

Increased Neural Efficiency with Repeated Performance of a Working Memory Task is Information-type Dependent

Unlike tasks in which practice leads to an automatic stimulus-response association, it is thought working memory (WM) tasks continue to require cognitive control processes after repeated performance. Previous studies investigating WM task repetition are in accord with this. However, it is unclear whether changes in neural activity after repetition imply alterations in general control processes common to all WM tasks or are specific to the selection, encoding and maintenance of the relevant information. In the present study, functional magnetic resonance imaging (fMRI) was used to examine changes during sample, delay and test periods during repetition of both object and spatial delayed recognition tasks. We found decreases in fMRI activation in both spatial and object-selective areas after spatial WM task repetition, independent of behavioral performance. Few areas showed changed activity after object WM task repetition. These results indicate that spatial task repetition leads to increased efficiency of maintaining task-relevant information and improved ability to filter out task-irrelevant information. The specificity of this repetition effect to the spatial task suggests a difference exists in the nature of the representation of object and spatial information and that their maintenance in WM is likely subserved by different neural systems.

Keywords: fMRI, object working memory, prefrontal cortex, spatial working memory, task repetition

Introduction

Working memory (WM) is the active maintenance of a limited amount of currently relevant information so it is available for immediate use. Maintaining this information is necessary for higher cognitive activities such as planning and problem solving. Working memory requires selecting and maintaining task-relevant information and inhibiting interference from task-irrelevant information. Thus, WM must be dynamic, constantly adjusting to reflect the demands relevant to the current situation. Little is known regarding how this inherently flexible WM system responds when task demands remain constant over an extended period of time (i.e. when the task-relevant and task-irrelevant dimensions do not change). Previous studies have examined the effects of repeated performance of various other cognitive tasks. Specifically, studies of repeated performance of motor and verbal tasks find evidence of behavioral as well as functional changes (Petersen *et al.*, 1998; Sakai *et al.*, 1998; van Mier *et al.*, 1998). In addition to its improvements on accuracy and reaction time, repetition has been found to alter neural activity in regions recruited by these tasks. Regions involved in the initial unskilled performance of the task showed a decrease in activation, while other regions increased their activity with increasingly skilled task performance. Repetition of the same stimulus-response association enabled more

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automatic performance of the task, and thus a functional reorganization of the areas involved (Petersen *et al.*, 1998; Sakai *et al.*, 1998; van Mier *et al.*, 1998).

Importantly, none of these tasks required the use of cognitive control after repetition. Repeated performance of a WM task does not evoke the same manner of neural or behavioral changes as those seen in studies of tasks in which performance becomes automatic with repetition. The information held in WM differs for each trial, and the stimulus-response association for one trial may not be the same for the next trial. For this reason, repetition of a WM task still includes cognitive control processes, and thus may rely on the same brain areas throughout repeated task performance, rather than switching to a more 'automatic' neural system. Previous work along these lines by Olesen *et al.* (2004) using functional magnetic resonance imaging (fMRI) found increases in brain activity after repeated performance of a visuo-spatial WM task, suggesting that extensive training can evoke plasticity in brain structures involved in WM. While that study assessed changes over a period of 5 weeks, other studies have found decreases in brain activation with short-term repetition (one day or less) of either an object (Landau *et al.*, 2004) or visuo-spatial (Garavan *et al.*, 2000) WM task. None of these studies found evidence for functional reorganization of the task, indicating that the use of cognitive control processes remained throughout the task. Accompanying behavioral changes with task repetition, such as alterations in response time and accuracy, were inconsistent, as improved behavioral performance was found in two studies (Garavan *et al.*, 2000; Olesen *et al.*, 2004) but not in the third (Landau *et al.*, 2004). Furthermore, because WM for only one type of information was assessed (either object WM or spatial WM, but not both in the same session), it is uncertain whether the effects of repeated performance are general to WM processes or specific to the type of information being maintained.

The present study uses fMRI to investigate the effects of repeated performance on both an object identity and a spatial location WM task. The task uses bidimensional (faces in locations) stimuli to assess how selection and maintenance of task-relevant information as well as suppression of the irrelevant stimulus dimension change over time. Previous studies have characterized functionally dissociable neural systems involved in the performance of object and spatial WM tasks (Courtney *et al.*, 1997; Carlesimo *et al.*, 2001; Mottaghy *et al.*, 2002; Sala *et al.*, 2003), with object WM preferentially activating ventral frontal regions and spatial WM preferentially activating dorsal frontal regions. Differences in repetition effects for object versus spatial WM tasks in these task-selective regions would further support the idea that these regions are differentially involved in spatial versus object WM. It was hypothesized that

changes in the pattern of brain activity with repeated performance would occur within these same neural systems, rather than result in recruitment of different neural systems. This prediction was based on the idea that, unlike repetition of some other cognitive tasks, repeated performance of a WM task is not expected to become automatic. The present study also tested for changes in behavioral performance after task repetition, and whether those changes might be correlated with activation.

Materials and Methods

Subjects

The 10 participants (four females), aged 20–34 years, were non-smokers in good health with no history of head injury, neurological or mental disorders, drug or alcohol abuse, and were not currently using medications that significantly affected central nervous system or cardiovascular function. The experimental protocol was approved by the Institutional Review Boards of the Johns Hopkins University and the Johns Hopkins Medical Institutions. Participants gave written informed consent and were compensated monetarily. All participants were given written and verbal instructions and completed a 30 min practice version of the task using the same stimuli, at least 24 h before the scanning session to minimize initial learning, strategy changes and priming effects in the scanner.

Stimuli

Stimuli consisted of 12 male and 12 female faces from a fixed set of 24 obtained from a high school yearbook and cropped to remove hair and clothing. All face stimuli were oriented in a similar position (roughly three-quarter profile, facing left), and displayed a neutral emotional expression. Stimuli, measuring $\sim 3.4^\circ$ of visual angle, were presented in a fixed set of 24 possible locations, arranged in an irregular grid with the greatest distance from fixation $\sim 18.2^\circ$ horizontally and 12.4° vertically. Control stimuli consisted of phase-scrambled images of the faces so that the luminance, contrast and frequency content of the visual images were constant. Stimuli were presented and behavioral data were collected on a Power Macintosh G4 desktop computer running SuperLab Pro software. An LCD projector located outside of the scanning room back-projected the stimuli onto a screen located inside the bore of the scanner. Subjects viewed the stimuli via a mirror mounted to the top of the head coil. Responses were made with left or right thumb presses of handheld button boxes that were connected via fiber optic cable to a Cedrus RB-610 Response Box.

