Neural System for Controlling the Contents of Object Working Memory in Humans

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Working memory (WM), the active maintenance of currently relevant information, is a flexible system allowing for fast and frequent goal-directed changes of rehearsed information. Successful WM maintenance prevents interference from distracting stimuli while allowing new task-relevant information to update the contents of WM. We used functional magnetic resonance imaging to show that when WM contents were updated, regardless of stimulus type (faces or houses), a frontoparietal network showed transient increases in activation. Some of these regions are highly similar to those identified in studies of shifting attention, supporting the idea that updating WM involves a change in the attentional priority afforded to the current perceptual input. A region within the mid-ventrolateral prefrontal cortex, near the junction of the inferior frontal sulcus and precentral sulcus (inferior frontal junction), that has previously been implicated in cognitive control, demonstrated transient increases in activity during updating as well as sustained maintenance activity. A more anterior prefrontal region, middle frontal gyrus, previously implicated in protecting the contents of WM from interfering stimuli during maintenance, demonstrated transient increases in activity during updating. The current study suggests that updating WM results from a combination of increased attention to the visual stimulus and a change in the system's interference protection state.

Keywords: attention, fMRI, frontal, maintenance, parietal, update

Introduction

The psychological construct that supports online representations of to-be-remembered stimuli is referred to as "working memory" (WM) and includes many cognitive processes, such as maintaining, manipulating, and updating information, within a limited-capacity storage buffer (Baddeley, 1992). The limited capacity of WM necessitates prioritizing which information is to be maintained and which is not. The current study examines the act of updating the contents of WM by replacing these contents with new information from the visual environment, a process that may involve multiple operations. The ability to maintain interference-resistant representations while also allowing some new information to enter the WM storage buffer are complementary abilities of the WM system. At the time of updating, the limited-capacity WM system must transition from protecting currently remembered items against interference (maintenance) to replacing a currently remembered item with a new item (updating). As a result, there is competition for representation between the items currently being maintained in WM and those items that are impinging on the system. Task instructions, goals and context determine whether the cur-

rently maintained information or the current perceptual input should be given greater relative priority in the competition for representation in the limited-capacity WM buffer. Currently it is unclear whether there is a single neural system that establishes this relative priority or separate systems: one that controls maintenance of items already in WM and another that controls the entry of new items into WM.

Insights into updating processes have been revealed previously by examining updating as part of a group of executive functions. A distinction must be made between different types of WM updating. First, WM may be updated by encoding additional items and/or eliminating items from WM. Second, WM may be updated through changing or manipulating the information which is already present in WM (Logie and others, 1994; Owen and others, 1996; Fürst and Hitch, 2000) such as reordering stimuli in alphabetical order (D'Esposito and others, 1999). In a recent set of experiments where participants consolidated information in WM with or without concurrent maintenance, the efficiency for encoding items into WM was not affected by the simultaneous maintenance of other, additional information until the WM capacity was reached (Woodman and Vogel, 2005). These results suggested that consolidation of information into a WM store and maintenance of information in WM are independent processes although both function under the same limited-capacity store. N-back and running span tasks require participants to replace old items with new ones while simultaneously maintaining other items and incrementing the serial position of items within the sequence. Studies using the running span task compared update-related activity (replacing old items with new items) with encoding-related activity (encoding new items without replacing items) (e.g., see Salmon and others, 1996; Cohen and others, 1997; D'Esposito and others, 1999; Van der Linden and others, 1999; Postle and others, 2001). Refresh tasks, which involve reviving the representation of an item which was recently encoded but was not being rehearsed (Raye and others, 2002; Johnson and others, 2004), may also be considered a type of updating of WM. Last, directed forgetting tasks require participants to stop remembering a subset of items within a memory set (Andrés and others, 2004) without encoding any new items to replace the forgotten ones. Thus, updating the contents of WM can be achieved in many different ways and is often confounded with other executive processes.

In addition, information in WM is susceptible to several types of interference that affect WM, potentially overwriting the information maintained and resulting in undesirable "updating." These other sources of competition and interference include

previously maintained information (through proactive interference) and incoming sensory stimuli. Interference is known to disrupt WM maintenance and resistance to interference in WM is a critical cognitive skill (see Jonides and Nee, 2005; Rougier and others, 2005). A recent study was reported in which participants were to maintain information while resisting interference from distracting stimuli (Sakai and others, 2002). Increased activation in part of the middle frontal gyrus (MFG) was found to be associated with improved performance and more coordinated activity across a frontoparietal network. Resolution of proactive interference is thought to involve a different prefrontal region, in the inferior frontal gyrus (IFG) (Jonides and Nee, 2005).

Together, these previous imaging studies support the notion that exerting control over the contents of WM, either for updating or for maintenance in the presence of distraction, results in additional prefrontal cortex activity beyond that involved in "simple" maintenance. However, because previous paradigms recruited additional cognitive operations—such as reordering stimuli already in WM during the n-back task—none of these studies isolated the operation of updating the contents of WM from these other executive processes. Therefore, it remains unclear whether the same neural systems are involved both in updating and in maintenance.

