

Effects of Memory Load and Distraction on Performance and Event-Related Slow Potentials in a Visuospatial Working Memory Task

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Abstract

■ Brain electrical activity related to working memory was recorded at 15 scalp electrodes during a visuospatial delayed response task. Participants ($N = 18$) touched the remembered position of a target on a computer screen after either a 1 or 8 sec delay. These memory trials were compared to sensory trials in which the target remained present throughout the delay and response periods. Distractor stimuli identical to the target were briefly presented during the delay on 30% of trials. Responses were less accurate in memory than sensory trials, especially after the long delay. During the delay slow potentials developed that were significantly more negative in memory

than sensory trials. The difference between memory and sensory trials was greater at anterior than posterior electrodes. On trials with distractors, the slow potentials generated by memory trials showed further enhancement of negativity, whereas there were minimal effects on accuracy of performance. The results provide evidence that engagement of visuospatial working memory generates slow wave negativity with a timing and distribution consistent with frontal activation. Enhanced brain activity associated with working memory is required to maintain performance in the presence of distraction. ■

INTRODUCTION

The term *working memory* is widely used to describe the brain processes involved in the temporary maintenance and manipulation of information selected from current events and previous experience. In animals, the neural substrates of working memory have been studied mainly using variations of the classic delayed response task (DRT) in which the animal was required to remember the location of a reward until a response was permitted (Fuster, 1991; Jacobsen, 1935). Experiments with monkeys indicate that an intact dorsolateral prefrontal cortex (PFC) is required for adequate performance on the visuospatial DRT (see Funahashi & Kubota, 1994). Monkeys with permanent or reversible (stimulation interference or cooling) lesions of the dorsolateral PFC cannot perform the task with a delay interposed between stimulus and response but perform it normally in the absence of a delay or when experimental interference is reversed (Diamond & Goldman-Rakic, 1989). Neurones in monkey PFC showed a sustained increase in firing during the delay period but no increase during a control task that did not require memory (Funahashi, Bruce, & Goldman-Rakic, 1989). Applying dopamine or

noradrenaline to the PFC enhanced the activity of PFC neurones during DRT performance (Sawaguchi, Matsuura, & Kubota, 1990). Conversely, pharmacological blockade of PFC dopamine receptors (Sawaguchi & Goldman-Rakic, 1991) or noradrenaline receptors (Li & Mei, 1994) caused a reversible decrement of spatial DRT performance.

There is some evidence that PFC control of spatial working memory in animals is contralaterally organized, with each hemisphere controlling memory for locations in the opposite visual field. Monkeys with unilateral PFC lesions were selectively impaired in DRT performance for targets appearing in the visual hemifield opposite to the lesion site (Funahashi, Bruce, & Goldman-Rakic, 1993). Some PFC cells fired during the delay only if targets fell within a preferred range of spatial positions, and these preferred spatial positions were most often in the contralateral visual hemifield (Funahashi, Charles, & Goldman-Rakic, 1991).

In humans, the crucial role of the dorsolateral PFC in working memory has been demonstrated by both clinical and experimental studies. DRT performance was selectively impaired in patients with diffuse lesions involving the PFC and/or its major subcortical connections

(Oscar-Berman, 1991). People with schizophrenia, who often have reduced PFC blood flow (Weinberger, Berman, & Daniel, 1991), had specific deficits on the DRT compared to people with bipolar disorder or normal controls (Park & Holzman, 1992, 1993). Patients with unilateral focal lesions in the dorsolateral PFC also showed impaired DRT performance (Partiot et al., 1992; Verin et al., 1993). In normal adults, DRT performance was impaired by applying transcranial magnetic stimulation to the PFC during the delay, whereas similar stimulation interference of motor cortex did not affect performance (Pascual-Leone & Hallett, 1994). DRT performance was improved in normal adult humans after ingestion of the dopamine D2 agonist, bromocriptine (Luciana, Depue, Arbis, & Leon, 1992). Few human studies have addressed the question of whether the PFC spatial memory is contralaterally organized, but there is some evidence for left PFC dominance rather than a contralateral organization (Pascual-Leone & Hallett, 1994; Pierrot-Deseilligny, Rivaud, Gaymard, & Agid, 1991).

Recent studies of brain activation in normal humans using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have confirmed PFC involvement in the control of working memory for letters, words, digits, faces, abstract shapes, and spatial position (see Awh et al., 1996; Cohen et al., 1994; Goldberg, Berman, Randolph, Gold, & Weinberger, 1996; McCarthy et al., 1994). While PET and fMRI can provide important spatial information about the distribution of activated regions, the temporal resolution of these techniques is insufficient to determine the sequence in which they are activated. Moreover, task performance may have to be maintained for up to several minutes to generate images. While event-related potentials (ERPs) lack the spatial resolution of PET and fMRI, they do have millisecond resolution that is better suited to the sequencing of evanescent cognitive processes.

Recent ERP studies have shown that certain slow potentials are associated with working memory (Lang, Starr, Lang, Lindinger, & Deecke, 1992; Rämä, Carlson, Kekoni, & Hämäläinen, 1995; Ruchkin, Canoune, Johnson, & Ritter, 1995; Ruchkin et al., 1994; Ruchkin, Johnson, Grafman, Canoune, & Ritter, 1992). These slow potentials were found to index working memory, not just preparatory processes (Ruchkin et al., 1995) and showed different topographies in visual compared to auditory tasks (Lang et al., 1992; Ruchkin et al., 1992). While several ERP studies have used delayed match to sample tasks (Lang et al., 1992; Ruchkin et al., 1992, 1994, 1995), there has been only one preliminary ERP study of a visuospatial DRT in humans (Rämä et al., 1995). They reported increased negative slow potential activity during the delay interval for memory compared to control trials (Rämä et al., 1995). However, the control task differed from the memory task in several respects, making it difficult to ascribe the increased negativity to working memory processes alone. Ruchkin et al. (1995) showed

that the best way to distinguish working memory operations from other processes was to manipulate memory load and demand, which highlights the importance of using a control task as similar as possible to the memory task and varying working memory load systematically.

One method of increasing the load on working memory is to employ distraction during the delay. Inhibition of distractor information in humans has been shown by behavioral methods to be difficult and selective (Tipper, Weaver, & Houghton, 1994). Distractor items had a greater effect on memory performance when they were more similar to the target, causing decreased recognition for the target in both auditory (Baddeley, 1990, p. 274) and visual (Loftus, 1979) modalities. Distractors decreased monkeys' performance on the DRT (Bartus & Dean, 1979; Arnsten & Contant, 1992). The detrimental effect of distraction was particularly marked in aged monkeys (Bartus & Dean), who have catecholamine depletion in the PFC (Arnsten & Goldman-Rakic, 1985). When aged monkeys were given $\alpha 2$ adrenergic agents before performing the DRT, their performance was restored to nondistracted levels (Arnsten & Contant, 1992).

The experiment reported in this paper used a visuospatial DRT that was formally the same as that used in the monkey studies referred to above and similar to the tasks used in human studies by Park and Holzman (1992) and Luciana et al. (1992). Whereas the latter studies used solely behavioral measures, both behavioral measures and ERPs were recorded in the present study. The task required the participant to fixate on a central spot on a computer screen. A target whose location had to be remembered was then presented briefly (150 msec) in peripheral vision. After a variable delay the fixation point disappeared. This was the signal for the participant to respond by touching the remembered location of the target. Sensory trials in which the target remained visible during the delay were randomly intermixed with memory trials to eliminate the adoption of different strategies that could occur if memory and sensory trials were presented in blocks as is necessary with functional imaging studies using PET and fMRI. We predicted that behavioral performance would be less accurate on trials requiring use of working memory and that the difference would be greater at long than short delay intervals. ERP slow wave amplitudes were expected to show a difference between memory and sensory trials, particularly at anterior electrodes.

