not significantly different from the 1-item control condition (all $ps > .3$). Paired t tests further confirmed that the response times to the probes in Remember Face or Remember Scene were faster than to the corresponding probes in Remember Both [face probe: $t(11) = -4.834, p = .001$; scene probe: $t(11) = -5.068, p < .001$]. The average accuracy for each condition was above 90% [$F(1, 11) = 2.98, p > .05$].

Similar behavioral performance was observed during the fMRI experiment (Figure 1C). We again found faster average response times for Remember Face (817.0 msec) and Remember Scene (870.7 msec) compared to Remember Both (overall mean = 939.2 msec; face probe = 901.31 msec; scene probe = 977.17 msec) [$F(1, 11) = 44.13, p < .001$]. Paired t tests again confirmed that the response times to probes in Remember Face or Remember Scene conditions were faster than to those in Remember Both [face probe: $t(11) = -4.985, p < .001$; scene probe: $t(11) = -5.163, p < .001$]. The average accuracies were above 89% for all conditions and the differences were insignificant [$F(1, 11) = 0.03, p > .1$]. The interaction between probe (face vs. scene) and cue (specific vs. non-specific) was marginally significant [$F(1, 11) = 5.05, p =$

.05]; the subjects were slightly more accurate in Remember Face than in Remember Both [$t(11) = 1.84, p = .05$, one-tailed], although the difference between Remember Scene and Remember Both was insignificant [$t(11) = 1.08, p = .15$, one-tailed]. As expected, the behavioral data showed that recognition performance was facilitated by the specific cues compared to the nonspecific cue.

To determine the fate of cued and noncued pictures in remember face and remember scene, we conducted a postexperiment memory test in another group of subjects outside of the magnet after they performed the main working memory task. Of primary interest were hit rates and correct rejection rates, which are proportion of correct recognition responses to pictures from the main task (old–cued and old–not cued) and new pictures, respectively. A one-way ANOVA revealed significant differences in recognition response to the three types of pictures [$F(2, 22) = 3.66, p = .04$]. Paired t tests showed that the hit rate for the old–cued pictures (i.e., those previously cued to remember; mean = 0.73, $SE = 0.03$) was significantly higher than that for the old–not cued items (i.e., those previously not cued; mean = 0.62, $SE = 0.05$) [$t(11) = 3.12, p = .01$, two-tailed]. Mean correct rejection rate for the new items was 0.76 ($SE = 0.03$). Differences between old–cued and new, as well as between old–not cued and new, were not significant ($ps > .05$).

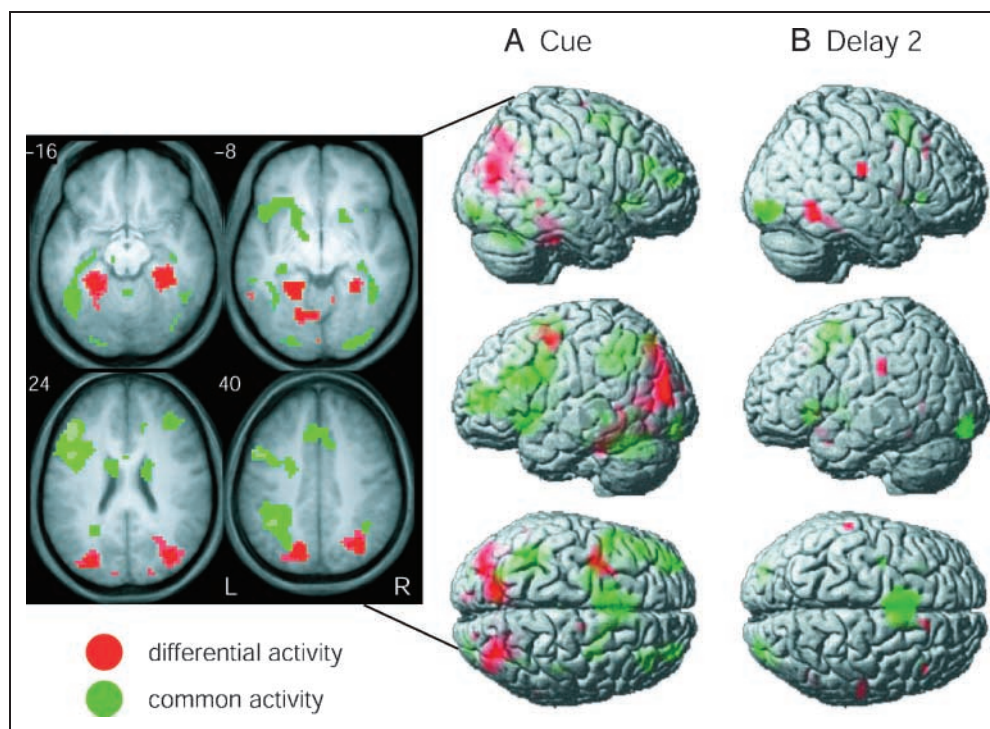
fMRI Results

Cue and Delay Period Activity: Common and Differential Activity across Conditions

Transient increases in response to all three task cues (“Face,” “Scene,” or “Both”) were observed in MFG, IFG, anterior insula, medial superior frontal gyrus (mSFG), superior parietal (SPL) and inferior parietal (IPL) lobes, FG, inferior occipital gyrus (IOG), striatum, and thalamus ($p < .001$, FDR corrected). Figure 2A illustrates these common activations in green color and Table 1A lists the peak coordinates and Z values of the suprathreshold activations. Among them, sustained activity during the delay period was observed in bilateral IFG/insula, left mSFG, bilateral IOG, and subcortical regions (Figure 2B and Table 1B). Similar patterns of activations have been previously observed in studies of object working memory (e.g., Courtney, Ungerleider, Keil, & Haxby, 1997).

In comparison, we conducted one-way ANOVAs to determine regions that showed differential responses to the task cues (Figure 2, red-colored activations). Left MFG (anterior to the frontal eye fields), left posterior SPL, and medial temporal and occipital regions showed differential responses to the different cues ($p < .01$, FDR corrected). Note that the part of SPL showing differential cue-related responses is more ventral and posterior to the part that is commonly activated across conditions (Figure 2A, inset). Differences in activation during the postcue delay period were revealed in several regions including PHG only when

Figure 2. Common and differential activity across the three cue conditions. Group composite maps are shown on the right and left lateral and dorsal surfaces of the rendered MNI single-subject brain for responses to the cue (A) and during the postcue delay period (B). Conjunction analysis was used to reveal suprathreshold activations (green) common to all three conditions (face, scene, and both). One-way ANOVA was used to reveal suprathreshold activations (red) differentiated across the three conditions. Threshold at $p < .001$ (uncorrected) is used for visualization and axial slices are shown to display activations in the medial temporal and occipital regions. Numbers indicate the Z-coordinates in millimeters. Note that the differential activation in SPL was found more posterior and ventral to the common activation. L = left; R = right.



the threshold was lowered to $p < .001$, uncorrected (Figure 2B and Table 1B). Taken together, the prefrontal areas responded about equally to the different cues, whereas the visual association regions showed the most differences in response to the cues (see below).