The relationship between the mechanisms for updating WM and for distractor-resistant maintenance is unclear. One can consider the information currently in WM and new perceptual inputs to be in competition with one another for representation within the limited-capacity system. Resolution of this competition in WM may involve processes similar to those involved in selective attention (Kastner and Ungerleider, 2000; Corbetta and Shulman, 2002; Yantis and others, 2002; Liu and others, 2003; Serences and others, 2004; Serences and Yantis, 2005). Attentional control and WM have been previously proposed to involve similar neural mechanisms (Awh and Jonides, 2001; Bisley and Goldberg, 2003; Derfuss and others, 2004; Sala and Courtney, 2006; Serences and Yantis, 2005). In a competition model of WM, similar to the "biased competition" model for visual attention (Desimone and Duncan, 1995), items with the highest priority are given access to and maintained in WM. Items with lower priority are replaced by other items, decay from the storage buffer, or are never allowed entrance (Shapiro and others, 1994; Chun and Potter, 1995).

The purpose of the current functional magnetic resonance imaging (fMRI) study was to elucidate the mechanisms involved in updating WM by replacing old information with new information and those involved in maintaining the contents of WM and to determine the extent to which these processes rely on similar or different neural mechanisms. Participants performed a continuous delayed recognition task that required frequent replacement of an item held in WM. Participants monitored a stream of stimuli (faces or houses) in order to respond to stimuli matching the sample stimulus maintained in WM. At random intervals (every 4–10 s) participants were cued either to update the contents of WM with a new sample or to continue to maintain the current sample. When the contents of WM were updated, regardless of stimulus type, a frontoparietal network showed transient increases in activation. Some of these regions overlapped with those showing sustained activity during maintenance of current information while others were uniquely modulated by the "update" events. The results demonstrate that WM maintenance and updating are subserved by partially overlapping neural systems. Furthermore, the current results suggest that updating of WM results from a combination of increased attention to the visual stimulus and a change in the interference protection state of the system.

Materials and Methods

Participants
Participants were 12 (7 females) nonsmoking Johns Hopkins University students in good health that had no history of head injury, neurological or mental disorders, or drug or alcohol abuse and no current use of medications that affect the central nervous system or cardiovascular function. The experimental protocol was approved by the institutional review boards of both the Johns Hopkins University and the Johns Hopkins Medical Institutions. Participants received compensation of $50 for the fMRI portion of the study. All participants gave written informed consent. Mean age of participants was 23 years with a range of 19–34 years.

Stimuli
Stimuli consisted of gray-scale photographs of 15 faces and 15 houses from the database created by the Max-Planck Institute for Biological Cybernetics in Tuebingen, Germany. Stimuli appeared within a white rectangle surrounded by a black background subtending a vertical visual angle of 3.9° and a horizontal visual angle of 3.2°. All faces were cropped to exclude hair and clothing, oriented forward, had neutral emotional expression, and appeared centrally on the screen. All stimuli were initially unfamiliar. An LCD projector located outside of the scanning room rear projected the stimuli onto a screen located inside the bore of the scanner, behind the participant's head. Participants viewed the stimuli via a mirror affixed to the top of the head coil. Responses were made on 3 handheld buttons that were connected via fiber optic cable to a Cedrus RB-6x0 Response Box. Stimuli were presented and behavioral data were collected on a PC desktop computer using Visual Basic software and the Microsoft DirectX graphics library (v7).

Stimuli were presented in a continuous morphing stream in which each stimulus appeared stationary for 1.5 s, then morphed (500 ms) into the next stimulus. The morph was produced with a series of 12 discrete images appearing in sequence for 42 ms each, creating a smooth spatiotemporal morph. Within the 500-ms morph time, each stimulus first morphed to a placeholder stimulus (another face or house, depending on the current block type) before continuing on to morph into the next stationary stimulus. This enabled 2 stationary stimuli in a row to be the same. This placeholder did not match any stimuli that were relevant to that portion of the task (the "update cue," the "maintenance cue," the sample held in WM, or the sample prior to the previous update cue).

