ELECTROPHYSIOLOGICAL MEASURES OF MAINTAINING REPRESENTATIONS IN VISUAL WORKING MEMORY

Andrew W. McCollough, Maro G. Machizawa and Edward K. Vogel

(University of Oregon, USA)

ABSTRACT

Visual working memory (WM) is a limited capacity system which maintains information about objects in the immediate visual environment. Recent neurophysiological and neuroimaging studies have identified sustained memory-item specific activity during the retention period of WM tasks, and this activity may be a physiological substrate of maintaining representations in WM. In the present study, we present an electrophysiological measure of delay activity using event-related potentials (ERPs). Subjects were asked to remember the items in a single hemifield presented within a bilateral display. Approximately 200 msec following the onset of the memory array, we observed a large negative wave at electrode sites that were contralateral with respect to the position of the memory items. This activity persisted throughout the retention period and appears to be an analog to delay activity observed in monkey single-unit and functional magnetic resonance imaging (fMRI) WM studies. The contralateral delay activity is modulated by the number of items in the memory array but reaches asymptote for arrays of 3 to 4 items. This activity is similar across different classes of simple objects and the amplitude is smaller on incorrect response trials relative to correct trials, suggesting that this activity is necessary for correct performance on a given trial. Together, these results appear to indicate an electrophysiological index of the maintained representations in visual WM.

Key words: visual working memory, attention, event related potentials, memory capacity, delay activity

Visual working memory (WM) is thought to be a system that facilitates our ability to maintain information about objects in the immediate visual environment so that they may be manipulated or acted upon. A fundamental property of this memory system is that it is subject to severe storage capacity limitations. Specifically, visual WM can accurately maintain approximately 3-4 object representations at any given time, and this information appears to be coded in the form of integrated object representations, rather than as a collection of disconnected visual features (Irwin and Andrews, 1996; Jiang et al., 2000; Lee and Chun, 2001; Luck and Vogel, 1997; Sperling, 1960; Vogel et al., 2001; Wheeler and Treisman, 2002; Xu, 2002). For example, Vogel et al. (2001) presented observers with a brief memory array of simple visual objects (colored squares, oriented bars, etc.). After a one-second blank-screen retention interval, a test array was presented that was either identical to the original memory array or differed in the color of one item. The observers then indicated whether the two arrays were the same or different. Memory capacity was measured by charting the observer's change detection accuracy as a function of the number of items in the memory array. Performance was near perfect for array sizes of up to 3 items, but declined substantially for larger arrays. From these and similar results, memory capacity is typically estimated to be slightly less than 3 items on average across the population (Vogel et al., 2001;

Cowan, 2001; Cowan et al., in press). However, memory capacity varies considerably across individuals, typically ranging from about 1.5 to 5 objects.

NEUROPHYSIOLOGICAL MEASURES OF VISUAL WM

Single Unit Recordings in Nonhuman Primates

Much of our knowledge of the neural substrates of WM has come from single-unit recording studies in awake, behaving monkeys. In these tasks, the monkey is trained to perform a delayed match-to-sample task in which a sample object is presented and the animal must preserve the item in WM across either a blank delay period or several intervening non-matching test items until the matching test item arrives. The firing rates of individual neurons are recorded throughout each trial, and under these circumstances many neurons show a sustained increase in firing rate above baseline that persists throughout the blank retention period until the test stimulus is presented. This increased activity is often referred to as *delay activity* (see Fuster, 1994 for a review) and was first demonstrated over thirty years ago (Fuster and Alexander, 1971; Kubota and Niki, 1971). Since then there have been a substantial number of studies that have reported delay activity across a broad range of cortical areas (Chafee and Goldman-Rakic, 1998; Constantinidis and Steinmetz, 1996;

Miller et al., 1993, 1996; Super et al., 2001; Chelazzi et al., 1998; Fuster and Jervey, 1982). The properties of the delay activity in certain neurons suggest that it contributes to the continued representation of information held in memory throughout the retention period. For example, the delay activity recorded from a given neuron is often highly specific to the identity or position of the item to be remembered, which suggests that this activity is specific to representations in memory rather than reflecting more task general processes such as arousal or the expectation of reward (Miller and Desimone, 1994). Moreover, several studies have shown that delay activity is reduced on trials in which behavioral performance is slow or incorrect suggesting that this activity contributes directly to memory performance on a given trial (Funahashi et al., 1989; Sakai et al., 2002).

While individual neurons in many cortical areas show delay activity, there appear to be three primary regions that have large populations of cells with this characteristic firing pattern: prefrontal cortex (Miller et al., 1996; Fuster, 1973), posterior parietal cortex (Chafee and Goldman-Rakic, 1998; Colby and Goldberg, 1999), and inferior temporal cortex (Chelazzi et al., 1998; Miller et al., 1993). Both across and within these cortical regions, the delay activity of a given neuron may have different properties, with differing degrees of robustness and selectivity of object features or location. The properties of this activity may directly contribute to different aspects of the maintained memory representation. For example, the activity of cells in the lateral intraparietal area (LIP) has been shown to be highly selective for the locations of task relevant items, and only weakly, if at all, responsive to irrelevant items (Constantinidis and Steinmetz, 1996; Gottlieb et al., 1998). While many of the neurons in LIP are strongly selective for particular locations, only small subsets of these cells also show delay activity that is highly sensitive to the identity of the memory item (Sereno and Maunsell, 1998). In contrast, a large proportion of neurons in inferior temporal cortex show identity-selective delay activity, with very few cells showing selectivity for the specific position of the to-be-remembered stimulus. Roughly equivalent proportions of neurons in the prefrontal cortex show delay activity that is selective for stimulus identity, location or both (Rao et al., 1997). However, the delay activity in these cells also appears to sensitive to even more complex aspects of the memory representation, such as the task-relevant categories (Freedman et al., 2001), the learned associations between stimuli (Asaad et al., 1998), as well as the maintenance of abstract rules (Wallis et al., 2001). Together, the task-specific delay activity of neurons in these different cortical areas appears to work in concert to give rise to representations that are maintained in visual WM.

fMRI Studies of WM

Neuroimaging studies in humans using functional magnetic resonance imaging (fMRI) have observed delay activity in WM tasks that appears to be analogous in response and anatomical locations to single unit delay activity observed in monkeys. For example, Sereno et al. (2001) found a location-specific signal in the posterior parietal cortex which showed strong retinotopic mapping of a remembered target location. The inferior temporal cortex, on the other hand, shows greater sensitivity to the identity and features of a stimulus, such as shape or color, independent of the stimulus location (Pessoa et al., 2002; Druzgal and D'Esposito, 2001). In contrast, the prefrontal cortex appears to reflect the complex control functions involved in the maintenance and manipulation of information in WM and does not appear to be the locus of stored memory representations (Postle et al., 1999; Rowe et al., 2000).

As in single unit studies, the degree of sustained fMRI delay activity also has strong correspondence to performance for WM tasks and is critical to the accuracy of the response. For instance, Pessoa et al. (2002) investigated differential fMRI activity during WM maintenance and found that the amplitude of the signal during the retention interval was reduced on trials in which the behavioral response was incorrect. This suggests that the delay activity reflects a process that is critical for correct memory performance on a given trial. In the prefrontal cortex, the magnitude of delay activity has been shown to vary parametrically with memory load, being greater for high-load conditions than low-load on a n-back task (Cohen et al., 1997), and to reflect activation of processes specific to the maintenance of WM (Braver et al., 1997). In addition, a study which examined prefrontal activation under sub- and supracapacity load conditions found higher overall activation for low-performing subjects compared to high performers, as well as a linear increase in activation as memory load increased (Rypma and D'Esposito, 2002). However, activation for low-performing subjects increased minimally as load increased compared to high-performing subjects, indicating that differences may be related to processing efficiency or cognitive strategy across individuals rather than the number of items in memory *per se*. Though delay activity in these studies was sensitive to memory load, the activity did not seem to reflect the known capacity limits of WM, and continued to increase even for arrays that exceed memory capacity. In contrast, a recent study found fMRI delay activity in the intra-parietal sulcus that is modulated by memory load and also appears to reach asymptote at approximately four items, which is highly similar to established capacity limits of visual WM (Todd and Marois, 2004). However, it is not clear

whether any one cortical area is responsible for memory capacity limits and future studies will be necessary to determine whether other cortical areas show similar limits (Lisman and Idiart, 1995; Nieder et al., 2002; Nieder and Miller, 2004).

ERP Studies of WM

Complementing the high spatial resolution of fMRI, event-related potentials (ERPs) provide an online measure of cognitive processing with excellent temporal resolution (Hillyard and Picton, 1987). Several ERP studies have observed a large, broadly distributed negative slow wave during the retention interval of WM tasks (Ruchkin et al., 1990, 1992). This component has been shown to be sensitive to task difficulty (Ruchkin et al., 1992), and appears to have a somewhat different scalp distribution for spatial and object WM tasks (Ruchkin et al., 1997). However, the degree to which this activity is specifically related to WM *per se* has not yet been definitively demonstrated. That is, there are several potential non-mnemonic processes that may occur during the retention period that could contribute to this activity. For example, during the retention period, in addition to maintaining the memory items the subject also anticipates the onset of the test display and prepares to make a response. Consequently, it is plausible that this negative slow wave may not only reflect the maintenance of information in WM, but is also partially due to this anticipation process. Indeed, the contingent negative variation (CNV) is a well studied ERP component that has similar characteristics to this negative slow wave (e.g., polarity, scalp distribution, timing) (Poon et al., 1974; Hillyard, 1969; Low and McSherry, 1968; Gaillard, 1977). It has been shown to precede the onset of a task relevant stimulus and is thought to reflect, in part, the anticipation of making a behavioral response. While it is possible that this negative slow wave does reflect a memory process, the general problem with using this activity as a neural correlate of WM is that it is non-specific with regard to the items that are being held in WM. Consequently, it is difficult to disentangle the memory processes from other task-general processes such as arousal, attention, or simply the anticipation of making a response.

