

Research Report

REHEARSAL IN SPATIAL WORKING MEMORY: Evidence From Neuroimaging

Edward Awh,¹ John Jonides,² Edward E. Smith,² Richard B. Buxton,³
Larry R. Frank,³ Tracy Love,⁴ Eric C. Wong,³ and Leon Gmeindl²

¹Department of Psychology, University of Oregon; ²Department of Psychology, University of Michigan; ³Department of Radiology, University of California, San Diego; and ⁴Department of Psychology, University of California, San Diego

Abstract—A variety of biological evidence has identified a frontal-parietal circuit underlying spatial working memory for visual stimuli. But the question remains, how do these neural regions accomplish the goal of maintaining location information on-line? We tested the hypothesis that the active rehearsal of spatial information in working memory is accomplished by means of focal shifts of spatial selective attention to memorized locations. Spatial selective attention has been shown to cause changes in the early visual processing of stimuli that appear in attended locations. Thus, the hypothesis of attention-based rehearsal predicts similar modulations of visual processing at memorized locations. We used functional magnetic resonance imaging to observe posterior visual activations during the performance of a spatial working memory task. In line with the hypothesis, spatial rehearsal led to enhanced activation in the early visual areas contralateral to the memorized locations.

The present work investigated a model of rehearsal in spatial working memory in which the active maintenance of location-specific representations is mediated by focal shifts of spatial selective attention to the memorized locations. Two sources of behavioral evidence suggest the plausibility of this model: First, recent studies (Awh, Jonides, & Reuter-Lorenz, 1998; Awh, Smith, & Jonides, 1995) have tested a clear prediction of the hypothesis of attention-based rehearsal in spatial working memory. If spatial selective attention is focused on memorized locations, then the typical effects of spatial selective attention—improved visual processing at attended locations—should also be observed at memorized locations. In line with this expectation, these studies confirmed that subjects were faster to discriminate a visual stimulus if that stimulus was presented in a location that was being stored in spatial working memory. Second, if subjects are hindered in their ability to direct attention toward a memorized location, memory accuracy for that location declines (Awh et al., 1998; Smyth, 1996; Smyth & Scholey, 1994). Smyth and her colleagues have shown that secondary tasks requiring shifts of attention disrupt performance of the Corsi Blocks Task, a traditional clinical measure of spatial memory span. Similarly, we (Awh et al., 1998) found that accuracy in spatial working memory showed greater impairments from a secondary task that required shifts of attention away from the memorized location than from a task that did not require attentional shifts. These interference experiments are a key complement to the first form of evidence because they show that the locus of selective spatial orienting is not merely correlated with the memorized locations. Rather, spatial attention plays a beneficial functional role in the active maintenance of location information.

The proposal that spatial working memory includes a component of spatial attention is also consistent with the putative neural substrates of these systems. It has been observed that there is considerable overlap between the cortical sites that mediate spatial working memory and spatial selective attention (Awh & Jonides, 1998; Awh et al., 1995), suggesting a relationship between the two systems. In particular, both mechanisms appear to be mediated by a frontal-parietal network of brain regions, and both show evidence of a marked right-hemispheric dominance. However, although this neuroanatomical correlation is consistent with the hypothesis of attention-based rehearsal, it does not demand this interpretation. Rather, a more direct test of the neuroanatomical relationship between attention and rehearsal is needed, a test that is provided by the present work.

Previous studies have shown that spatial selective attention leads to modulation of activity in early visual areas contralateral to the attended regions of space (e.g., Gratton, 1997; Heinze et al., 1994; Hillyard & Mangun, 1987; Moran & Desimone, 1984; Petersen, Corbetta, Miezin, & Shulman, 1994). We focused on this change in early visual processing as a signature for the operation of spatial selective attention. On this basis, we predicted that if spatial rehearsal involves the deployment of spatial attention toward the locations held in working memory, we would observe modulation of the visual responses to stimuli falling in these memorized locations.