Tasks

Each run contained WM trials of a single type, either object or spatial WM but not both within a single run. There were two conditions, performed in separate scanning sessions, each consisting of a different sequence of runs and classified according to which WM task was being repeated: (i) 'object repetition' and (ii) 'spatial repetition'. The 'object repetition' condition consisted of a spatial run followed by five object runs, two additional spatial runs and a final object run. The 'spatial repetition' condition consisted of the same sequence, but with the trial types for each run reversed. Thus, object trials in the sequence used in the previous scanning session were replaced with spatial trials, and vice versa (Fig. 1B).

In this sequence of runs only one of the tasks has an extended period of repetition within a single scanning session. However, both tasks were performed within each scan session to enable identification of brain regions that were preferentially activated by spatial versus object WM. The initial run in which participants performed the task that would not be repeated ensured that the beginning of the repetition period was not confounded by possible effects of adjusting to the conditions of the scanner itself. In addition, this initial run ensured that at the beginning of the repetition period participants had to switch the relevant and irrelevant information domains. During the 'repetition' period, what was repeated were the instructions regarding the relevant domain. The last three runs were included in order to evaluate whether any repetition effects in activation and/or performance remained after performing the other task for a short period of time and then switching

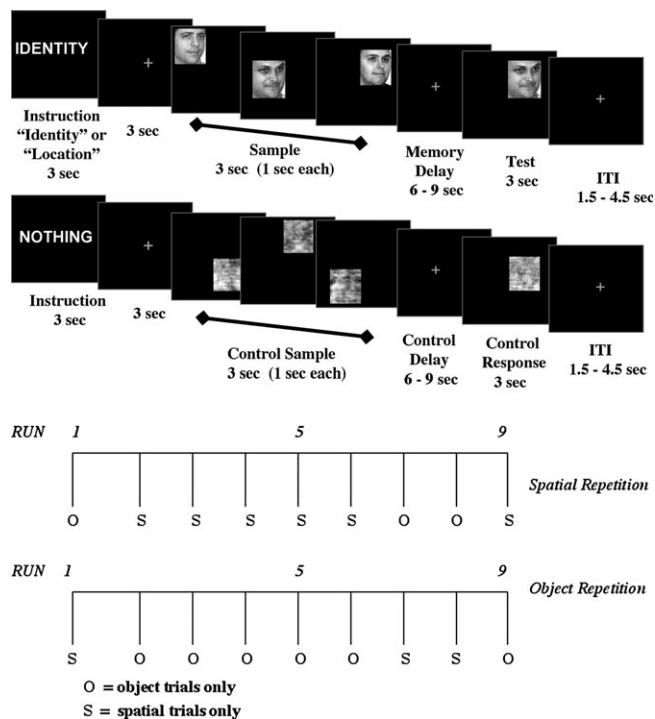


Figure 1. Schematic of task. (A) Sequence of events for each trial. (B) Sequence of type of trials for each run across the experimental session for the spatial repetition and the object repetition conditions.

back to the previously repeated task. Participants performed the object and spatial repetition conditions during two scanning sessions (each session separated by at least 1 week). The order of the conditions was counterbalanced across participants.

A delayed recognition paradigm was used for both spatial and object WM tasks (Fig. 1A). In object WM trials, participants were instructed to remember only the identity of the faces and ignore the location, and to respond as to whether the test face was the same as (match) or different from (non-match) any of the three sample faces. In the spatial WM trials, participants were instructed to remember only the locations of the faces and ignore identity, and to indicate whether the location of the test face was the same as (match) or different from (non-match) any of the three sample locations. In both object and spatial trials, a match corresponded to a left button press, while a non-match corresponded to a right button press. In control trials, participants were instructed to press both buttons during the test stimulus, which acted as a sensorimotor control. Each individual trial consisted of (i) one of three instruction cues — 'NOTHING', 'IDENTITY' or 'LOCATION' — for the control, object and spatial WM trials, respectively, lasting 3 s; (ii) an instruction delay of 3 s consisting of a blank screen with a fixation cross in the center; (iii) the presentation of three sample face stimuli for 1 s each; (iv) a WM delay with equal numbers of 6, 7.5, or 9 s delays pseudorandomly intermixed consisting of a blank screen with a fixation cross in the center; (v) the presentation of a test stimulus for 3 s; and (vi) an intertrial interval (ITI), equally likely to be either 1.5, 3, or 4.5 s long, consisting of a blank screen with a fixation cross at the center. Within each run, WM tasks were grouped into two blocks of four object or spatial trials each. Each block began and ended with two control task trials. Thus within each run, there were eight memory trials and eight control trials. Each run began and ended with a 12 s fixation cross at the center of the screen.

Subjects were instructed to fixate on the cross in the center of the screen any time it was present (during ITIs and memory delays). Half of the trials were non-matches and half were matches. In the object trials, half of the time the test face could appear in one of the three sample locations, and similarly for the location trials, half of the time the test location would be occupied by one of the three sample faces. Thus, in one-quarter of the trials the test face would appear in the same location

as where that face had appeared at sample. Participants were instructed to base their match/nonmatch decision only on the cued relevant information dimension.

In order to increase statistical power to observe possible changes in performance that might not have been evident in the group of 10 fMRI participants, additional behavioral data were collected on a separate group of 20 participants (aged 18–29 years). Outside of the scanner, 10 of these participants performed 16 object trials (equivalent to two fMRI runs) followed by 96 spatial trials (twice as many during the fMRI repetition period). The other 10 participants performed 16 spatial trials and then 96 object trials.