Memory Task
Task design is illustrated in Figure 1. Prior to the beginning of the experiment, participants memorized 2 faces and 2 houses as update and maintenance cues. Participants monitored a continuous stream of 15 repeating morphing stimuli in order to respond to a stimulus that matched the sample stimulus held in WM in a modified delayed recognition task. The first stimulus in the stream was the first sample to be held in WM. Every 4–10 s participants were cued either to update the contents of WM by replacing the old sample with a new sample, or to maintain the sample they had encoded previously. When they saw an update cue, they were to update the contents of WM with the subsequent stimulus in the stream, which became the new sample. When they saw a maintenance cue they were to continue to maintain the previously encoded sample. When participants saw an update cue, maintenance cue or match to the current sample, they pressed 1 of 3 buttons. Participants were instructed to evaluate each stimulus by responding to each in 1 of 4 ways: update cue = press "update" button, maintenance cue = press "maintenance" button, match to sample = press "match" button, nonmatch to sample = no response. The update cue and maintenance cue buttons were held in one hand and the match button was held in the other hand. The mapping of buttons to event types was counterbalanced across participants.
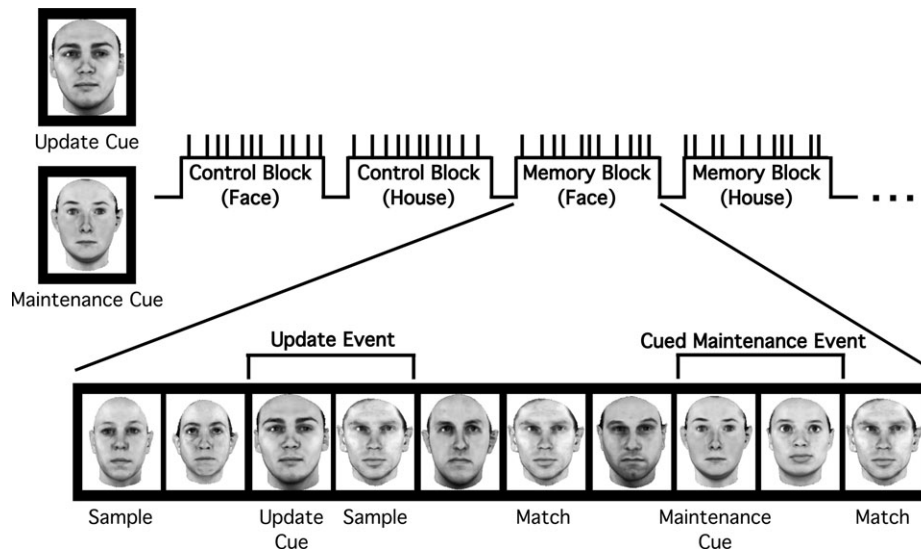
Figure 1. Task design. Participants monitored a stream of stimuli (faces or houses in different blocks) to respond to a sample held in WM in a modified delayed recognition task. Every 4–10 s participants were cued either to update the contents of WM with a new sample or continue to maintain the sample currently maintained in WM.

The appearance of maintenance cues and update cues was pseudo-random. After one cue appeared, the next cue occurred at a random interval 4, 6, 8 or 10 s later. There could be no more than 2 update or 2 cued maintenance events in a row. The mean length of time a participant was required to maintain any one stimulus (time between update cues) was 10.6 s with a range of 0–22 s. To minimize proactive interference effects, the sample face prior to the most recent update event could not appear again until after the subsequent update event. Token stimuli, which were either matches to sample or nonmatches, were pseudo-randomly interspersed with the update and cued maintenance events. Match and nonmatch tokens appeared with equal probability throughout the trials.

Category Discrimination Task

Participants also performed blocks of a category discrimination task for faces and houses, separately, as a control task. As in the memory task, they saw separate streams of morphing faces or houses. For house blocks they pressed a button when the house on the screen had a garage. For faces they pressed a button if the face was female. Half of the houses contained garages. Half of the faces were female. Before the practice session, participants were asked to tell the experimenter which faces they believed to be female in order to ensure that participants were responding to half of the faces.

Procedure

Participants performed 6–10 practice runs (146 s each) of the memory task until they reached criterion performance (greater than 80% accuracy in all conditions), using the same stimuli as were later used during scanning. They then performed 1 run containing 1 block of each condition outside of the scanner immediately before participating in the fMRI portion of the experiment. Each of the 6 fMRI experimental runs lasted 592 s. Within each run there were 4 blocks, each 146 s long, one of each of the 4 task conditions: memory for houses, memory for faces, category discrimination for houses, and category discrimination for faces. Between each block was a blank screen followed by a word cueing the participant which task was about to begin. Order of task block type was counterbalanced across runs and subjects. There were 10 update and 10 cued maintenance events within each memory block, for a total of 120 events of each type.

Data Collection

During the performance of the cognitive tasks, T_2*-weighted, gradient echo, echo planar imaging (EPI) scans (time to repetition [TR] = 2 s, time to echo [TE] = 40 ms, flip angle = 90°, twenty-one 4-mm axial slices, 1-mm gap, 80 × 80 matrix, SENSE factor = 2 [sensitivity encoding

technique for fast acquisition; Pruessmann and others, 1999]) were collected. One high-resolution T_1-weighted MPRAGE anatomical scan (TR = 8.2 ms, TE = 3.7 ms, flip angle = 8°, prepulse time to inversion delay = 852.5 ms, time between inversions = 3 s, inversion time = 748 ms, SENSE factor = 2, scan time = 385 s) was collected between the middle 2 experimental runs to allow for anatomical localization. All scans were conducted at the F.M. Kirby Research Center for Functional Brain Imaging on a 3-T Philips Intera.

Data Analysis

Behavioral Analysis

Data from reaction time and error rates were analyzed separately. A within-subject analysis of variance (ANOVA) was conducted to test for differences between stimulus types (faces vs. houses) and WM conditions (update vs. cued maintenance events). Match events were analyzed separately to test for differences between stimulus types. Greenhouse-Geisser corrected P values are reported.

A separate within-subject ANOVA was conducted on behavioral performance for match events to test for differences in performance as a function of time from the previous update event. Factors included time (4, 6, 8, 10, 12, 14, 16, 18, and 20 s) and stimulus type (faces and houses). Data for reaction times and error rates were analyzed separately.