More recently, Klaver et al. (1999) have reported a similar ERP component that appears to provide a more specific measure of maintaining information in visual WM. In this study, subjects were presented a display containing two abstract shapes (one in each hemifield) and were cued to remember the item on either the left or right side of the display over a 1500 msec blank interval. Shortly following the onset of the memory array, a negative wave was observed at posterior electrode sites that were contralateral to the position of the memory item which persisted throughout the retention period.

This sustained contralateral activity is potentially a good candidate for a neural correlate of visual WM because it provides more specific information with regard to the position of the remembered item, which makes it less likely to be due to more task-general processes. Nevertheless, further demonstrations of the specificity of this activity are necessary to determine whether this is truly mnemonic activity, and if so what aspect of the memory process it reflects.

Overview of the Present Study

The goal of the present study is to establish an electrophysiological correlate of visual WM in humans that is specific to the representations that are being held in memory on a given trial. Recently, we have reported lateralized ERP activity that appears to be analogous to the delay activity observed in single unit studies as well as in fMRI studies (Vogel and Machizawa, 2004). This activity is similar to that described by Klaver et al. (1999), but we have extended this by showing that it is highly sensitive to known memory capacity limitations. It is also strongly predictive of individual differences in memory capacity, which makes it a good candidate for a neural correlate of memory representations. In this series of experiments, we continue to test the specificity of this activity as a measure of the current number of items in visual WM as well as provide further details regarding our previous analyses and results. In Experiment 1, we describe this lateralized ERP delay activity (contralateral delay activity – CDA) and also provide topographical analyses of the distribution of the activity observed across the scalp. In Experiment 2 we test whether this activity generalizes to other types of simple visual objects. In the third experiment[1], we measure whether this activity is modulated by the number of items being held in memory and also whether it is sensitive to behavioral performance measures. In the final experiment, we test whether this activity is modulated by the overall size of the attentional "spotlight" necessary to include each of the items in the memory array.

EXPERIMENT 1

In this experiment we provide an initial demonstration of the ERP contralateral delay activity as a plausible analog to the delay activity observed in both single unit and fMRI studies. In this and each of the subsequent experiments we isolate this activity by presenting subjects with a

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[1]Portions of the results of Experiment 3 were described previously in Vogel and Machizawa (2004). Here, we present a more complete description of that experiment along with several new analyses of the results. In addition, we present the results from three new experiments that serve to extend and strengthen the conclusions of the previously reported study.
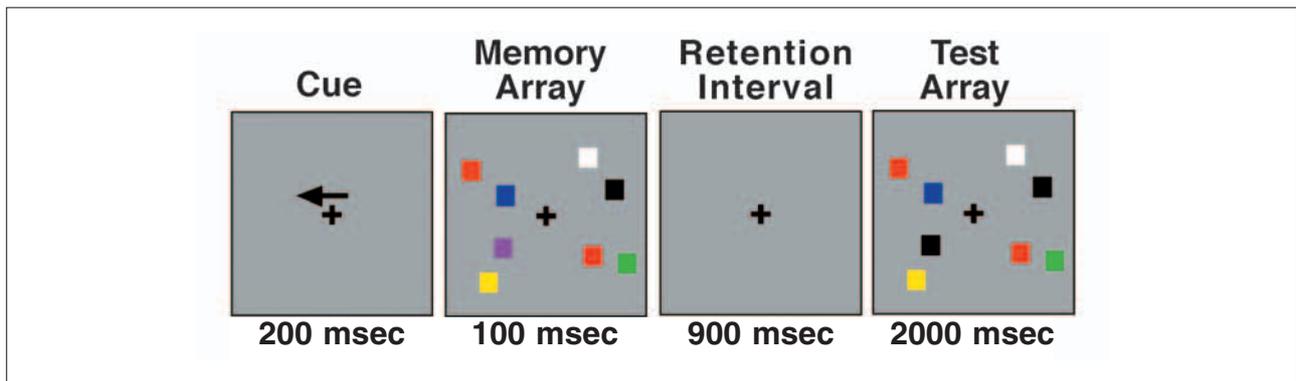
Fig. 1 – *Example of a change trial for the left hemifield in Experiment 1.*

bilateral display of memory items and asking the subjects to remember the items within only a single hemifield. This bilateral presentation provides balanced perceptual stimulation to both hemispheres and allows us to measure the activity that is specific to the hemisphere that is contralateral with respect to the hemifield that contains the to-be-remembered items. This procedure affords us the ability to separate the contralateral memory-related activity from the bilateral non-specific activity that occurs during the retention period.

Here, we will examine the contralateral delay activity for a task in which the subjects must hold four simple objects in visual WM on each trial. Previously, Klaver et al. (1999) reported that while this contralateral activity was present and robust when the subject held one object in memory, the activity was completely diminished when the subject attempted to hold two items in memory simultaneously. The authors suggested that the diminishing of this activity was due to the two item arrays exceeding memory capacity. However, many previous studies have shown that visual WM capacity is generally within the range of 3-4 items. More importantly, in the Klaver et al. (1999) study, in the two-item condition each of the items was presented in a different hemifield (one on the left, one on the right). Given the known contralateral nature of this activity, it is likely that the absence of this activity was simply due to the contralateral activity from the left hemisphere (coding the right item) canceling out the contralateral activity from the right hemisphere (coding the left item), thus rendering ipsilateral and contralateral activity indistinguishable. Therefore, in Experiment 1, we examined whether this contralateral activity persisted when subjects remember multiple objects presented within the same hemifield.

Methods

Participants

Twelve college undergraduates, ages ranging from 18-33, were paid to participate in this experiment. These participants reported no history of neurological problems, reported having normal color vision and normal or corrected-to-normal visual acuity and gave informed consent according to procedures approved by the University of Oregon

Stimuli and Procedure

Stimulus arrays were presented within $4° \times 7.3°$ rectangular regions that were centered 3° to the left and right of a central fixation cross on a gray background (8.2 cd m^2) viewed at a distance of 70 cm. The memory array consisted of 4 colored squares in each hemifield (see Figure 1). The color of each square was selected at random from a set of highly discriminable colors (red, blue, violet, green, yellow, black and white) and a given color could appear no more than twice in an array (see Vogel et al., 2001, for color coordinates). Stimulus positions were randomized on each trial, with the constraint that the distance between squares within a hemifield was at least 2° (center to center). Each square subtended $.49° \times .49°$ of visual angle.

Each trial began with a 200 msec arrow cue presented over a fixation point, followed by a 100 msec memory array, a 900 msec blank period and finally, a 2,000 msec test array. The 900 msec retention period exceeds the duration of iconic memory which necessitates that the items were held in WM (Sperling, 1960; Vogel et al., 2001). The arrow cue pointed to either the left or right and preceded the memory array with a variable delay ranging from 300-400 msec. Subjects were instructed to keep their eyes fixated while remembering the squares in the hemifield indicated by the arrow cue. On half of the trials, the memory and test arrays were identical; on the other half of trials the color of one item in the test array in the memorized hemifield was different from the memory array. Subjects responded by pressing one of two buttons on each trial to indicate whether the memory and test arrays were the same or different. When a color changed between the memory and test arrays the new value was selected at random from all of the other color values. The responses were

unspeeded, with the accuracy rather than the speed of the response stressed during instruction. Each of the participants were tested in a single session of 90 minutes, with each trial block lasting ~ 6 minutes with two short breaks of 20 sec spaced evenly throughout each block. Each subject performed at least 240 trials per condition in each experiment.

Recording and Analysis

Electroencephalographic (EEG) activity was recorded from 64 tin electrodes mounted in an elastic cap (Electrocap International), using the International 10/20 System, along with several custom locations. In addition to the standard sites, four additional sites were used: OL and OR, positioned midway between O1 and T5 on the left hemisphere and O2 and T6 on the right; POz, located on the midline between Pz and O1-O2, and PO3 and PO4, located halfway between POz and T5 on the left and POz and T6 on the right. All sites were recorded with a left-mastoid reference, and the data were re-referenced offline to the algebraic average of the left and right mastoids. The horizontal electrooculogram (EOG) was recorded from electrodes placed approximately 1 cm to the left and right of the external canthi of each eye to measure horizontal eye movements. In order to detect blinks and vertical eye movements the vertical EOG was recorded from an electrode mounted beneath the left eye and referenced to the right mastoid. Trials containing artifacts: ocular, movement, or amplifier saturation (blocking) were excluded from further analysis, which accounted for the exclusion of an average of 13% of trials. Subjects with trial rejection rates in excess of 25% were excluded from the sample. The EEG and the EOG were amplified with a SA Instrumentation amplifier with a bandpass of .01-80 Hz and were digitized at 250 Hz in LabView 6.1 running on a Macintosh.

Results

Behavior

Behavioral performance on the cued WM task was very accurate and comparable to what we have observed using similar tasks with a memory load of four items (Vogel et al., 2001). Mean accuracy was 87%, and performance did not significantly differ for remember-left and remember-right displays (F < 1).