Imaging Protocol

All scans were performed at the F.M. Kirby Research Center for Functional Brain Imaging on a 3 T Philips Gyroscan. Structural scans were taken after acquisition of functional data, and consisted of a T1-weighted MP-RAGE anatomical sequence (200 coronal slices, 1 mm thickness, $T_r = 8.1$ ms, $T_E = 3.7$ ms, flip angle = 8° , 256×256 matrix, FOV = 256 mm). The functional T2*-weighted MR scans were interleaved gradient echo, echo planar images (27 axial slices, 3 mm thickness, 1 mm gap, $T_R = 1500$ ms, $T_E = 30$ ms, flip angle = 65° , 80×80 matrix, FOV = 240 mm). All functional scans were acquired in the axial plane and aligned parallel to the line from the anterior commissure to the posterior commissure.

fMRI Analysis

Identifying Regions of Activation

Functional MRI data were phase-shifted using Fourier transformation to correct for slice acquisition time, and motion-corrected using 3D volume registration (Cox, 1996). Multiple regression analysis was performed on the time series data at each voxel using Analysis of Functional NeuroImages (AFNI) software (Cox, 1996; B.D. Ward, <http://afni.nimh.nih.gov/afni/doc/manual/>). Regressors of no interest included six regressors derived from the movement parameters and one for linear drift. The WM and control tasks were broken down into four cognitive components: instructional cue, sample stimuli presentation, delay period and test stimulus presentation. Two sets of regressors were used. For both sets of regressors, the runs were concatenated so that a single reference baseline was used across all runs. The first set consisted of vectors representing the time series of each component for each task, across all runs, convolved with a gamma function model of the hemodynamic response. The second set consisted of vectors representing the time series for each component of each task, separate for each run, convolved with a gamma function model of the hemodynamic response. The second set of regressors totaled 72 (four task components per two tasks yielding eight regressors per run, with a total of nine runs). Scalar beta weights for each of these regressors were converted into percent signal change from the average baseline coefficient (comprised of unmodeled timepoints, i.e. ITI, across all runs combined) for each of the runs. Individual subject maps were transformed into the Talairach coordinate system, resampled to 2 mm^3 , and spatially smoothed with a Gaussian kernel (6 mm full-width half-maximum).

Before assessing changes in activation with repetition, functionally defined regions of interest were identified, using the first set of regressors, within which we assessed changes in activation across runs related to task repetition, using the second set of regressors. Four sets of regions were identified: (i) areas showing more activation during both WM tasks combined relative to the control task; (ii) areas showing more activation during the control task relative to both WM tasks combined; (iii) areas showing more activation during the spatial than the object WM task; and (iv) areas showing more activation during the object than the spatial WM task. Activated regions within parietal cortex were quite large and appeared to contain two distinct foci, one more anterior than the other. Because of the possibility that this cluster of voxels encompassed two distinct functional regions that might respond differently to task repetition, we separated them at the point of narrowest connectivity, yielding an anterior and posterior parietal region on both right and left sides. See Figure 2.

Furthermore, to assess any changes in the regions activated as a result of task repetition, we contrasted activation from the beginning

of the repetition period to the end of the repetition period for both the spatial repetition and the object repetition conditions.

For all comparisons, individual voxel significance was held to $P < 0.01$ (t -threshold of 2.85) and corrected for multiple comparisons via spatial extent of activation, holding each cluster of voxels to an experiment-wide $P < 0.05$. Based upon a Monte Carlo simulation run via AFNI on the union of all subjects' brain volumes (as classified using the EPI signal intensity threshold), it was estimated that a $1013 \mu\text{l}$ contiguous volume (72 voxels, each measuring $1.875 \times 1.875 \times 4$ mm) would meet the $P < 0.05$ threshold.

Assessing Changes in Activation across Runs

From the analysis with the set of regressors defined separately for each run, beta weight coefficients for each defined region of interest, averaged across all voxels within a region for each WM and control delay (and sample and test period) for each run, were extracted. This allowed subsequent analysis of each region's change in activation across runs (compared with the baseline coefficient estimated across the entire session). Because a single baseline was used across all runs, changes in WM activation were independent of any changes in baseline activation across runs. We tested for main effects of repetition across runs and an interaction between repetition and task condition using an ANOVA. The percent signal change values during the repetition period (runs 2–6) were averaged across runs 2 and 3 and compared with the average percent signal change across runs 5 and 6, to assess the effects of task repetition. The difference in activation from runs 2 and 3 to runs 5 and 6 within a condition is referred to as a 'repetition effect'. Furthermore, to measure the effects of repetition within each task condition, paired t -tests were computed for the average of runs 2 and 3 compared with the average of runs 5 and 6. We also assessed any further effects of repetition by comparing activation during the last run of the task repetition period to activity after switching to the non-repeated task (run 6 versus run 7). Additionally, we compared activity during the last run of the repetition period to activation after switching back to the repeated task in the final run (run 6 versus run 9).

Correlating Activation with Behavioral Performance

We assessed whether overall behavioral performance on each WM task was correlated with fMRI activity for each of the regions obtained. Participants were classified according to whether their behavioral performance (combined accuracy and reaction time score) was above or below the median performance score and the subsequent correlation with fMRI activity was measured. Furthermore, we tested whether, within each participant, any changes in fMRI activity were significantly correlated with changes in behavioral performance across runs by measuring the correlation between the difference in activity and the corresponding difference in behavioral performance for that participant with regard to the beginning of the repetition period (runs 2 and 3) and the end of the repetition period (runs 5 and 6).