Activity Unique to the Selection Process

To further determine whether PFC and/or visual association regions are uniquely involved in the process of selecting visual information in working memory, we compared responses to the specific cues (Face/Scene) with the nonspecific cue (Both). A conjunction analysis of contrasts [Remember Face–Remember Both] and [Remember Scene–Remember Both] did not reveal any regions in common to them for the cue period even at a lower threshold ($p < .01$, uncorrected). A common cluster (due to less deactivation) was found in postcentral gyrus ($x = 54$, $y = -18$, $z = 24$) during the postcue delay period ($p < .005$, uncorrected, cluster size ≥ 20), although a close examination of the time courses showed only weak differences. Our data therefore provide little or no evidence supporting a unique neural substrate for selecting/ignoring information in working memory.

Activity in PHG and FG during Selective Maintenance of Face or Scene

Using the individually defined ROIs that showed preferential responses to scene and face stimuli during the localizer

task, we examined whether they were modulated by the different cues in the main working memory task. The results are shown in Figure 3. PHG in both hemispheres showed differential activity in response to the different cues [left PHG: $F(2, 22) = 6.43$ and $p = .006$; right PHG: $F(2, 22) = 8.48$ and $p = .002$]. Student's t tests indicated that activity in PHG during the cue and delay periods was significantly stronger in response to Remember Scene in comparison to Remember Face (left PHG: $p = .01$; right PHG: $p = .02$, with Bonferroni correction) but insignificant in comparison to Remember Both after multiple comparison correction (left PHG: $p = .10$; right PHG: $p = .12$). Activity in PHG during Remember Face was lower than that during Remember Both (approaching significance, $p = .06$ with Bonferroni correction). Thus, the level of activation in PHG during Remember Both was in between the specific cue conditions, with the picture scene relevant in one case (Remember Scene) but no longer relevant in another (Remember Face).

In contrary, activity in FG, an area considered preferential for face perception and recognition, did not differentiate between the different cues, except during the probe stage [right FG: $F(2, 22) = 8.354$, $p = .002$; left FG: $F(2, 22) = 4.355$, $p = .025$]. No other regions showed significantly greater responses in correspondence to Remember Face than to Remember Scene. However, direct contrast of Remember Face to Remember Scene revealed activations in MFG (BA 46), anterior PFC (BA 10), and caudate nucleus during the postcue delay period at a lower threshold ($p < .005$, uncorrected).

Table 1. Results of Conjunction Analysis for Active Regions in All Three Cue Conditions

<i>Lobe</i>	<i>Region</i>	<i>BA</i>	<i>Cluster Size</i>	<i>MNI Coordinates</i>			<i>t</i>	<i>Z</i>
				<i>x</i>	<i>y</i>	<i>z</i>		
<i>(A) Cue Period</i>								
Frontal	MFG	46	824	-45	30	27	8.72	6.24
	MFG	10		-42	48	12	8.07	5.95
	PrCS	44/9/6		-48	6	33	6.74	5.31
	MFG ^a	9/8	94	-18	-3	45	7.22	5.55
		6		-30	-3	60	6.08	4.95
	MFG	46	27	33	36	24	5.5	4.6
	MFG	10	17	33	54	18	5.15	4.38
	mSFG	6/8	190	0	18	48	6.25	5.04
		6		-9	9	54	4.75	4.12
		SFG	6	8	24	0	57	4.65
	Insula/IFG ^b		89	27	30	3	4.52	3.96
Parietal	IPL	40	358	-39	-51	39	7.66	5.76
	SPL/IPS	7		-24	-75	51	6.68	5.28
	SPL/PCu	7		-12	-75	54	6.32	5.08
Temporal	MTG	21	154	39	-51	-3	7.88	5.87
	ITG/MTG	37/19	157	-36	-60	-3	6.99	5.44
	FG/Cblm	37		-42	-54	-24	6.14	4.98
	Cblm			-39	-69	-30	5.45	4.57
	FG		7	-39	-27	-21	4.59	4.01
Occipital	IOG	18	49	30	-93	-9	6.6	5.24
	IOG	18	30	-27	-93	-9	6.49	5.18
Subcortical	Lent Nuc ^c		65	-18	12	0	6.72	5.3
				-18	-3	12	5.86	4.82
	Caudate			-12	-3	24	5.03	4.3
	Lent Nuc		10	18	12	-9	4.59	4.01
	Pulvinar		81	-21	-36	0	5.45	4.57
				-15	-30	9	5.07	4.33
	Pulvinar ^c		25	24	-33	0	6.29	5.06
			18	-33	6	5.07	4.33	
	Cblm/FG		58	39	-69	-30	5.57	4.64
<i>(B) Delay-2 Period</i>								
Frontal	mSFG	6	368	-3	12	57	5.7	4.72
	ACG	8/32		-9	15	45	5.08	4.34
	ACG	32/24		9	18	36	3.76	3.41
	Insula/IFG	47	59	-30	21	-3	4.71	4.09
	IFG	47	7	42	24	0	3.75	3.4

Table 1. (continued)

Lobe	Region	BA	Cluster Size	MNI Coordinates			t	Z
				x	y	z		
Occipital	IOG	18	65	-30	-90	-15	8.64	6.21
	IOG	18	101	27	-96	-9	6.65	5.26
				36	-87	-9	5.73	4.74
Subcortical	SC		81	-3	-24	-12	4.48	3.93
				-3	-30	-6	4.44	3.9
				6	-27	-9	4.19	3.73
	Lent Nuc		76	-18	0	3	4.32	3.82
				-18	-3	-9	4.12	3.67
				-18	-3	15	3.88	3.5
	midbrain		9	-6	-9	-3	3.97	3.56
Lent Nuc		6	18	12	-3	3.71	3.36	