Electrophysiology

We time-locked the ERPs to the onset of the memory array and used a recording epoch that extended through the retention period until the test array was presented. The waveforms for the remember-left and remember-right conditions for all electrode sites are shown in Figure 2. As can be seen in the figure, the activity for the two memory conditions diverge after approximately 200 msec at the lateral posterior electrode sites and this difference persists throughout the retention period. At posterior electrode sites along the right hemisphere, the voltage observed for the remember-left condition was significantly more negative than the remember-right condition. Conversely, at the left hemisphere electrode sites we observed that the remember-right condition produced a significantly more negative voltage than the remember-left condition. We tested whether these differences were reliable by performing a 2-way analysis of variance (ANOVA) on the mean amplitudes of activity from 300-900 msec with the factors of Hemisphere (left, right) and memory condition (remember-left, remember right). The results yielded no significant main effects of either Hemisphere or memory condition (both F's < 1). However, there was a highly significant cross-over interaction of hemisphere by memory condition [F (1, 11) = 23.10; p < .001], indicating a strong contralateral relationship between the spatial position of the memory items and the hemisphere of the activity during the memory delay period. This relationship does not appear to be present at more anterior electrodes. A 2-way ANOVA on the mean amplitudes at anterior electrode sites (anterior to the Cz plane) yielded no significant main effects of Hemisphere or memory condition (both F's < 1), nor was there a significant interaction between these two conditions [F (1, 11) = 1.13; p > .25].

Scalp Topography

We compared the scalp topography of the activity across several time periods following the onset of the memory array. Figure 3 shows isocontour voltage maps of the posterior scalp distribution of the periods of 200-300 msec and 300-900 msec. As can be seen in the figure, the 200-300 msec period shows a negativity that is contralateral with respect to the attended side of the display. This activity appears to reflect the N2pc; a contralateral component in the N2 time range, which is thought to index the orienting of attention to targets presented within a bilateral display (Luck and Hillyard, 1994; Woodman and Luck, 1999). While the 300-900 msec period shows a similar contralateral negativity, this later sustained activity has a more dorsal and medial distribution than the 200-300 msec period. To test whether these differences in scalp topography were reliable, we isolated the contralateral activity by constructing difference waves (Remember Right – Remember Left) and normalized the activity according to the procedure described by McCarthy and Wood (1985). In an ANOVA, we found a highly significant interaction between time window (200-300 msec *vs.* 300-900 msec) and electrode site [F (61, 549) = 7.56; p < .0001], indicating that these
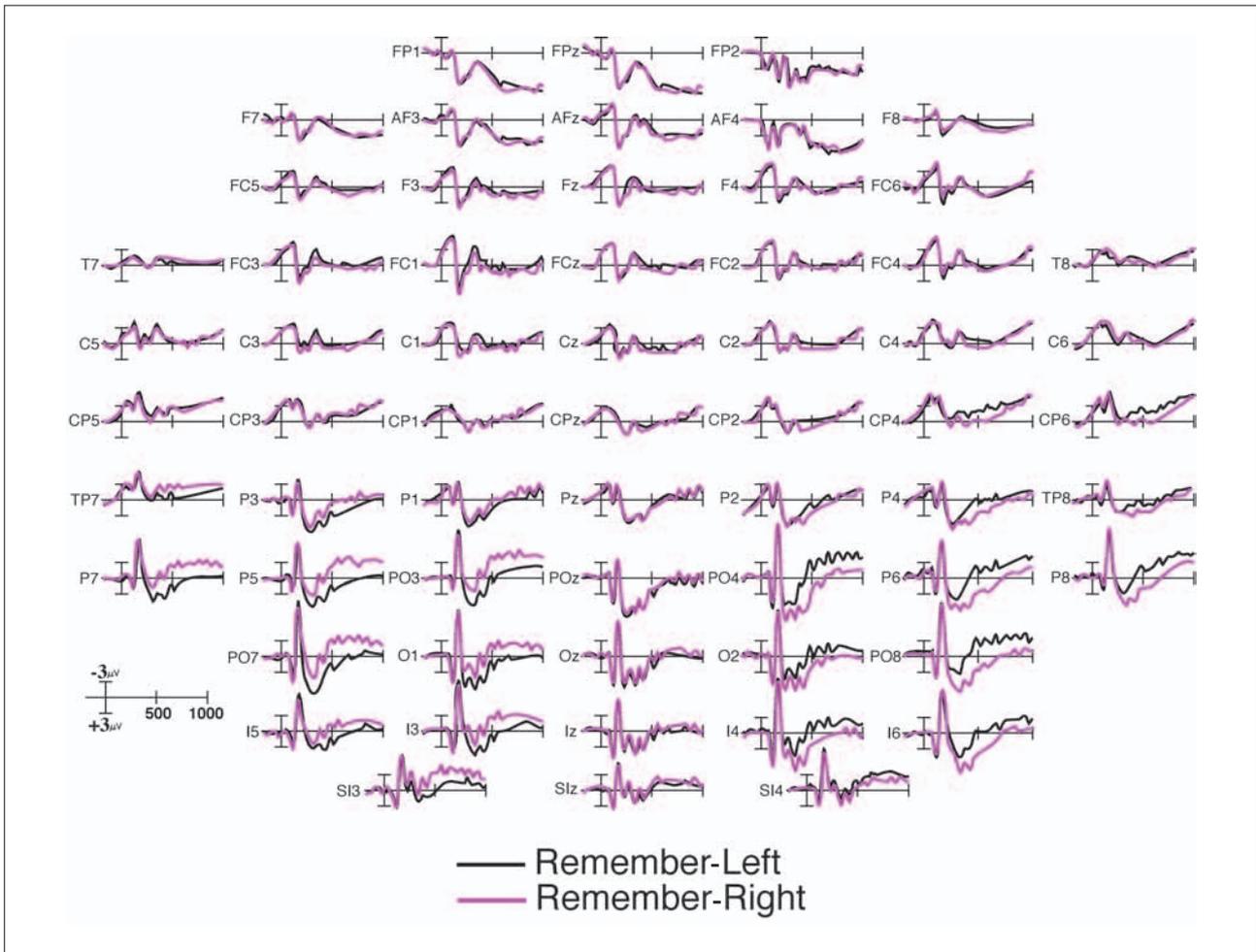
Fig. 2 – *Grand averaged waveforms for remember-left and remember-right conditions for all electrode sites in Experiment 1. Note that in this and all subsequent figures, negative voltage is plotted upwards.*

two time windows likely have distinct scalp distributions. In follow-up analyses, we divided the 300-900 msec period into three phases: 300-500 msec, 500-700 msec, 700-900 msec to determine whether these three periods share the same scalp distribution or have distinct distributions. We found no significant time window × electrode interaction [$F (122, 1098) = .63$; $p > .5$], suggesting that these three periods share a common scalp distribution. Because the sustained activity during the delay period persists until the test array is presented, we also compared the 300-900 msec period to the 1000-1200 msec period. This much later period reflects the first 200 msec following the onset of the test array. Here, we found a significant time window × electrode position interaction [$F (61, 549) = 3.26$; $p < .05$], indicating that the contralateral effect following the test array has a distinct scalp distribution from the sustained contralateral activity during the memory delay period.