Results

Behavioral Results

All subjects performed at no worse than 33% incorrect. The average error rates for the object repetition condition and spatial repetition condition (across nine runs including both object and spatial tasks) were nearly identical at $18.33 \pm 3.14\%$ (mean \pm SEM) and $18.33 \pm 3.04\%$, respectively. Average reaction times for the object repetition condition and spatial repetition condition were 1327 ± 74.1 and 1381 ± 85 ms. No significant differences in reaction times [$t(9) = 0.62$, $P > 0.1$] or errors [$t(9) = 0.86$, $P > 0.1$] were found between the two repetition conditions. Similarly, average reaction times for the object and spatial WM tasks (including only runs of the same information type across both repetition conditions) were 1357 ± 140.5 and 1335.3 ± 165.4 ms, respectively. Error rates for the object and

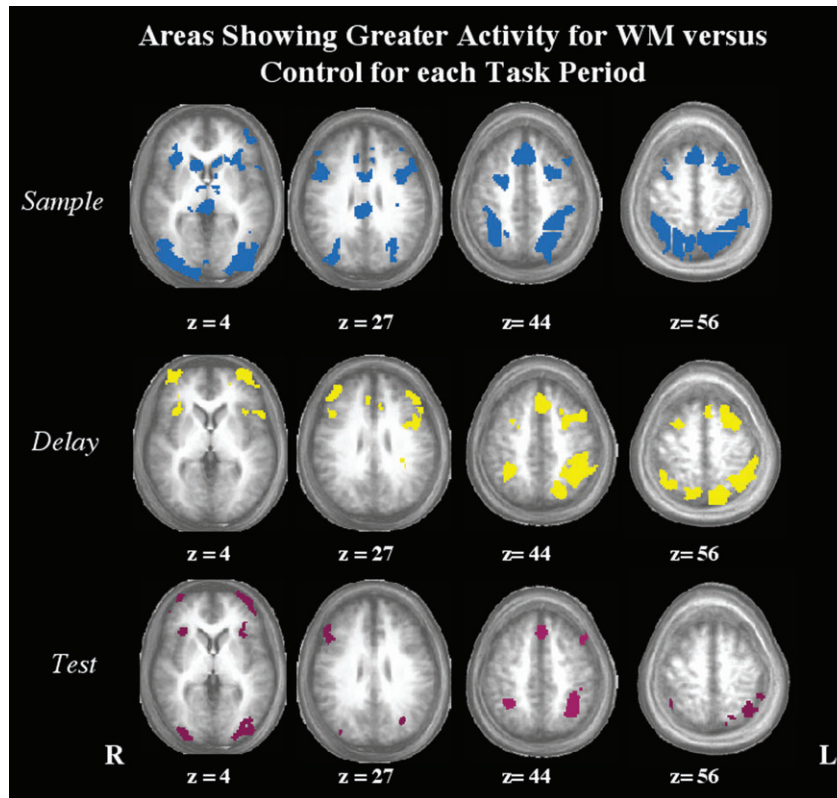


Figure 2. Random-effects activation maps during the sample, delay and test period during both working memory tasks (compared with the control task) overlaid on an averaged Talairach normalized anatomical image.

spatial tasks were 15.8 ± 3.59 and $20.7 \pm 3.17\%$. No significant differences in reaction time or error rate were found between the two task types [$t(9) = 0.42, 0.17$ respectively, $P > 0.1$]. No significant gender- or age-related differences in performance were found.

There were no significant changes in performance between the first two runs and the last two runs of the repetition period during fMRI scanning. There were also no significant changes from the beginning to the end of the repetition period in the additional behavioral data collected outside the scanner, despite having twice as many trials as during the fMRI scanning.

fMRI Results

Regions of Activation

The regions of activation identified by comparing either both WM tasks to control or the spatial and object WM tasks to each other, are shown in Figures 2 and 3 and listed in Supplementary Tables 1–5. Regions of activation were slightly different for the sample, delay and test periods of the tasks. The regions of activation are similar to those identified by previous neuroimaging studies of spatial and object WM. Activation changes across runs within the repetition period (runs 2–6) were analyzed within each of these regions of activation.

A voxelwise random effects analysis was performed to test whether any regions showed greater activation at the end of the repetition period as compared with the beginning. No such activations were found, indicating that the regions utilized during the WM tasks did not change as a function of repetition.

That is, there were no brain regions active after the task repetition period that were not also active at the beginning.

Repetition Effects within Object and Spatial WM Relative to Control Regions

Sample and Delay Periods. Many of the regions showing greater activity for both WM tasks relative to the control task also showed a main effect of repetition, decreasing in activity from runs 2 and 3 to runs 5 and 6. Almost all of these regions also showed an effect of repetition for the spatial repetition condition alone. Some of these regions also showed a repetition \times condition interaction, having a greater decrease for the spatial repetition condition than in the object repetition condition. Only one region (right precentral sulcus/inferior frontal gyrus (IFG)) during the sample period and a different region (right insula) during the delay (Fig. 4) showed a significant repetition effect for the object WM task when that condition was analyzed separately (Supplementary Tables 1 and 2). These results suggest that, even in those areas that did not show a significant repetition by condition interaction, the main effect of repetition was likely driven primarily by the spatial WM task. Activation changes across runs during the delay period are plotted in Figure 4 for the right posterior parietal and superior frontal sulcus, presupplementary motor area/anterior cingulate cortex (preSMA/ACC) and right insula. Areas with greater activation for the control task than the WM tasks showed similar results. Two regions, covering much of lateral and superior temporal cortex during the sample period and one region, including the posterior cingulate and precuneus, during the delay showed significant repetition-related decreases in activation for the spatial WM task only.