Subjects memorized locations in either the right visual field (RVF) or the left visual field (LVF) while brain activation was measured by means of functional magnetic resonance imaging (fMRI). During the retention interval, a bilateral flickering grid occluded all the potential memorized locations. Measuring the visual responses to this flickering stimulus enabled us to observe whether spatial rehearsal in working memory causes location-specific modulations of visual activity. This experimental rationale follows from previous neuroimaging studies of spatial selective attention (e.g., Gratton, 1997; Heinze et al., 1994; Petersen et al., 1994). These studies have revealed modulations of ongoing visual activity contralateral to attended regions of space. Thus, the flickering stimulus served to drive visual responses over both memorized and nonmemorized locations (i.e., over opposite sides of visual fixation). We reasoned that if spatial rehearsal was accomplished by directing spatial attention to the memorized locations, then the flicker-driven visual responses should be larger contralateral to these locations. These studies could extend the behavioral evidence by showing another shared functional consequence of memory and attention—the top-down modulation of early visual processing.

We recognized that the predicted contralateral activations in the spatial memory task could arise, in part, as a result of encoding processes for a unilateral stimulus display. That is, for example, activations might arise in right occipital cortex by virtue of the fact that the memoranda were presented in the LVF. In order to assess the contributions of encoding versus rehearsal processes, the same subjects

Address correspondence to Edward Awh, 1227 University of Oregon, Eugene, OR 97403-1227; e-mail: awh@darkwing.uoregon.edu.

were scanned while they performed a nonspatial memory task that was matched to the spatial task in all relevant respects. This nonspatial memory condition provided a baseline estimate of the amount of encoding-driven activation in early visual areas resulting from the perceptual processing of the memory cues. Once this baseline was set, we were able to determine whether the spatial memory condition caused rehearsal-related memory activations.

Our primary dependent measure involved a comparison of the visual activations elicited by right and left sides of the flickering grid. These activations should, by hypothesis, be modulated by the rehearsal involved in the spatial memory task. One complication with this measure is that recent demonstrations have shown substantial between-subjects variability in the functional morphology of early visual areas (Sereno et al., 1995). In recognition of this fact, we included in our experiment a separate visual-stimulation condition so that we could identify (on a within-subjects basis) which regions of occipital cortex responded to the flickering grid. Once these regions were identified, they could serve as the basis for an analysis of contralateral visual activations in response to the flickering grid in the memory conditions. This analysis strategy follows *sensory gain-control* models of spatial attention (e.g., Hillyard & Mangun, 1987; Wijers, Lange, Mulder, & Mulder, 1997), which assert that the effect of spatial attention is to change the excitability of the neural populations that participate in the early perceptual analysis of visual information. The implication is that attentional effects should be observed within the same neuronal structures that respond in a bottom-up fashion to sensory stimulation. The visual-stimulation condition made it possible to identify these neuronal structures using a functional criterion.

METHOD

Subjects

Four volunteers (2 males) were paid to participate in this study. All subjects were right-handed and had normal or corrected-to-normal vision.

Tasks

Spatial memory task

Throughout all trials in every experimental condition, subjects were instructed to maintain fixation on a cross in the center of the screen. A single trial of the spatial memory task (illustrated in Fig. 1a) proceeded as follows: First, three false-font characters (0.5° tall and 0.4° wide) were sequentially presented within one visual field for 500 ms each (interstimulus interval = 300 ms). Subjects were instructed to remember the locations of these memory cues. Within each visual field, there were 42 possible memory locations that were equally spaced within an imaginary rectangle (6.6° tall and 6° wide). One of these rectangles was on the left of the fixation point, and the other was on the right. The distance between the two rectangles was 2.0° (i.e., the shortest distance from fixation was 1° for each rectangle), and their vertical position was centered across the horizontal meridian of the screen. Then, 500 ms after the offset of the third memory cue, a counterphased flickering grid (flicker rate = 8 Hz) that occluded all possible memory locations in both visual fields was presented for 6 s. Five hundred milliseconds after the offset of the grid, a single false-font

character was presented for 2 s. Subjects used a two-button keypad held in their right hand to indicate whether this memory probe occupied any of the three locations they were holding in memory. The locations of nonmatch probes (occurring with a probability of .5) were randomly selected from all nonmemorized locations within the visual field of the memory set. Rather than using a control condition, we contrasted the same memory task in the right versus the left visual fields.