Hemispheric Effects

In the first analysis, we found no significant main effect of hemisphere at posterior electrode sites, suggesting that the left and right hemispheres produce equivalent activity during the memory delay when the to-be-remembered items were in the contralateral visual field. However, while the overall amplitude did not differ across hemispheres, it is possible that there are hemispheric asymmetries in terms of the difference in amplitude when the memory items were in the contralateral field as compared to the ipsilateral visual field with respect to a given electrode site. Indeed, we designed the memory displays to be bilateral so that there would be identical visual stimulation to both hemispheres, allowing us to isolate the unilateral memory-related activity during the delay period from the bilateral perceptual activity evoked by the display items. Thus, memory-related activity in this paradigm is best defined as the difference in amplitude between memory items in the contralateral visual field and items in the ipsilateral visual field for a given electrode site. We examined whether memory-related hemispheric asymmetries were present by constructing two difference waves: Remember-Right minus Remember-Left for the left hemisphere electrode sites; Remember-Left minus Remember-Right for the right hemisphere electrode sites. These two difference waves isolate the
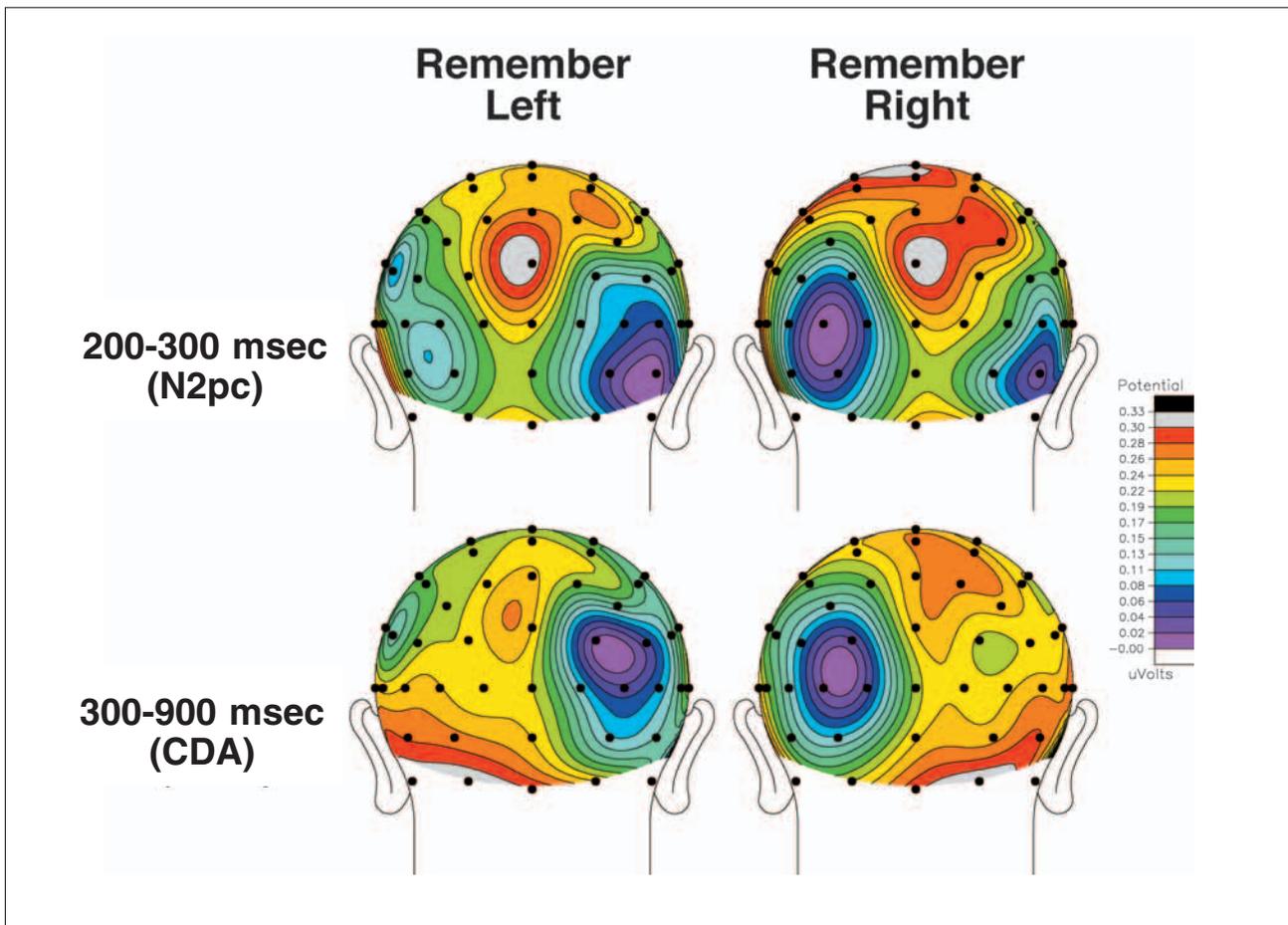
Fig. 3 – *Isocontour voltage maps of the posterior scalp distribution for remember left and right conditions in Experiment 1, created by means of the spherical spline method of Perrin et al. (1989). Voltage was measured as the mean amplitude from 200-300 msec following onset of the memory array in the upper row and from 300-900 msec in the lower row and was normalized to put the two periods on the same scale. Larger amplitude negative voltage is drawn in the purple and blue shaded regions.*

contralateral memory activity for each hemisphere, which allows us to compare the relative magnitude of activity across the two hemispheres. This analysis revealed that the right hemisphere produced slightly but not significantly larger activity during the memory delay than the left hemisphere (– 1.52 µV *vs.* – 1.27 µV; F < 1). These results further indicate that the contralateral memory delay activity observed in this experiment is equivalent for the left and right hemispheres.

Contralateral Activity to Memory and Test Arrays

Figure 4 shows the contralateral and ipsilateral activity at posterior electrode sites collapsed across visual field and hemisphere. We computed contralateral waveforms by averaging the activity recorded at right hemisphere electrode sites when subjects were cued to remember the left side of the memory array with the activity recorded from the left hemisphere electrode sites when they were cued to remember the right side. Conversely, we computed ipsilateral waveforms by averaging the activity recorded at right hemisphere electrode sites when subjects were cued to remember the right side of the memory array with the activity recorded from

the left hemisphere electrode sites when they were cued to remember the left side. As can be seen in the figure, contralateral activity diverges from ipsilateral activity approximately 200 msec following the onset of the memory array and persists throughout the memory delay period. As expected from the initial analyses, this difference yielded a highly significant main effect of condition for the period of 300-900 msec [contralateral *vs.* ipsilateral; F (1, 11) = 25.41, p < .001]. However, this difference appears to decrease towards the end of the memory delay period. We therefore divided the 300-900 msec period into three time windows: 300-500 msec; 500-700 msec; 700-900 msec and performed an ANOVA with the factors of time window and contralaterality. This analysis yielded a significant time window × contralaterality interaction [F (2, 22) = 7.55; p < .01]. In subsequent pairwise comparisons, we found a significant contralateral effect (i.e., Contra > Ipsi) for each time window (all p's < .01). However, while still significant this difference was smaller at the 700-900 msec window than at the earlier time periods. This decrease in the contralateral effect near the end of the delay period was not due to a decrease in the activity at the contralateral electrodes, but appears
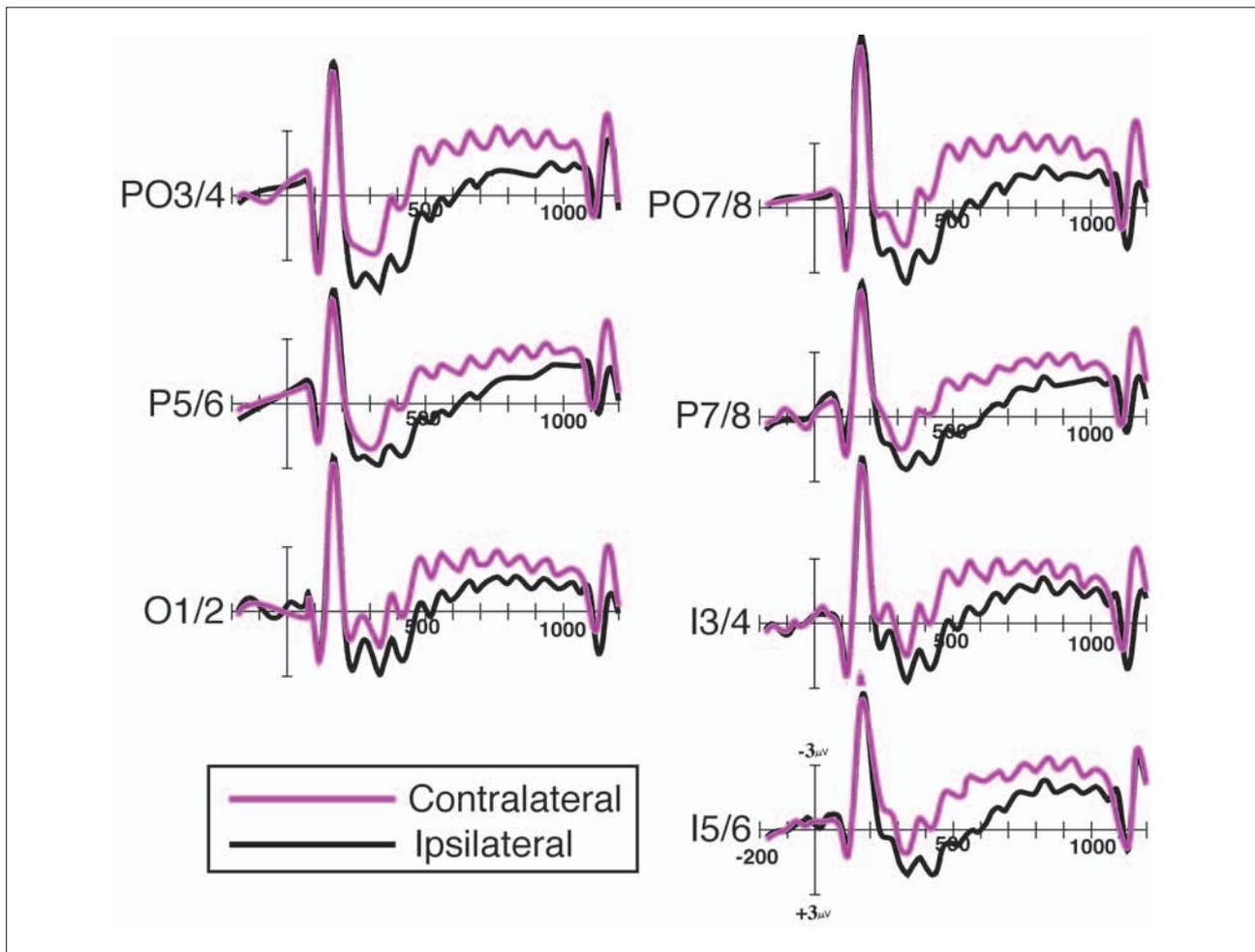
Fig. 4 – *Contralateral and ipsilateral activity at posterior electrode sites time-locked to the memory array and collapsed across visual field and hemisphere in Experiment 1.*

to be the result of an increase in the ipsilateral activity prior to the onset of the test array. Overall amplitude at the contralateral electrode sites increased significantly from the 300-500 msec period to the 500-700 msec period (p < .001), but this activity did not increase from the 500-700 msec to the 700-900 msec period (F < 1). In contrast, overall amplitude at the ipsilateral electrode sites increased significantly across all three time windows (all p's < .01), thus producing a smaller difference between contralateral and ipsilateral activity at the end of the trial.

We also compared the contralateral *versus* ipsilateral activity evoked by the test array at the posterior electrode sites. The N1 component evoked by the test array appears to be larger for the contralateral electrode sites than for the ipsilateral electrode sites. We confirmed this effect with an ANOVA on the mean amplitudes from 150-220 msec (following test array onset) [F (1, 11) = 9.36; p < .01].