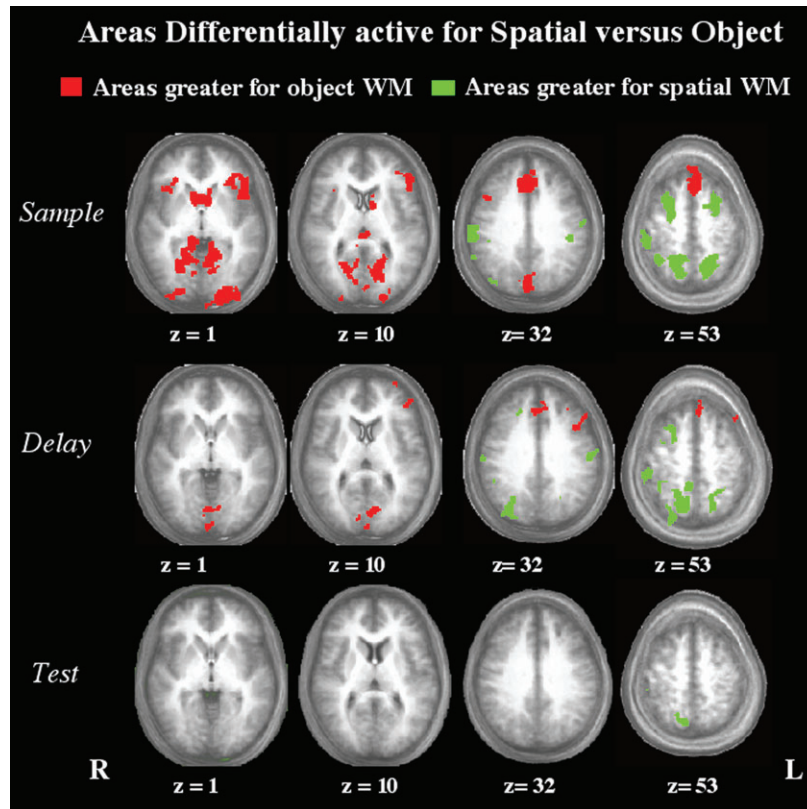


Figure 3. Random-effects activation maps of areas differentially activated during the sample, delay and test periods for object versus spatial working memory tasks overlaid on averaged Talairach normalized anatomical images. Areas showing greater activity for the object working memory task (compared with the spatial working memory task) are depicted in red. Areas showing greater activity for the spatial task (as compared with the object task) are shown in green. No regions showed a difference during the test period for object versus spatial working memory.

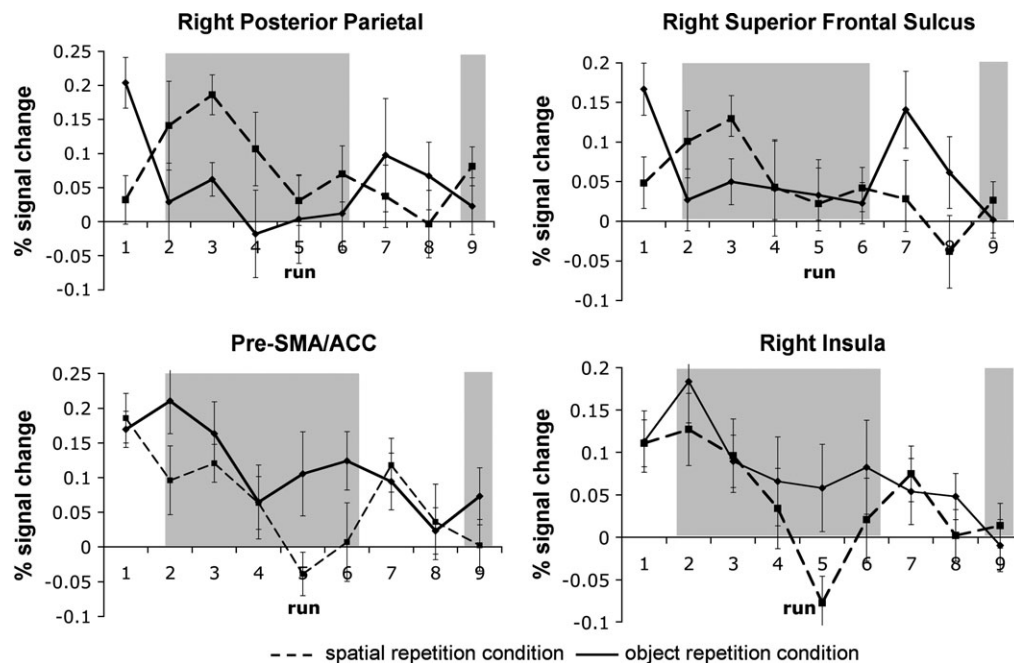


Figure 4. Average percent signal change relative to baseline in areas greater during the working memory delay (compared with control) for each run for each condition. Shaded areas indicate where the same type of task (object or spatial) is being performed. Therefore, runs 2–6 and run 9 constitute the same working memory task. The solid line depicts activity for each run during the object repetition condition and the dashed line depicts activity for the spatial repetition condition. (A) Right posterior parietal with a significant main effect of repetition and a significant spatial repetition decrease. (B) Right superior frontal sulcus with a significant main effect of repetition, significant interaction and significant spatial repetition decrease. (C) Pre-SMA/ACC with a significant main effect and significant spatial repetition decrease. (D) Right insula with a significant main effect, significant object repetition decrease and significant spatial repetition decrease.

Test Period. Unlike during the sample and delay periods, during the test period there was no indication that the repetition effects were primarily during the spatial WM task. The right insula, left insula/IFG and the preSMA regions all showed a main effect of repetition. No regions yielded a significant repetition \times condition interaction. The right insula showed decreases for both spatial and object repetition conditions. The left middle frontal gyrus (MFG) was the only region showing a decrease for the spatial repetition condition alone, and the preSMA and right inferior parietal lobule (IPL) both showed decreases for the object repetition condition (Supplementary Table 3). No regions identified as having greater activation during control than WM during the test period showed repetition related changes.

Repetition Effects within Regions More Active for Object WM

Many regions that had greater object than spatial activity also showed a main effect of repetition. The cuneus/lingual gyrus during the sample period and a cuneus/lingual gyrus region (encompassing the one found during the sample period) during the delay period showed a repetition \times condition interaction, indicating that the repetition effect was larger during spatial than object WM. Other regions showing such an interaction included right insula/IFG, right IFG/MFG and caudate/ACC. Similar to the analysis of the regions showing greater activity for both WM tasks relative to control, almost all of these 'object-selective' regions that showed a main effect of repetition also showed an effect of repetition for the spatial repetition condition alone during sample and delay (Fig. 5). However, none of these regions showed a significant repetition effect when the object repetition condition was analyzed separately (Supplementary Table 4). Contrasting run 6 with run 7 for the spatial repetition condition revealed increases in activation for several regions when switching to the object WM task after repetition of the spatial task (see Figs 4 and 5). Activation changes across runs during the delay period in left IFG/MFG are plotted in Figure 5.

Repetition Effects within Areas More Active for Spatial WM

Sample and Delay Periods. As in the previous analyses, several regions with greater spatial than object activity showed a main effect of repetition during both sample and delay periods (Supplementary Table 5). The right precuneus during the

sample period and the left postcentral sulcus during both sample and delay also showed a repetition \times condition interaction. The left postcentral sulcus during the sample period was the only region to show an interaction but no main effect of repetition.