The difficulty of the task was increased by presenting the target at up to 360 possible positions separated by 1° intervals instead of the eight or sixteen discrete positions used in previous studies. Response accuracy was measured by the extent of position displacement from the target (see Luciana et al., 1992), as well as by the more commonly used percentage correct measure, because we thought the latter might not be sensitive enough in motivated young university students. Incen-

tive for students to perform at their best was achieved by giving a monetary reward that was graded and dependent on accuracy. The effect of delay length was investigated by including a short (1 sec) and a long (8 sec) delay. The 8-sec delay was chosen because DRT performance of normal adults was significantly less accurate at an 8-sec delay than at a 0-sec delay in previous studies (Luciana et al., 1992; Spitzer, 1993). Performance and ERPs were compared for left visual field (LVF) and right visual field (RVF) targets. Distracting stimuli were presented during the delay on some trials to further engage working memory functions. We predicted that distractors would decrease accuracy, particularly on memory trials, and would change ERP amplitudes.

RESULTS

Excluded Trials

Trials containing either incorrect motor responses or electrical artifacts were excluded from further analysis. The 26.3% rejected trials were made up as follows: electrooculogram (EOG) artifact 10.8%; electroencephalogram (EEG) artifact 9.1%; inaccurate response ($>2^\circ$ radius from target) 4.0%; too slow (>1500 ms) 1.4%; too fast (<200 msec) 0.9%; perseveration of previous response 0.16%; distractor position touched 0.02%.

Motor Performance

Accuracy measures were Percentage Correct and Position Displacement. Percentage Correct was the proportion of artifact-free trials that had responses within timing and accuracy limits. Position Displacement was the distance between the screen touch point and the target center. Reaction times were divided into Response Initiation and Movement Time. Response Initiation was

the time taken to lift the hand off the response pad after the fixation point disappeared. Movement Time was the time between lifting the hand off the response pad and touching the screen. All the performance measures were analyzed using four-way ANOVAs for Trial type (sensory, memory) \times Delay interval (1 sec, 8 sec) \times Visual field (left, right) \times Distractor (distractor present, distractor absent; see results in Tables 1 and 2). Position Displacement and reaction time measures were based on correct, artifact-free trials only.

Accuracy

Percentage of trials correct was significantly greater for sensory than memory trials and significantly greater than 1-sec than 8-sec trials. These effects interacted because the decrease in Percentage Correct with the longer delay was larger on memory trials ($F(1, 17) = 45.22, p < 0.001$) than on sensory ones ($F(1, 17) = 6.50, p < 0.025$; see means in Table 2). Distractor presence interacted with Delay. Presentation of a distractor significantly reduced the percentage of trials correct (from 89 to 85%) in long-delay trials ($F(1, 17) = 6.67, p < 0.025$). The presence or absence of a distractor did not affect the Percentage Correct of short-delay trials (96% correct for both nondistractor and distractor trials; $F < 1.00$). Visual field did not affect Percentage Correct.

Of correct responses, pointing responses were more accurate for sensory than memory trials (Position Displacement) and were more accurate at the 1-sec than the 8-sec delay. The interaction between these effects showed that the longer delay increased Position Displacement on memory trials ($F(1, 17) = 39.99, p < 0.001$) but not on sensory trials ($F < 1.00$; see means in Table 2). Position Displacement was also increased for targets in RVF (7.9 ± 0.4 mm) compared to the LVF (6.9 ± 0.3

Table 1. *F* values for ANOVAS on Accuracy and Reaction Time Measures.

Source of Variation	df	Accuracy		Reaction Time	
		% Correct	Position	Initiation	Movement
Trial type (TT)	1, 17	24.34 ^a	194.74 ^a	<1.00	<1.00
Delay (D)	1, 17	43.88 ^a	22.59 ^a	18.49 ^a	15.24 ^a
Visual field (VF)	1, 17	<1.00	4.76 ^b	7.19 ^b	7.46 ^c
Distractor (DT)	1, 17	4.34	1.41	18.53 ^a	3.41
TT \times D	1, 17	16.68 ^a	27.07 ^a	9.44 ^c	1.22
TT \times VF	1, 17	<1.00	4.37 ^b	<1.00	1.63
TT \times DT	1, 17	2.17	<1.00	31.43 ^a	<1.00
D \times DT	1, 17	6.61 ^b	<1.00	13.96 ^c	<1.00

^a $p < 0.001$.

^b $p < 0.05$.

^c $p < 0.01$.

Table 2. Means (\pm SE) for Accuracy and Reaction Time Measures

Measure	Delay	Means (\pm SE)	
		Sensory	Memory
Accuracy			
Percentage Correct	1	97.9 \pm 0.4%	94.5 \pm 1.0%
	8	93.8 \pm 1.5%	80.0 \pm 2.8%
Position Displacement	1	3.6 \pm 0.2 mm	6.9 \pm 0.3 mm
	8	3.6 \pm 0.2 mm	8.0 \pm 0.3 mm
Reaction Time			
Response Initiation			
Distractor	1	357.7 \pm 9.0 msec	365.3 \pm 8.5 msec
	8	378.8 \pm 8.2 msec	391.2 \pm 6.6 msec
Nondistractor	1	382.3 \pm 10.2 msec	366.6 \pm 7.1 msec
	8	383.0 \pm 9.1 msec	383.7 \pm 8.2 msec
Movement Time			
	1	790.1 \pm 18.9 msec	777.1 \pm 17.6 msec
	8	808.7 \pm 17.7 msec	805.8 \pm 14.4 msec

mm) on memory trials ($F(1, 17) = 6.64, p < 0.025$) but was not affected by Visual field on the sensory trials (RVF 3.6 \pm 0.4 mm, LVF 3.5 \pm 0.2 mm; $F < 1.00$). Distractors had no effect on pointing accuracy.

Reaction Time

Response Initiation and Movement Time were faster at the short than the long delay, and faster for RVF targets (Initiation 373.4 \pm 7.9 msec; Movement 789.8 \pm 15.1 msec) than for LVF targets (Initiation 379.0 \pm 7.8 msec; Movement 801.1 \pm 14.8 msec). Faster Response Initiation for the short delay trials was more pronounced on memory trials ($F(11, 17) = 29.55, p < 0.001$) than on sensory ones ($F(1, 17) = 6.07, p < 0.025$; see means in Table 2). Responses were also initiated more quickly in the presence of a distractor in sensory trials ($F(1, 17) = 35.66, p < 0.001$) but not in memory trials ($F(1, 17) = 3.70, ns$) and at the short delay ($F(1, 17) = 22.68, p < 0.001$) but not at the long delay ($F < 1.00$; see means in Table 2).

Event-Related Potentials

Short Delay

The grand mean waveforms for the short delay, pooled over 1- and 8-s delay trials, are shown in Figure 1. Presentation of the target in both sensory and memory trials elicited a negative peak (N2) with a latency of approximately 200 msec and a positive peak (P3) with a latency

of 300 to 400 msec. No analysis of these components was performed. Following the P3 a slow wave was evoked and was present throughout the delay. The grand mean waveforms showed marked differences between sensory and memory trials in slow wave amplitude and topography during the delay. The slow wave was quantified by dividing the delay into two 500-msec epochs over two latency ranges (150 to 650 and 650 to 1150 ms posttarget). ANOVA results for midline (Trial type \times Visual field \times Midline Site) and lateral (Trial type \times Visual field \times Lateral Site \times Hemisphere) analyses of these epochs are shown in Table 3. Distractor trials were excluded from these analyses because of the variable time of distractor onset during the first second of the delay.