Discussion

In this experiment, we observed a large negative component at posterior electrode sites that

were contralateral to the positions of the to-be-remembered items. This component persisted throughout the retention interval and resembles delay activity recorded from individual neurons in monkey visual cortex (Miller et al., 1993). This contralateral delay activity was restricted to the posterior portions of the scalp and was equivalent for both the left and right hemispheres. The spatial specificity of this activity suggests that it receives contributions from cortical areas with at least a moderate topographic mapping of space, but further experiments will be necessary to determine both the sources of this activity as well as its specific spatial properties. This activity appears to be similar to that described by Klaver et al. (1999). However, in contrast to their report, we found that the activity is robust and observable for arrays of four items when they are presented within the same hemifield.

The contralateral delay activity persisted throughout the memory delay period while the subjects were maintaining the items in visual WM. However, this activity decreased near the end of the trial prior to the onset of the test array. However, this decrease does not necessarily reflect a decay of the contralateral memory trace, but

appears to be due to an increase in amplitude at the ipsilateral electrode sites prior to the onset of the test array. Indeed, in a recent unpublished study, our laboratory has found that this contralateral delay activity persists for memory delay intervals of up to 3 seconds, and that the ipsilateral activity again significantly increased prior to the onset of the test array. One possibility for this increase in ipsilateral activity is the presence of a CNV-like wave in anticipation of the onset of the test array. This wave may be bilateral in distribution, but may have a negligible effect upon the contralateral electrode sites because they already may be near ceiling. Further follow-up studies will be necessary to determine the underlying cause of this increase in amplitude at the ipsilateral electrode sites.

The difference between the contralateral and ipsilateral activity persisted even following the presentation of the test array. This effect was restricted to the N1 component. While there are likely numerous memory processes that are involved in comparing the memory representations with the incoming test array, it is currently unclear whether this N1 effect reflects a mnemonic process or an interaction between spatial attention and the perceptual response to the test array. Numerous previous studies have found that the visual N1 component is modulated by selective attention even in bilateral arrays (Heinze et al., 1990; Mangun and Hillyard, 1991; Vogel and Luck, 2000). It is highly plausible that subjects maintained attention to the side of the display containing the memoranda throughout the delay period until the test was presented, resulting in an enhanced N1 response to the test array. Indeed, Awh et al. (1998, 2000) have shown that the maintenance of items in spatial WM tasks involves sustained spatial attention towards the remembered locations.

Experiment 2

In Experiment 1 we demonstrated an ERP measure of delay activity in a task in which subjects must maintain the individual colors of an array of squares in visual WM. In Experiment 2 we sought to replicate this effect with a task in which the subjects must remember the orientations of several rectangles so that we could determine whether this activity generalizes across different classes of simple visual features. We have previously shown using similar tasks that behavioral performance is highly comparable for maintaining colors and orientations in visual WM (Vogel et al., 2001). Therefore, we expected that the delay activity observed for this task would be more or less comparable to what we observed in the color memory task. On the other hand, evidence from single-unit physiology has shown that delay activity observed in inferotemporal cortex is particularly selective for stimulus identity

(Chelazzi et al., 1998; Miller et al., 1993), and it is therefore possible that this ERP delay activity may be selective for stimulus identity as well.

Methods

Participants

A new group of 12 college students participated in this experiment. Participants reported no history of neurological problems, reported having normal color vision and normal or corrected-to-normal visual acuity (ages ranging from 18-33) and gave informed consent according to procedures approved by the University of Oregon.

Stimuli and Procedure

The method in this experiment is identical to Experiment 1, with the exception that the stimuli consisted of black oriented rectangles (Figure 5a). Each rectangle subtended .65° × 1.15° of visual angle and was presented at orientations of 0°, 45°, 90° or 135°. Subjects were instructed to report whether or not the orientation of any one of the rectangles had changed between the memory array and the test array.

Recording and Analysis

EEG activity was recorded from tin electrodes mounted in an elastic cap (Electrocap International), using the International 10/20 System. 10/20 sites F3, Fz, F4, T3, C3, Cz, C4, T4, P3, Pz, P4, T5, T6, O1, and O2 were used, along with 5 additional non-standard sites: OL midway between T5 and O1, OR midway between T6 and O2, PO3 midway between P3 and OL, PO4 midway between P4 and OR, POz midway between PO3 and PO4. Otherwise, the recording and analysis was carried out in the same manner as in Experiment 1.

Results and Discussion

Behavior

Behavioral performance on the orientation WM task was very accurate and comparable to what we observed in Experiment 1. Mean accuracy was 83%, and performance did not significantly differ for remember-left and remember-right displays (F < 1).

Electrophysiology

Figure 5b shows the grand-averaged waveforms for the contralateral and ipsilateral activity plotted for an averaged posterior electrode site. As in Experiment 1, approximately 200 msec following the onset of the memory array the contralateral activity became more negative than the ipsilateral
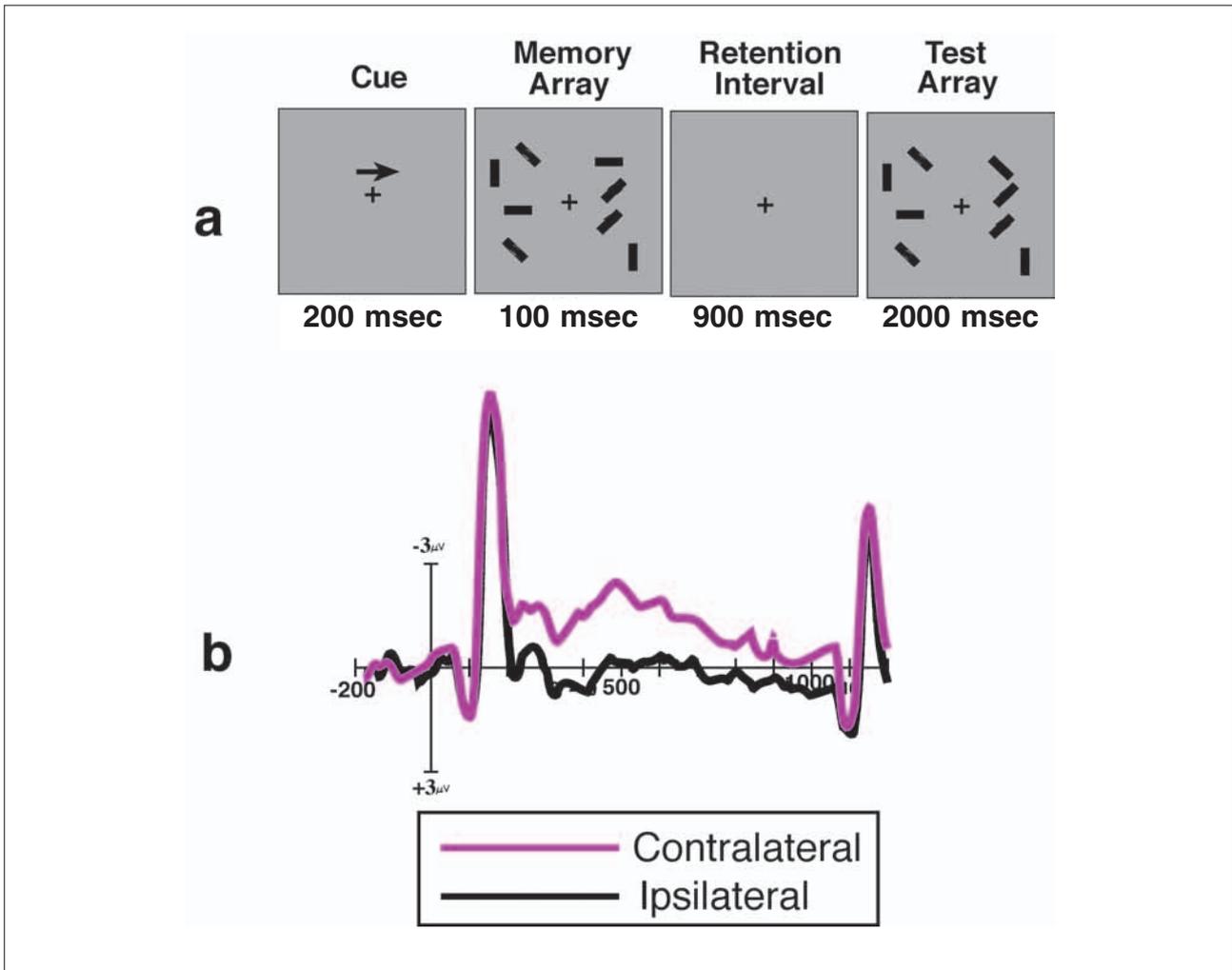
Fig. 5 – *Stimulus and results for Experiment 2. a) Example of an orientation "change" trial for the right hemifield. b) Grand-averaged waveforms for contralateral and ipsilateral activity plotted for an averaged posterior electrode site: averaged across O1/2, OL/R, T5/6, PO3/4.*

activity and this difference persisted throughout the memory delay period until the test array was presented. An ANOVA on the mean amplitudes (300-900 msec) confirmed that this difference was reliable, yielding a significant main effect of condition [contralateral *vs.* ipsilateral; F (1, 11) = 24.54, p < .001]. These results appear to be highly similar to those we observed for colored squares in Experiment 1, suggesting that the contralateral delay activity generalizes across different stimulus types. To establish whether these results were similar to those we observed in Experiment 1, we compared the scalp distributions of the activity from 300-900 msec across the two experiments. An ANOVA on the normalized difference waveforms found neither a main effect of Experiment nor an Experiment × electrode position interaction (both F's > 1), indicating that the overall amplitudes and scalp distributions of the activity observed during the memory delay period were similar for maintaining colors and orientations. While this by no means conclusively demonstrates that all aspects of this activity are completely equivalent for color and orientation memory, it does provide initial evidence

that this activity is comparable for different types of simple objects. Moreover, the lack of an obvious difference between color and orientation memory does not necessarily indicate that this delay activity is entirely insensitive to the identity of the memory items and future experiments will be necessary to examine the response of this activity to a much broader range of stimulus types.