Similar to the other within-condition analyses, most spatially selective regions that showed a main effect of repetition also showed an effect of repetition for the spatial repetition condition alone during sample and delay. The left superior parietal lobule (SPL) was the only region to show a significant decrease for the object repetition condition as well as for the spatial repetition condition (Fig. 5). Again, this finding suggests that the significant main effects of repetition were primarily driven by the spatial repetition condition.

Test Period. No significant repetition effects were found in either of the two regions significantly more active during the spatial relative to the object WM test period.

Activation for Repeated Task after Task Switch

Repetition effects on activation remained after switching to the non-repeated task for two runs and then back to the repeated task for the final run. Specifically, there was no increase in activation from run 6 to run 9 for any region that showed a repetition-related decrease (a decrease from runs 2 and 3 to runs 5 and 6). However, one region (left occipital, WM > control in the sample period) showed an additional decrease in activation in run 9 for the spatial repetition condition. See Figures 4 and 5.

Correlations between Behavioral Performance and Activation

Reaction time and error rate were analyzed separately, and also assessed in a combined performance score that was independent of any speed-accuracy trade-offs. Within each repetition condition for the repeated task, participants performing better than the median (combined accuracy and RT performance score) had greater activation than those performing below the median. No systematic changes in behavioral performance were found and no correlation between fMRI activity and any of these behavioral measures was found. Although activation decreased during the repetition period, no changes in performance were observed. Thus, within-participant repetition-related changes in activation were largely uncorrelated with changes in behavioral performance.

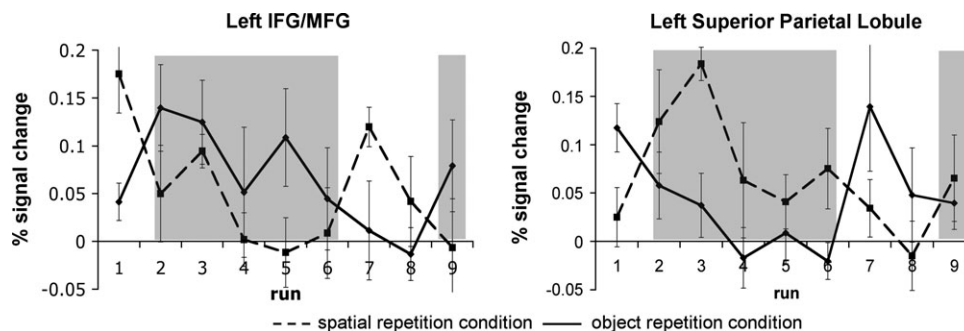


Figure 5. Average percent signal change relative to baseline during delay period for the object-selective left IFG/MFG and the spatially selective left SPL for each run for each condition. (A) Left IFG/MFG area with a significant main effect of repetition and a significant spatial repetition decrease. (B) Left SPL with a significant main effect, significant object and spatial repetition decrease.

For both the fMRI and behavior-only data, trials in which the relevant and irrelevant aspects of the test image either both matched or both mismatched the sample image were compared with those trials in which the relevant and irrelevant features were incongruent regarding a match or mismatch to the sample items. There were no accuracy or reaction time differences between congruent and incongruent trials for either the spatial or object task and no effects of repetition.

Discussion

Summary

The aim of the present study was to assess the effects of repetition on a WM task. We investigated the effect of task repetition for both object and a spatial WM to determine if these effects were general to WM processes, or specific to the type of information being maintained. We assessed these effects during sample, delay and test periods, in areas that showed greater activation for all WM tasks compared with control, as well as areas that showed greater activation for one WM task over the other. The effect of repetition was most pronounced during the sample and delay periods, where we found decreasing activation with task repetition in many of these areas during the spatial WM task, regardless of whether the region appeared to be spatially selective, object selective or domain independent. A subset of these areas also showed decreased activation with repetition of the object WM task, but this effect occurred in far fewer regions than in the spatial repetition condition. No regions showed increased activation for either task and no areas became active toward the end of the repetition period that had not been active at the beginning of the scanning session. No changes in behavioral performance with task repetition were observed.

Relevant and Irrelevant Information during Spatial Working Memory

Our results indicate that in regions selective for spatial encoding as well as those selective for maintaining spatial information, repeated performance of a spatial WM task results in decreases in the brain activity of these areas. This decrease in activity, along with a lack of change in behavioral performance, could indicate increasing neural efficiency during encoding and maintenance of spatial information. With repetition, less neurons would be needed to encode and represent spatial locations. This idea is similar to the finding of Rainer and Miller (2000) that, with repeated exposure, fewer neurons were recruited to perceive and recognize familiar objects compared with novel ones. However, in contrast to Rainer and Miller's study, the decreases in activation with repetition of our spatial WM task were not accompanied by improvements in behavioral performance; instead, it appears that fewer neurons were employed to maintain the same level of performance.

These decreases may also indicate changes in attentional processes during the sample and delay period. In the current study, the use of bidimensional stimuli required that participants maintain either the object or the spatial information according to the instructional cues and ignore the irrelevant information. The behavioral data indicates that, independent of repetition, the presence of matching or mismatching irrelevant information at test does not significantly affect performance on this task. Nevertheless, incidental encoding of irrelevant in-

formation could still be occurring. In addition, the control processes necessary to filter out this information could be affected by repetition. Task repetition could have one of two effects on processing of the irrelevant information. Repetition of the spatial task could enable participants to become better able to filter out the irrelevant (face identity) information. Alternatively, as subjects become more efficient at maintaining the relevant information they may have excess capacity with which to maintain irrelevant information, and thus encode and maintain more of this information incidentally. The latter explanation suggests that with repetition, the attentional filter may become 'leaky' over time, without detriment to performance. The decreases during the spatial WM task noted in the object-selective areas, however, argue against this second hypothesis. We posit that the decreases found in these areas for the spatial WM task are indicative of less incidental encoding and maintenance of object information during the spatial WM task. Therefore, both the representation of spatial information and the filtering out of the object information improve over time when these same types of information continue to be relevant and irrelevant, respectively.