In the first 500 msec of the delay, although Trial type had no main effect, it varied with both Visual field and Site. Slow wave negativity was greater on memory than sensory trials when targets were presented to the LVF (midline difference = 1.0 μ V, $F(1, 17) = 10.66, p < 0.01$; lateral difference = 0.6 μ V, $F(1, 17) = 6.94, p < 0.025$), but Trial type did not affect amplitude for RVF targets, $ps > 0.10$. The interaction with Lateral Site indicated at Anterior Lateral sites (F7 and F8) memory trials had greater positive amplitudes (0.5 \pm 0.6 μ V) than sensory trials (0.0 \pm 0.6 μ V; $F(1, 17) = 9.88, p = 0.006$). Inspection of the grand mean waveforms revealed that the difference may be due to a negative peak that was more prominent in sensory trials to targets presented in the RVF (see Figure 1).

In addition to the Trial type effects at midline sites a Site main effect indicated maximal slow wave negativity

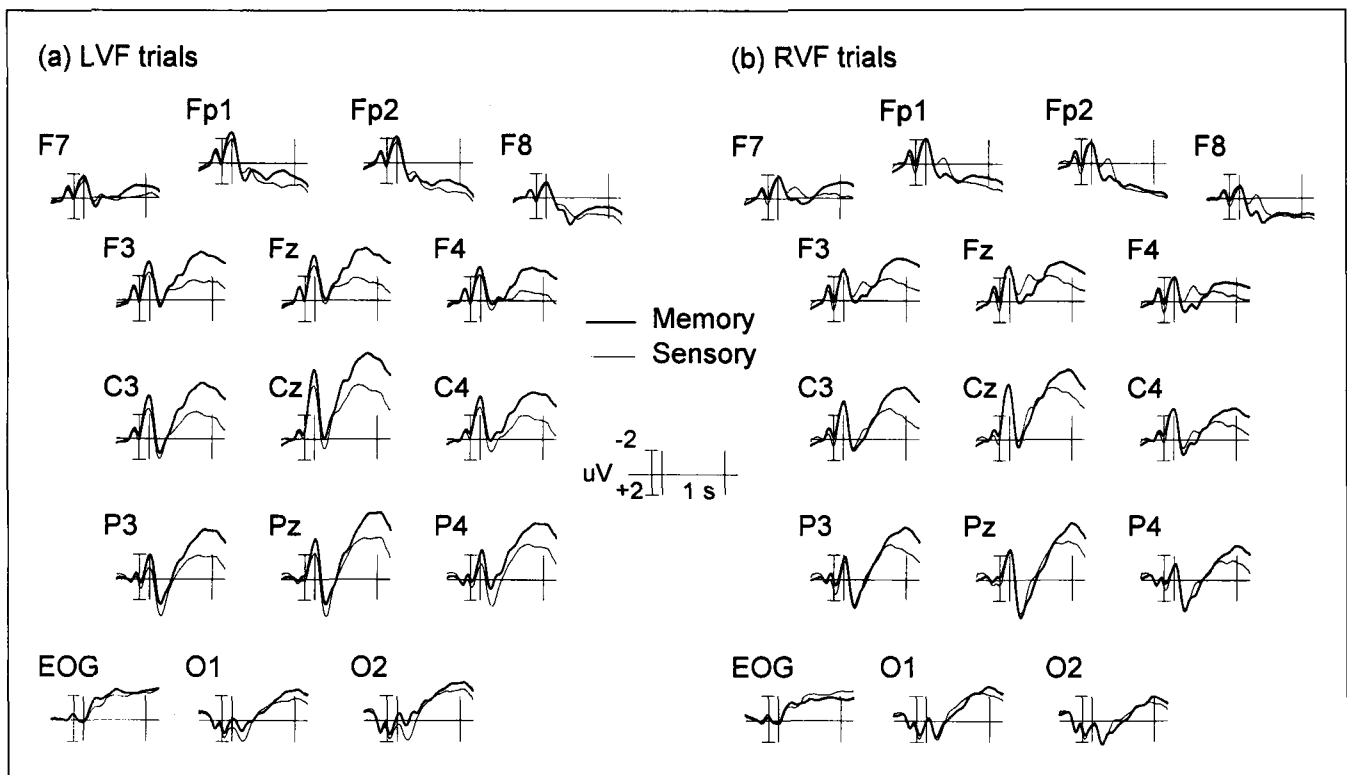


Figure 1. Grand mean waveforms obtained in 18 participants to (a) LVF and (b) RVF targets in sensory (thin) and memory (thick) trials. Waveforms were pooled over 1-sec and 8-sec delays and averaged with respect to target onset (time 0), using a 350-msec pretarget baseline. Vertical markers at 150 and 1150 msec indicate the beginning (time of target offset in memory trials) and end (fixation offset) of the delay, respectively. ERP recordings were from 15 electrode sites (10/20 electrode system), referenced to linked ears. EOG was recorded from the upper orbital ridge and outer canthus of the left eye.

at Cz, and a Visual field \times Site interaction indicated a trend toward greater negativity for LVF than RVF targets at Pz (difference = 0.7 μ V; $F(1, 17) = 4.15, p = 0.057$). At lateral sites Visual field, Site, and Hemisphere interacted with each other. Negativity was greater over left than right hemisphere at Prefrontal, Anterior temporal, and Frontal sites and was maximal at F3 (see Figure 1). Left hemisphere sites were not affected by the Visual field of the target, but two right hemisphere posterior electrodes, P4 and O2, showed greater negativity after the LVF than RVF targets (P4 difference = 1.3 μ V, $F(1, 17) = 16.05, p < 0.001$; O2 difference = 1.2 μ V, $F(1, 17) = 12.55, p < 0.004$).

In the second 500 msec of the delay there was a main effect of Trial type due to greater negativity on memory than sensory trials at midline (difference = 1.7 μ V) and lateral (difference = 1.1 μ V) sites. At midline sites, the greater negativity of memory trials was significant for LVF targets (difference = 2.4 μ V; $F(1, 17) = 21.69, p < 0.001$) but not RVF targets (difference = 1.0 μ V, $p > .05$). At lateral sites, the Trial type effect was localized to Frontal and Central sites, $ps < 0.001$ (see Figure 1). The Trial type \times Site interaction at Lateral sites also indicated a topography difference between memory and sensory

trials since slow wave negativity had a more anterior maximum on memory trials than on sensory trials (Central versus Central-Parietal maximum).

The main effects of Site in the second 500 msec indicated maximum negativity at Central sites for both midline and lateral sites. Negativity was greater over the left ($-1.7 \pm 0.6 \mu$ V) than over right hemisphere ($-0.8 \pm 0.6 \mu$ V). Interactions involving Visual field, Site, and Hemisphere were similar to the interactions in the first 500 msec. The greater negativity over left hemisphere was significant at Prefrontal, Anterior temporal, Frontal and Central sites. There was greater negativity for LVF than RVF targets at the right hemisphere posterior electrodes, P4 and O2, $ps < 0.001$, but the Visual field did not affect left hemisphere or anterior electrodes.