While the *delay activity* appears comparable between the two experiments, there does appear to be a difference in the initial activity following the onset of the test array. That is, in Experiment 1, we found a large contralateral effect on the N1 elicited by the test array. In contrast, in Experiment 2 there appears to be no difference between the contralateral and ipsilateral activity for the evoked response to the test array. We confirmed this pattern of results with an ANOVA on the mean amplitude of activity from 150-220 msec in which we found no significant effect of contralaterality [F (1, 11) = 3.01; p < .15]. As described in the previous experiment, it is currently unclear whether the modulation of the N1 following the test reflects mnemonic processes or attentional processes. At

this point, we can only speculate regarding the lack of an N1 effect in this experiment. One possibility is that subjects adopt a somewhat different strategy of spatially attending the arrays of orientations than the arrays of colors resulting in more or less focused spatial attention prior to the onset of the test array. However, future studies that specifically target this modulation of the N1 will be necessary to determine what these differences reflect.

EXPERIMENT 3

The two previous experiments have suggested that the contralateral delay activity can be reliably observed and that it is similar for different types of simple objects. However, while suggestive, these results do not indicate whether this activity reflects mnemonic activity or whether it reflects some other spatially-specific activity that occurs during the retention period. To that end, in Experiment 3, we tested whether this activity was sensitive to the number of memory items that the subject must hold in visual WM on a given trial. If it does indeed reflect a process that is involved in maintaining items in visual WM, we would expect that the magnitude of the activity would increase as the number of memory representations increases. However, as the number of the items in the memory array increases, the task difficulty also increases. Consequently, it is difficult to determine whether an increase in activity reflects the additional representations in memory or the additional difficulty of the task. To account for this possibility, in this experiment we presented subjects with arrays of two, four, or six items within each hemifield. Previously, we have shown that most subjects can accurately hold up to four colored squares in visual WM (Vogel et al., 2001). Therefore, if this activity is sensitive to the number of representations being held in memory, we would expect an increase in the amplitude of the activity from two to four items. However, because an array of six items exceeds memory capacity, only four representations from the array (i.e., capacity's worth) should be held in memory on a given trial. Consequently, we would expect that the amplitude of the contralateral delay activity would be equivalent for arrays of four and six items because the same number of representations is held on each trial. On the other hand, if the contralateral delay activity reflects the overall difficulty of the task rather than the number of representations, we would expect the amplitude of the activity to be larger for arrays of six items than for four items because six item arrays pose a significantly more difficult task than do four item arrays. Therefore, by examining the contralateral delay activity across multiple array sizes we will essentially determine whether this activity is sensitive to the known psychometric properties of visual WM capacity.

Methods

Participants

A new group of 12 college students participated in this experiment. Participants reported no history of neurological problems, reported having normal color vision and normal or corrected-to-normal visual acuity (ages ranging from 18-33) and gave informed consent according to procedures approved by the University of Oregon.

Stimuli and Procedure

The stimuli and procedure were identical to Experiment 1 with the exception that arrays of 2, 4, and 6 colored squares in each hemifield were used. These three conditions were mixed randomly within a given block.

Results

Behavior

Performance on the memory task varied as a function of the number of items in the array, with highest accuracy for 2 items (96%), slightly lower accuracy for 4 items (86%), and poorest performance for 6 items (79%). Performance levels here were highly comparable to what we have previously observed with equivalent array sizes (Vogel et al., 2001). These differences were found to be highly reliable in a 1-way ANOVA [F (2, 22) = 19.06; p < .01].

Electrophysiology

Figure 6 shows the ipsilateral and contralateral activity for the three memory array sizes observed at posterior electrode sites. As in the previous experiments, 200 msec following the onset of the memory array we observed a large negative wave at electrodes sites that were contralateral to the position of the remembered items. This contralateral delay activity was present for all three set sizes. However, upon visual inspection the magnitude of the activity (in terms of the difference between ipsilateral and contralateral) appeared smaller for the two-item arrays than for either the 4- or 6-item arrays. To more directly compare the magnitude of this activity across the array sizes, we computed difference waves in which the ipsilateral activity was subtracted from the contralateral activity (Figure 7a). Contralateral delay activity was considerably larger for arrays of 4 or 6 items than for arrays of 2 items. However, the amplitude for arrays of 4 or 6 items was highly comparable. We tested whether this pattern of results was reliable in a 1 factor ANOVA on the mean amplitude of the difference waves for the three array sizes and found a highly significant effect of array size [F (1, 11) = 6.63; p < .01]. In subsequent pairwise tests, we
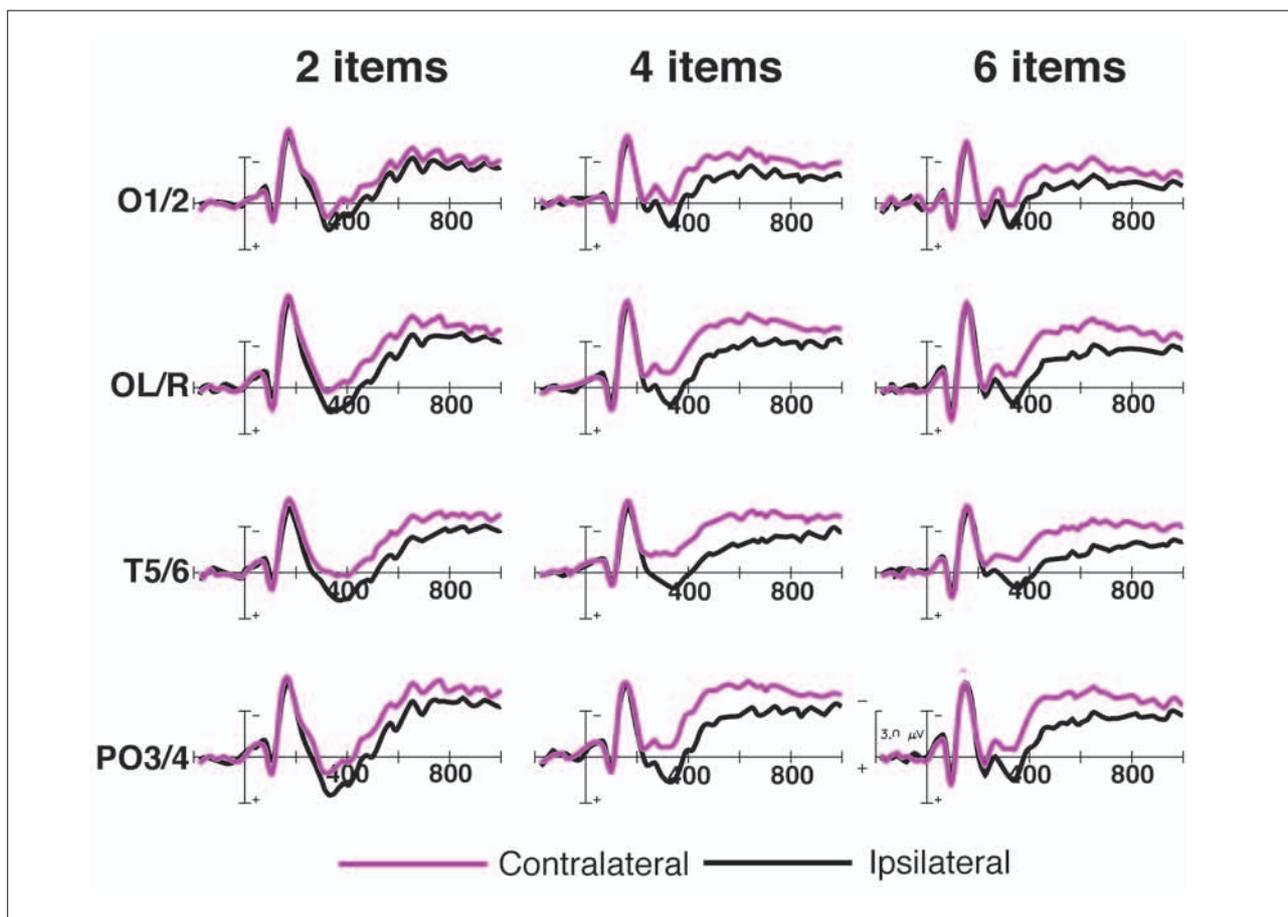
Fig. 6 – *Ipsilateral and contralateral activity for the three memory array sizes observed at posterior electrode sites in Experiment 3.*

found that while the amplitude for 2 items was significantly smaller than 4 items [F (1, 11) = 21.12; p < .001], there was no significant difference between arrays of 4 and 6 items (F < 1).