The activity observed in object selective areas during the spatial task may not reflect incidental encoding of the object information, however. This activity may instead reflect inputs to the ventral object-selective areas from dorsal areas that are more directly involved in spatial encoding and maintenance. Such interconnections between temporal and parietal visual areas and among prefrontal cortex regions are common (e.g. Barbas and Pandya, 1989; Webster *et al.*, 1994). If the activity in object selective areas during the spatial task reflects input from spatially selective regions, then the decreasing pattern of activation seen in the spatially selective areas would be expected to be reflected in the activation measured in those object-selective areas. Thus, the effects of repetition in the spatial WM task could relate only to the representation of the task-relevant information, but this information is subsequently distributed across both dorsal and ventral regions of the prefrontal cortex (see also Sala *et al.* 2003; Sala and Courtney, forthcoming).

Cognitive Control and Conflict Resolution

Two areas, preSMA and right IPL, showed decreases that were significant only for the object WM task during the test period, in areas greater for both WM tasks compared with control. Although this effect was only significant during the object WM task, the repetition \times condition interaction was not significant, so there may have been a small decrease during the spatial task as well. A very similar preSMA/ACC region showed decreases during sample and delay periods for the spatial task. The preSMA/ACC has been implicated in conflict monitoring, and in signaling an increasing need for cognitive control processes (Fassbender *et al.*, 2004; Garavan *et al.*, 2003; Kerns *et al.*, 2004). The decrease in activation in preSMA/ACC implies a reduction in the need for control or increased efficiency of control after repetition. Decreases observed during the test period suggests increasing efficiency in filtering out irrelevant information because our test stimuli could either match or mismatch the irrelevant information, independent of whether the test stimulus matched according to the relevant information. Thus, improved filtering out of the irrelevant information would lead to less response conflict and presumably less activity in preSMA/ACC.

Increased Efficiency Specific to Spatial Working Memory?

Our results are somewhat different from those of Landau *et al.*, who found decreases with repetition during their object WM task, which also used faces as stimuli. Participants in that study performed 96 trials, whereas the repetition period in the present study contained 48 trials. It is possible that the repetition of object WM differs from spatial WM repetition in that more trials are necessary to evoke object WM repetition-related decreases. If the repetition period of the current study had contained more trials we might have seen more decreases related to object WM repetition. In addition, the object WM tasks used in the two studies were different. In the current study, participants were instructed to ignore the location information during the object WM task whereas in the Landau *et al.* study the location of the faces was kept constant at the fovea. Therefore, the underlying demands (attending to object information, filtering out location information) differ between the two studies, and the lack of effects in our object task might be due to slower or smaller changes in the efficiency of this selective attention demand with repetition.

While most of the repetition effects were specific to the spatial task, decreases during both the object and spatial WM tasks were found in right precentral sulcus/IFG during the sample period, and in the right insula during both the delay and test periods in the regions defined by the comparison of both WM tasks versus control. There were also significant decreases for both object and spatial tasks in the spatially selective left SPL during the delay period. The changes seen in the right precentral sulcus/IFG and right insula during the sample, delay and test periods may indicate general changes in WM control processes, such as attentional selection, encoding, rehearsal of task-relevant information or retrieval of information. The decrease observed in the spatially selective SPL area during the object WM delay could be a result of decreasing maintenance of the irrelevant spatial locations during the object WM task, analogous to the apparent decrease in the processing of faces during the spatial task. Therefore, while the repetition-related effects were either greater or faster in the current study for spatial WM, there is some indication that similar changes may occur during object WM.

No Increases in Activation or New Regions Activated

Neither the current study nor the Landau *et al.* (2004) study, both of which examined changes in activation within a single scanning session lasting <1 h, observed any increases in activation with task repetition. Increases in brain activation were observed in a study by Olesen *et al.* (2004) in which participants received extensive practice on a visuospatial WM task outside of the scanner for a period of 5 weeks. This is similar to the effects that have been reported for motor sequence learning in which a decrease in activation during a scanning session may be followed by an increase in the extent of activation after weeks of practice (Karni *et al.*, 1995). Our results, therefore, do not preclude the possibility of increased activation with more extensive task practice, but rather demonstrate the effects of WM task repetition on a short-term scale.

The network of regions activated for each of the WM tasks did not change from beginning (runs 2 and 3) to the end (runs 5 and 6) of the repetition period. This result differs from those of previous studies that found a shift in the regions activated

during the beginning and end of a period of task repetition using tasks in which fixed stimulus–response associations are learned (Petersen *et al.*, 1998; van Mier *et al.*, 1998). However, studies that specifically target repeated performance of a WM task are in accord with our findings (Garavan *et al.*, 2000; Jansma *et al.*, 2001; Landau *et al.*, 2004; Olesen *et al.*, 2004). The results of the current study and these previous studies confirm our hypothesis that the inability to develop an automatic stimulus–response association with repetition necessitates the continued use of cognitive control mechanisms to adequately perform a WM task. Repetition of a WM task may result in the processes subserving WM becoming more efficient, but does not abolish the role of cognitive control in the task completely. This idea is supported by the finding of other studies of WM repetition (McEvoy *et al.*, 1998; Jansma *et al.*, 2001). These studies found that with practice, the demand for higher-order processes remained, and the regions involved remained the same throughout task performance. Changes were instead elicited in terms of efficiency, as the effectiveness of the processes involved in WM task performance improved with repetition.

Changes in Neural Activation Independent of Changes in Performance

The results of the current study and those of earlier studies (Landau *et al.*, 2004; Olesen *et al.*, 2004) indicate that neural changes with repetition of a WM task are not necessarily reflected in behavioral performance. We observed no changes in performance in both the fMRI portion of our experiment and the additional behavioral data collected outside the scanner which contained twice as many trials (96). Previous work showing correlations between changes in activation related to changes in performance within participants employed large amounts of practice over several weeks (e.g. Haier *et al.*, 1992; Petersen *et al.*, 1998; Olesen *et al.*, 2004), which differs from our single-session study. Importantly, the lack of correlation further supports the hypothesis that the changes in activation are related to changes in neural efficiency due to task repetition, and are not reflective of changes in performance. In accordance with Olesen *et al.* (2004)'s explanation, these changes reflect changes in the neural substrate of performance and cannot simply be accounted for by changes in behavioral performance. Perhaps the participants chose a criterion level of performance and, despite the increased efficiency, maintained that level of performance with reduced 'effort' instead of maintaining a high level of effort in order to improve performance. If the experiment had included incentives or continuous feedback, we might have been more likely to observe such performance changes. Alternatively, results may indicate that practice-related changes in the neural substrates of the task precede improved performance.

