

Attention Biases Visual Activity in Visual Short-term Memory

Bo-Cheng Kuo^{1,2}, Mark G. Stokes¹, Alexandra M. Murray^{1*},
and Anna Christina Nobre¹

Abstract

■ In the current study, we tested whether representations in visual STM (VSTM) can be biased via top-down attentional modulation of visual activity in retinotopically specific locations. We manipulated attention using retrospective cues presented during the retention interval of a VSTM task. Retrospective cues triggered activity in a large-scale network implicated in attentional control and led to retinotopically specific modulation of

activity in early visual areas V1–V4. Importantly, shifts of attention during VSTM maintenance were associated with changes in functional connectivity between pFC and retinotopic regions within V4. Our findings provide new insights into top-down control mechanisms that modulate VSTM representations for flexible and goal-directed maintenance of the most relevant memoranda. ■

INTRODUCTION

Selective attention is important for biasing perceptual processing in favor of the most relevant sensory information (Posner, 1980). Similarly, attention can bias internal representations in visual STM (VSTM; Gazzaley & Nobre, 2012; Stokes & Nobre, 2012; Griffin & Nobre, 2003; Landman, Spekreijse, & Lamme, 2003). Behavioral evidence has demonstrated that the focus of attention during maintenance has a great impact on the probability that a specific item will be successfully retained in VSTM (Murray, Nobre, Clark, Cravo, & Stokes, 2013; Pertzov, Bays, Joseph, & Husain, 2013; Astle, Summerfield, Griffin, & Nobre, 2012). Results from electrophysiological recordings in humans have also revealed that cueing the relevant item being maintained in VSTM modulates delay-related activity, consistent with reducing the VSTM load to the relevant item or location (Kuo, Stokes, & Nobre, 2012). However, the neural substrates for attentional biasing in VSTM remain poorly understood. Here, we investigate the underlying neural mechanisms that support top-down attentional modulation of VSTM representations using fMRI.

A prevailing neural account of attention proposes that top-down modulation of visual activity relies on long-range functional interactions with control brain regions including prefrontal and parietal cortices (Serences & Yantis, 2006; Corbetta & Shulman, 2002; Nobre, 2001; Kastner & Ungerleider, 2000; Desimone & Duncan, 1995). Neuroimaging evidence suggests that similar top-down attentional biases may continue to operate and support VSTM representations. In particular, interactions between

prefrontal and visual cortices have been implicated in the selective gating of relevant information into VSTM in the active maintenance of relevant information (Postle, 2005, 2006; Gazzaley, Rissman, & D'Esposito, 2004; Curtis & D'Esposito, 2003; Awh & Jonides, 2001). For example, in tasks requiring selective encoding and maintenance of a specific stimulus category or feature dimension in VSTM, visual association areas with relevant specializations show similar patterns of modulation as during selective attention in perceptual tasks (Gazzaley, 2011; Zanto & Gazzaley, 2009; Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005; Ranganath, DeGutis, & D'Esposito, 2004). Areas with relevant specializations for the attended stimulus category or dimension also display stronger functional connectivity with prefrontal regions, especially around the inferior frontal sulcus (IFS). Finally, the critical role that pFC plays in modulating and supporting VSTM representations has been confirmed by studies using TMS (Lee & D'Esposito, 2012; Zanto, Rubens, Thangavel, & Gazzaley, 2011).

Functional interactions between prefrontal and visual cortices may, therefore, provide a natural structure for top-down signals to continue to bias internal representations after the initial encoding of VSTM events according to changing task goals and priorities. Studies introducing retrospective cues (retro-cues) to shift attention to locations or categories of stimuli being maintained in VSTM have reported corresponding modulation in the levels and patterns of activity in relevant visual areas (Lewis-Peacock, Drysdale, Oberauer, & Postle, 2012; Higo, Mars, Boorman, Buch, & Rushworth, 2011; Lepsien, Thornton, & Nobre, 2011; Munneke, Heslenfeld, & Theeuwes, 2008, 2010; Serences, Ester, Vogel, & Awh, 2009; Sligte, Scholte, & Lamme, 2009; Yi, Turk-Browne, Chun, & Johnson, 2008; Johnson, Mitchell, Raye, D'Esposito, & Johnson, 2007; Lepsien & Nobre, 2007). These changes in the activity

¹University of Oxford, ²National Taiwan University

*Current affiliation: University Medical Center Hamburg-Eppendorf and the Schön Klinik Hamburg Eilbeke, Germany.

of posterior brain regions may reflect reweighting of maintenance-related activity or the selective anticipation of subsequent relevant probe items against which memory contents need to be compared (Stokes et al., 2013; Lewis-Peacock et al., 2012; Lepsien et al., 2011; Lepsien & Nobre, 2007).

In this study, we tested whether shifts of the internal focus of attention in VSTM involve changes in the functional interaction between pFC and retinotopic regions within visual areas. We used retro-cues to trigger shifts of spatial attention to locations of items being maintained in VSTM and measured the biasing of activity within retinotopically specific regions of visual areas (V1–V4) as well as changes in the strength of functional coupling between these retinotopic areas and areas implicated in the control of VSTM content (IFS, FEFs, and posterior parietal cortex [PPC]).

METHODS

Experiment 1: Behavioral Validation Experiment

Participants

All participants in Experiment 1 were right-handed, according to the Edinburgh handedness inventory (Oldfield, 1971). Eighteen healthy volunteers with normal or corrected-to-normal visual acuity were recruited (age range = 19–35 years, 12 women). Written informed consent was obtained from all participants before the study, and they were financially reimbursed for their time or received course credit. All experimental methods and procedures were approved by the Central University Research Ethics Committee of the University of Oxford.

Task Design

A purely behavioral experiment was conducted to ensure that the long ISIs required for disambiguating neural responses in the fMRI experiment were adequate for yielding adequate performance based on VSTM and that performance was not dependent on verbalization. Each trial began with the onset of a centrally displayed asterisk (500-msec duration), which signaled the onset of the trial. After a randomized variable interval (500- to 1000-msec duration), participants viewed a memory array containing four different shapes presented peripherally (200-msec duration). Participants were instructed to remember as many of the shapes as possible. Following an initial retention interval (2000 msec), an informative, symbolic retro-cue appeared for 500 msec at the center of the screen. The retro-cue indicated a stimulus shape from the memory array that would be required to perform the subsequent comparison to the probe stimulus. When 8000 msec of a second retention interval following the retro-cue had elapsed, the probe array was presented for 200 msec. The participants' task was to decide whether the cued item appeared at the same location in the memory and probe

arrays. The same stimuli always appeared in the memory and probe arrays; however, two items always swapped location. The six possible swaps between pairs of items occurred with equal probability and in random order. On 50% of trials, this swap included the cued item. Participants were instructed to respond “match” by pressing the left mouse button or “nonmatch” by pressing the right mouse button, using their right hand, according to whether the item at the cued location was the same (50% of trials) or different (50% of trials) as the corresponding item from the previous memory array. Shape stimuli were drawn from a set of 100 novel, difficult to verbalize, meaningless, closed-shape contours previously developed by Endo and colleagues (Endo, Saiki, Nakao, & Saito, 2003). In memory and probe arrays, each stimulus subtended a visual angle of 1.72° and appeared with equal probability at one of four quadrant peripheral locations at 2.58° of lateral eccentricity and 2° of elevation. All stimulus contours were white. A black background was used throughout the experiment.

To test for verbalization effects, we included a secondary digit task in which participants were required to remember three digits presented at the beginning of the trial for later test after the probe array on 50% of trials. This dual-task manipulation was based on a previously used procedure for a similar purpose (Magen, Emmanouil, McMains, Kastner, & Treisman, 2009). Each dual-task trial started with the onset of a centrally displayed asterisk for 500 msec, followed, at a variable interval (500- to 1000-msec duration), by the presentation of three digits side-by-side in the center of the display (500 msec). The string of digits was approximately 1° in width and 0.3° in height. All digits were white. Following the probe array after a randomized variable interval (3500- to 4000-msec duration), three digits were then presented for 1500 msec. Participants were instructed to respond “match” or “nonmatch” relative to the three digits presented at the beginning of the trial, using the same response keys (left button for match response and right button for nonmatch response). The interval between trials varied randomly between 3000 and 3500 msec. The task schematic of the behavioral validation experiment is illustrated in Figure 1A.

Experimental Procedure

Stimuli were presented on a CRT screen using Presentation software (Neurobehavioral Systems, Inc., Albany, CA). Participants were comfortably seated in a dimly illuminated experimental booth, facing a computer monitor placed 100 cm in front of them. They were given written as well as verbal instructions regarding the task requirements and completed 16 practice trials to ensure they understood the task. They were also instructed to maintain fixation on a small fixation marker at the center of the monitor during the active parts of the experiment and to respond as accurately as possible.