In a subsequent analysis, we compared the amplitude of the contralateral delay activity on correct performance trials with the amplitude observed on incorrect trials. Because of the relatively small number of incorrect trials (e.g., only 4% errors on 2-item arrays), we collapsed correct and incorrect trials across the three set sizes. The mean amplitudes for correct and incorrect trials are plotted in Figure 7b. The amplitude of the contralateral delay activity was significantly smaller on trials in which the subject's report was incorrect than when it was correct [F (1, 11) = 7.13; p < .01].

Discussion

The results of Experiment 3 provide strong evidence that the contralateral delay activity is a sensitive index of the number of representations that are currently held in visual WM. The amplitude of this activity showed a significant increase from two item arrays to four item arrays. However, this activity did not continue to increase for arrays of six items and appears to have reached asymptote at approximately four items. These results suggest that

the activity is modulated by the number of items that can be accurately held in visual WM rather than the increase in overall difficulty imposed by arrays containing larger numbers of items. In addition, we found that the amplitude of the contralateral delay activity on a given trial was highly sensitive to the subject's accuracy in performing the task on that trial. Amplitude was significantly reduced on error trials relative to correct trials, suggesting that the representation indexed by this activity may be a necessary antecedent to correct WM performance in this task. Together these results indicate that the contralateral delay activity provides a highly specified measure of visual WM performance; it is sensitive to the spatial positions of the memory items, the number of items that are currently being remembered, the limitations of visual WM capacity, and is also predictive of accurate memory performance.

Experiment 4

The results of Experiment 3 indicate that the contralateral delay activity increases in magnitude as the number of objects increases, but reaches asymptote at the memory capacity limit (see also Vogel and Machizawa, 2004). These results are consistent with the hypothesis that the delay activity
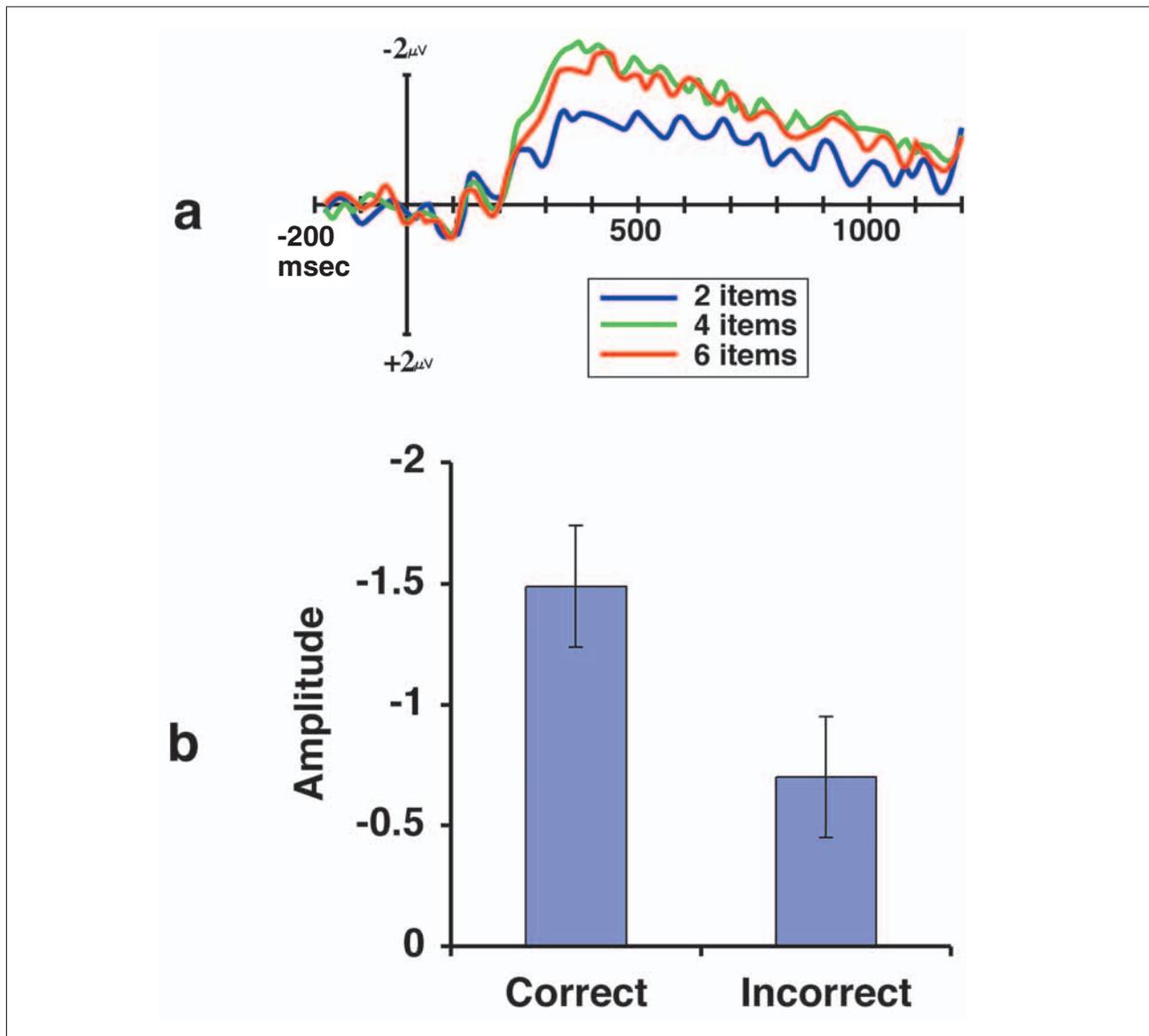
Fig. 7 – *a) Difference waves of contralateral minus ipsilateral activity for arrays of 2, 4, and 6 items for an averaged posterior electrode site in Experiment 3. b) The mean amplitudes for correct and incorrect trials collapsed across the three array sizes.*

indexes the number of active representations currently being held in memory rather than being sensitive to the general difficulty of the task. However, it is plausible that the amplitude of this activity is not actually determined by the number of items in memory, but rather is determined by the size of the "attentional spotlight" necessary to encompass the items within the memory array (Eriksen and St. James, 1986; Hillyard et al., 1998). In the previous experiment, on average across trials, arrays with only two items encompassed a smaller overall area within the hemifield than did arrays with four items. Consequently, it was necessary to broaden the focus of spatial attention across a larger area of space in the four-item condition than the two-item condition and this may account for the observed increase in amplitude from two to four items. However, one aspect of the results from Experiment 3 suggests that this counter-interpretation is unlikely. Specifically, arrays of six

items on average encompass a greater area than do arrays of four items, and yet there was no observed increase in amplitude from four to six. Nevertheless, one could argue that the spatial extent of attention has reached ceiling for areas at or near that imposed by arrays of four items.

In Experiment 4, we tested this hypothesis directly by varying the distance between memory items within a given array to determine whether the amplitude of the CDA was modulated by the number of items or the overall size of area that the items encompassed.

Methods

Participants

A new group of 12 college students participated in this experiment. Participants reported no history of neurological problems, reported having normal
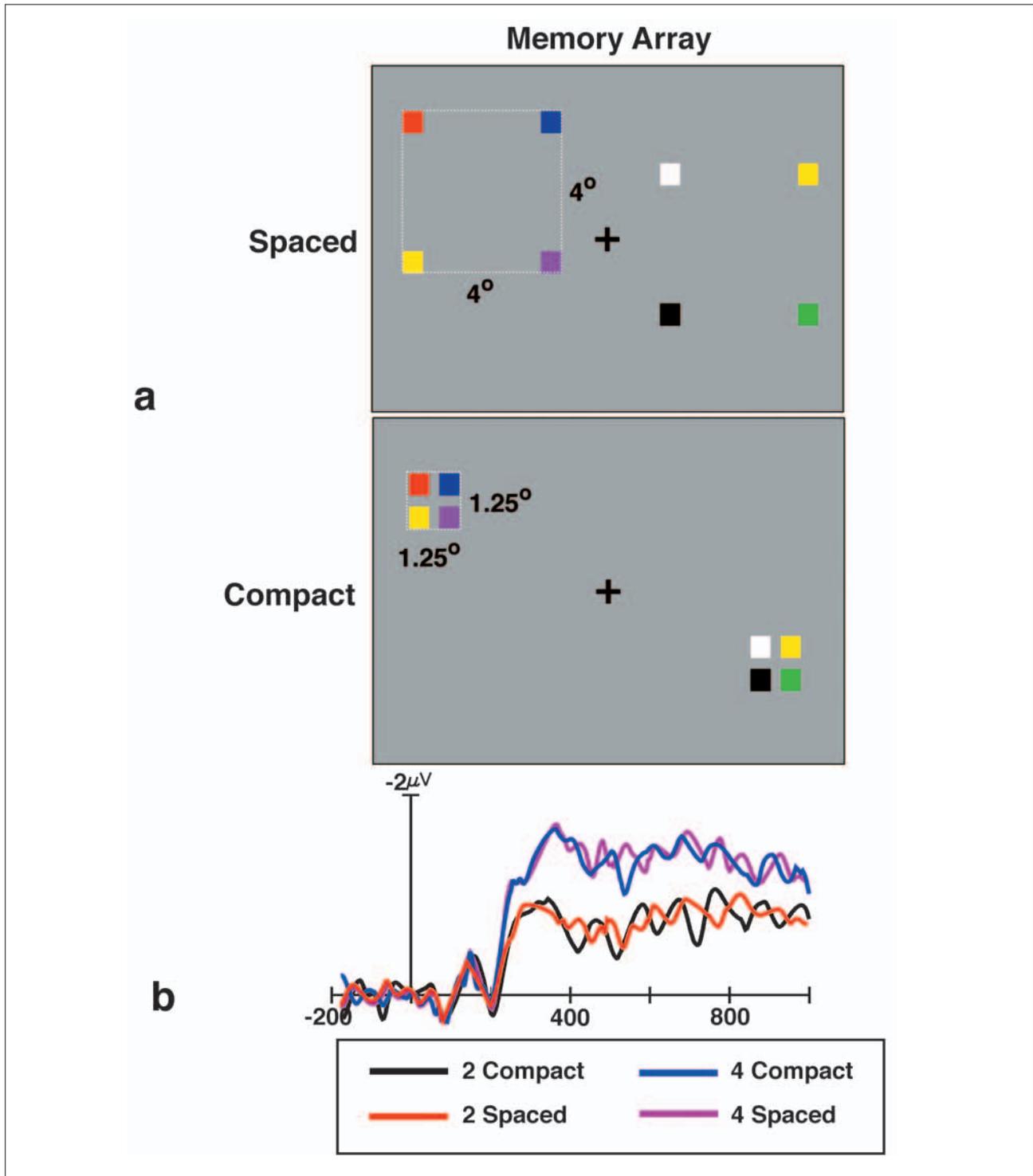
Fig. 8 – *a) Memory arrays in the spaced and compact conditions in Experiment 4. In the spaced condition the total area of the configuration of squares was 4° by 4° of visual angle. In the compact condition the total area was 1.25° by 1.25°. b) Difference waves for the four conditions of Experiment 4 plotted for an averaged posterior electrode site.*