Long Delay

Grand mean waveforms for the long delay are shown in Figure 2 (nondistractor trials) and Figure 3 (distractor trials). After the first second, the negative slow wave previously described peaked and then decreased in amplitude, becoming positive in polarity around 3 to 4 sec

Table 3. ANOVA Results for Average Amplitudes During the Short Delay^a

Source of Variation	150-650 msec		650-1150 msec	
	df	F	df	F
Midline Electrodes				
Trial type (TT)	1, 17	<1.00	1, 17	16.88 ^b
Site (S)	2, 34	10.69 ^b	2, 34	13.42 ^b
TT × Visual field (VF)	1, 17	14.84 ^b	1, 17	5.51 ^c
VF × S	1, 25	5.23 ^c	1, 23	1.69
Lateral Electrodes				
Trial type (TT)	1, 17	<1.00	1, 17	14.74 ^b
Site (S)	2, 26	1.13	2, 29	13.20 ^b
Hemisphere (H)	1, 17	2.59	1, 17	21.75 ^b
TT × VF	1, 17	8.22 ^c	1, 17	2.17
TT × S	2, 25	3.63 ^c	2, 32	6.57 ^d
VF × S	2, 31	3.38 ^c	2, 30	1.08
VF × H	1, 17	11.40 ^d	1, 17	38.89 ^b
S × H	3, 53	4.11 ^c	3, 54	5.48 ^d
VF × S × H	2, 42	13.86 ^b	2, 39	26.85 ^b

^a Target offset in memory trials occurred at 150 msec, which represents the start of the delay interval.

^b $p < 0.001$.

^c $p < 0.05$.

^d $p < 0.01$.

Figure 2. Grand mean waveforms obtained in 17 participants, for sensory (thin) and memory (thick) trials without distractors, over the 8-sec delay. Vertical markers at 150 and 8150 msec indicate the beginning (time of target offset in memory trials) and end (fixation offset) of the delay, respectively.

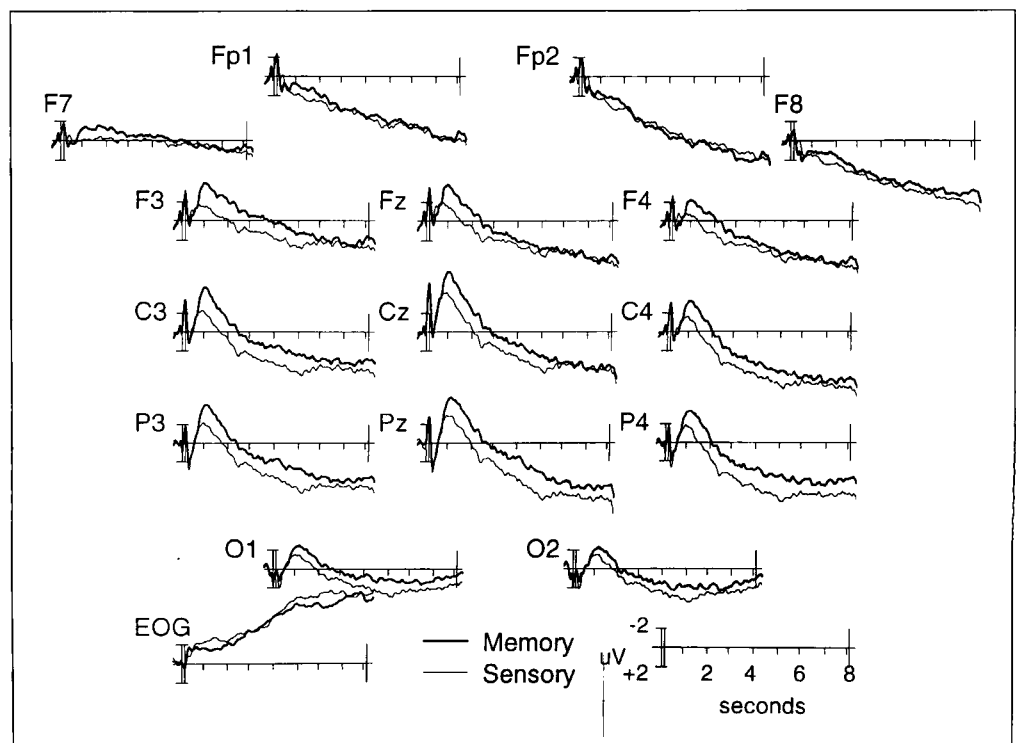


Figure 3. Grand mean waveforms obtained in 17 participants, for sensory (thin) and memory (thick) trials with distractors, over the 8-sec delay.

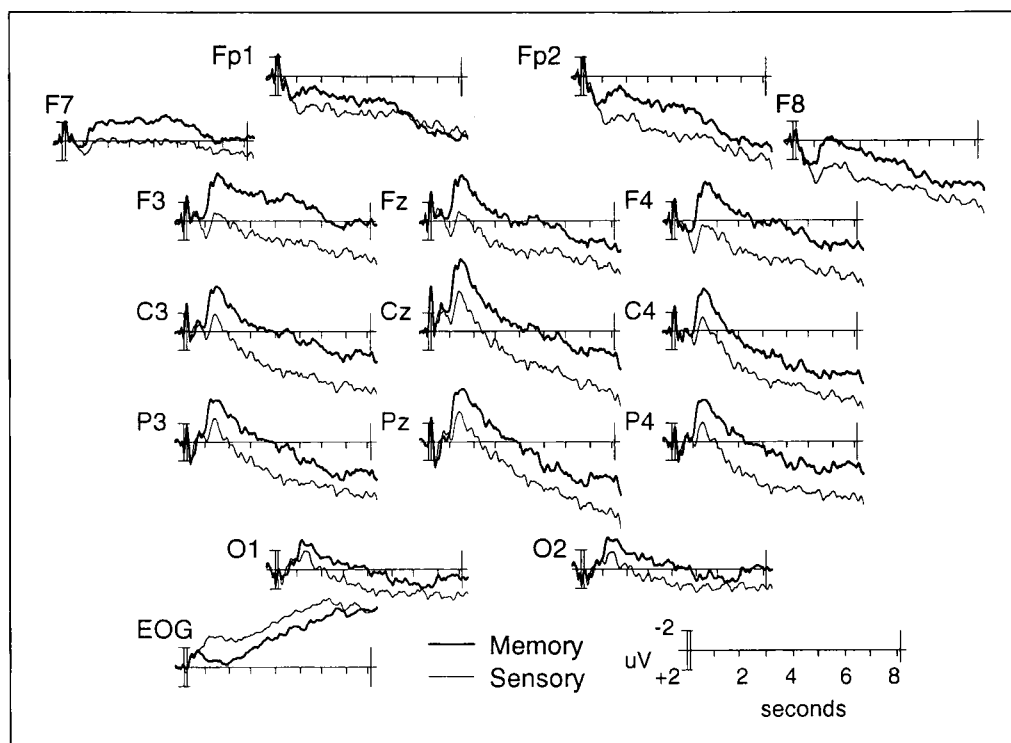


Table 4. ANOVA Results for Average Amplitudes During the Long Delay.