Voxelwise General Linear Model

Data were analyzed using Analysis of Functional NeuroImages (AFNI) software (Cox, 1996). First, functional EPI data were phase shifted using Fourier transformation to correct for slice acquisition time, and motion corrected using three-dimensional volume registration. Multiple regression analysis was performed on the time series data at each voxel, for all voxels in the brain volume. Block regressors modeled sustained activity across all time points within a block. There were 4 block regressors: house memory, face memory, house category discrimination, and face category discrimination. There were separate event-related regressors for each of the following: update cue, stimulus following the update cue, maintenance cue, stimulus following the maintenance cue, match to sample preceding a nonmatch stimulus, nonmatch after a match-to-sample stimulus, all other matches to sample, errors, and, within the category discrimination blocks, button-press events where participants detected a female face or a house with a garage. (For a schematic of the regressors, see supplementary materials Table 1.) Regressors were convolved with a gamma function model of the hemodynamic response which included the 10 s following events (delay time of 2 s, rise time of 3 s and a fall time of 5 s). The unmodeled

time points (i.e., interblock intervals) defined the baseline. Mixed effects analyses, with subjects as a random factor, were performed on the imaging data, with all regressors modeled separately for the 2 stimulus types. Simultaneous modeling of the block regressors and the individual event regressors allows for sustained and transient components of the activity to be identified (Visscher and others, 2003). Individual participant data were spatially smoothed using a smoothing kernel of 3 mm.

General linear tests were performed on the regression coefficients to make direct comparisons of activation across tasks and events. An update event consisted of the update cue and the subsequent stimulus (sample) to be encoded into WM. A cued maintenance event consisted of the maintenance cue and the subsequent stimulus, which was always a nonmatch (did not match either update or maintenance cue, or sample held in WM). Both conditions contained a button press, recognition of an item stored in long-term memory (cue), the representation of the meaning of the cues, which was also likely to have been active in WM for the duration of the WM blocks, and a subsequent stimulus. In an update event this subsequent stimulus is to be encoded into WM, whereas in the cued maintenance event this subsequent item is to be ignored, while the participant continues to maintain the previously encoded sample. The following contrasts were performed: update events versus cued maintenance events and memory blocks versus category discrimination blocks. Update refers to the results of the contrast of update events greater than cued maintenance events. The "sustained memory component" refers to the results of the contrast of memory block activity greater than category discrimination block activity. Individual voxel thresholds were set at $P < 0.05$. Data were corrected for multiple comparisons by spatial extent of contiguous suprathreshold individual voxels (experiment-wise $P < 0.05$ for a cluster). In a Monte Carlo simulation within the AFNI software package, using a smoothing kernel of 3 mm, a connection radius of 5.20 mm on $3 \times 3 \times 3$-mm voxels, it was determined that an activation volume of 575 μL satisfied the $P < 0.05$ threshold.

ANOVA on Regional Time Courses

Time courses were created for regions of activation using deconvolution analysis on individual participant's data (Ward, 2002). To calculate percent signal change, all voxels were normalized to have a mean signal of 100. Estimates of the impulse response function for each event type were obtained for 8 time points (16 s) following the beginning of each event within each voxel. Data were coded into the following events of interest separately for face and house stimuli: update cue, maintenance cue, match, errors, and block regressors for the memory and category discrimination blocks. Each participant's model estimate of the percent signal change for each region of activation, averaged across voxels within the region, was entered into a $2 \times 2 \times 8 \times 12$ ANOVA with participants ($n = 12$) as a random factor. ANOVAs were conducted to determine the effects of time (8 time points), memory condition (update and cued maintenance) and stimulus type (faces and houses).

Results

Behavioral Results

Behavioral data are reported for reaction time and error rate by stimulus type (face and house stimuli) and WM cue type (update cues and maintenance cues). Match events were analyzed separately to test for differences between stimulus types.

Data are reported as the group mean ± SEM. Participants were similarly accurate with both face and house stimuli at detecting update cues (95.4 ± 2.5% and 97.1 ± 1.6%, respectively) and maintenance cues (95.7 ± 1.6% and 97.4 ± 1.3%, respectively). Likewise similar reaction times were measured for detecting update cues with either face or house stimuli (RT = 682 ± 27.5 ms and 685 ± 25.5 ms, respectively) and for detecting maintenance cues (RT = 698 ± 32.7 ms and 666 ± 24.0 ms, respectively).

In a within-subject ANOVA for reaction times, including stimulus type and WM cue type, there were no significant differences in reaction times between face and house stimuli ($F_{1,11} = 1.27$, $P = 0.283$). Furthermore, there were no significant differences between WM conditions (update cues vs. maintenance cues) in reaction times ($F_{1,11} = 0.004$, $P = 0.951$). In a separate within-subject ANOVA for error rates, including stimulus type and WM cue type, error rates between faces and houses approached significance ($F_{1,11} = 4.48$, $P = 0.058$). There were no significant differences between WM conditions (update cues vs. maintenance cues) for error rates ($F_{1,11} = 0.10$, $P = 0.753$). There was also no interaction between stimulus type (face vs. house) and WM condition for reaction times ($F_{1,11} = 1.79$, $P = 0.209$) or error rates ($F_{1,11} = 0.00$, $P = 1$).