color vision and normal or corrected-to-normal visual acuity (ages ranging from 18-33) and gave informed consent according to procedures approved by the University of Oregon.

Stimuli and Procedure

This experiment was highly similar to Experiment 3 with the following exceptions. Two

array sizes were tested (2 or 4 colored squares) across two levels of array area (compact *vs.* spaced). Figure 8a shows examples of 4 item arrays in the spaced and compact conditions. In the spaced condition, on each trial the positions of the memory items (.49° by .49° each) were constrained so that the distance between the items within the array was exactly 3° in both directions. This resulted in a configural square that encompassed a

total area of approximately 4° by 4° of visual angle. This configuration of squares was presented at new random locations within the hemifield on each trial. The compact condition was identical to the spaced condition with the critical exception being that the distance between the items was .25° which resulted in a total area of approximately 1.25° by 1.25°.

Results and Discussion

Behavior

Memory performance across all four conditions was very high. As in the previous experiments accuracy was higher for the two item arrays than for the four item arrays (p < .01). However, there was no difference in accuracy between the compact and spaced conditions for either array sizes (both p's > .25).

Electrophysiology

Figure 8b shows the difference waves isolating the contralateral delay activity for the four conditions. As in the previous experiment, the amplitude of the delay activity was larger for arrays of four items than for arrays of two items. However, the compact and spaced conditions produced equivalent amplitudes for each of the array sizes. We tested whether this was a reliable pattern in a 2-way ANOVA with the factors of array size (2 *vs.* 4) and distance (compact *vs.* spaced) on the mean amplitudes (300-900 msec) of the difference waves. While there was a highly significant main effect of array size [F (1, 11) = 23.71, p < .001], there was neither a main effect of distance (F < 1) nor an interaction between array size and distance (F < 1). These results indicate that the contralateral delay activity is primarily modulated by the number of memory items in the array rather than the overall attended area of the array. That is, despite the fact that the overall attended area in the two items spaced condition was dramatically larger than that of the four items compact condition, contralateral delay activity amplitude was still significantly larger for the four item condition than the two item condition.

GENERAL DISCUSSION

The primary goal of this study was to establish a specific electrophysiological measure of maintaining visual WM representations in humans. To this end we described a series of experiments that examined the properties of the contralateral delay activity to determine if this activity indexes the representations held in visual WM. The specific properties of this activity across several different stimulus and task manipulations suggest that it is a strong candidate for a specific neural correlate of the number of items held in visual WM on a given trial and that it can be separated from other non-mnemonic activity that occurs during the retention period. For example, the contralateral nature of this activity indicates that it is sensitive to the positions of the remembered items. This location-sensitivity suggests that this activity receives contributions from cortical areas with retinotopically organized representations, which is consistent with the primarily posterior locus of this activity across the scalp. Previous single-unit and fMRI studies have observed location selective delay activity in both the posterior parietal and prefrontal cortices (Sereno et al., 2001; Funahashi et al., 1989; Rao et al., 1997) and it is plausible that this activity receives inputs from one or both of these areas. In addition, this activity is not specific to memory for colors, but also generalizes to memory for other visual attributes (i.e., orientations). These results suggest that this activity is not highly sensitive to the identity of the memoranda. However, at present we have examined this activity across only a very limited set of stimuli and further experiments will be necessary to examine the sensitivity of this activity across a much broader range of stimulus classes.

An important feature of the contralateral delay activity that indicates that it is a sensitive measure of visual WM representations is that its amplitude modulates as a function of the number of items that the subject is holding in memory for that trial. Specifically, as the number of maintained memory representations increases, we observed a corresponding increase in the amplitude of this activity. Indeed, in addition to the results of Experiment 3, we have previously demonstrated that the amplitude of this activity can reliably distinguish between arrays of 1, 2, 3 and 4 items, indicating that this activity is a highly sensitive measure of the number of items held in memory (Vogel and Machizawa, 2004). Of course, simply demonstrating that this activity is modulated by the number of memory items is not sufficient to allow us to conclude that this activity specifically reflects memory representations because it is possible that the amplitude is actually modulated by task difficulty, which also increases with array size. However, the results of Experiment 3 demonstrate that while the amplitude increases from two items to four items, there is no increase from four to six items despite a substantial increase in difficulty between these two array sizes. Indeed, in our previous study (Vogel and Machizawa, 2004) we have shown that the contralateral delay activity reaches an asymptotic limit at approximately three items and does not increase for even larger array sizes (e.g., 8 or 10 items) which is equivalent to the average memory capacity in this task (Vogel et al., 2001; Jiang et al., 2000; Irwin, 1992; Xu, 2002; Cowan et al., in press). These results indicate that

this activity is highly sensitive to previously established behavioral limitations in visual WM tasks, and suggest that this activity reflects the number of representations that can be accurately held in memory at one time. We provided further evidence of this sensitivity in our previous study by demonstrating that there is a very strong positive correlation (r = .78) between an individual's memory capacity and the precise point at which this delay activity reaches asymptote, with high memory capacity individuals reaching asymptote for larger arrays than low memory capacity individuals.

The present study also provides further evidence that this activity strongly corresponds with behavioral performance on the memory task by demonstrating that its amplitude is considerably reduced on incorrect trials relative to correct trials. These results indicate that strong, sustained contralateral delay activity is necessary for accurate memory in this visual WM task. Similar demonstrations of task performance sensitivity have been recently observed in both the prefrontal and posterior parietal cortices in both single unit and neuroimaging studies (Pessoa et al., 2002; Sakai et al., 2002; Todd and Marois, 2004). Moreover, in Experiment 4 we demonstrated that the amplitude of this activity is not at all sensitive to the overall area that the memory items encompass, which further indicates that this activity reflects the number of memory representations rather than the spatial properties of the attentional "spotlight" (Eriksen and St. James, 1986).

Together, the current results characterize the contralateral delay activity as a strong candidate for a highly specific electrophysiological index of the number of memory representations that are active in visual WM on a given a trial. This activity may provide a powerful new "online" measure of the moment-by-moment contents of visual WM across different task and stimulus manipulations. Its fine sensitivity to memory capacity limitations may also provide a vehicle for exploring how memory capacity is allocated to different types of objects as well as potentially providing insight into how memory capacity differs across individuals. However, while this activity may hold promise for addressing these questions, many fundamental questions remain regarding the nature of this activity. For example, what aspect of the memory representations does this activity reflect? At present, while we have evidence that the spatial locations of the items are represented, it still remains to be seen whether the identity of the memory items is also present within this activity or whether it reflects "pointers" to the remembered items. Moreover, the cortical sources of this activity are still presently unknown and will require further exploration. While the scalp topography reveals a focus of activity over the posterior parietal and occipital areas, it is technically plausible that this activity receives inputs from prefrontal cortex as well. The fact that we found no contralateral activity at frontal electrode sites during the memory delay period by no means suggests that there was no frontal activity present during this task. This simply means that we were unable to isolate any mnemonic activity at these areas: either because the biophysics of the neural generators were such that the activity was not detectable at the scalp or because there was bilateral activation of the prefrontal cortex during the maintenance period. The functional properties of this activity are similar to reports of delay activity in both prefrontal and posterior parietal cortices and it seems likely that this activity receives contributions from several cortical areas. For example, a recent study found that single unit delay activity observed in extrastriate cortex was phase-locked to theta oscillations recorded in the local field potential (Lee et al., 2005). These results suggest a mechanism linking increases in the firing rates of individual neurons to more large-scale firing patterns across populations of neurons. It is plausible that oscillatory activity in the local field potential across several cortical areas gives rise to the complex memory representations maintained in visual WM. Indeed, theta oscillations have been proposed as a neural computational mechanism that underlies capacity limitations in WM and these oscillations may contribute to the contralateral delay activity that we observe at the scalp (Lisman and Idiart, 1995; Vogel et al., 2001; Raffone and Wolters, 2001; Tallon-Baudry et al., 2001).

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Edward K. Vogel, Department of Psychology, 1227 University of Oregon, Eugene, OR 97403-1227, USA. e-mail: vogel@darkwing.uoregon.edu