Source of Variation	df ^a	Second of the Delay						
		2	3	4	5	6	7	8
Midline Electrodes								
Trial type (TT)	1, 16	8.28 ^b	5.37 ^b	3.71	4.34	3.15	2.77	4.03
Distractor (DT)	1, 16	13.21 ^c	9.30 ^c	1.89	2.87	2.68	<1.00	<1.00
Site (S)	2, 32	8.55 ^c	2.29	<1.00	5.11 ^b	7.84 ^c	5.49 ^c	3.41 ^b
Lateral Electrodes								
Trial type (TT)	1, 16	7.28 ^b	4.71 ^b	3.89	4.45	3.34	2.33	3.33
Distractor (DT)	1, 16	9.41 ^c	14.36 ^c	3.79	4.48 ^b	3.99	<1.00	<1.00
Site (S)	5, 80	9.52 ^d	5.13 ^c	5.08 ^c	5.74 ^c	5.70 ^c	6.27 ^d	7.66 ^d
Hemisphere (H)	1, 16	24.26 ^d	18.67 ^d	20.73 ^d	19.78 ^d	20.84 ^d	17.92 ^d	16.53 ^d
TT × S	5, 80	4.49 ^b	4.53 ^c	3.79 ^b	3.08 ^b	3.01 ^b	3.39 ^b	4.58 ^c
DT × S	5, 80	4.11 ^b	1.97	<1.00	<1.00	<1.00	<1.00	<1.00
DT × H	1, 16	4.85 ^b	2.62	1.54	<1.00	<1.00	<1.00	1.27
S × H	5, 80	7.09 ^d	7.28 ^d	10.29 ^d	12.78 ^d	16.88 ^d	19.21 ^d	18.76 ^d
TT × S × H	5, 80	<1.00	1.36	1.99	2.23	2.32 ^b	2.62 ^b	2.40 ^b

^a Uncorrected degrees of freedom.

^b $p < 0.05$.

^c $p < 0.01$.

^d $p < 0.001$.

in the delay. The grand mean waveforms showed differences between memory and sensory trials that were enhanced in the presence of distractors (compare Figures 2 and 3). Average amplitudes were compared at 1-sec epochs for the second through eighth seconds of the delay. ANOVA results for midline (Trial type \times Distractor \times Midline Site) and lateral (Trial type \times Distractor \times Lateral Site \times Hemisphere) analyses of these epochs are shown in Table 4. Because only 30% of the trials contained a distractor, LVF and RVF trials were pooled for these analyses to ensure reliable slow potential measurement for the distractor trials.

Negativity was significantly greater for memory than sensory trials at both midline and lateral sites in the second and third epochs of the delay (differences of 2.3 to 3.3 μ V). Topography of the slow wave at midline sites was the same for both sensory and memory trials, showing maximal negativity at Cz in the second and third epochs and maximal positivity at Pz in the fourth through eighth epochs. Midline electrodes showed no Trial type effects in the fourth through eighth epochs. At lateral electrodes, negativity was maximal at Parietal sites (P3, P4) in the second epoch. The positivity at lateral electrodes in the third through eighth epochs had two maxima: Prefrontal (Fp1, Fp2) and Central (C3, C4) sites (see Figures 2 and 3). Negativity was greater over the left hemisphere in all epochs examined. This hemispheric effect was significant at the anterior electrodes (Prefrontal, Anterior temporal, Frontal, and Central) but not the posterior electrodes (Parietal, Occipital). Trial type interacted with Lateral Site in all epochs. The simple effect of Trial type was closest to significance at the Frontal sites (F3, F4) in each epoch (p s < 0.05; a Bonferroni-corrected alpha level of 0.008 was required for significance). In the final 3 sec of the delay the Trial type effect was lateralized to the left hemisphere Frontal electrode, F3 ($F(1, 16) = 8.63, p = 0.01; 5.45, p = 0.033; \text{and } 7.37, p = 0.015$; for the sixth, seventh and eighth seconds respectively).

Trials in which a distractor was presented elicited greater slow wave negativity compared to nondistractor trials in the second and third seconds of the delay (midline and lateral sites, differences of 0.7 to 1.7 μ V) and the fifth second (difference = 1.4 μ V at lateral sites). Visual inspection of Figures 2 and 3 suggests that the distractor effect was more pronounced on memory than sensory trials (also see Figure 4). Therefore separate ANOVAs were run for sensory and memory trials, with the factors of Distractor \times Site (midline sites) and Distractor \times Site \times Hemisphere (lateral sites). These analyses showed greater negativity after distractors occurred on memory but not sensory trials, in the second epoch of the delay (midline and lateral sites) and the third through fifth epochs (lateral sites only). The Distractor effects in the second epoch were significant over Central and Parietal electrodes only, p s < 0.001 and were significant over the right hemisphere ($F(1, 16) = 13.94, p < 0.01$)

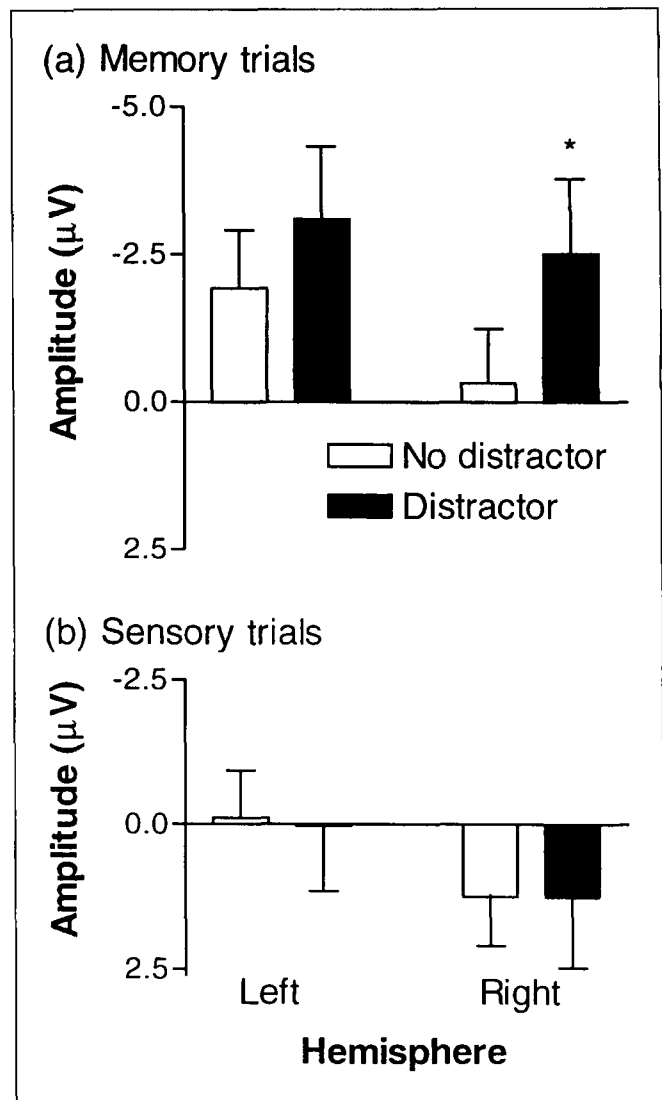


Figure 4. Distractor effect over each hemisphere in (a) memory and (b) sensory trials for the epoch 1150 to 2150 msec after target onset. Means (\pm Standard Errors) of slow potential average amplitudes are shown, with negative amplitudes above the x axis. *Significantly different from memory no distractor trials, $p = 0.028$.

but not over the left hemisphere ($F(1, 16) = 3.27, ns$; see Figure 4).