Single- and dual-task conditions were presented in a block design. To minimize fatigue, the experiment was

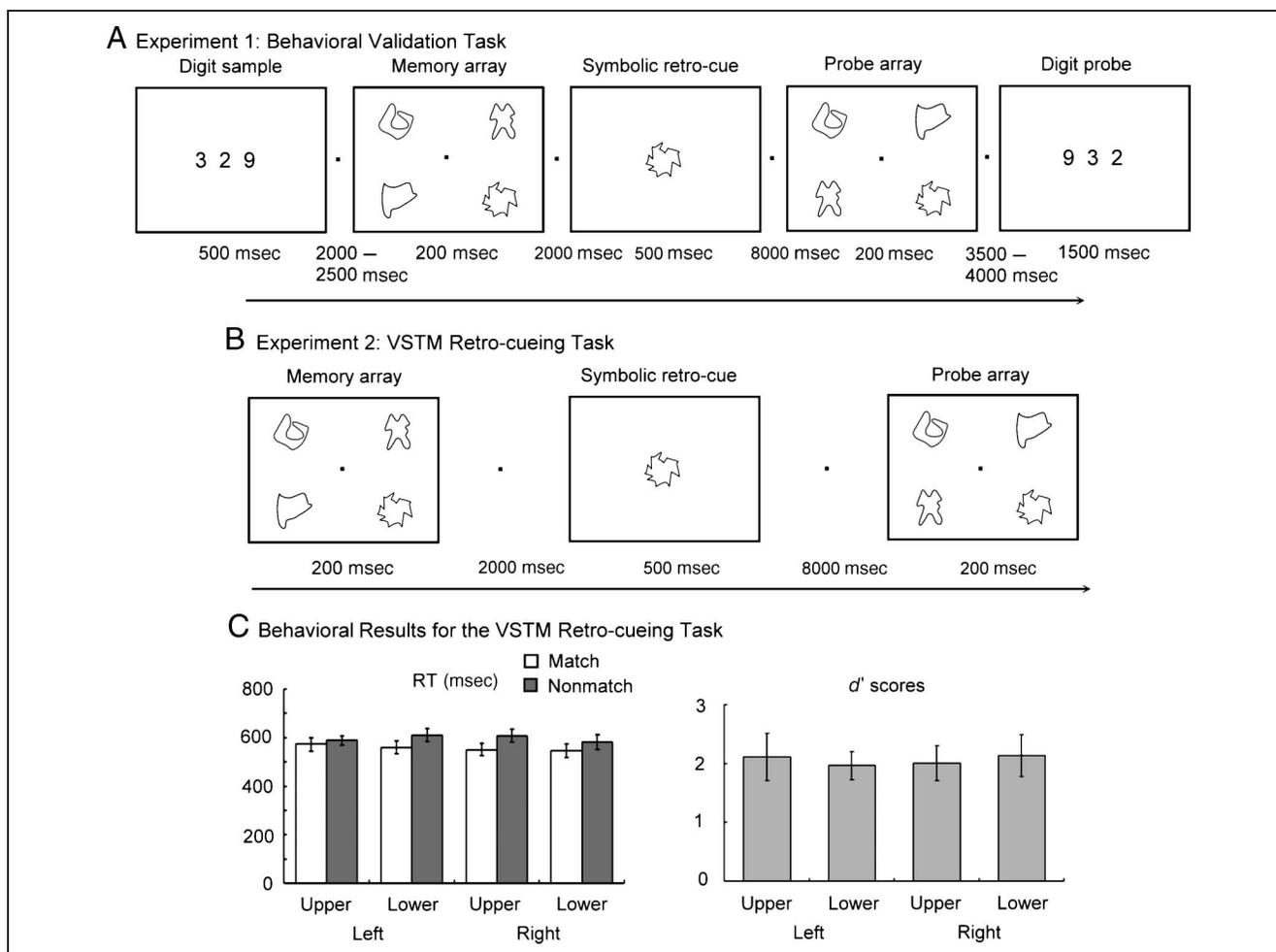


Figure 1. Tasks and behavioral results. Schematic illustration of the (A) behavioral validation task (Experiment 1) and (B) VSTM retro-cueing fMRI task (Experiment 2). Participants viewed a memory array containing four different peripheral shapes at the beginning of the trial (200-msec duration). Following an initial retention interval (2000 msec), an informative, symbolic retro-cue appeared centrally for 500 msec. When 8000 msec of a second retention interval had elapsed following the retro-cue, the probe array was presented for 200 msec. Participants' task was to decide whether the cued item appeared at the same location in the memory and probe arrays. To test for verbalization effects, we included a secondary digit task in which participants were required to remember three digits presented at the beginning of the trial (500-msec duration) for later test after the probe array. (C) Behavioral results of the VSTM retro-cueing task for both mean RT (msec, left) and sensitivity measures (d' scores, right). Error bars represent standard errors of the means.

completed in eight short blocks of 16 trials, which participants could self-initiate (four blocks for each task type). There were 128 trials in total (32 match and 32 nonmatch trials in each task type). Task order was counter-balanced across participants (half of the participants performed the single-task condition first). Blocks and response types were intermixed in a randomized and unpredictable order. Total experimental time for each participant was approximately 1 hr.

Behavioral Analyses

Behavioral measures, including accuracy and mean RTs, were analyzed by a 2 (Task Type: single, dual) \times 2 (Response Type: match, nonmatch) repeated-measures ANOVA. Only correct responses were included for RT analyses. We also analyzed the sensitivity score for match/nonmatch discrimi-

nation responses ($d' = Z[\text{hit rate}] - Z[\text{false alarm rate}]$; Green & Swets, 1966), using a paired t test (single vs. dual task). Hit rate was defined as the conditional probability that the participants responded "match" when the target item was the same, and the false-alarm rate was defined as the conditional probability that the participants responded "match" when the target item was different.

Experiment 2: fMRI Experiment

Participants

Sixteen healthy, right-handed (Oldfield, 1971) volunteers with normal or corrected-to-normal visual acuity participated in Experiment 2. Written informed consent was obtained from all participants before the study, and they were financially reimbursed for their time. Data

from four participants were excluded because of excessive head movement in the scanner or technical failure. The behavioral and fMRI analyses were performed on the remaining 12 participants (age range = 23–38 years, seven women). One volunteer participated in both the behavioral validation and fMRI experiments. All experimental methods and procedures were approved by the Central University Research Ethics Committee of the University of Oxford.

Task Design

The main VSTM retro-cueing task used in the fMRI experiment was identical to the single-task condition in the behavioral validation experiment (see Figure 1B). Response assignment was counterbalanced across participants in the fMRI experiment. Half of the participants were instructed to respond “match” by finger-pressing the left response button or “nonmatch” by finger-pressing the right response button. This mapping was reversed for the other half of participants. Participants were instructed to respond as accurately as possible. The interval between trials varied randomly between 5000 and 11,000 msec.

Visual Localizer and Retinotopic-Mapping Tasks

To identify ROIs in early visual cortex, participants performed two additional tasks: a visual localizer and a retino-

topic mapping task (Figure 2). Participants were instructed to view the stimuli passively without making any responses.