When detecting "match-to-sample" stimuli, there were similar reaction times (RT = 562 ± 19.3 ms for faces, 535 ± 22.5 ms for houses) and error rates (88.3 ± 2.9% for faces, 90.4 ± 3.3% for houses) for face and house stimuli with no significant difference in reaction time ($t(11) = -1.44$, $P = 0.179$) or error rate ($t(11) = 1.08$, $P = 0.303$) between stimulus types.

In another set of within-subject ANOVAs to test for changes in performance on match events as time progressed from the previous update event, there were changes in reaction times but no changes in error rates and no differences between
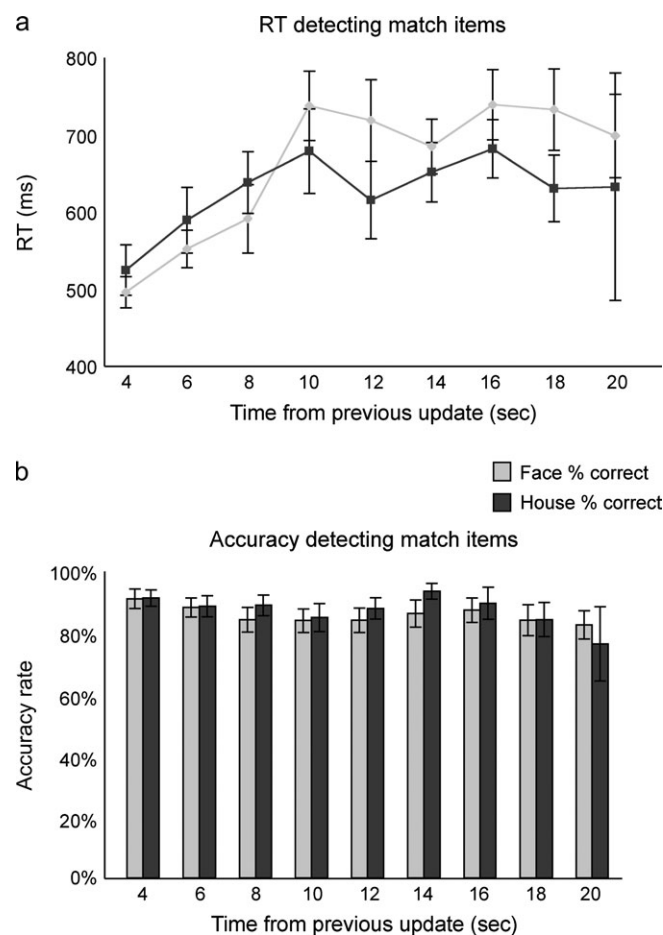

Figure 2. Performance detecting match events as a function of time from the most recent previous update event. (*a*) Reaction time (RT). RT increases as time from the previous update event. (*b*) Percent correct. There is no significant change in performance on detecting match items over time.

stimulus types. These results are shown in Figure 2. There were no significant differences in reaction times between face and house stimuli ($F_{1,11}$ = 0.01, P = 0.922). However, there were significant changes in reaction time over time ($F_{1,8}$ = 5.85, P = 0.006). In a separate within-subject ANOVA for error rates, there was no significant difference in error rates between faces and houses ($F_{1,11}$ = 0.44, P = 0.52). Furthermore, there were no significant differences over time for error rates ($F_{1,8}$ = 1.83, P = 0.18), indicating that the change in RT over time was not due to a speed-accuracy trade-off. There was no interaction between stimulus type (face vs. house) and time for reaction times ($F_{1,8}$ = 1.20, P = 0.33) or error rates ($F_{1,8}$ = 0.62, P = 0.63).

Identification of Active Areas

Sustained Maintenance-Related Activity
To examine both the sustained and transient components of the WM task-related activity, block regressors modeled the WM task blocks and the control blocks, whereas additional regressors simultaneously modeled transient events within each task block (see Materials and Methods). A large network of regions was active when comparing the sustained component of the WM task with the sustained component of the category discrimination task (Fig. 3 and supplementary materials Table 2). This network of regions corresponds well with activations observed in previous block-design neuroimaging studies of object WM, including areas in frontal, parietal, and inferior temporal cortices (for reviews, see, e.g., D'Esposito and others, 1998; Courtney, 2004).

Transient Update-Related Activity
Update-related activity was found by collapsing across stimulus types and directly comparing update events with cued maintenance events. For a list of all active areas, see supplementary materials Table 3. Update areas (update > cued maintenance) include the supplementary and presupplemetary motor areas (SMA/PreSMA), left inferior frontal junction (IFJ), intraparietal sulcus (IPS), and left middle (MFG) and bilateral inferior frontal gyri (IFG) (Fig. 4a). None of these regions demonstrated a significant difference in activation between houses and faces for either update events or cued maintenance events in a voxelwise analysis. Finally, there were areas of extrastriate cortex that were more active for update relative to cued maintenance events.

Several areas showed a pattern of activation where the activity level for update events was significantly less than the activity level for cued maintenance events. These regions are shown in shades of blue and include posterior and inferior regions of occipital and temporal cortices and medial frontal cortex. For a list of all active areas, see supplementary materials Table 4. Many of these regions showed a relative transient decrease in activity following the update events (Fig. 4c), compared with pre-event sustained block activation levels. In addition, there were common areas of activity in cued maintenance relative to baseline and update relative to baseline, primarily in supplementary motor area and bilateral motor cortex, reflecting the common button-press component of these events.