Suprathreshold activations across all three conditions in comparison to baseline were identified using conjunction analysis for (A) cue and (B) delay-2 events of the delayed recognition task. A higher threshold was used for the cue period in order to distinguish the regions commonly active across the three task conditions ($p < .001$, FDR corrected). A lower threshold was used for the delay period ($p < .05$, FDR corrected). Clusters were 6 contiguous voxels or larger. The table shows the peak coordinates in millimeters, t values, Z scores, and anatomical names of the major clusters. BA = Brodmann's area; IFG = inferior frontal gyrus; MFG = middle frontal gyrus; SFG = superior frontal gyrus; PrCS = precentral sulcus; mSFG, medial SFG; ACG = anterior cingulate gyrus; IPL = inferior parietal lobe; SPL = superior parietal lobe; IPS = intraparietal sulcus; PCu = precuneus; ITG = inferior temporal gyrus; MTG = middle temporal gyrus; FG = fusiform gyrus; Cblm = cerebellum; IOG = inferior occipital gyrus; SC = superior colliculus; Lent Nuc = lentiform nucleus.

^aCluster found in the white matter.

^bCluster revealed at a lower threshold FDR $p < .01$.

^cCluster separated at a higher threshold FDR $p < .0001$.

Activity in Other Visual Association Regions during Selective Maintenance

Besides PHG and FG, the localizer task revealed two other regions that showed differentially greater activations in Remember Scene than in Remember Face. The left lingual gyri ($x = -24, y = -51, z = -18$) and posterior SPL ($x = -15, y = -72, z = 57$) were significantly more active during Remember Scene compared to Remember Face (all $ps < .05$). Although the localizer task revealed greater activations in middle occipital and temporal gyri including FG during the face 1-back condition compared to the scene 1-back condition ($p < .05$, FDR corrected), these regions were not influenced by the cue conditions in the main working memory task.

One-way ANOVA also revealed that left posterior SPL/precuneus (PCu) ($x = -12, y = -75, z = 42$) and bilateral PHG ($x = 33, y = -36, z = -18$ and $x = -30, y = -42, z = -18$) were more active during Remember Scene than during the other two conditions. Besides, left MOG ($x = -33, y = -84, z = 21$) and right SPL/SOG ($x = 33, y = -69, z = 39$) showed main effects of cue and the differences were confirmed by ROI analysis. Activity in left MOG was greater in Remember Scene than in Remember Face ($p = .043$) and slightly enhanced during Remember Scene compared to Remember Both ($p = .069$) during the postcue delay period. Activity in right SPL/

SOG was also greater during Remember Scene than during Remember Face ($p = .012$) throughout the delay period (Figure 4).

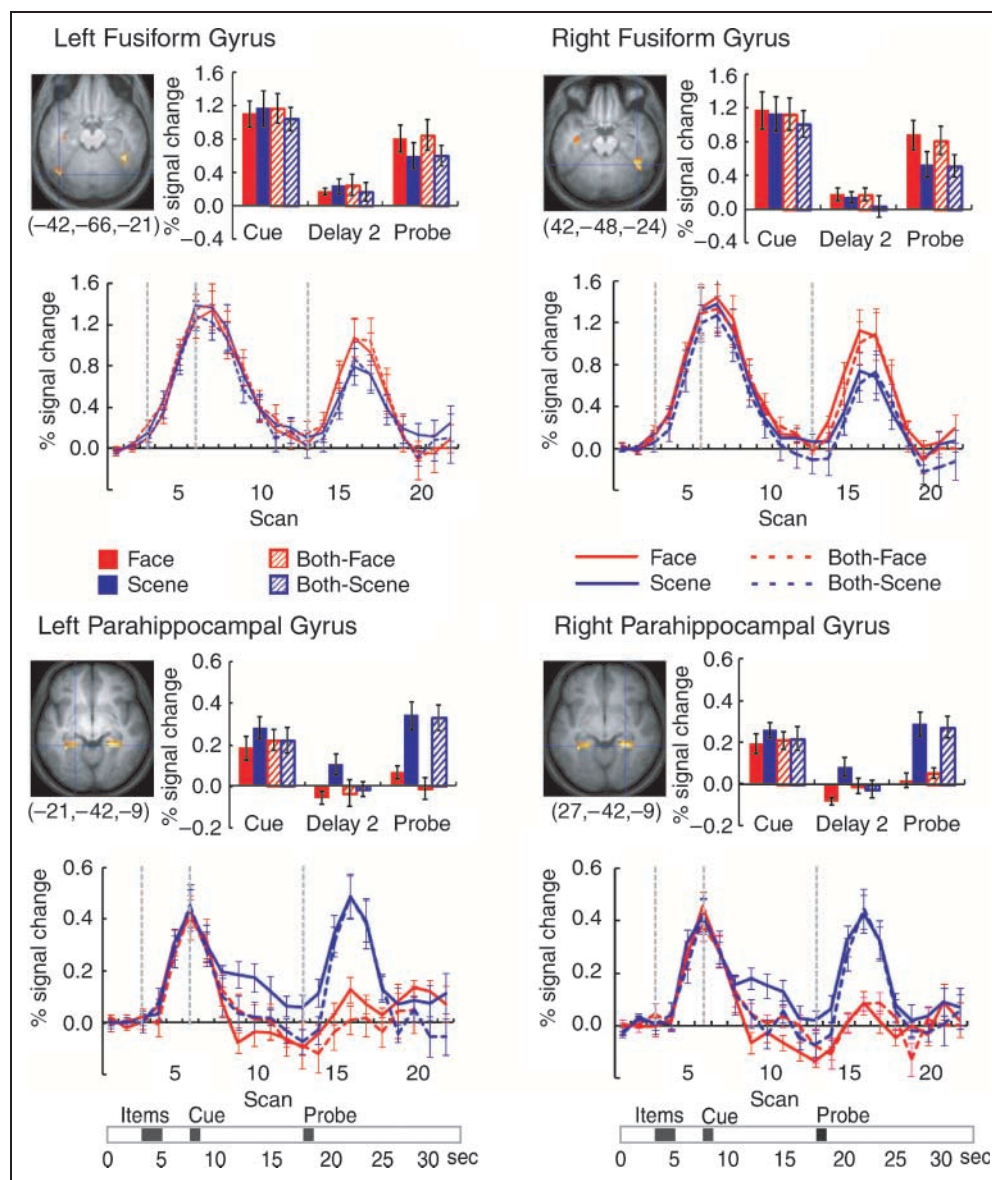
Activity Related to Remembering Both Face and Scene

To determine whether PFC and other areas would reflect a reduction of memory load in the selective maintenance conditions, as it was associated with better behavioral performance, we contrasted Remember Both with Remember Face and Remember Scene. Right dorsal MFG ($x = 45, y = 24, z = 30$) and left MFG ($x = -45, y = 30, z = 27; x = -42, y = 48, z = 12$) showed the main effects of cue during the postcue delay period [$F(2, 22) = 2.997, p = .07; F(2, 22) = 5.160, p = .015; F(2, 22) = 5.458, p = .012$, respectively] (Figure 5). Further t tests with Bonferroni correction indicated that activity in left MFG was significantly stronger during Remember Both in comparison to Remember Scene (all $ps < .05$) but insignificant in comparison to Remember Face (all $ps > .05$).