The trial structure during a single run of the scanner is illustrated in Figure 1b. One right-left sequence consisted of three RVF trials followed by three trials in the LVF. Each scan series consisted of four consecutive right-left sequences. During scanning, the average memory accuracy was 73%.

Nonspatial memory task

The nonspatial memory task employed a stimulus display identical to that of the spatial memory task, except that Geneva-font letters were presented instead of false-font letters. In addition, subjects were instructed to remember the identity of the letters rather than their locations. Subjects used a two-button keypad to indicate whether the memory probe matched the identity of any of the three letters they held in memory. The probe matched the identity of the memory cue with a probability of .5. (Average accuracy during scanning was 95%.) This condition allowed us to assess the extent to which there were any stimulus-driven activation differences between the RVF and LVF memory trials.

The nonspatial memory task provides a valid estimate of the effects of unilateral encoding only to the extent that encoding letters was at least as demanding as encoding spatial locations. A separate behavioral study suggests that encoding was, in fact, more difficult in the nonspatial task. Six subjects performed 80 trials of the spatial and nonspatial memory tasks while the exposure duration of the memoranda was randomly varied between 10 and 500 ms. The accuracies exhibited a significant interaction of exposure duration and task, $t(5) = 3.3$, $p = .01$: Faster exposures led to a 10% decrement in letter memory accuracy, but there was no effect of exposure duration on spatial memory accuracy. Thus, we conclude that the letter task required more demanding encoding than the spatial task did. This result validates the use of the letter memory task to assess the extent to which encoding-related activity contributed to the activation of visual areas contralateral to the memory cues in the spatial memory condition.¹

Visual-stimulation condition

Subjects were scanned while they viewed alternating 30-s presentations of the right side of the flickering grid and the left side of the flickering grid. This procedure allowed us to establish regions of interest (ROIs) within the left and right hemispheres of each subject that corresponded to the cortical regions stimulated by the right and left sides of the bilateral grid. We used the ROIs from the visual-stimula-

1. Although there was a difference in overall memory accuracy between the spatial and letter memory tasks, it should be noted that the difficulty of the memory tasks would be unlikely to influence the extent to which encoding of the memory cues caused contralateral activation of early visual areas. Thus, the letter memory task provides an appropriate control for this alternative source of contralateral visual activation in the spatial memory condition.