Overlap Analysis
To ascertain whether WM maintenance and WM updating are subserved by similar neural systems, we analyzed the overlap in activity of these 2 conditions. A subset of the regions showing a transient update-related increase in activity overlapped partially with those showing sustained WM activity including SMA/PreSMA, bilateral IPS/superior parietal lobule and left IFJ (Fig. 5). In contrast, none of the regions showing transient decreases in update-related activity overlapped with regions showing sustained WM activity.

Time Course Analysis within Functionally Defined Regions

Update Events > Cued Maintenance Events
There are similar characteristic time courses across regions showing more activation for update events than cued maintenance events (Fig. 3). Most regions had a significant WM condition by time interaction, indicating a different time course of activity for the 2 memory event types. Update events elicited a positive, sharp rise to peak, whereas cued maintenance events elicited a much lower amplitude response that remained close to baseline. Only 2 of these update regions (IFJ and cingulate) exhibited a main effect of stimulus type (face vs. house) and only one region (R inferior occipitotemporal) had a stimulus by memory condition interaction. There were no significant 3-way interactions between stimulus type, WM condition and time (supplementary materials Table 3).

Cued Maintenance Events > Update Events
The interaction of memory condition and time in most of the regions showing less activation for update than cued maintenance events again indicates that the time course of response
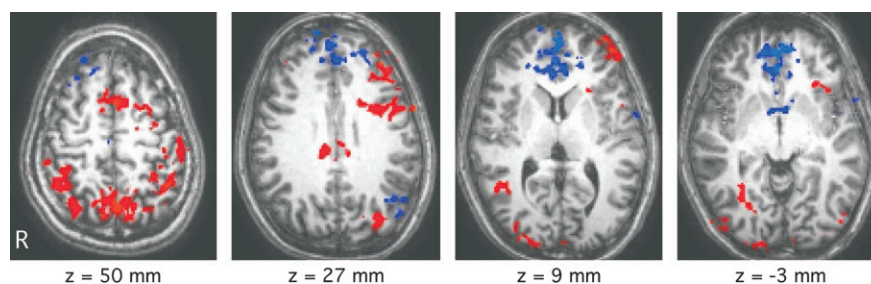

z = 50 mm   z = 27 mm   z = 9 mm   z = −3 mm

Figure 3. Sustained effect of WM task. Regions more active in the WM blocks are shown in shades of red. Regions more active in the category discrimination blocks are shown in shades of blue.
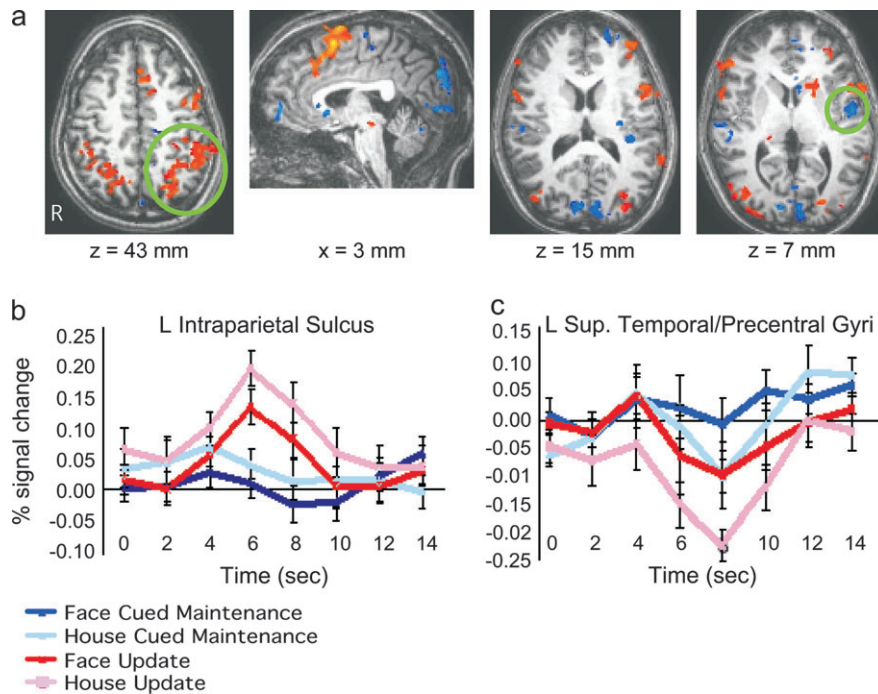
Figure 4. Update versus cued maintenance. (*a*) Regions more active for update events are shown in shades of red. Regions less active for update events relative to cued maintenance events are shown in shades of blue. (*b*) Example time course for one region more active in the update events. (*c*) Example time course for one region where activation decreased significantly more following the onset of update events relative to the onset of cued maintenance events. Error bars represent SEM.
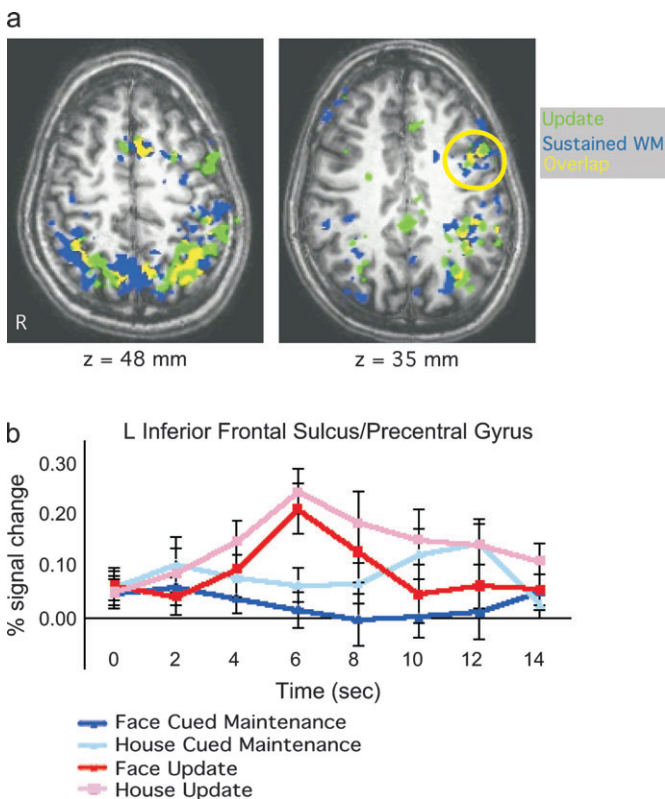