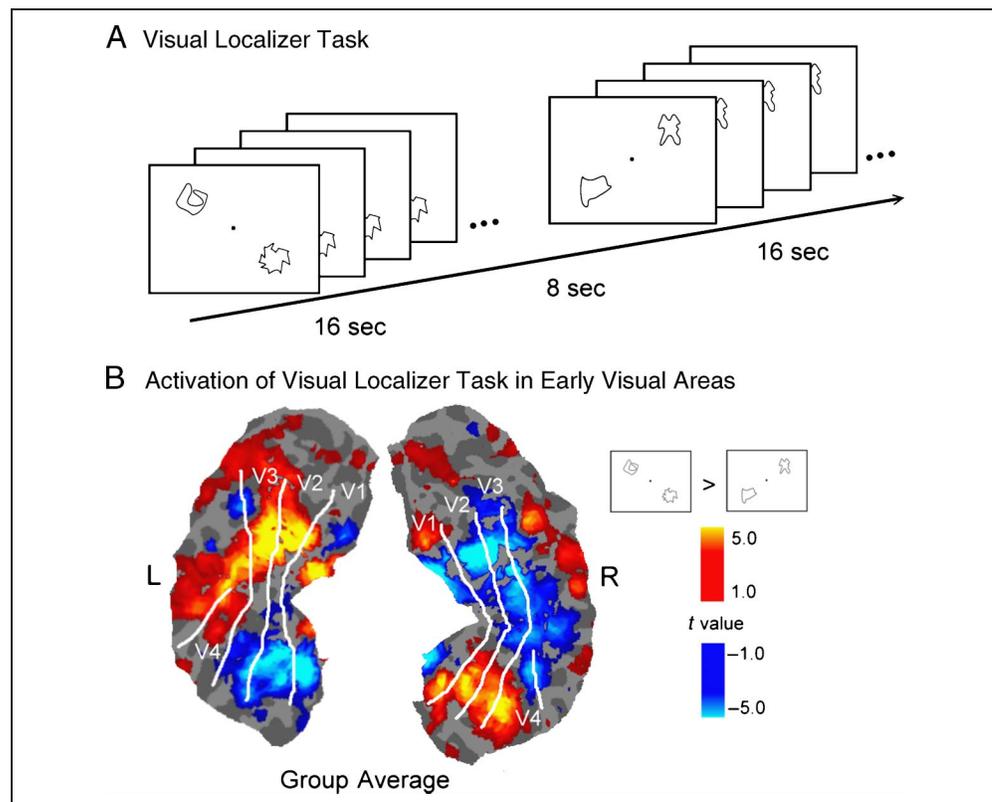
In the visual localizer task, the same shape stimuli used in the main fMRI task were presented in two-item arrays, arranged along a diagonal (left upper and right lower or left lower and right upper) on a black background in a block design. Eccentricity and elevation were the same as in the main task. Each two-item array was presented for 500 msec followed by a 500-msec blank interval, and each array was repeated 16 times in each block (16-sec duration for each block). The same shape stimuli and locations were used in each block. The interval between blocks was 8000 msec.

We employed a standard retinotopic mapping procedure to estimate polar angle maps in visual cortex and determine the boundaries of early visual areas V1, V2, V3, and V4 (Engel, Glover, & Wandell, 1997). We mapped the boundaries of visual areas using a slowly rotating black/white checkerboard wedge, with an angle of 45°, which completed six rotations in 144 sec, stimulating the entire visual field. In total, 12 sets (six rotations for each set) were repeated. A gray background was used throughout the retinotopic mapping experiment.

Experimental Procedure

Participants completed Experiment 2 over two separate fMRI sessions. In the first session, participants completed three runs of the VSTM retro-cueing task (48 trials per

Figure 2. (A) In the visual localizer task, we showed two-item arrays containing the same shape stimuli presented along a diagonal (upper left and lower right or upper right and lower left) at the same locations of the main VSTM retro-cueing fMRI task. (B) The activation corresponding to the stimulus locations was found in early visual areas (red color scale: upper left and lower right > upper right and lower left; blue color scale: upper right and lower left > upper left and lower right). Here, we present the group-level data of the visual localizer task on a normalized flattened surface of occipital cortex (for illustration purpose) with boundaries between early visual areas (V1–V4) in white. L = left; R = right.



run, 144 trials in total) and three runs of the visual localizer task (24 blocks per run, 72 blocks in total). The retro-cueing and localizer tasks were performed in alternating order. The trial order for the VSTM retro-cueing task and the block order for the localizer tasks were randomized within runs and across participants. Before fMRI scanning, participants completed one practice session (32 trials) of the VSTM retro-cueing task outside the scanner to ensure that they could perform the task as instructed. Retinotopic mapping was performed in the second fMRI session. Participants were instructed to maintain fixation on a small fixation marker at the center of the screen during the presentation of the visual stimuli.

fMRI Acquisition and Scanning Parameters

Images were acquired on a Siemens 3T Tim Trio scanner with a 12-channel head coil at the University of Oxford Centre for Clinical Magnetic Resonance Research. Functional data were collected using a T2*-weighted gradient EPI sequence (repetition time = 2000 msec, echo time = 30 msec, flip angle = 90°) to measure BOLD response. EPI images were obtained from 32 contiguous axial-oblique slices (3-mm thick with no gap) acquired in descending order with in-plane resolution of 3 × 3 mm (matrix size = 64 × 64). High-resolution anatomical images (1 × 1 × 1 mm) were also acquired for each participant using a T1-weighted magnetization prepared rapid gradient echo sequence (field of view = 192 × 192 mm).

Stimuli were presented with Presentation software (Neurobehavioral Systems, Albany, CA). Visual stimuli were rear-projected on to a screen via a Hitachi CP-X80 LCD projector at 1024 × 768 resolution at a 60-Hz refresh rate. Participants in the MR scanner viewed the screen through a mirror fixed to the head coil. If required, MR-compatible corrective lenses were used to ensure normal visual acuity during the experiment. Behavioral responses were recorded using an MR-compatible response button box. Participants were also instructed to minimize their head movements during scanning and to maintain central fixation through the experiment. Scanning time for each participant was approximately 1 hr for the first session and approximately 40 min for the second session.

Behavioral Analyses

Behavioral measures, including accuracy and mean RTs, were analyzed by a 2 (Stimulus Side: left, right) × 2 (Stimulus Elevation: upper, lower visual field) × 2 (Response Type: match, nonmatch) repeated-measures ANOVA. Only correct responses were included for RT analyses. We analyzed d' scores using a 2 (Stimulus Side: left, right) × 2 (Stimulus Elevation: upper, lower visual field) repeated-measures ANOVA.

fMRI Data Analyses

fMRI data processing and analyses were carried out with SPM5 software (Wellcome Department of Cognitive Neurology, London, U.K.) in MATLAB (MathWorks, Inc., Natick, MA). The FreeSurfer software package (surfer.nmr.mgh.harvard.edu) was used for structural analysis and for projecting results onto flattened cortical surfaces.

fMRI data were processed separately for the VSTM retro-cueing task, the visual localizer task, and the retinotopic mapping task. Three types of analysis were performed on the functional data of the VSTM retro-cueing task. A whole-brain univariate analysis was used to identify brain areas activated during the retroactive orienting of attention to an individual object and location in VSTM. ROI-based analyses were used to detect spatially specific modulation of activity in early visual areas involved in maintaining VSTM representations triggered by retro-cues. Finally, a functional connectivity analysis tested whether the degree of correlation between areas implicated in controlling shifts of attention in VSTM (IFS, FEF, PPC) and retinotopically specific areas of visual cortex changed when attention was oriented to a specific object location in VSTM.

Preprocessing. The first four volumes of each run were discarded to allow for magnetic saturation effects. The remaining functional images were corrected for head movement artifact and timing differences in slice acquisitions. Preprocessed functional images were coregistered to the individual anatomical image. Images for the VSTM retro-cueing task were then normalized to the standard SPM/Montreal Neurological Institute (MNI) brain template (Collins, Neelin, Peters, & Evans, 1994) and resampled to a 2-mm isotropic voxel size. Normalized images were spatially smoothed with a Gaussian kernel of 8-mm FWHM to accommodate any anatomical variability across participants (Hopfinger, Buchel, Holmes, & Friston, 2000; Worsley et al., 1996). The time-series data were then high-pass filtered with a frequency cutoff at 128 sec and prewhitened by means of an autoregressive model AR(1). Images from the visual localizer task and retinotopic mapping experiment were analyzed in the participants' native space with no spatial normalization or smoothing.

Whole-brain Univariate Analysis for the VSTM Retro-cueing Task

In the first analysis, we identified retro-cue-related brain areas in a standard SPM univariate analysis. The neural responses to events of interest were modeled using the canonical hemodynamic response function. The model of the VSTM retro-cueing task included regression functions for the retro-cue events according to the stimulus position (left upper, left lower, right upper, right lower visual field). Probe arrays were also modeled by regression functions for

response type (match, nonmatch) according to stimulus side and elevation for the retro-cue events (left upper, left lower, right upper, right lower visual field). Movement parameters were also used to construct six regressors to model variance caused by head movements during scanning. We did not model the memory array immediately preceding the retro-cue because the interval was too short to disambiguate the two events (2000 msec). Specific contrasts were calculated for single participants' data at the first level, and group results were determined using a random effects analysis at the second level. To determine retro-cue-related effects, all retro-cue events were averaged and compared with the implicit baseline using one-sample t test, with a threshold of $p < .05$, correcting for multiple comparisons using the false discovery rate correction.

ROI Localization for Retinotopic Visual Modulation by Retro-cues

The aim of the next analysis was to measure changes in activity at cued (i.e., attended) and uncued (i.e., unattended) retinotopic locations throughout the visual hierarchy. First, we used retinotopic mapping to determine the boundaries between early visual areas (V1, V2, V3, and V4). Second, we used the visual localizer results to identify the retinotopic locations associated with the main task. Finally, we tested the spatially specific modulation of visual areas elicited by the retro-cues.