Alternative Explanations

The decreases seen during encoding were unlikely to be a result of priming, since participants were exposed to 48 trials of the same stimuli before the scanning session. We see decreases during the delay period also, when no stimuli are present, a further indication that priming is not an explanation for our results. In addition, priming would be expected to affect the object task at least as much as the spatial task.

General participant fatigue is also unlikely to explain the decreases in activation observed in this study for three reasons.

First, the decreases were largely restricted to the spatial task. Second, behavioral performance remains constant throughout the repetition period. Finally, increased activation is seen in object selective areas when subjects switch to the object task in run 7 after the spatial task repetition period, further indicating that this decrease is specific to the repeated spatial task and not the result of generalized fatigue, or decreased attention or motivation.

While we did not find any difference between the spatial and object tasks in either overall performance or repetition-related changes in performance, it is possible that the asymmetry in the repetition effects observed in this experiment are related to these particular tasks rather than spatial versus non-spatial information more generally. For example, if the encoding and WM systems for faces were already maximally efficient from extensive experience, then one might not expect to see additional decreases in activation with task repetition as for a more novel task. The lack of any differential effects of repetition time on performance of the two tasks, even during training, argues against any difference in novelty for the tasks in this study. Answering this question definitively will require more research using similar repetition paradigms with multiple other types of spatial and non-spatial WM tasks.

Conclusions

The selectivity of the repetition effects in the spatial WM task supports the idea of separable neural systems for object and spatial WM. Repetition effects are either greater or occur at a faster rate for spatial WM than for object WM. This result suggests either a difference in the nature of the representation of spatial versus object information or separable neural systems for the maintenance of these two information types in WM. In addition, the results of the current experiment provide evidence for repetition- or practice-related increased efficiency of the representation of task-relevant spatial information and improved attentional filtering of irrelevant object information.

Supplementary Material

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

Notes

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References

Barbas H, Pandya DN (1989) Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *J Comp Neuro* 286:353-375.

- Carlesimo GA, Perri R, Turriziani P, Tomaiuolo F, Caltagirone C (2001) Remembering what but not where: independence of spatial and visual working memory in the human brain. *Cortex* 37:519-534.
- Courtney SM, Ungerleider LG, Keil K, Haxby JV (1997) Transient and sustained activity in a distributed neural system for human working memory. *Nature* 386:608-611.
- Cox RW (1996) AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res* 29:162-173.
- Fassbender C, Murphy K, Foxe JJ, Wylie GR, Javitt DC, Robertson IH, Garavan H (2004) A topography of executive functions and their interactions revealed by functional magnetic resonance imaging. *Brain Res Cogn Brain Res* 20:132-143.
- Garavan H, Kelley D, Rosen A, Rao SM, Stein EA (2000) Practice-related functional activation changes in a working memory task. *Microsc Res Tech* 51:54-63.
- Garavan H, Ross TJ, Kaufman J, Stein EA (2003) A midline dissociation between error-processing and response-conflict monitoring. *Neuroimage* 20:1132-1139.
- Haier RJ, Siegel BV Jr, MacLachlan A, Soderling E, Lottnerberg S, Buchsbaum MS (1992) Regional glucose metabolic changes after learning a complex visuospatial/motor task: a positron emission tomographic study. *Brain Res* 570:134-143.
- Jansma JM, Ramsey NF, Slagter HA, Kahn RS (2001) Functional anatomical correlates of controlled and automatic processing. *J Cogn Neurosci* 13:730-743.
- Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG (1995) Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature* 377:155-158.
- Kerns JG, Cohen JD, MacDonald AW 3rd, Cho RY, Stenger VA, Carter CS (2004) Anterior cingulate conflict monitoring and adjustments in control. *Science* 303:1023-1026.
- Landau SM, Schumacher EH, Garavan H, Druzgal TJ, D'Esposito M (2004) A functional MRI study of the influence of practice on component processes of working memory. *Neuroimage* 22:211-221.
- McEvoy LK, Smith ME, Gevins A (1998) Dynamic cortical networks of verbal and spatial working memory: effects of memory load and task practice. *Cereb Cortex* 8:563-574.
- Mottaghy FM, Gangitano M, Sparing R, Krause BJ, Pascual-Leone A (2002) Segregation of areas related to visual working memory in the prefrontal cortex revealed by rTMS. *Cereb Cortex* 12:369-375.
- Olesen PJ, Westerberg H, Klingberg T (2004) Increased prefrontal and parietal activity after training of working memory. *Nat Neurosci* 7:75-79.
- Petersen SE, van Mier H, Fiez JA, Raichle ME (1998) The effects of practice on the functional anatomy of task performance. *Proc Natl Acad Sci USA* 95:853-860.
- Rainer G, Miller EK (2000) Effects of visual experience on the representation of objects in the prefrontal cortex. *Neuron* 27:179-189.
- Sakai K, Hikosaka O, Miyauchi S, Takino R, Sasaki Y, Putz B (1998) Transition of brain activation from frontal to parietal areas in visuomotor sequence learning. *J Neurosci* 18:1827-1840.
- Sala JB, Courtney SM (Forthcoming) Binding of what and where during working memory maintenance. *Cortex*.
- Sala JB, Rama P, Courtney SM (2003) Functional topography of a distributed neural system for spatial and nonspatial information maintenance in working memory. *Neuropsychologia* 41:341-356.
- van Mier H, Tempel LW, Perlmutter JS, Raichle ME, Petersen SE (1998) Changes in brain activity during motor learning measured with PET: effects of hand of performance and practice. *J Neurophysiol* 80:2177-2199.
- Webster MJ, Bachevalier J, Ungerleider LG (1994) Connections of inferior temporal areas TEO and TE with parietal and frontal cortex in macaque monkeys. *Cereb Cortex* 4:470-483.