DISCUSSION

Using a delayed recognition task with a cue presented during the delay period, we found both specific and non-specific activities related to the selective maintenance of dif-

Figure 3. Activity in FG and PHG during the cue, postcue delay, and probe periods of the three task conditions (face, scene, and both). Each panel shows an axial slice with a cross-hair marking the location of the average peak coordinate, a bar graph of the averages of percent signal change during the different periods and time courses across conditions. Red solid bar and line = Remember Face; blue solid bar and line = Remember Scene; red hatched bar and dashed line = Remember Both with face probes; blue hatched bar and dashed line = Remember Both with scene probes. The vertical dashed gray lines from left to right mark the onset times of the visual items (a face and a scene), cue and probe in their order of presentation during the task. A time scale (sec) is shown in the bottom of the figure.



ferent visual information in working memory. PHG, along with other visual association areas (LG, posterior SPL, MOG, and SOG), showed differentially stronger activity during selective maintenance of a picture of a scene in comparison to selective maintenance of a picture of a face or nonselective maintenance of both pictures. In contrast, the prefrontal areas (MFG, IFG, mSFG) and ventral occipito-temporal regions (IOG) responded indiscriminately to all three cues. Although we did not find any region that responded uniquely to the selection process independent of the type of visual information, right dorsal MFG showed heightened activity during maintaining two pictures compared to selectively maintaining one of the two pictures. These findings thus suggest that the mechanism of selecting visual information in working memory may rely on the enhancement of functionally specialized regions such as PHG, perhaps through their interactions

with a nonspecific system involving frontal, visual association, and subcortical areas.

Control of Information Processing

Control of information processing such as attending to or updating of the contents in working memory in order to meet a task goal has been characterized as one of the major operations constituting executive functions (Wager & Smith, 2003; Miyake et al., 2000). This process has been further characterized in recent neuroimaging studies by showing enhancement of neural activity to task-relevant information in the presence of interference (Egner & Hirsch, 2005) and change in neural activity following task instructions during the delay period (Lepsien & Nobre, 2007). Current theories have postulated that dorsolateral PFC plays an important role in mediating

Figure 4. Additional regions showed preferential activity during selective maintenance of pictures of scenes. rIOG is shown for comparison; it was active at about the same level in all three conditions. Averages of percent signal change are plotted for the cue and postcue delay periods (see Tables 1 and 2 for abbreviations). * indicates significant difference at $p < .05$ with multiple comparison correction.

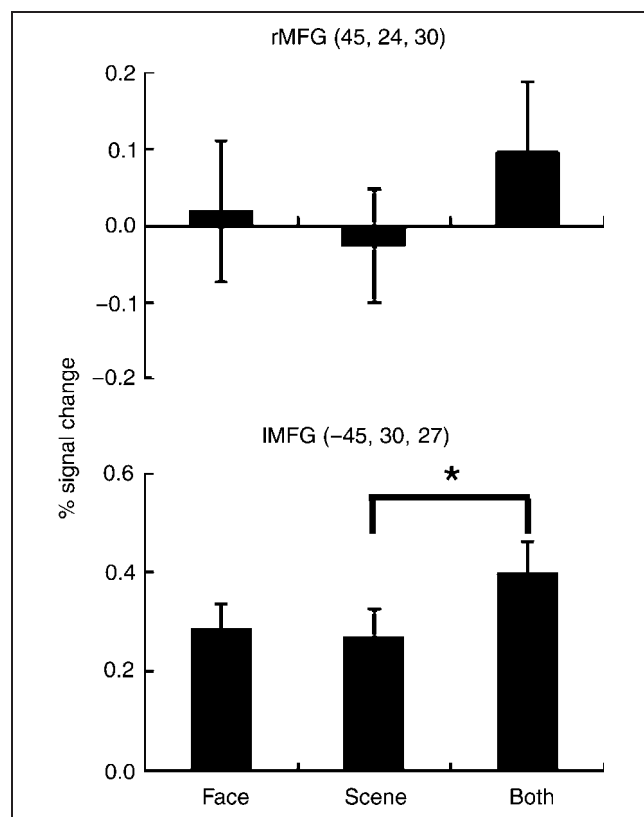
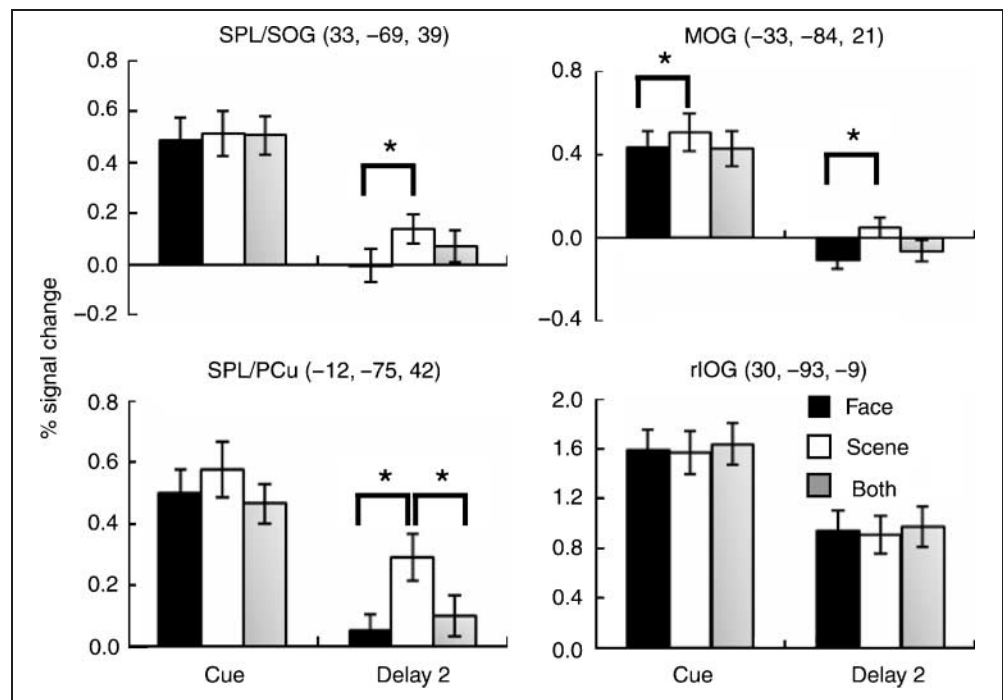