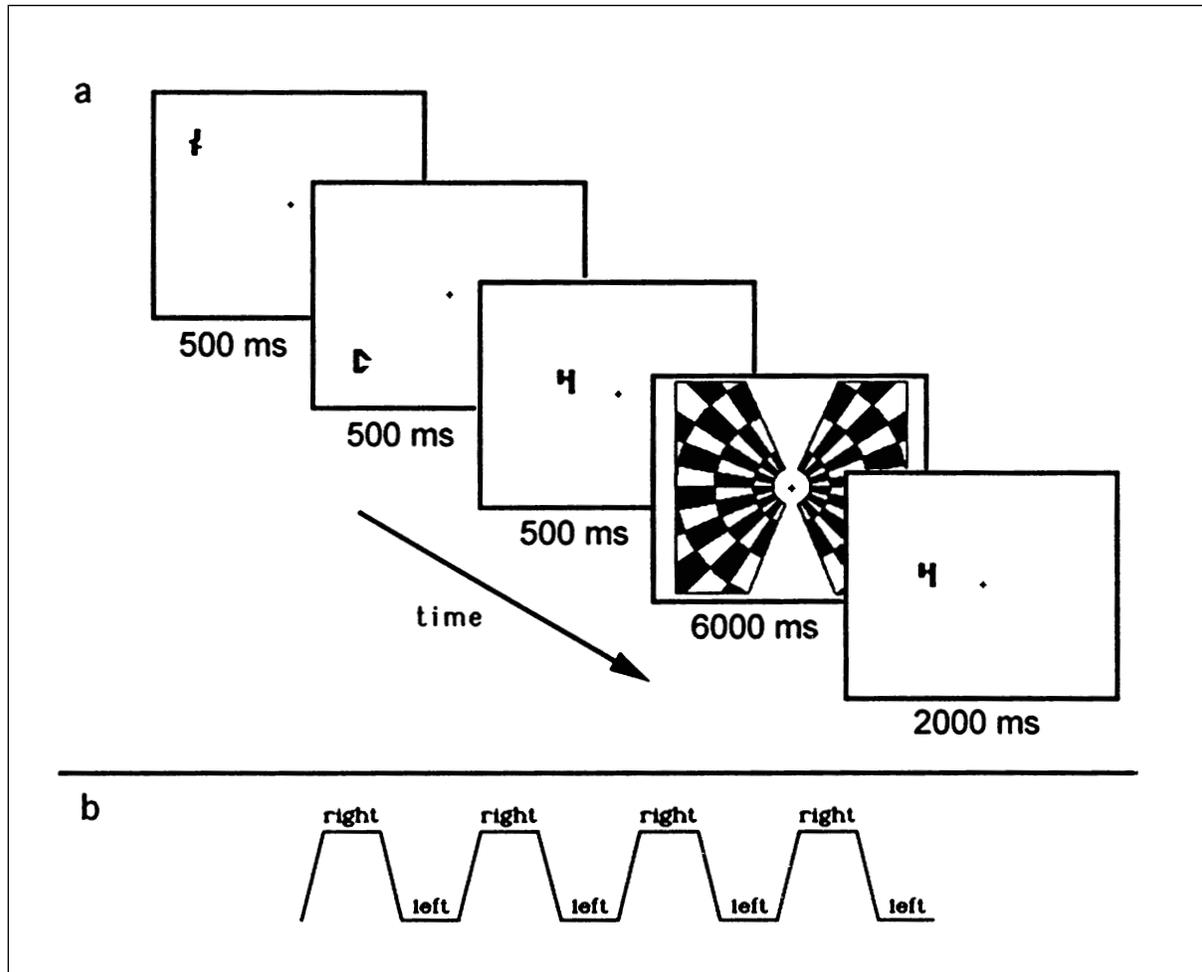


Fig. 1. Schematics of a spatial memory trial in the left visual field (a) and the trial structure during a single run of the scanner (b). During each trial, three false-font characters were presented sequentially for 500 ms each (interstimulus interval = 300 ms) in randomly selected locations. Five hundred milliseconds after the offset of the last memory cue, the bilateral flickering grid was presented for 6,000 ms. Five hundred milliseconds after the offset of the grid, the memory probe was presented for 2,000 ms, and subjects indicated whether it was in the same location as any of the three locations they were asked to remember. Each task cycle consisted of three right-visual-field trials followed by three left-visual-field trials. This right-left cycle was repeated four times per scan. The height of the square wave (b) at any given point is the predicted activation level of a brain region that is activated during a memory trial in the right visual field.

tion condition to compare activity in left- and right-hemisphere visual areas during the memory tasks.²

2. We used these empirically determined ROIs rather than Brodmann's Areas because Brodmann's Areas can be misleading as a result of the large intersubject variability in the morphology of striate and extrastriate functional borders. That is, although it is relatively obvious that the visual-stimulation condition should activate contralateral brain regions in posterior visual cortex (including striate and extrastriate regions), the assignment of Brodmann's regions to these activations should be somewhat suspect. These arguments notwithstanding, we implemented a standard Talairach transformation of individual subjects' data. This analysis revealed that the activations in the visual-stimulation condition were confined to Brodmann's Areas 17, 18, and 19.

Scanning and Analysis

Imaging was performed on a GE 1.5-T SIGNA clinical MRI scanner fitted with a high-performance local head gradient and RF coils (Wong, Bandettini, & Hyde, 1992; Wong, Boskamp, & Hyde, 1992). Functional T2*-weighted images were acquired using an echo-planar single-shot gradient-echo pulse sequence with a matrix size of 64×64 , in-plane resolution of 5×5 mm, echo time (TE) of 40 ms, flip angle of 90° , and field of view of 24 cm. A total of 136 images was acquired for each of 14 adjacent 5-mm-thick coronal slices (extending from the most posterior slice forward) in an interleaved mode with a repetition time (TR) of 2 s. All subjects were first scanned in the visual-stimulation condition. Two scan series were acquired for each memory condition; the order of the spatial and letter tasks was counterbalanced across subjects.