Retinotopic mapping. To delineate the boundaries of visual areas V1, V2, V3, and V4, the response of each voxel within the early visual areas was characterized by the amplitude and the phase using fast Fourier transformation. The amplitude determines to what extent the voxels are related to retinotopy, and the phase determines which frequency is coded by the voxels. Next, we constructed a 3-D cortical surface for both hemispheres of each participant individually according to the boundary between gray and white matter in the cortex using FreeSurfer. We then segmented and unfolded the 3-D cortical surface. After that, fMRI data from the retinotopic mapping task were projected on the flattened cortical maps to identify the visual areas for V1, V2, V3, and V4 in each of the two hemispheres.

Visual localizer task. We analyzed the localizer task using a GLM and a block design for modeling in native space. The purpose of the localizer task was to define the retinotopic regions within the visual areas that were selectively responsive to the locations of the visual stimuli presented in the memory array. We selected the activated voxels that were sensitive to the four visual-field locations by contrasting activations in the two blocks (upper left and lower right vs. lower left and upper right). A liberal threshold was used to ensure identification of the relevant retinotopic regions in all individual partici-

pants ($t = 1.0$). The functional activation from the visual localizer task was plotted on each early visual area (V1, V2, V3, and V4, respectively). In total, 16 ROIs were delineated in each participant: 4 visual fields (left upper, left lower, right upper, right lower visual field) \times 4 visual areas (V1, V2, V3, V4). Combining the localizer data with the retinotopic maps allowed us to determine the sets of voxels that were most sensitive to the stimulated portion of the visual field.

Time-course analysis. We used finite impulse responses to model the time course of activations in each visual ROI according to the attention condition (attended, unattended) and probe-type condition (match, nonmatch). Data from all three unattended locations were averaged together. The finite impulse response model was used to estimate the time course from the onset time of the memory array and lasting over twelve 2-sec time bins (24 sec in total), thereby including all phases of a trial: memory array, retro-cue, and probe array.

To test for retinotopically specific modulation of early visual areas during the retention interval (after the retro-cues), we analyzed time-course data in a 2 (Attention) \times 4 (ROI) repeated-measures ANOVA using the mean beta estimates of the maintenance-related activity between 8 and 12 sec after the onset of the memory array (approximately between 6 and 10 sec after the appearance of the retro-cue). To explore the relationship between the modulation of maintenance-related neural activity in early visual areas and behavioral performance, we conducted additional analyses in which we further separated trials according to fast versus slow RTs relative to the median RT. These data were analyzed in a three-way (Attention, ROI, RT [fast, slow]) repeated-measures ANOVA. Finally, we tested the impact of retinotopically specific modulation of early visual areas on the processing of the incoming probe stimulus in a three-way (Probe Type, Attention, and ROI) repeated-measures ANOVA. For this analysis, we used the mean beta estimates of the probe-related activity between 16 and 22 sec after the onset of the memory array (i.e., approximately between 5 and 11 sec after the appearance of the probe array).

Functional Connectivity Analysis

The final set of analyses used a psychophysiological interaction (PPI) procedure to test for changes in interregional correlation between VSTM control regions (IFS, FEF, PPC) and retinotopically specific visual areas. PPI is a regression-based method to test for differences in functional connectivity between conditions without assuming a direction of influence. PPI examines the changes in the contribution of activation in one brain region to that in another region (physical factor) because of the changes in the experimental context (psychological factor; Gitelman, Penny, Ashburner, & Friston, 2003; Friston et al., 1997). This method estimates functional correlation between the time-series

signal of the seed voxels and the time-series signals of all other voxels.

We were particularly interested in testing changes in the top-down influence of IFS on retinotopically specific regions of visual areas, but for completeness, we also tested other possible sources of top-down influence from FEF and PPC. We selected seed regions in the network associated with the control of attention in VSTM guided by previous retro-cue studies (Gazzaley & Nobre, 2012; Nobre et al., 2004) and based on our univariate analyses of activations triggered by retro-cues. Peak areas of activations within these regions were identified within individual participants (mean MNI coordinates $[x, y, z]$: left IFS = $-42.50 \pm 6.11, 8.75 \pm 7.93, 29.17 \pm 7.13$ mm; right IFS = $51.50 \pm 4.58, 12.25 \pm 4.69, 33.25 \pm 3.93$ mm; left FEF = $-30.75 \pm 6.90, -2.50 \pm 3.80, 56.33 \pm 6.00$ mm; right FEF = $31.00 \pm 5.00, 0 \pm 4.21, 56.00 \pm 7.16$ mm; left PPC = $-27.50 \pm 4.01, -58.75 \pm 5.79, 51.75 \pm 6.09$ mm; right PPC = $30.25 \pm 4.14, -58.25 \pm 3.93, 53.00 \pm 6.98$ mm). Seed regions were spheres with a radius of 6 mm.

To perform the PPI analyses, the deconvolved time-series data (a time-series “physiological” variable) for

the seed regions were extracted from each participant. We then constructed an interaction term that represents the interaction of psychological (attended vs. unattended location for retro-cues) and physiological variables (Gitelman et al., 2003; Friston et al., 1997). Finally, the estimates of PPI values were extracted from each visual ROI from each individual participant. We analyzed PPI data in a three-way (Attention, ROI, Hemisphere [left, right]) repeated-measures ANOVA for each seed region: IFS, FEF, and PPC.

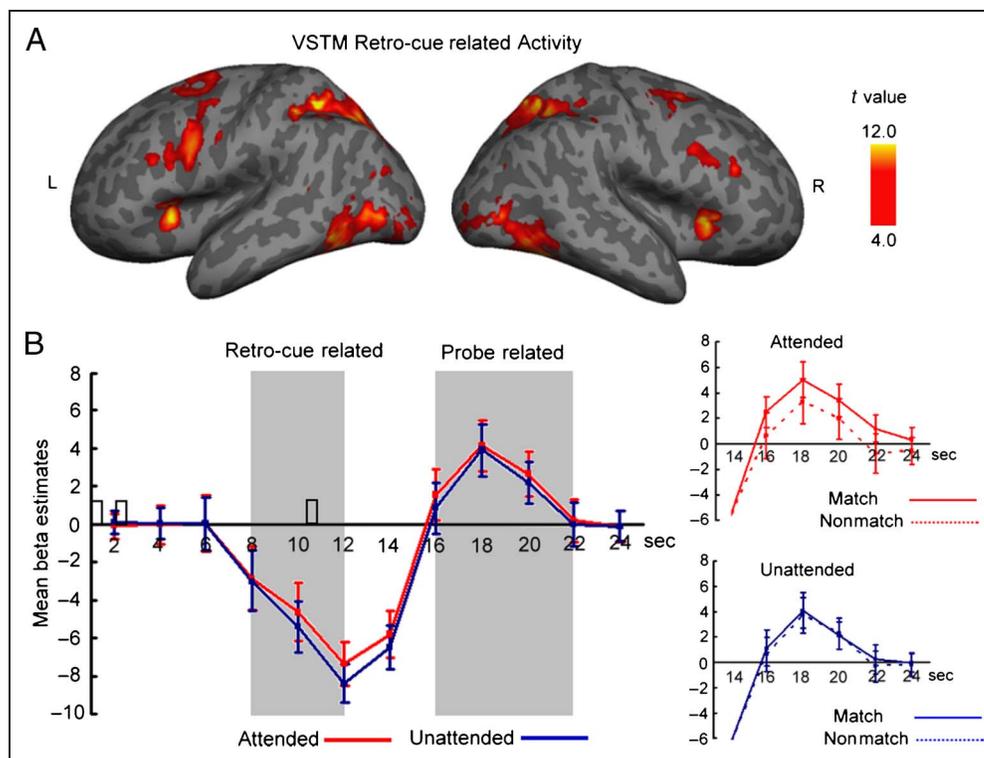
RESULTS

Behavioral Results

Experiment 1

The behavioral validation experiment confirmed that it was possible to use long VSTM delays and that the behavioral performance in the task used for fMRI was equivalent to that under conditions that discouraged verbalization. The repeated-measures ANOVA revealed that there were no Task-Type main effects or interactions for Accuracy or

Figure 3. (A) Whole-brain univariate results for VSTM retro-cueing. A distributed and extensive bilateral activation in cortical regions was found after the presentation of retro-cues. This activation pattern included SFG, MFG, and IFG, which surround the IFS, FEF, anterior insula/ventrolateral pFC, and ACC within frontal regions; SPL, IPS, and PCu within parietal regions; fusiform and MTG, IOG, and MOG within occipito-temporal regions; and left thalamus and bilateral cerebellum. (B) Time-course results of ROI analysis in early visual areas (V1–V4). Analysis of time-course data (gray areas) revealed a significant modulatory effect by retro-cues in early visual areas measured at the attended locations compared with unattended locations during the retention interval (left). Time-course data also showed a significant interaction between cued locations and item types during the probe period (right). These results indicated a greater difference in beta estimates for detecting match versus nonmatch items at the corresponding attended locations (top) in contrast to unattended locations (bottom). Error bars represent standard errors of the means. L = left; R = right.