Figure 5. Load-related activity in MFG ROIs. Bar graphs show averages of percent signal change during the postcue delay period across the three cue conditions. * indicates significant difference at $p < .05$ with multiple comparison correction.

the control of selective information processing (Miller & Cohen, 2001; Koehlin, Basso, Pietrini, Panzer, & Grafman, 1999).

Our data, however, did not reveal a specific prefrontal area for biasing visual information processing. Although several areas in PFC, including MFG, IFG, and mSFG (or pre-SMA), were active during our working memory task, none of them were particularly more involved in the selective maintenance conditions (Remember Face or Scene) in comparison to the nonselective condition (Remember Both). This seems in contrast with a recent study by Lepsien and Nobre (2007). They suggested that the prefrontal (e.g., mSFG) and parietal (e.g., SPL) areas, similar to the common activations revealed by our data (Table 1), are important for controlling selection or orientation of attention in working memory, although their study did not include a control condition (such as Remember Both) as a comparison. Our data suggest that these regions are involved in both selection and maintenance processes in working memory.

There is probably not a single region (or mechanism) responsible for the selective control of information processing. Perhaps selective maintenance is manifested through interactions between prefrontal areas and posterior visual association areas. There are some evidence supporting this notion from electrophysiological studies of nonhuman primates (Tomita, Ohbayashi, Nakahara, Hasegawa, & Miyashita, 1999) and neuroimaging studies of humans (Gazzaley et al., 2007; Gazzaley, Rissman, & Desposito, 2004; Rissman, Gazzaley, & D'Esposito, 2004). Tomita et al. (1999) have shown that in the absence of visual

Table 2. Results of One-way ANOVA for the Effects of Cue

Lobe	Region	BA	Cluster Size	MNI Coordinates			<i>t</i>	<i>Z</i>
				<i>x</i>	<i>y</i>	<i>z</i>		
<i>(A) Cue Period</i>								
Frontal	MFG	6	58	-33	-3	54	28.89	4.82
Parietal	SPL/PCu	7	319	-12	-75	42	34.23	5.09
	SPL/SOG ^a	19		33	-69	39	26.4	4.68
Temporal	PHG	36	150	33	-36	-18	38.31	5.27
	Cblm			27	-36	-30	38.3	5.27
	PHG	36	173	-30	-42	-18	27.44	4.74
Occipital	MTG ^b	37/31		-39	-69	6	17.37	4.01
	OG	19	372	33	-78	24	34.73	5.12
	PCG			18	-60	15	27.12	4.72
	MOG ^b	19		-33	-84	21	33.84	5.08
	PCG	31	114	-6	-69	12	19.55	4.2
				-15	-66	12	19.48	4.2
	LG	19		-6	-57	6	18.68	4.13
	LG	19	46	-18	-72	-12	18.31	4.1
LG	19		-9	-66	-6	16.53	3.94	
LG	18	8	15	-75	6	14.14	3.69	
<i>(B) Delay-2 Period</i>								
Frontal	IFG	47	16	-15	15	-18	14.16	3.69
	DFG	8	10	12	27	42	12.93	3.55
	ACG	24	8	9	6	36	12.08	3.44
Parietal	PoCG	43	22	54	-18	21	14.45	3.72
	IPL	40	9	-63	-27	33	13.04	3.56
Temporal	FG	37	87	39	-45	-15	18.77	4.14
	ITG	37		51	-51	-12	17.2	4
	PHG	36		30	-33	-24	11.19	3.32
Occipital	LG	19	11	-21	-57	0	13.31	3.59
Subcortical	Caudate		15	6	9	3	13.42	3.61
	Caudate		6	-18	21	-3	11.6	3.38

Differential activity across the three cue conditions were identified for (A) cue and (B) delay-2 events of the delayed recognition task. A higher threshold was used for the cue period ($p < .01$, FDR corrected) and lowered for the delay period ($p < .001$, uncorrected; FDR = 0.25). Clusters were 6 contiguous voxels or larger. PHG = parahippocampal gyrus; PCG = posterior cingulate gyrus; DFG = dorsal frontal gyrus; OG = occipital gyrus; SOG = superior occipital gyrus; MOG = middle occipital gyrus; LG = lingual gyrus; PoCG = postcentral gyrus; See Table 1 for other abbreviations and notations.

^aFrom the OG cluster.

^bFrom the SPL/PCu cluster.

input, top-down signal exerted by PFC was critical for activating neurons in the inferotemporal cortex during retrieval of visual information. For selective encoding of pictures of faces, Gazzaley et al. (2004, 2007) have shown that activity

in FG correlated with activity in several PFC regions including SFG, MFG, and IFG during a delayed recognition task, and for selective encoding of scenes, activity in PHG correlated with activity in left MFG (peak coordinates: $x = -44$,

$y = 38, z = 32$). It is possible that PFC areas and FG/PHG interacted similarly during the Remember Face and Remember Scene conditions of our task. However, we do not have enough statistical power for determining this relationship in this dataset.

Selective Maintenance of Visual Information in Working Memory

Our selective working memory paradigm is similar to the directed forgetting paradigm, which is commonly used in memory research (Bjork, Bjork, & Anderson, 1998; Brown, 1954). By inserting a cue (remember or forget) after the presentation of each study item, researchers found that such manipulations produced a behavioral effect in which items directed to be remembered were more likely to be successfully recalled than those directed to be forgotten (MacLeod & Daniels, 2000; MacLeod, 1989). However, it has been shown that the to-be-forgotten items can resurface under certain situations, suggesting that these items were poorly rehearsed or inhibited rather than completely removed from the memory system (see MacLeod et al., 2003). Similarly, we incorporated a cue manipulation in a typical delayed recognition task and have shown data suggesting enhancement of relevant items (potentially through selective rehearsal) and disregard of no-longer-relevant or to-be-forgotten information (potentially through inhibition or lack of rehearsal) at the maintenance stage.