A motion-correction algorithm was applied to each scan's data, and an averaged data set was compiled for each memory task within each subject. Because a poststimulus undershoot (i.e., the lowering of baseline activity after the first cycle of activation) is a documented characteristic of the MR signal (Buxton, Wong, & Frank, 1997), the final 96 images (during which the baseline was stable) of the averaged scan were used for data analysis. ROIs were identified by correlating the functional data from the visual-stimulation condition with a three-cycle trapezoidal reference waveform (Bandettini et al., 1994). Clusters of two or more cortical pixels that exhibited a correlation value of at least .40 (i.e., responsive to stimulation in the RVF) or below $-.40$ (i.e., responsive to stimulation in the LVF) were included in the ROIs. The statistical analyses we present are based on the mean fractional signal change for pixels within each ROI.

RESULTS AND DISCUSSION

The right-left stimulus alternation in the memory conditions was modeled with a modified repeating square-wave function (see Fig. 1b), and this function was correlated with the fMRI signal (Bandettini et al., 1994). This analysis provided a quantitative measure of how well the time course of activation in each voxel was predicted by the model function in Figure 1b. Because the memory trials were initiated in the RVF, we predicted that signal change in visual areas of the left hemisphere would be positively correlated with the model function, and activity in the right hemisphere would be negatively correlated. This contrast in the time course of activation in the right and left hemispheres should be manifest as a positive difference between the signal change observed in these brain regions throughout the course of these

scans. That is, this difference is predicted by the hypothesis that remembering a location in the RVF leads to greater activation in left- than right-hemisphere visual areas, whereas remembering a location in the LVF causes greater right- than left-hemisphere activation.

Consistent with the hypothesis of attention-based rehearsal, every tested subject showed a statistically significant enhancement of visual responses contralateral to the memorized locations (see Fig. 2). A correlational analysis of signal change with experimental events (Bandettini et al., 1994) revealed the same pattern. The nonspatial memory task also resulted in contralateral activation (as expected, given the unilateral stimulation that occurred during the memory tasks). Thus, the key result is that this contralateral activation was significantly larger in the spatial condition than in the nonspatial condition, according to both the signal-change analysis, $t(25) = 6.5, p < .001$, and the correlational analysis, $t(25) = 4.9, p < .001$. This result was also statistically significant within each subject tested, and it suggests that the contralateral modulation observed during the spatial memory task reflected more than stimulus-driven processing.

As Figure 2 illustrates, the visual modulation in the spatial task tended to increase as the slices became more anterior, whereas the effect in the nonspatial task was relatively flat. In order to assess the statistical significance of this divergence, we grouped the three most posterior slices and the three most anterior slices into bins. An analysis of variance with subject, hemisphere (right vs. left), task (spatial vs. nonspatial), and position (anterior vs. posterior) as factors showed a significant three-way interaction among task, hemisphere, and position in both signal change, $F(1, 3) = 4.2, p < .05$, and correlation, $F(1, 3) = 6.4, p < .05$. This divergence between the spatial and letter tasks provides further evidence that the source of these contralateral effects