DISCUSSION

Memory Effects

Pointing accuracy on memory trials was significantly decreased at the 8-sec delay compared to the 1-sec delay, with a magnitude comparable to previous findings in normal adults (Luciana et al., 1992; Spitzer, 1993). Responses on sensory control trials did not decrease in accuracy with the longer delay and were significantly more accurate than the memory trial responses even with a 1-sec delay. These results suggest that the visuo-

spatial memory representation of the target degrades rapidly. In contrast to previous studies that have found no accuracy differences with visual hemifield (Park & Holzman, 1992; Rämä et al., 1995), performance on memory trials was found to be more accurate for LVF than RVF targets. The use of a greater number of target locations than in previous studies may have increased the sensitivity of the DRT to a right hemisphere advantage for visuospatial working memory.

Reaction time did not differ between memory and sensory trials, although previous studies have found slower reaction times on memory than sensory trials (Park & Holzman, 1992; Rämä et al., 1995) and with greater working memory load (Roberts, Hager, & Heron, 1994). Distractor trials showed trends toward faster responses on sensory than memory trials, but nondistractor trials did not. Reaction times may have been affected by a performance strategy whereby participants attempted to maximize their accuracy reward in the easiest conditions (sensory trials without distractors) by taking longer to respond. The faster responses found on short-delay trials may have been partly due to target onset acting as a forewarning signal for the response signal (fixation offset). Reaction time benefits from a forewarning signal are greater with fixed than variable delays, and are greater at a 1-sec than 8-sec delay (Rockstroh, Elbert, Birbaumer, & Lutzenberger, 1982).

Greater negativity of slow potentials in memory than sensory trials presumably reflects activation of working memory processes. Increased negativity is consistent with previous findings (Rämä et al., 1995; Ruchkin et al., 1992, 1995). The increased negativity cannot be attributed to preparatory processes during the delay or before each trial since the sensory trials required similar response preparation to the memory trials and were intermixed with memory trials. Greater negativity on memory trials may be the human equivalent of the sustained excitation seen in microelectrode recordings of monkey PFC neurons. PFC neurons show a sustained increase in firing during the delay of memory but not sensory control trials (Funahashi et al., 1989).

The topography of the negative slow potential in this study was consistent with frontal activation during working memory trials. Enhanced negativity for memory trials compared to sensory trials was significant at Frontal (F3, F4) and Central (C3, C4) lateral electrodes in the second 500 msec of the delay. In the second through eighth seconds, the effect was strongest at Frontal electrodes. This finding thus replicates and extends the findings of Rämä et al. (1995), who found greater negativity on memory than sensory trials at F3, F4, and C3 but did not include lateral posterior electrodes. ERP studies using delayed matching tasks found that the increase in slow potential negativity with increased memory load had a posterior maximum after visual stimuli and an anterior maximum after phonological stimuli (Lang et al., 1992; Ruchkin et al., 1992, 1994, 1995). The topographical dif-

ferences between visuospatial delayed matching and visuospatial delayed response could be due to the requirement to remember a visual array rather than one location or to different memory strategies when recognition rather than recall is required.

The Trial type effect on amplitude was largest relatively early in the delay, from 0.5 to 3 sec after target onset, although all epochs had significant interactions involving Trial type. This timing suggests that working memory activity is most important early in the delay. Supporting evidence comes from the finding that electrical stimulation of the PFC was most disruptive to DRT performance in monkeys when the interference occurred early in the delay (Stamm, 1969). The early part of the delay may be used for encoding the memory trace, while the later part of the delay is used for rehearsal and maintenance, which may take less effort. The early onset of working memory effects in both performance and ERP results suggests that delays of 1 to 3 sec would be sufficient for future studies.

Interpretation of the Trial type difference relies on matching of sensory and memory trials. The sensory trials were not perfectly matched with the memory trials since they had a sustained visual stimulus that may have made it more difficult to inhibit the response until the imperative signal. Inhibitory processes would be expected to involve working memory and PFC functioning (Diamond, 1990) and could therefore decrease the difference in working memory demand between sensory and memory trials. The smaller Trial type effects later in the delay could be due to increased effort of inhibiting the response in sensory trials. However, participants were well trained, and anticipatory responses occurred on less than 1% of trials, suggesting that inhibition of responding until the appropriate time was relatively easy. Also, in easy trials participants used the sensory condition to their advantage by responding more slowly to increase their accuracy.

Effects of Distraction

Distraction reduced the percentage of correct trials on long-delay trials but did not affect accuracy on the short-delay trials. Position Displacement of correct trials was not affected by distraction, and responses to the distractor position rather than the target position were rare. The small effect of distractors on accuracy suggests that overcoming the distraction of the extra stimulus was relatively easy for the young adult participants. When distractors require more effort to distinguish them from targets, performance declines, showing decreased accuracy (Baddeley, 1990, p. 274) and increased reaction time (Tipper et al., 1994). Greater effects of distraction on performance would be expected with distractors that were more similar to the target (e.g., could appear close to the target as well as in the opposite visual field to the target), under conditions of greater working memory

load, or with older participants (Arnsten & Contant, 1992; Daigneault & Braun, 1993).

An unexpected effect of distractors was found on Response Initiation. Distractors decreased reaction times on sensory but not memory trials and at the short but not the long delay, suggesting that the distractor interfered with the speed accuracy trade-off strategy of taking more time to respond to visible targets. It seems counterintuitive to associate slower reaction times with easier trials and faster reaction times with more difficult trials. However, this interpretation holds because participants were rewarded for accuracy within a fixed time limit. A subsequent experiment that rewarded speed as well as accuracy decreased slow responses on sensory trials (Watson, 1996).

In contrast to its small effects on performance, distraction produced an obvious enhancement of slow potential negativity on memory trials. The increased negativity suggests that maintaining performance in the presence of distraction was difficult, requiring increased brain activity associated with working memory. The duration of the distractor effect for several seconds after distractor offset was too long to be explained by simple visual processing alone. Increased slow wave negativity also occurs with increased working memory load (Ruchkin et al., 1995), suggesting that the distractor further loaded working memory. The distraction and Trial type effects differed in their topographies. Enhanced negativity on memory trials was largest at Frontal sites, whereas enhanced negativity due to distraction was largest at Central and Parietal sites in the second epoch and was widespread in later epochs. Thus early processing of the distractor may have involved the parietal cortex, which was activated during working memory for visual stimuli in previous ERP (Ruchkin et al., 1992, 1995) and functional imaging studies (Goldberg et al., 1996).

Laterality Effects

Laterality effects can be explained most parsimoniously as a combination of right-hand response effects and right hemisphere superiority for visuospatial working memory encoding. Faster responses to RVF targets were probably due to the right unimanual response. More direct pathways for RVF targets due to left hemisphere reception and response execution, and crossing the body midline for left target pointing probably combined to make the right target location faster. With oculomotor responses, equivalent reaction times for left and right targets were found (Rämä et al., 1995). The greater negativity at anterior electrodes over the left hemisphere than over the right hemisphere, from 0.5 to 8 sec of the delay, was probably due to left frontal preparation for the right-hand motor response. A similar effect has been reported with an onset of 0.5 to 3 sec before a smooth, goal-directed movement (Rockstroh et al., 1982), but preparation for a response at either a 1- or 8-sec delay

may have extended its duration in this experiment. Further research that manipulates the response hand is required to clarify whether these effects were due to the response hand.

The greater accuracy on memory trials with LVF than RVF targets implies right hemisphere superiority for visuospatial target location. Behavioral studies have supported right hemisphere superiority for a range of visuospatial tasks (Bradshaw & Nettleton, 1983). It could be argued that slower responses to LVF targets could be responsible for increased accuracy in the LVF. If this had occurred, LVF targets should have been more accurately located on sensory as well as memory trials. However, the visual field affected accuracy only on memory trials, whereas LVF reaction time was slower on both sensory and memory trials. Therefore it is reasonable to suggest that the effect of the visual field on accuracy was independent of speed of response and was not simply due to the right-hand response.