Our data seem to support a key role of the visual association regions in the selective representation of visual information in working memory (Postle, 2006). We found that activity in PHG reflects selective processing of pictures of scenes during postcue delay period. This observation corroborates previous findings of differential activity in PHG during selective encoding of pictures of scenes versus selective encoding of pictures of faces, nonselective encoding, and passive viewing (Gazzaley et al., 2005), and during selective maintenance of pictures of scenes versus faces (Lepsien & Nobre, 2007). Similar to the encoding effects observed by Gazzaley et al., our data not only showed enhancement in activity during Remember Scene but also reduction in activity in PHG during Remember Face, where the scene picture was no longer needed to be held in working memory. The heightened responses to a specific cue (i.e., Remember Scene) compared to a nonspecific cue (i.e., Remember Both) suggest that the cued item may become more accessible when a piece of information is being selected, as manifested in a faster recognition time. This interpretation agrees with behavioral findings of “focus of attention” as a mechanism for making one or few items more accessible momentarily in working memory (Oberauer, 2002; Cowan, 1995, 1999) and with the *refresh* process proposed as an elementary memory mechanism (Johnson et al., 2005; Johnson & Hirst, 1993; Johnson, 1992).

In contrast to our expectation, activity of FG was not modulated by the task cues. Although we can determine the part of FG that showed greater responses to face stimuli in comparison to scene stimuli in most individuals, the individually defined ROIs did not show differential activity during the delay interval but did show preferential activation to the face probes. Numerous studies have shown that the fusiform area is involved in perception and recognition of faces (Kanwisher, 2000; Kanwisher et al., 1997) or in processing complex visual stimuli that observers have acquired expertise to discriminate (Gauthier, Skudlarski, Gore, & Anderson, 2000; Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999). Our data thus further suggest that FG may be involved in processing different kinds of complex visual stimuli, but it may not play a unique role in maintaining faces in working memory as implicated in previous studies (Druzgal & D’Esposito, 2003). Similar to a previous study (Jha & McCarthy, 2000), we also found that the activity in FG returned to baseline by the end of the delay period. Although there was no task-related enhancement of activity in FG, we did observe facilitation in recognition performance for Remember Face. Perhaps the maintenance of faces in working memory requires the interaction between PFC and FG (Gazzaley et al., 2004 and see above). Our data support this notion by showing that, albeit statistically insignificant, left MFG seemed more active during Remember Face (and remember both) than during Remember Scene. However, it is unclear from our data whether left MFG and FG correlate with each other during Remember Face. Another possibility of why we did not observe selective enhancement of activity in FG is that the participants might have held the pictures of faces in all conditions even though it was unnecessary in the Remember Scene condition.

The finding of posterior SPL showing greater responses to Remember Scene than to Remember Face and Remember Both in the present study was novel in this type of working memory studies. Previous studies have reported activations in SPL (extending to PCu) during shifting attention between faces and houses (Serences, Schwarzbach, Courtney, Golay, & Yantis, 2004; Yantis & Serences, 2003) and during object working memory tasks requiring either simple maintenance (e.g., Xu & Chun, 2006) or both maintenance and manipulation (e.g., Lepsien & Nobre, 2007). We previously have also shown that right SPL is modulated by updating load (Leung, Oh, Ferri, & Yi, 2007) and by familiarity-based interference (Leung & Zhang, 2004) during spatial working memory tasks, although the peak activations in these studies were more anterior compared to the activation peak reported here. Because the level of activity in posterior SPL was about the same for Remember Face and Remember Both but only heightened during Remember Scene, it cannot be solely attributed to the attentional processes involved in working memory as previous studies have implicated.

Although posterior occipital cortex was commonly activated in visual tasks, from passive viewing to manipulation

and maintenance of visual information, PFC–occipital interaction in maintaining visual information did not receive much attention. Several neuroimaging studies have postulated the possibility of PFC–IOG and PFC–MOG connections for holding or reactivating visual representations. Ishai, Ungerleider, and Haxby (2000) have shown a category-sensitive activity in ventral occipital cortex including IOG and MOG in perceiving visual stimuli from different categories (e.g., faces and chairs). This category-sensitive activity in these cortical regions was also observed during visual imagery, although the activation volume was smaller. They also observed increased activity in MFG during visual imagery, suggesting that PFC may interact with the occipital regions in reviving visual representations. Johnson, Mitchell, Raye, D’Esposito, and Johnson (2007) examined top–down bias on posterior regions using a refresh paradigm involving face and scene stimuli. As expected, they found enhanced activity in FG, PHG, and dorsolateral PFC in response to a refresh cue compared to a repeated visual stimulus. They also found significantly stronger activity in left MOG and right IOG responding to the refresh cues for scenes and faces, respectively. Taken together, our results are in line with previous findings suggesting that the visual association areas including MOG, posterior SPL, and PHG may be involved in reactivating specific visual representations in working memory, which is potentially an important process required in visual search and imagery.

Nonselective Maintenance of Visual Information

As discussed above, the contrast between the selective maintenance conditions (Remember Face or Scene) and the nonselective condition (Remember Both) in our study did not reveal any suprathreshold activations within PFC for selective processing. However, slightly but significantly greater activation was observed in right dorsal MFG during Remember Both compared to the two selection conditions. These results are consistent with previous findings in suggesting that right dorsal MFG is involved in supporting higher load working memory (Leung, Seelig, & Gore, 2004; Rypma & D’Esposito, 1999).

Dorsal MFG has been highly implicated in refreshing of memory, which may be more demanding in the selective maintenance conditions. The peak activation in this area is very close to that observed in studies designed to isolate the refresh component process in delayed recognition tasks (Raye, Mitchell, Reeder, Greene, & Johnson, 2008; Raye, Johnson, Mitchell, Greene, & Johnson, 2007; Johnson et al., 2005). If, indeed, right dorsal MFG was involved in both refreshing memory and processing higher load of information, it would explain why we only observed a slight difference in activation between our selective and nonselective maintenance conditions.

Dorsomedial PFC (pre-SMA) was active during all three conditions in the main task and the localizer tasks. In particular, sustained activity was found in this region above the significance threshold over the entire postcue delay

period. The exact role of pre-SMA in working memory is unclear. Pre-SMA has been implicated in cognitive control and particularly in guiding response plans (e.g., Sakai et al., 2000). A few studies have shown activations in pre-SMA during object-related attention (Schubotz & von Cramon, 2001) and rote maintenance of verbal items (Davachi, Maril, & Wagner, 2001). Perhaps, pre-SMA’s role is in maintaining task rules such as the selection cues in our study, which is important for guiding later response sequence and plans (see Tanji, 2001).