RT ($ps > .1$). The only significant main effect we observed was the difference in RT according to Response Type: match (617.45 ± 130.89 msec) versus nonmatch (681.06 ± 153.61 msec) [$F(1, 17) = 17.54, p < .005$]. There was no significant effect of Task Type for d' scores ($p > .1$).

Experiment 2

Behavioral results for the main fMRI task showed that participants performed reliably well but were not at ceiling in the task (match response: $82.18 \pm 11.15\%$, non-match response: $82.18 \pm 11.62\%$, accuracy: 2.04 ± 0.93 d' score). There was no significant effect of either side or elevation of the target stimulus in accuracy, RT, or d' scores ($ps > .1$). There was no significant effect for Response Type in Accuracy ($p > .1$). No significant interaction effect was found in Accuracy, RTs, or d' scores ($ps > .1$). The only significant effect was observed in RTs between match (606.77 ± 90.81 msec) versus nonmatch (672.57 ± 115.37 msec) responses [$F(1, 11) = 29.65, p < .005$]. Behavioral data for the main fMRI task are illustrated in Figure 1C.

fMRI Results

Whole-brain Univariate Results for the VSTM Retro-cueing

We found that retro-cues elicited a bilateral, distributed, and extensive activation pattern in cortical regions (Figure 3A and Table 1). These activations included superior, middle, and inferior frontal gyri (SFG, MFG, and IFG); FEF; anterior insula/ventrolateral pFC; and ACC within the frontal cortex. We also found significant activation in the superior parietal lobule (SPL) and inferior parietal lobule, intraparietal sulcus (IPS), and precuneus (PCu) within the PPC. Occipito-temporal areas included middle temporal gyrus (MTG), fusiform gyrus, and inferior and middle occipital gyrus (IOG and MOG). Significant subcortical activations occurred in the left thalamus and bilateral cerebellum. These whole-brain univariate results replicated previous findings characterizing the control network for orienting spatial attention to item locations in VSTM (Gazzaley & Nobre, 2012; Nobre et al., 2004).

ROI Localization Results for Retinotopic Visual Modulation by Retro-cues

Analysis of the visual localizer task combined with retinotopic mapping successfully yielded nonoverlapping visual ROIs related to the processing of each of the four visual fields in four different early visual areas (V1, V2, V3, and V4). We tested for the presence of retinotopically specific modulation of early visual areas during the retention interval and probe period.

Analysis of time courses of activations in these retinotopically specific regions of early visual areas revealed

Table 1. Brain Areas and MNI Coordinates (x, y, z) Significantly Activated by Retro-cues during VSTM

Brain Areas		x	y	z	t
<i>Frontal Regions</i>					
ACC	Med	-6	24	45	8.30
	Med	9	18	49	6.40
SFG	L	-15	12	60	7.63
MFG	L	-39	18	23	5.50
	R	39	30	23	6.45
IFS	L	-48	6	26	7.59
	R	54	15	34	5.09
FEF	L	-36	0	64	5.31
	R	33	6	60	6.86
Insula	L	-30	18	4	8.46
	R	30	18	8	8.32
<i>Parietal Regions</i>					
SPL	L	-18	-69	56	6.56
	R	21	-57	56	8.78
IPS	L	-42	-36	41	8.41
	R	36	-42	45	6.05
PCu	L	-27	-75	30	7.94
	R	12	-60	53	9.77
<i>Occipito-temporal Regions</i>					
MOG	L	-45	-75	4	6.98
	R	48	-75	0	6.91
IOG	L	-39	-87	-8	5.8
	R	33	-93	-8	4.67
MTG	L	-42	-60	8	4.37
	R	45	-60	-4	7.31
Fusiform gyrus	L	-48	-60	-15	10.00
	R	48	-57	-19	8.31
<i>Others</i>					
Thalamus	L	-9	-12	0	5.62
Cerebellum	L	-33	-60	-30	5.42
	R	30	-63	-30	7.46
	Med	-6	-78	-30	5.30
	Med	12	-75	-26	6.29

Med =medial; L =left hemisphere; R = right hemisphere; $t = t$ score.

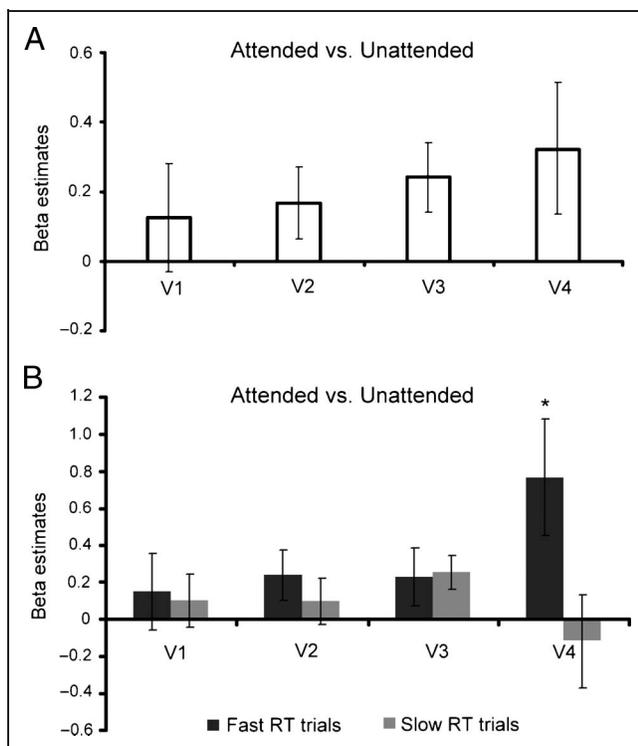


Figure 4. (A) Attentional modulation of activity in V1–V4 during retro-cues. (B) Modulation of visual activity during retro-cues in fast versus slow RT trials. Attentional modulation in V4 (but not in other visual areas) was associated with RTs (fast and slow RT trials based on the median split for each participant; $p < .05$). Error bars represent standard errors of the means.

significant modulation of visual activity by attention to locations of objects maintained in VSTM (Figure 3B). During the retention interval, the activation profiles measured at the attended and unattended locations diverged after retro-cues [$F(1, 11) = 9.88, p < .05$], resulting in greater activation for attended compared with unattended locations. We also observed a significant effect of ROI [$F(3, 33) = 8.11, p < .005$], showing overall stronger activation in V4 compared with V1. There was no significant interaction between Attention and ROI ($p > .1$). Equivalent results were observed when we directly compared the attended location with the diagonally opposite unattended quadrant

[main effect of Attention: $F(1, 11) = 6.97, p < .05$]. We also observed a significant effect of ROI [$F(3, 33) = 9.48, p < .005$]. Again, the interaction between attention and ROI was not significant ($p > .1$). As in previous VSTM studies, overall activity levels dropped below baseline during the retention interval, before returning to above-baseline levels during the probe period (Munneke, Belopolsky, & Theeuwes, 2012; Sligte et al., 2009; Lepsien & Nobre, 2007).

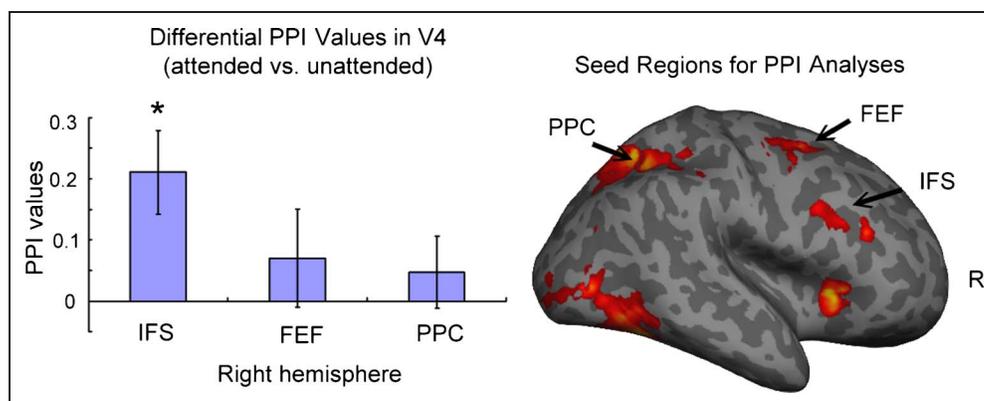
In a subsidiary analysis including RT as a factor, we found that the modulation of activation in visual area V4 was related to a performance measure of efficient selection in VSTM (see Figure 4). In addition to a main effect of Attention [$F(1, 11) = 6.50, p < .05$], there was a significant three-way interaction among Attention, ROI, and RT [$F(3, 33) = 3.00, p < .05$]. Follow-up contrasts showed the effect to be specific to V4, with significant differences in activity between attended and unattended locations on the fast RT trials [$t(11) = 2.42, p < .05$] but not on slow RT trials ($p > .1$).