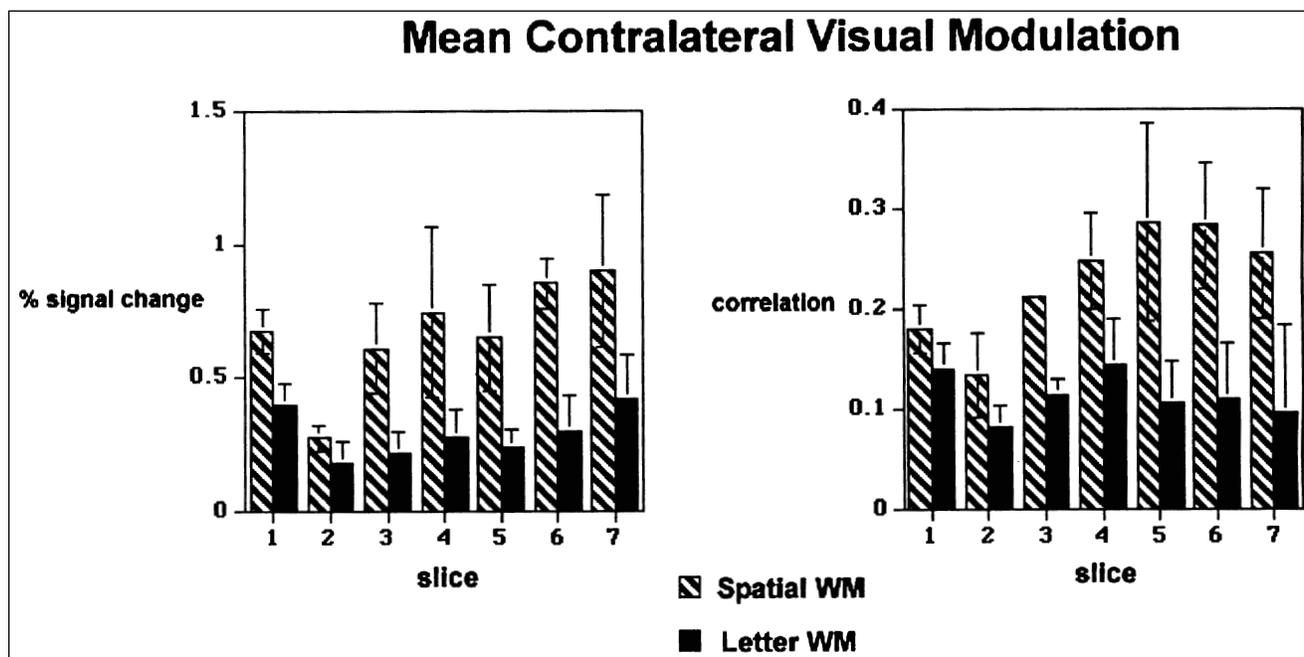


Fig. 2. The mean difference between left- and right-hemisphere activation (i.e., the degree of contralateral modulation of visual responses to the bilateral flickering display) across all subjects tested. Slices 1 through 7 cover the most posterior to the most anterior coronal sections containing visually responsive voxels. The graph on the left depicts the results in terms of the percentage of signal change, and the graph on the right depicts the results of the same comparison using correlational data (r values). "Spatial WM" refers to the results of the spatial working memory condition. "Letter WM" refers to the results of the letter working memory condition.

is qualitatively different in the two memory tasks.³ We interpret the contralateral enhancement in the letter condition to be a result of the unilateral presentation and encoding of stimuli with this display. The fact that the modulation of contralateral responses was greater in the spatial condition cannot be explained merely on the basis of the stimulus display; an attentional explanation is warranted. These data converge with previous behavioral evidence that has implicated spatial selective attention in the rehearsal of spatial information in working memory. Furthermore, the present work provides direct evidence that these spatial rehearsal effects include a modulation of early perceptual processing contralateral to memorized locations, consistent with previous studies of the neural substrates of spatial selective attention.

In sum, our results reveal a contralateral modulation of early visual processing by spatial rehearsal in working memory. We observed some visual activations during the nonspatial working memory task, an effect that provides a baseline measure of the stimulus-driven visual activations in this procedure. Thus, the fact that the modulation was reliably larger in the spatial than in the nonspatial task implicates a direct influence of a component of spatial working memory. We propose that the process in question corresponds to spatial rehearsal, and furthermore that spatial rehearsal in working memory amounts to focal shifts of spatial attention to the memorized locations.

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3. The Talairach transformations suggest that Area 17 (i.e., striate cortex) activations were largely confined to the most posterior slices measured. Although striate cortex cannot be conclusively identified on this basis, these data taken at face value suggest that the divergence between activations in the spatial and nonspatial tasks was greatest in extrastriate rather than striate cortex. Given the interpretation that attention-based rehearsal drives these differences, these data are consistent with previous evidence suggesting that attention modulates extrastriate but not striate activity (Clark & Hillyard, 1996).

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