Summary

In the present study, we examined whether or not there is a common neural substrate specifically involved in selective processing of visual representations in working memory. Our data suggest that there are nonspecific activations in IFG, MFG, FG, and IOG during the maintenance and selection of visual representations in working memory regardless of stimulus type. We also found more specific activations associated with selective processing of pictures of scenes in visual association areas including PHG, LG, posterior SPL/PCu, and MOG. To further elucidate these specific and nonspecific networks engaged in selective processing of visual information in working memory, a multivariate approach can be adopted in future studies.

Acknowledgments

This work was supported by the State University of New York at Stony Brook and a Drescher Award. We thank Dr. Mark Wagshul and the staff of Department of Radiology for their generous support, and John Borghi for data collection assistance.

Reprint requests should be sent to Hoi-Chung Leung, SUNY Stony Brook, Department of Psychology, Stony Brook, NY 11794-2500, or via e-mail: hoi-chung.leung@sunysb.edu.

REFERENCES

- Aguirre, G. K., Zarahn, E., & D’Esposito, M. (1998). An area within human ventral cortex sensitive to “building” stimuli: Evidence and implications. *Neuron*, *21*, 373–383.
- Baddeley, A. D., & Hitch, G. (1974). Working memory. In G. Bower (Ed.), *The psychology of learning and motivation* (Vol. 8, pp. 47–90). New York: Academic Press.
- Bjork, E. L., Bjork, R. A., & Anderson, M. C. (1998). Varieties of goal-directed forgetting. In J. M. Golding & C. M. MacLeod (Eds.), *Intentional forgetting: Interdisciplinary approaches* (pp. 103–137). Mahwah, NJ: Erlbaum.
- Brett, M., Anton, J. L., Valabregue, R., & Poline, J. B. (2002). *Region of interest analysis using an SPM toolbox [abstract]*. Paper presented at the Presented at the 8th International Conference on Functional Mapping of the Human Brain.
- Brown, J. (1954). The nature of set-to-learn and of intra-material interference in immediate memory. *Quarterly Journal of Experimental Psychology*, *6*, 141–148.
- Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed

- neural system for human working memory. *Nature*, 386, 608–611.
- Cowan, N. (1995). *Attention and memory: An integrated framework*. New York: Oxford University Press.
- Cowan, N. (1999). An embedded-processes model of working memory. In A. Miyake & P. Shah (Eds.), *Models of working memory: Mechanisms of active maintenance and executive control* (pp. 62–101). New York: Cambridge University Press.
- Davachi, L., Maril, A., & Wagner, A. D. (2001). When keeping in mind supports later bringing to mind: Neural markers of phonological rehearsal predict subsequent remembering. *Journal of Cognitive Neuroscience*, 13, 1059–1070.
- D'Esposito, M., Postle, B. R., Jonides, J., & Smith, E. E. (1999). The neural substrate and temporal dynamics of interference effects in working memory as revealed by event-related functional MRI. *Proceedings of the National Academy of Sciences, U.S.A.*, 96, 7514–7519.
- Druzgal, T. J., & D'Esposito, M. (2003). Dissecting contributions of prefrontal cortex and fusiform face area to face working memory. *Journal of Cognitive Neuroscience*, 15, 771–784.
- Egner, T., & Hirsch, J. (2005). Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. *Nature Neuroscience*, 8, 1784–1790.
- Epstein, R., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, 392, 598–601.
- Friston, K. J., Ashburner, J., Frith, C. D., Poline, J. B., Heather, J. D., & Frackowiak, R. S. J. (1995). Spatial registration and normalization of images. *Human Brain Mapping*, 3, 165–189.
- Fuster, J. M. (1989). *The prefrontal cortex: Anatomy, physiology, and neuropsychology of the frontal lobe* (2nd ed.). New York: Raven Press.
- Gauthier, I., Skudlarski, P., Gore, J. C., & Anderson, A. W. (2000). Expertise for cars and birds recruits brain areas involved in face recognition. *Nature Neuroscience*, 3, 191–197.
- Gauthier, I., Tarr, M. J., Anderson, A. W., Skudlarski, P., & Gore, J. C. (1999). Activation of the middle fusiform “face area” increases with expertise in recognizing novel objects. *Nature Neuroscience*, 2, 568–573.
- Gazzaley, A., Cooney, J. W., McEvoy, K., Knight, R. T., & D'Esposito, M. (2005). Top-down enhancement and suppression of the magnitude and speed of neural activity. *Journal of Cognitive Neuroscience*, 17, 507–517.
- Gazzaley, A., Rissman, J., Cooney, J., Rutman, A., Seibert, T., Clapp, W., et al. (2007). Functional interactions between prefrontal and visual association cortex contribute to top-down modulation of visual processing. *Cerebral Cortex*, 17(Suppl. 1), i125–i135.
- Gazzaley, A., Rissman, J., & Desposito, M. (2004). Functional connectivity during working memory maintenance. *Cognitive, Affective & Behavioral Neuroscience*, 4, 580–599.
- Goldman-Rakic, P. S. (1987). Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In V. B. Mountcastle & F. Plum (Eds.), *Handbook of physiology: The nervous system, higher functions of the brain* (Vol. 5, pp. 373–417). Bethesda, MD: American Physiological Society.
- Ishai, A., Ungerleider, L. G., & Haxby, J. V. (2000). Distributed neural systems for the generation of visual images. *Neuron*, 28, 979–990.
- Jha, A. P., & McCarthy, G. (2000). The influence of memory load upon delay-interval activity in a working-memory task: An event-related functional MRI study. *Journal of Cognitive Neuroscience*, 12(Suppl. 2), 90–105.
- Johnson, M. K. (1992). MEM: Mechanisms of recollection. *Journal of Cognitive Neuroscience*, 4, 268–280.
- Johnson, M. K., & Hirst, W. (1993). MEM: Memory subsystems as processes. In A. F. Collins, S. E. Gathercole, M. A. Conway, & P. E. Morris (Eds.), *Theories of memory* (pp. 241–286). Hillsdale, NJ: Erlbaum.
- Johnson, M. K., Raye, C. L., Mitchell, K. J., Greene, E. J., Cunningham, W. A., & Sanislow, C. A. (2005). Using fMRI to investigate a component process of reflection: Prefrontal correlates of refreshing a just-activated representation. *Cognitive, Affective & Behavioral Neuroscience*, 5, 339–361.
- Johnson, M. R., Mitchell, K. J., Raye, C. L., D'Esposito, M., & Johnson, M. K. (2007). A brief thought can modulate activity in extrastriate visual areas: Top-down effects of refreshing just-seen visual stimuli. *Neuroimage*, 37, 290–299.
- Jonides, J., Smith, E. E., Marshuetz, C., Koeppe, R. A., & Reuter-Lorenz, P. A. (1998). Inhibition in verbal working memory revealed by brain activation. *Proceedings of the National Academy of Sciences, U.S.A.*, 95, 8410–8413.
- Kanwisher, N. (2000). Domain specificity in face perception. *Nature Neuroscience*, 3, 759–763.
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, 17, 4302–4311.
- Koechlin, E., Basso, G., Pietrini, P., Panzer, S., & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. *Nature*, 399, 148–151.
- Lepsien, J., & Nobre, A. C. (2007). Attentional modulation of object representations in working memory. *Cerebral Cortex*, 17, 2072–2083.
- Leung, H. C., Oh, H., Ferri, J., & Yi, Y. (2007). Load response functions in the human spatial working memory circuit during location memory updating. *Neuroimage*, 35, 368–377.
- Leung, H. C., Seelig, D., & Gore, J. C. (2004). The effect of memory load on cortical activity in the spatial working memory circuit. *Cognitive, Affective & Behavioral Neuroscience*, 4, 553–563.
- Leung, H. C., & Zhang, J. X. (2004). Interference resolution in spatial working memory. *Neuroimage*, 23, 1013–1019.
- MacLeod, C. M. (1989). Directed forgetting affects both direct and indirect tests of memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 15, 13–21.
- MacLeod, C. M., & Daniels, K. A. (2000). Direct versus indirect tests of memory: Directed forgetting meets the generation effect. *Psychonomic Bulletin & Review*, 7, 354–359.
- MacLeod, C. M., Dodd, M. D., Sheard, E. D., Wilson, D. E., & Bibi, U. (2003). In opposition to inhibition. In B. H. Ross (Ed.), *The psychology of learning and motivation: Advances in research and theory* (Vol. 43, pp. 163–214). New York, NY: Elsevier Science.
- Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, 24, 167–202.
- Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “frontal lobe” tasks: A latent variable analysis. *Cognitive Psychology*, 41, 49–100.
- Nelson, J. K., Reuter-Lorenz, P. A., Sylvester, C. Y., Jonides, J., & Smith, E. E. (2003). Dissociable neural mechanisms underlying response-based and familiarity-based conflict in working memory. *Proceedings of the National Academy of Sciences, U.S.A.*, 100, 11171–11175.
- Oberauer, K. (2002). Access to information in working memory: Exploring the focus of attention. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 28, 411–421.