Figure 5. Overlap of 2 contrasts. (*a*) Regions more active for update events than cued maintenance events are shown in green. Regions more active for WM blocks than category discrimination blocks are shown in purple. The overlap of these 2 contrasts is shown in yellow. Overlap was found only in bilateral superior parietal, SMA/PreSMA and L IFS/Precentral Gyrus. (*b*) Example time course. Time courses of activity in all overlap regions is similar. Error bars represent SEM.

was different for the 2 memory event types (Fig. 3 and supplementary materials Table 4). For most regions, activation decreased following the onset of both event types. This decrease was greater for the update events than the cued maintenance events. There were no significant main effects or interactions for stimulus type.

Discussion

In the current study we find qualitative differences as well as similarities in the neural activity when participants update WM by replacing an old item with a new item versus when participants maintain the contents of WM. First, there were transient increases in activity following a cue to update the contents of WM that were greater than changes in activity following similar cued events which required perceptual encoding and motor response but not updating of WM. Second, the regions demonstrating this transient update-related activity overlapped with a subset of regions (bilateral superior parietal, SMA/PreSMA and left IFJ) that showed sustained activity across the WM task blocks. Third, regions showing transient update-related activity are similarly activated for two different stimulus types (faces and houses).

In the current experiment all tasks, including updating WM, involve perceptual encoding. The relationship between encoding and WM, however, was different for different task conditions. Cued maintenance events required perceptual encoding while maintaining other information in WM, whereas update events required perceptual encoding for the purpose of entering the newly encoded item into WM. A previous study suggested that update-related activity (replacing old items with new items) was more spatially extensive but localized to similar regions as encoding-related activity (updating WM without discarding items) in a WM running span task (Postle and others,

2001). However, in that study both conditions involved entering items into WM, perhaps contributing to the high degree of similarity between the activations. In contrast, the events of interest in the present study both required perceptual encoding of identical visual stimuli but only the update event involved entering that stimulus into WM for future use.

One can consider the information currently in WM and new perceptual inputs to be in competition with one another for representation within the limited-capacity system. Perhaps during updating, increased attention to the current perceptual input results in a more robust representation of the new information that enables it to overwrite the current contents of WM through a change in the interference-resistant maintenance state. We observed increases in activity in the extrastriate cortex (inferior occipitotemporal and parahippocampal gyri, see supplementary materials Table 2) that were greater for update than cued maintenance events. These extrastriate activations indicate more attention to or processing of the current stimulus during updating.

In the current study, update-related activity that was not stimulus dependent was observed in superior frontal and parietal regions that are highly similar to regions activated in previous studies of attention switching (Kastner and Ungerleider, 2000; Corbetta and Shulman, 2002; Yantis and others, 2002; Liu and others, 2003; Serences and others, 2004; Serences and Yantis, 2005). According to a competition model of WM, items with the highest priority are given access to and maintained in WM. Items with lower priority are replaced by interference, decay from the storage buffer, or are never allowed entrance (Shapiro and others, 1994; Chun and Potter, 1995). The results of the current study, therefore, suggest that areas transiently more active during the update events relative to the cued maintenance events may be associated with a change in priority for the new information over the old information, enabling the entry of new information into WM. In a computational modeling study, Rougier and others (2005) demonstrated that an adaptive gating mechanism allowing for updating of actively maintained patterns of activity can allow for flexible cognitive control, without the need for a "homunculus." These transient increases in activity in the current experiment may reflect such an adaptive gating mechanism and may be related to previous reports of an update-related signal in the event related potential literature (P300 is a signal thought to index loading information into WM, see, e.g., Luck and others, 1996; Vogel and others, 1998).