During the probe period, analysis of the time courses of activations in the visual ROIs showed that directing attention to item locations in VSTM enhanced the discrimination between match versus nonmatch subsequent stimuli at the same retinotopic locations. A main effect of Attention [$F(1, 11) = 14.69, p < .005$] reflected larger responses overall for probe stimuli at attended compared with unattended locations. However, this main effect was qualified by a significant interaction between Attention and Probe Type [match vs. nonmatch; $F(1, 11) = 4.78, p = .05$]. Follow-up analyses revealed greater differences in beta estimates for detecting match versus nonmatch items at the attended locations (1.73 ± 1.15) than in the unattended locations [$-0.32 \pm 0.29; t(11) = 2.19, p = .05$; Figure 3B]. The main effect of visual ROIs was also significant [$F(3, 33) = 4.36, p < .05$], showing stronger activations to probe stimuli in V1 compared with V4. No other significant effects were found ($ps > .1$).

Functional Connectivity Analysis

Functional connectivity results are illustrated in Figure 5. Our main question was whether functional connectivity between control regions and retinotopic regions of visual

Figure 5. In the current PPI analysis, we selected seed regions in the network associated with the control of attention in VSTM guided by our univariate analyses of activations triggered by retro-cues, focusing on IFS, FEF, and PPC (right; R = right hemisphere). The right IFS showed stronger functional coupling with V4 at the corresponding attended locations compared with the unattended locations (left).



areas was altered by orienting attention during VSTM. We tested this in a PPI analysis using time courses from ROIs in control regions and retinotopically specific visual areas in a three-way repeated-measures ANOVA that assessed the effects of Cued Location (attended, unattended) \times Visual ROIs (V1, V2, V3, V4) \times Hemisphere (left, right). We were particularly interested in the IFS, but for completeness, we conducted equivalent analyses for FEF and PPC.

For the IFS, the PPI analysis showed that retro-cues triggered significant changes in its functional connectivity with retinotopic visual areas. A main effect of Attention showed stronger coupling between IFS and retinotopic regions related to attended versus unattended locations maintained in VSTM [$F(1, 11) = 7.45, p < .05$]. A main effect of Visual ROI [$F(3, 33) = 4.90, p < .05$] indicated that coupling was also stronger overall for V4 than V1, V2, or V3 ($ps < .05$). A significant three-way interaction among attention, visual ROI, and hemisphere indicated that the strongest attention-related modulation of functional coupling between IFS and retinotopic coding of remembered stimuli occurred with V4 in the right hemisphere [$F(3, 33) = 4.95, p < .05$]. Follow-up analyses confirmed significant differences in IFS–V4 functional coupling between attended and unattended locations in the right hemisphere [$t(11) = 3.07, p < .05$], but not in the left hemisphere ($p > .1$). When tested separately, functional connectivity between IFS and other visual ROIs was not found to differ significantly for attended versus unattended locations ($ps > .1$).

No significant modulations of functional connectivity were observed for FEF or PPC ($ps > .1$).

DISCUSSION

Using a memory-based retro-cueing task adapted for event-related fMRI, we showed that changes in long-range connections between frontal cortex and retinotopically specific regions of visual areas accompany shifts of attention during VSTM maintenance. Responses in early visual areas were significantly elevated when the corresponding memory items were attended versus unattended. Furthermore, modulation of maintenance-related activity in V4 was related to the speed of responses based on selected memoranda. Importantly, retro-cues modulated the strength of functional coupling between frontal control areas and these retinotopically organized visual areas. In particular, activity in the right IFS became more strongly coupled to the portion of V4 coding the stimulus instructed to be relevant for the subsequent comparison. Focusing attention during VSTM maintenance also led to increased differentiation between matching versus nonmatching probe items in retinotopic visual areas. Together, these findings provide new insights into top–down modulation within VSTM that can influence the maintenance of relevant memoranda and the expectation of subsequent probe stimuli to guide behavior in a flexible and goal-directed fashion.

Our experimental design guaranteed that spatial shifts of attention were internally generated, based on information being maintained in VSTM. The cue was an object that appeared at the center of the screen and instructed participants to discriminate whether this item and a subsequent probe appearing at the same location matched or not. There was no spatial information in the cue itself. Instead, it was necessary to access the location of the cued memory item in the mnemonic code to shift attention to the relevant item location. Similar designs have been used successfully in previous studies (Lewis-Peacock et al., 2012; Munneke et al., 2012; Lepsien & Nobre, 2007). This aspect of the design is important to ensure that the effects observed are not simply the results of a spatial cue merely biasing activity in anticipation of a probe stimulus. Given the tight functional coupling between VSTM maintenance and probe anticipation in these tasks, these details become important for interpreting the results (see Lewis-Peacock et al., 2012; Nobre & Stokes, 2011; Stokes, 2011).

Performance in the task was also unlikely to be supported by, or dependent on, verbalization strategies. In our first behavioral experiment, we found no change in behavioral performance when verbal strategies were discouraged by a concurrent verbal memory task. Furthermore, the fMRI analyses were primarily aimed at revealing retinotopically specific modulatory mechanisms, toward which verbalization is unlikely to contribute.

In accordance with previous findings (Lepsien et al., 2011; Nee & Jonides, 2009; Lepsien & Nobre, 2007; Raye, Johnson, Mitchell, Greene, & Johnson, 2007; Roth & Courtney, 2007; Roth, Serences, & Courtney, 2006; Lepsien, Griffin, Devlin, & Nobre, 2005; Nobre et al., 2004), we found that retro-cues increased activity across a network of brain regions similar to that implicated in attentional control in perceptual tasks, including posterior parietal cortices and FEF (Corbetta & Shulman, 2002; Nobre, 2001; Kastner & Ungerleider, 2000) as well as more anterior prefrontal regions, especially around the IFS. These findings give additional support to the notion that retro-cues trigger VSTM-based attentional shifts via top–down control mechanisms. Moreover, our ROI analyses showed that the retro-cues bias activity in retinotopically specific regions in early visual cortex. Specifically, the comparisons of attended versus unattended locations demonstrated that the memory-based shifts of attention may modulate activity in multiple early visual areas (V1–V4). These results replicate and extend previous findings of retinotopically specific modulation of visual activity during VSTM retro-cueing tasks (Munneke et al., 2012; Sligte et al., 2009).

An important novel aspect of our study was the ability to investigate changes in the strength of functional connectivity between areas implicated in attentional control and the specific retinotopic regions within visual areas coding the location of attended versus unattended stimuli during VSTM maintenance. Our results showed that spatiotopically specific biases can be established between

prefrontal and visual areas. Our findings also pointed to the most likely connection points for top-down modulation of VSTM maintenance by spatial attention. Our functional connectivity analysis emphasized changes in the strength of coupling between the right IFS and retinotopic coding within V4. Recent findings using electrophysiological recordings in macaques have also suggested that functional coupling between pFC and V4 may mediate effective VSTM maintenance and synchronization in low-frequency oscillatory activity may play a mediating role in enhancing interregional communication (Liebe, Hoerzer, Logothetis, & Rainer, 2012). The retinotopic specificity of our findings is a significant advance on previous demonstrations of interregional correlation between prefrontal and visual areas during VSTM maintenance (Sneve, Magnussen, Alnæs, Endestad, & D'Esposito, 2013; Gazzaley et al., 2004) and its enhancement by effective retro-cues (Kuo, Yeh, Chen, & D'Esposito, 2011).

Accumulating evidence has shown that pFC is involved in attention, memory, and many other cognitive domains (Duncan, 2010; Duncan & Owen, 2000). To accommodate such diversity, it has been hypothesized that a basic principle of pFC function is adaptive coding (Duncan, 2001). According to this account, pFC functions as a global workspace and is associated with diverse cognitive demands in different task contexts. Prefrontal neurons become tuned to code relevant inputs and thus are highly adaptable. pFC adapts its function to support the processing of task-relevant information in other cortical systems of the brain. Our functional connectivity data support this adaptive-coding hypothesis, suggesting that the right IFS might selectively enhance processing of task-relevant VSTM representations by biasing neural activity in retinotopically specific subregions of early visual cortex. In our task, prefrontal and visual connectivity is modulated flexibly to accommodate changes in task demands. Within an adaptive coding framework, our results could reflect rapid reconfiguration of neural tuning profiles in pFC, with task-dependent connectivity patterns (e.g., Stokes et al., 2013). Although our findings highlight changes in functional connectivity between prefrontal and visual areas, we cannot rule out the possible contribution of other control areas in modulating early visual areas during shifts of attention in VSTM. Our task or methods may have lacked the sensitivity to reveal contributions from other regions that have been implicated in the control of attention and VSTM maintenance, such as in the parietal cortex (e.g., Bledowski, Rahm, & Rowe, 2009; Magen et al., 2009; Leung, Oh, Ferri, & Yi, 2007; Nobre et al., 2004; Johnson, Raye, Mitchell, Greene, & Anderson, 2003).