Two ERP findings were consistent with the performance data in suggesting right hemisphere superiority for maintaining target location in working memory. First, in the first 500 msec of the delay, negativity was greater on memory than on sensory trials for LVF but not RVF targets. This effect for LVF targets cannot be attributed to right-hand responding. If the hand of response was implicated in the visual field difference, both sensory and memory trials should have shown increased negativity for LVF targets. Second, greater negativity over Parietal (P4) and Occipital (O2) electrodes occurred for LVF compared to RVF targets in both epochs of the short delay. This finding suggests asymmetrical encoding of target location with greater activation of right posterior brain regions. Right hemisphere dominance for visuospatial working memory is supported by imaging studies (Jonides et al., 1993; McCarthy et al., 1994).

However, hemispheric asymmetry was not restricted to an early right hemisphere advantage. In the final 3 sec of the 8-sec delay the greatest difference between sensory and memory trials was recorded over the left hemisphere at F3. Retrieval of the target location might be controlled in the left hemisphere. PET imaging has shown changes in hemispheric control at different stages of memory processing. During a verbal memory task, left PFC activation was found during encoding and right PFC activation was found during retrieval (Shallice et al., 1994). The nonverbal ERP asymmetries observed in this study are consistent with right hemisphere encoding coupled with left frontal retrieval. Lesion and stimulation studies in humans have previously suggested that left PFC damage is more disrupting to DRT performance than right PFC damage (Pascual-Leone & Hallett, 1994; Pierrot-Deseilligny et al., 1991). The present results suggest that the left and right hemispheres have different roles in working memory, so different task designs could show greater effects of either left or right hemisphere disruption. There was no clear support for the finding in

monkeys that the PFC in each hemisphere predominantly maintains contralateral targets in working memory (Funahashi et al., 1991, 1993).

Conclusions

Demand on working memory when a series of target locations need to be memorized and the responses were delayed were shown by decreased response accuracy and increased negativity of slow potentials generated by anterior brain areas. Accuracy of target localization declined substantially within 1 sec, and working memory potentials were greater relatively early during the delay. Distractors increased the negativity on memory trials but had few effects on sensory control trials or on performance. These results are consistent with active maintenance of location information by a working memory processor located in the anterior cortex. The results suggested different roles of the right and left hemispheres in visuospatial working memory, but further investigation of hemispheric differences using bilaterally controlled responses is needed.

MATERIALS AND METHODS

Participants

Ten male and eight female participants were recruited from tertiary institutions and paid \$15 per session plus incentive money dependent on performance (\$34 to \$49) for their participation. They were aged between 18 and 29 years ($M = 22.1 \pm 3.2$ SD), were right-handed (Annett, 1970), had corrected-to-normal vision (better than 6/12 Snellen equivalent), and were screened at interview for psychiatric or neurological abnormalities. Participants were requested to abstain from caffeine on the day of testing and from alcohol for 24 hours prior to testing. Participants gave informed written consent.

Task Description

Participants sat facing a touch-sensitive computer monitor, with their right hand resting on a 5 × 5-cm response pad placed centrally in front of them. A black hood with a 205-mm-diameter hole in the middle was fastened to the monitor face to ensure that targets at all locations were an equal distance from the edge of the screen. Each trial began with presentation of a filled black circle (0.5° visual angle in diameter), positioned in the center of the gray screen. Fixation had to be maintained on this point until it disappeared. The target, a checkered black and gray circle with a visual angle diameter of 1.5°, was presented 250 msec after fixation point onset anywhere (pseudorandomly) on an annulus (9.25° radius) from the

fixation point. The target disappeared after 150 msec on memory trials or remained visible until the end of the trial on sensory trials. A delay period of either 1 or 8 sec followed during which the fixation point remained on the screen. At the end of the delay, the fixation point disappeared, signaling to the participant to lift his or her hand off the response pad and touch the screen with a rubber tipped pointer (5-mm diameter), where the target had been presented (memory trials) or was still present (sensory trials). Once the fixation point had disappeared, eye movements to the target location were permitted.

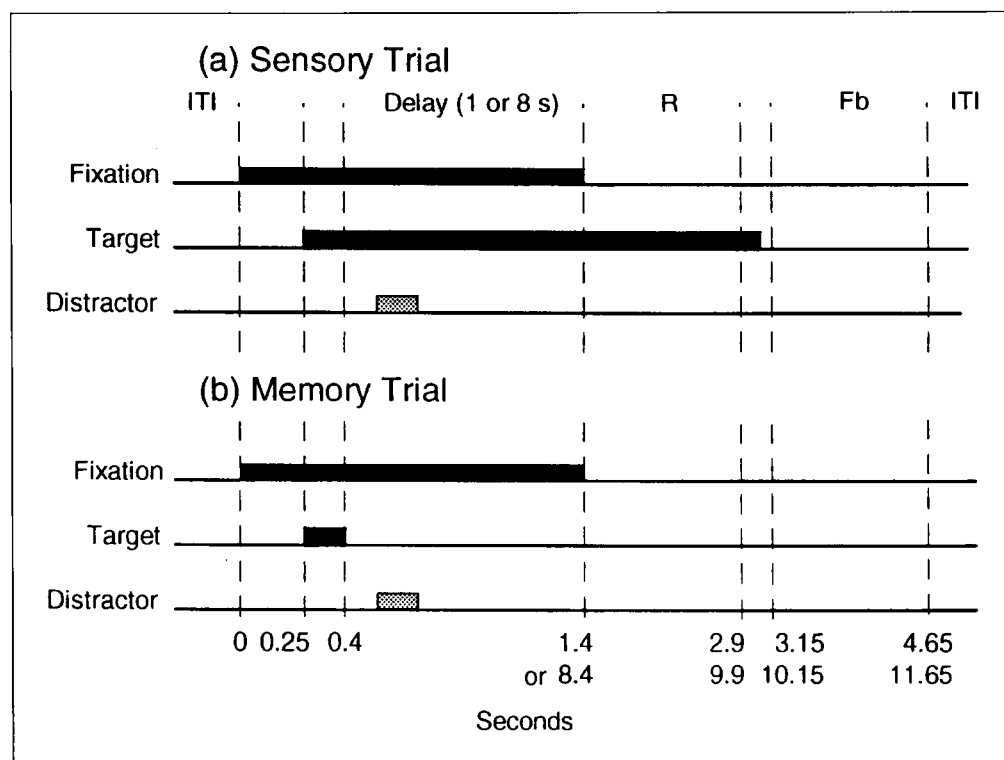
On 28.6% of the trials, a distractor, identical to the target, was presented in the opposite visual field on the same 9.25° annulus. Distractors were 150 msec long with an onset between 300 to 700 msec after target onset. Participants were instructed to ignore this “second target” if it occurred.