- Postle, B. R. (2006). Working memory as an emergent property of the mind and brain. *Neuroscience*, *139*, 23–38.
- Postle, B. R., Zarahn, E., & D'Esposito, M. (2000). Using event-related fMRI to assess delay-period activity during performance of spatial and nonspatial working memory tasks. *Brain Research, Brain Research Protocols*, *5*, 57–66.
- Puce, A., Allison, T., Gore, J. C., & McCarthy, G. (1995). Face-sensitive regions in human extrastriate cortex studied by functional MRI. *Journal of Neurophysiology*, *74*, 1192–1199.
- Raye, C. L., Johnson, M. K., Mitchell, K. J., Greene, E. J., & Johnson, M. R. (2007). Refreshing: A minimal executive function. *Cortex*, *43*, 135–145.
- Raye, C. L., Mitchell, K. J., Reeder, J. A., Greene, E. J., & Johnson, M. K. (2008). Refreshing one of several active representations: Behavioral and functional magnetic resonance imaging differences between young and older adults. *Journal of Cognitive Neuroscience*, *20*, 852–862.
- Rissman, J., Gazzaley, A., & D'Esposito, M. (2004). Measuring functional connectivity during distinct stages of a cognitive task. *Neuroimage*, *23*, 752–763.
- Rypma, B., & D'Esposito, M. (1999). The roles of prefrontal brain regions in components of working memory: Effects of memory load and individual differences. *Proceedings of the National Academy of Sciences, U.S.A.*, *96*, 6558–6563.
- Sakai, K., Hikosaka, O., Takino, R., Miyauchi, S., Nielsen, M., & Tamada, T. (2000). What and when: Parallel and convergent processing in motor control. *Journal of Neuroscience*, *20*, 2691–2700.
- Schubotz, R. I., & von Cramon, D. Y. (2001). Functional organization of the lateral premotor cortex: fMRI reveals different regions activated by anticipation of object properties, location and speed. *Cognitive Brain Research*, *11*, 97–112.
- Serences, J. T., Schwarzbach, J., Courtney, S. M., Golay, X., & Yantis, S. (2004). Control of object-based attention in human cortex. *Cerebral Cortex*, *14*, 1346–1357.
- Tanji, J. (2001). Sequential organization of multiple movements: Involvement of cortical motor areas. *Annual Review of Neuroscience*, *24*, 631–651.
- Thompson-Schill, S. L. (2003). Neuroimaging studies of semantic memory: Inferring “how” from “where”. *Neuropsychologia*, *41*, 280–292.
- Thompson-Schill, S. L., D'Esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *Proceedings of the National Academy of Sciences, U.S.A.*, *94*, 14792–14797.
- Tomita, H., Ohbayashi, M., Nakahara, K., Hasegawa, I., & Miyashita, Y. (1999). Top-down signal from prefrontal cortex in executive control of memory retrieval. *Nature*, *401*, 699–703.
- Wager, T. D., & Smith, E. E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive, Affective & Behavioral Neuroscience*, *3*, 255–274.
- Xu, Y., & Chun, M. M. (2006). Dissociable neural mechanisms supporting visual short-term memory for objects. *Nature*, *440*, 91–95.
- Yantis, S., & Serences, J. T. (2003). Cortical mechanisms of space-based and object-based attentional control. *Current Opinion in Neurobiology*, *13*, 187–193.
- Zhang, J. X., Leung, H. C., & Johnson, M. K. (2003). Frontal activations associated with accessing and evaluating information in working memory: An fMRI study. *Neuroimage*, *20*, 1531–1539.