Previous studies of macaques have revealed that attention can increase the effective contrast of a stimulus and improve perceptual discriminability of attended items (Reynolds & Chelazzi, 2004; McAdams & Maunsell, 1999; Motter, 1993). This type of attentional modulation of perceptual sensitivity has also been reported in humans

in V1–V4 (Pestilli, Carrasco, Heeger, & Gardner, 2011; Liu, Larsson, & Carrasco, 2007; Liu, Pestilli, & Carrasco, 2005). Our results pointed to analogous modulatory effects during memory-based shifts of attention during VSTM delays. Retro-cues affected the subsequent comparison process of probed objects, indexed by an enhanced difference in neural processing of matching versus nonmatching objects within attended retinotopic visual locations than in unattended locations. One intuitive explanation of our results is that modulation of memory-related representations triggers retinotopically specific anticipatory spatial biases to prioritize or facilitate perceptual discrimination of the relevant probe stimulus and its comparison with the corresponding memorandum.

Although top-down modulatory effects in early visual areas are observed in both attention and VSTM, the role that these contribute in each case is not fully understood. Attending to an expected visual target/location can lead to anticipatory activation in occipital cortex (Ruff & Driver, 2006; Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999). This is thought to contribute to the “bias” that is essential for resolving competitive perceptual interactions in favor of task-relevant items (Desimone & Duncan, 1995). Persistent activity in sensory cortices is also observed during VSTM (Lepsien & Nobre, 2007) and has been implicated in supporting the maintenance of visual contents during VSTM (Ester, Serences, & Awh, 2009; Harrison & Tong, 2009; Serences et al., 2009; Pasternak & Greenlee, 2005). However, VSTM and attention tasks share many functional similarities (Gazzaley & Nobre, 2012; Stokes, 2011; Kuo, Rao, Lepsien, & Nobre, 2009; Awh & Jonides, 2001). Most VSTM tasks also involve anticipating probe stimuli to be compared with the relevant memoranda. After all, VSTM is an inherently proactive function for maintaining information to guide future perception and action. In many, if not most cases, therefore, sustained visual activity in VSTM tasks may reflect anticipation of the probe stimulus (Lewis-Peacock et al., 2012; Lepsien et al., 2011; Stokes, 2011). In our task, it is not possible to differentiate between retroactive modulation of maintenance-related activity and proactive anticipatory activity. We suggest that top-down modulatory mechanisms may provide the functional bridge between boosting the relevant VSTM representation and preparing the visual system for upcoming probe demands.

Summary

Using retro-cues to trigger memory-based shifts of attention in VSTM, we replicate and extend previous studies identifying brain networks involved in controlling attention in VSTM. We show, for the first time, that dynamic adjustments in functional connectivity take place between pFC and retinotopically specific regions of early visual areas during VSTM maintenance as a consequence of changing expectations and task demands. Attentional modulation during VSTM also leads to enhanced discrimination and

comparison of subsequent control stimuli to relevant memoranda.

Acknowledgments

This work was supported by the Wellcome Trust (Grant WT082791MA to A. C. N.). The research was also supported by the National Institute for Health Research (Oxford Biomedical Research Centre based at Oxford University Hospitals Trust Oxford University). B. C. K. was supported by a grant from the National Science Council, Taiwan (NSC 100-2410-H-004-221-MY2). M. G. S. was supported by St. John's College, Oxford. A. M. M. was supported by a Commonwealth Scholarship.

Reprint requests should be sent to Bo-Cheng Kuo, Department of Psychology, National Taiwan University, No. 1, Sec. 4, Roosevelt Road, 10617, Taipei, Taiwan, or via e-mail: bckuo@ntu.edu.tw.

REFERENCES

- Astle, D. E., Summerfield, J., Griffin, I., & Nobre, A. C. (2012). Orienting attention to locations in mental representations. *Attention, Perception, & Psychophysics*, *74*, 146–162.
- Awh, E., & Jonides, J. (2001). Overlapping mechanisms of attention and spatial working memory. *Trends in Cognitive Sciences*, *5*, 119–126.
- Bledowski, C., Rahm, B., & Rowe, J. B. (2009). What “works” in working memory? Separate systems for selection and updating of critical information. *Journal of Neuroscience*, *29*, 13735–13741.
- Collins, D. L., Neelin, P., Peters, T. M., & Evans, A. C. (1994). Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. *Journal of Computer Assisted Tomography*, *18*, 192–205.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, *3*, 201–215.
- Curtis, C. E., & D’Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Sciences*, *7*, 415–423.
- Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annual Review of Neuroscience*, *18*, 193–222.
- Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. *Nature Reviews Neuroscience*, *2*, 820–829.
- Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: Mental programs for intelligent behaviour. *Trends in Cognitive Sciences*, *14*, 172–179.
- Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*, *23*, 475–483.
- Endo, N., Saiki, J., Nakao, Y., & Saito, H. (2003). Perceptual judgments of novel contour shapes and hierarchical descriptions of geometrical properties. *The Japanese Journal of Psychology*, *74*, 346–353.
- Engel, S. A., Glover, G. H., & Wandell, B. A. (1997). Retinotopic organization in human visual cortex and the spatial precision of functional MRI. *Cerebral Cortex*, *7*, 181–192.
- Ester, E. F., Serences, J. T., & Awh, E. (2009). Spatially global representations in human primary visual cortex during working memory maintenance. *Journal of Neuroscience*, *29*, 15258–15265.
- Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage*, *6*, 218–229.
- Gazzaley, A. (2011). Influence of early attentional modulation on working memory. *Neuropsychologia*, *49*, 1410–1424.
- 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., & Nobre, A. C. (2012). Top-down modulation: Bridging selective attention and working memory. *Trends in Cognitive Sciences*, *16*, 129–135.
- Gazzaley, A., Rissman, J., & D’Esposito, M. (2004). Functional connectivity during working memory maintenance. *Cognitive, Affective, & Behavioral Neuroscience*, *4*, 580–599.
- Gitelman, D. R., Penny, W. D., Ashburner, J., & Friston, K. J. (2003). Modeling regional and psychophysiological interactions in fMRI: The importance of hemodynamic deconvolution. *Neuroimage*, *19*, 200–207.
- Green, D. M., & Swets, J. A. (1966). *Signal detection theory and psychophysics*. Huntington, NY: Robert E. Krieger Publishing Company.
- Griffin, I. C., & Nobre, A. C. (2003). Orienting attention to locations in internal representations. *Journal of Cognitive Neuroscience*, *15*, 1176–1194.
- Harrison, S. A., & Tong, F. (2009). Decoding reveals the contents of visual working memory in early visual areas. *Nature*, *458*, 632–635.
- Higo, T., Mars, R. B., Boorman, E. D., Buch, E. R., & Rushworth, M. F. S. (2011). Distributed and causal influence of frontal operculum in task control. *Proceedings of the National Academy of Sciences, U.S.A.*, *108*, 4230–4235.
- Hopfinger, J. B., Buchel, C., Holmes, A. P., & Friston, K. J. (2000). A study of analysis parameters that influence the sensitivity of event-related fMRI analyses. *Neuroimage*, *11*, 326–333.
- Johnson, M. K., Raye, C. L., Mitchell, K. J., Greene, E. J., & Anderson, A. W. (2003). fMRI evidence for an organization of prefrontal cortex by both type of process and type of information. *Cerebral Cortex*, *13*, 265–273.
- 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.
- Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R., & Ungerleider, L. G. (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron*, *22*, 751–761.
- Kastner, S., & Ungerleider, L. G. (2000). Mechanisms of visual attention in the human cortex. *Annual Review of Neuroscience*, *23*, 315–341.
- Kuo, B.-C., Rao, A., Lepsien, J., & Nobre, A. C. (2009). Searching for targets within the spatial layout of visual short-term memory. *Journal of Neuroscience*, *29*, 8032–8038.
- Kuo, B.-C., Stokes, M. G., & Nobre, A. C. (2012). Attention modulates maintenance of representations in visual short-term memory. *Journal of Cognitive Neuroscience*, *24*, 51–60.
- Kuo, B.-C., Yeh, Y.-Y., Chen, A. J. W., & D’Esposito, M. (2011). Functional connectivity during top-down modulation of visual short-term memory representations. *Neuropsychologia*, *49*, 1589–1596.
- Landman, R., Spekreijse, H., & Lamme, V. A. F. (2003). Large capacity storage of integrated objects before change blindness. *Vision Research*, *43*, 149–164.
- Lee, T. G., & D’Esposito, M. (2012). The dynamic nature of top-down signals originating from prefrontal cortex: A combined fMRI-TMS study. *Journal of Neuroscience*, *32*, 15458–15466.
- Lepsien, J., Griffin, I. C., Devlin, J. H. T., & Nobre, A. C. (2005). Directing spatial attention in mental representations: Interactions between attentional orienting and working-memory load. *Neuroimage*, *26*, 733–743.