Once information enters WM, it must be maintained and protected from interference until any other information becomes more relevant. In the current experiment there is no significant change over time following an update event in error rates for detecting match items. However, increasing reaction times suggest that the memory representation, or access to it, changes over time. Although participants refresh their memory representation with the frequent match events between update events, interference may accumulate from the nonmatch stimuli and/or the representation may degrade over time. A recent fMRI study of interference-resistant WM (Sakai and others, 2002) demonstrated that greater activity in Brodmann area (BA) 46 is associated with a tighter coupling of activity between the intraparietal sulcus (labeled IPS in the current study) and BA 8 (corresponding to the dorsal part of the region labeled IFJ in the current study) when participants attempt to maintain locations in WM in the presence of distracting stimuli compared with trials

without distracting stimuli. This interaction of activity across these regions may allow for interference-resistant maintenance.

In the current study, a region in the MFG that appears highly similar to the BA 46 region identified in the Sakai study responds transiently to updating WM in the current task. In the current study, participants maintained items in WM while viewing a constant stream of items, some of which matched the contents of WM, whereas others did not (and were therefore "distracting" because they must not overwrite the contents of WM). However, this MFG region did not show differential amounts of sustained activity for the WM task compared with the categorization task. This region may be involved in the control of both WM and sustained attentional selection of perceptual information (and therefore there was no significant difference in sustained activity between memory task blocks and categorization task blocks). The transient increases in activation observed during update events may reflect a reconfiguration in the representation of cognitive priorities. The interpretation that this area is involved in changing representations and priorities in WM and attention is consistent with the Sakai results as participants may have alternated attention between the distracting stimuli and the contents of WM. This interpretation is also consistent with previous reports implicating the MFG in manipulation of information (D'Esposito and others, 1999; Bor and others, 2003), in shifting attention from one stimulus attribute to another (Nagahama and others, 2001; Serences and others, 2005), and in task switching (Braver and others, 2003). Furthermore, we did not find the same prefrontal region (left IFG) activated as has been implicated in proactive interference experiments (for a review, see Jonides and Nee, 2005). The type of protection from interference here is more specific to interference from perceptual input (Sakai and others, 2002).

Other regions, particularly the IPL and IFJ, demonstrated both sustained and transient activation changes in the current study. A similar set of regions was also found to elicit transient "refresh"-related activity in a set of studies by Johnson and her colleagues when participants refreshed a just-read word in WM compared with when they simply read a word (Raye and others, 2002; Johnson and others, 2004). Refresh may be another form of updating as it involves reviving the representation of an item which was not being rehearsed and the priority of the refreshed item changes from low to high. The IFJ has also been implicated in other tasks requiring a high degree of control over potential interference from irrelevant information such as the Stroop task, task switching, WM tasks such as n-back (Derfuss and others, 2004), task preparation (Brass and von Cramon, 2004), and changes in stimulus-response mapping (Dove and others, 2000; Nagahama and others, 2001). Derfuss and others (2004) suggest that the reason for similar IFJ activation in such a wide variety of tasks is that the IFJ is involved in cognitive control, but more specifically, it is sensitive to "updating of task rules," which is consistent with transient activity associated with task switching (Braver and others, 2003) and with the update events in the current study. Furthermore, our results suggest that IFJ is involved both in the maintenance of information and in transient updates of information. The regions of transient and sustained activity within IFJ in the current study overlapped only slightly, however. This result suggests that there may be a functional topography within IFJ. Distribution of activity across this area may depend on whether the current information in WM or the new information is task relevant.

WM updating may involve active inhibition of irrelevant stimuli. Although none of the areas showing sustained maintenance-related activity showed transient decreases in activity at the time of updating, active inhibition may still be occurring. First, the temporal resolution of fMRI may not be sufficient to distinguish inhibition at the time of the update cue from the subsequent encoding of the new stimulus. Second, the observed increases in activation could reflect inhibitory synaptic input, rather than increases in neural activity because inhibitory synaptic activity can also increase blood flow and, therefore, the blood oxygen level-dependent fMRI signal (Caesar and others, 2003). Such inhibitory input could disrupt the maintenance of the current contents of WM, thereby allowing current perceptual information access to the buffer. Third, it is possible that representations in WM are mutually inhibitory (analogous to the biased competition model for attentional selection) and thus inhibition of the old, now irrelevant stimulus may result from the biased enhancement of the activation of the new, relevant stimulus. Changes in relative priority could result from either enhancement, inhibition, or both.

In summary, changes in the contents of WM in response to explicit cues to replace an old item in WM with a new item appear to result from transient increases in activity in a parieto-frontal network that partially overlaps with regions that demonstrate sustained activity during WM maintenance. Distribution of activity within these areas suggests a functional topography which may depend on whether the current information in WM or the new information is task relevant. The cues may trigger a change in the representation of task priorities resulting in greater allocation of attention to current perceptual input and a change in the interference-resistant maintenance state. Representations of task priorities are likely to be relative, where multiple relevant items may have varying degrees of priority, and may be influenced by highly salient visual stimuli (Bisley and Goldberg, 2003) as well as by task instructions or other sources of motivation.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/

Notes

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