Responses had to be initiated (hand lifted off response pad) between 0.2 and 1.5 sec after fixation offset, and the screen had to be touched within 1.5 s and in a 2° radius of the target center. Correct responses earned a reward of 2 to 10 cents, depending on accuracy. The 2° radius around target center was divided into five concentric rings, with radii of 0.4, 0.8, 1.2, 1.6, and 2.0° respectively. Responses within the innermost ring gained 10 cents, then 8, 6, 4, and 2 cents as responses fell within rings successively further from target center. Five cents were deducted for all incorrect responses (i.e., whether responses were too fast, too slow, or located incorrectly). After the response, feedback appeared on the screen for 1500 msec. Reaction time and the amount of money won for the response were shown after correct responses. The type of incorrect response and the message “lose 0.05 c” were displayed after incorrect responses. The intertrial interval (between feedback offset and fixation onset for the next trial) varied randomly within a range of 350 to 850 msec. The events during the trial are shown in Figure 5.

Amount of Measurement

A total of 560 trials (10 blocks of 56 trials) was presented to each participant. There were 240 sensory and 240 memory trials. For both sensory and memory trials there were 120 trials at each of the delays (1 or 8 sec); thus 240 trials were presented at each delay. For each Trial type and delay, 40 trials contained a distractor and 80 trials contained no distractor; thus there were a total of 160 distractor trials and 320 nondistractor trials. Within these 480 trials, targets occurred equally often in the LVF (240 trials) and the RVF (240), excluding the positions within 7.5° of the horizontal or vertical meridia. Eighty additional nondistractor trials were presented in these meridian areas to prevent the absence of stimulation in these areas being learned (making a total of 560 trials), but the responses were excluded from analysis.

Figure 5. Sequence of events during an (a) sensory and (b) memory trial of the delayed response task. Fixation and Target were presented on every trial. Distractor (0.15 sec) occurred on 28.6% of trials. The intertrial interval (ITI) was 2.1 to 2.5 sec. Fixation point came on 0.25 sec before the Target. Memory trial target duration 0.15 sec, Sensory trial target durations of 2.65 sec at 1-sec delay and 9.65 sec at 8-sec delay. The response window interval (R) was 1.5 sec commencing 0.2 sec after fixation offset. The feedback (Fb) period of 1.5 sec informed the participant of speed, accuracy, and amount of reward.



Within each block of 56 trials, Trial type, Delay, Visual field, Distractor versus nondistractor, and meridian versus nonmeridian location occurred pseudorandomly within the a priori probability constraints described above. Each block of 56 trials lasted approximately 10 min.¹

Procedure

Participants were trained on the task in a separate session 1 to 3 days before the experimental session. In addition to training, participants were screened and assessed on various psychometric tasks including written word fluency (Thurstone & Thurstone, 1962), the National Adult Reading Test (Nelson, 1982), and the Speed and Capacity of Language Processing Test (Baddeley, Emslie, & Nimmo-Smith, 1993). Training involved the completion of one block of 56 sensory control trials, then one block of 56 memory trials, and finally two blocks containing 56 trials of sensory and memory type randomly intermixed. In all blocks, trials with 1- and 8-sec delays and distractors were included, and targets appeared pseudorandomly in the LVE/RVE, and meridians. The training session was designed to familiarize participants with the testing and recording procedures and to ensure asymptotic performance (minimum of 85% trials correct). The experimental session consisted of one practice block and ten experimental blocks. Participants rested briefly between blocks, with a refreshment break between blocks five and six.

Performance Measurement

Performance measures were defined as follows:

1. Percentage Correct: The number of correct trials without electrical artifacts, divided by the total number of artifact-free trials, multiplied by 100.
2. Position Displacement: Distance in millimeters between screen touch point and target center (calculated by Pythagorean theorem from the vertical and horizontal displacement from target center; see Luciana et al., 1992).
3. Response Initiation: Latency between fixation offset and break of hand contact with the response pad.
4. Movement Time: Latency between break of contact with the response pad and the screen touch time.

ERP Recording

Testing took place in an electrically shielded, sound attenuated cubicle with controlled temperature and humidity. EOG activity was recorded by placing 10-mm tin cup electrodes on the upper orbital ridge and outer canthus of the left eye. The Electrocap system was used to record EEG activity at 15 sites: left and right Prefrontal (Fp1, Fp2), Anterior temporal (F7, F8), Frontal (F3, F4), Central (C3, C4), Parietal (P3, P4), and Occipital (O1, O2) and midline Frontal (Fz), Central (Cz) and Parietal (Pz) sites. Recording sites had impedances below 5 k Ω and were referenced to linked ears.

Grass preamplifiers (model P511K) with a bandpass

of 0.01 to 100 Hz (down 3-dB attenuation points and 6 dB per octave roll-off rate) amplified the EOG Fp1 and Fp2 signals 5000 times and all other EEG channels 20,000 times. Amplified signals were then passed through an analogue-to-digital converter (± 5 -V input, 12-bit resolution) and sampled every 2 msec from 100 msec before the fixation point onset to 200 msec after the fixation point offset. Trials were rejected off-line if the root mean square amplitude of any EEG or EOG channel (measured over 1-sec intervals from the end of the baseline) exceeded 30 μ V. Eyeblink artifacts were removed using an eyeblink correction procedure.

Data Reduction

Data were averaged separately for Trial type, Delay, Visual field, and Distractor presence using a pretarget baseline of 350 msec. Separate averages for the LVF and RVF trials were produced, using weighting for the proportion of accepted trials in the upper and lower quadrants. ERP waveform amplitudes during the delay interval were then averaged over selected epochs for analysis. Data from the first second of the delay, grand meaned over 1- and 8-sec delay trials, were analyzed over two 500-msec epochs (i.e., relative to target onset, averages from 150 to 650 and 650 to 1150 msec). Eight-second delay trials were analyzed over 1-sec epochs (i.e., relative to target onset, averages from 1150 to 2150, 2150 to 3150, 3150 to 4150, 4150 to 5150, 5150 to 6150, 6150 to 7150, and 7150 to 8150 msec).

Statistical Analyses

To assess the effects of Trial type (sensory, memory), Delay (1 sec, 8 sec), Visual field (LVF, RVF) and Distractor (present, absent) on behavioral measures, four-way repeated measures ANOVAs were performed. Two sets of ERP analyses were performed, one for midline and one for lateral electrodes. Lateral electrodes were defined by a combination of the factors of Lateral Site (Prefrontal, Anterior temporal, Frontal, Central, Parietal, and Occipital) and Hemisphere (left, right). Midline electrodes were defined by the single factor of Midline Site (Frontal, Central, Parietal). Each time interval was analyzed separately. Epochs in the first second of the delay were analyzed at midline sites with three-way repeated measures ANOVAs (Trial type \times Visual field \times Midline Site) and at lateral sites with four-way ANOVAs (Trial type \times Visual field \times Lateral Site \times Hemisphere). The later epochs in the 8-sec delay were analyzed by three-way (Trial type \times Distractor \times Midline Site) and four-way (Trial type \times Distractor \times Lateral Site \times Hemisphere) ANOVAs. The factor of Distractor was excluded from the analyses of the first second of the delay because of the variable timing of distractor presentation during the first second. Visual field was excluded from analyses of the 8-sec delay to ensure reliable slow potential measurement for

the distractor trials. One participant with very large positive amplitudes in the last 4 sec of the delay was excluded from analysis of the 1-sec epochs but was included in the behavioral analyses and analysis of the short delay.

Greenhouse-Geisser corrections to degrees of freedom were used when Mauchly's test indicated violation of the sphericity assumption of repeated measures ANOVA ($p < .05$). Simple effects analyses were used post hoc to examine significant interactions. Pairwise comparisons were used for post hoc tests on factors with more than two levels. A familywise alpha level of 0.05 was adopted. Bonferroni corrections were used to determine the significance of post hoc tests.

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Notes

1. Only 54 trials per block were presented to the first six participants.

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