- Lepsien, J., & Nobre, A. C. (2007). Attentional modulation of object representations in working memory. *Cerebral Cortex*, *17*, 2072–2083.
- Lepsien, J., Thornton, I., & Nobre, A. C. (2011). Modulation of working-memory maintenance by directed attention. *Neuropsychologia*, *49*, 1569–1577.
- 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.
- Lewis-Peacock, J. A., Drysdale, A. T., Oberauer, K., & Postle, B. R. (2012). Neural evidence for a distinction between short-term memory and the focus of attention. *Journal of Cognitive Neuroscience*, *24*, 61–79.
- Liebe, S., Hoerzer, G. M., Logothetis, N. K., & Rainer, G. (2012). Theta coupling between V4 and prefrontal cortex predicts visual short-term memory performance. *Nature Neuroscience*, *15*, 456–464.
- Liu, T., Larsson, J., & Carrasco, M. (2007). Feature-based attention modulates orientation-selective responses in human visual cortex. *Neuron*, *55*, 313–323.
- Liu, T., Pestilli, F., & Carrasco, M. (2005). Transient attention enhances perceptual performance and fMRI response in human visual cortex. *Neuron*, *45*, 469–477.
- Magen, H., Emmanouil, T.-A., McMains, S. A., Kastner, S., & Treisman, A. (2009). Attentional demands predict short-term memory load response in posterior parietal cortex. *Neuropsychologia*, *47*, 1790–1798.
- McAdams, C. J., & Maunsell, J. H. R. (1999). Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *Journal of Neuroscience*, *19*, 431–441.
- Motter, B. C. (1993). Focal attention produces spatially selective processing in visual cortical areas V1, V2, and V4 in the presence of competing stimuli. *Journal of Neurophysiology*, *70*, 909–919.
- Munneke, J., Belopolsky, A. V., & Theeuwes, J. (2012). Shifting attention within memory representations involves early visual areas. *PLoS One*, *7*, e35528.
- Munneke, J., Heslenfeld, D. J., & Theeuwes, J. (2008). Directing attention to a location in space results in retinotopic activation in primary visual cortex. *Brain Research*, *1222*, 184–191.
- Munneke, J., Heslenfeld, D. J., & Theeuwes, J. (2010). Spatial working memory effects in early visual cortex. *Brain and Cognition*, *72*, 368–377.
- Murray, A. M., Nobre, A. C., Clark, I. A., Cravo, A. M., & Stokes, M. G. (2013). Attention restores discrete items to visual short-term memory. *Psychological Science*, *24*, 550–556.
- Nee, D. E., & Jonides, J. (2009). Common and distinct neural correlates of perceptual and memorial selection. *Neuroimage*, *45*, 963–975.
- Nobre, A. C. (2001). The attentive homunculus: Now you see it, now you don't. *Neuroscience and Biobehavioral Reviews*, *25*, 477–496.
- Nobre, A. C., Coull, J. T., Maquet, P., Frith, C. D., Vandenberghe, R., & Mesulam, M. M. (2004). Orienting attention to locations in perceptual versus mental representations. *Journal of Cognitive Neuroscience*, *16*, 363–373.
- Nobre, A. C., & Stokes, M. G. (2011). Attention and short-term memory: Crossroads. *Neuropsychologia*, *49*, 1391–1392.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, *9*, 97–113.
- Pasternak, T., & Greenlee, M. W. (2005). Working memory in primate sensory systems. *Nature Reviews Neuroscience*, *6*, 97–107.
- Pertsov, Y., Bays, P. M., Joseph, S., & Husain, M. (2013). Rapid forgetting prevented by retrospective attention cues. *Journal of Experimental Psychology: Human Perception and Performance*, *39*, 1224–1231.
- Pestilli, F., Carrasco, M., Heeger, D. J., & Gardner, J. L. (2011). Attentional enhancement via selection and pooling of early sensory responses in human visual cortex. *Neuron*, *72*, 832–846.
- Posner, M. I. (1980). Orientating of attention. *The Quarterly Journal of Experimental Psychology*, *32*, 3–25.
- Postle, B. R. (2005). Delay-period activity in the prefrontal cortex: One function is sensory gating. *Journal of Cognitive Neuroscience*, *17*, 1679–1690.
- Postle, B. R. (2006). Working memory as an emergent property of the mind and brain. *Neuroscience*, *139*, 23–38.
- Ranganath, C., DeGutis, J., & D'Esposito, M. (2004). Category-specific modulation of inferior temporal activity during working memory encoding and maintenance. *Cognitive Brain Research*, *20*, 37–45.
- Raye, C. L., Johnson, M. K., Mitchell, K. J., Greene, E. J., & Johnson, M. R. (2007). Refreshing: A minimal executive function. *Cortex*, *43*, 135–143.
- Reynolds, J. H., & Chelazzi, L. (2004). Attentional modulation of visual processing. *Annual Review of Neuroscience*, *27*, 611–647.
- Roth, J. K., & Courtney, S. M. (2007). Neural system for updating object working memory from different sources: Sensory stimuli or long-term memory. *Neuroimage*, *38*, 617–630.
- Roth, J. K., Serences, J. T., & Courtney, S. M. (2006). Neural system for controlling the contents of object working memory in humans. *Cerebral Cortex*, *16*, 1595–1603.
- Ruff, C. C., & Driver, J. (2006). Attentional preparation for a lateralized visual distractor: Behavioral and fMRI evidence. *Journal of Cognitive Neuroscience*, *18*, 522–538.
- Serences, J. T., Ester, E. F., Vogel, E. K., & Awh, E. (2009). Stimulus-specific delay activity in human primary visual cortex. *Psychological Science*, *20*, 207–214.
- Serences, J. T., & Yantis, S. (2006). Selective visual attention and perceptual coherence. *Trends in Cognitive Sciences*, *10*, 38–45.
- Sligte, I. G., Scholte, H. S., & Lamme, V. A. F. (2009). V4 activity predicts the strength of visual short-term memory representations. *Journal of Neuroscience*, *29*, 7432–7438.
- Sneve, M. H., Magnussen, S., Alnæs, D., Endestad, T., & D'Esposito, M. (2013). Top-down modulation from inferior frontal junction to FEFs and intraparietal sulcus during short-term memory for visual features. *Journal of Cognitive Neuroscience*, *25*, 1944–1956.
- Stokes, M. G. (2011). Top-down visual activity underlying VSTM and preparatory attention. *Neuropsychologia*, *49*, 1425–1427.
- Stokes, M. G., Kusunoki, M., Sigala, N., Nili, H., Gaffan, D., & Duncan, J. (2013). Dynamic coding for cognitive control in prefrontal cortex. *Neuron*, *78*, 364–375.
- Stokes, M. G., & Nobre, A. C. (2012). Top-down biases in visual short-term memory. In G. R. Mangun (Ed.), *The neuroscience of attention: Attentional control and selection* (pp. 209–228). New York: Oxford University Press.
- Worsley, K. J., Marrett, S., Neelin, P., Vandal, A., Friston, K. J., & Evans, A. (1996). A unified statistical approach for determining significant signals in images of cerebral activation. *Human Brain Mapping*, *4*, 58–73.
- Yi, D.-J., Turk-Browne, N. B., Chun, M. M., & Johnson, M. K. (2008). When a thought equals a look: Refreshing enhances perceptual memory. *Journal of Cognitive Neuroscience*, *20*, 1371–1380.
- Zanto, T. P., & Gazzaley, A. (2009). Neural suppression of irrelevant information underlies optimal working memory performance. *Journal of Neuroscience*, *29*, 3059–3066.
- Zanto, T. P., Rubens, M. T., Thangavel, A., & Gazzaley, A. (2011). Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. *Nature Neuroscience*, *14*, 656–661.