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Research Report

Control processes in verbal working memory: An event-related potential study

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ABSTRACT

Event-related potentials (ERPs) were recorded using a large electrode array while subjects engaged in tasks designed to dissociate control from storage/maintenance processes in verbal working memory (WM). Increased ERP negativity (450–900 ms post-stimulus onset) over left frontal regions emerged only when required dynamic updating/revision of WM stores was initiated, with augmentation of right frontal negativity in the same epoch relative to more general overall task demands. Increased ERP positivity in a similar time window over parietal regions reflected initiation of required rehearsal/maintenance of memory set contents, with progressive amplitude increases with repeated dynamic updating/revision of memory stores, suggesting increased effortful activity to resist proactive interference effects. These findings are consistent with a left frontal-parietal network for process control in verbal working memory.

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1. Introduction

Higher cognitive functions such as reasoning and language require working memory (WM), a set of cognitive processes involving short-term information storage and maintenance and process control. [Baddeley's \(2000\)](#) WM model postulates several short-term stores, including the phonological loop (PL), containing current, auditory/verbal information that decays within seconds unless store-intrinsic maintenance (subvocalization-like rehearsal) mechanisms are brought to bear. This subvocalization mechanism is also thought to permit entry into the PL of visually presented verbal material. The role in WM of a distinct central executive (CE), based in part on [Norman and Shallice's \(1986\)](#) "supervisory attentional system", includes selection and coordination of processes applied to PL contents ([Baddeley, 2000](#)). Although the model requires elaboration, it is demonstrably of considerable

heuristic value and has generated a body of generally supportive evidence involving multiple technologies and methodologies (e.g., [Gruber and Von Cramon, 2003](#); [Gupta and MacWhinney, 1995](#); [Morris and Jones, 1990](#); [Murray, 1968](#); [Salmon et al., 1996](#)).

Behavioral, neuropsychological, neuroimaging and electrophysiological findings provide general support for Baddeley's notion of distinct storage/rehearsal and process control mechanisms in verbal WM. [Morris and Jones \(1990\)](#) showed that both storage requirements and information manipulation demands affected error rates in recall of strings of letters, and the absence of an interaction suggests that these are engaging separate processes. Coordination of processing, a CE function, has been assessed using dual task paradigms and shown to be impaired despite intact storage/rehearsal under a number of circumstances, including neuropathological conditions such as Alzheimer dementia ([Morris, 1994](#)).

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More recently, the spatial resolution capabilities of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been utilized for the study of brain regions responsible for a range of cognitive activities, including WM. For example, Garavan et al. (2000) have attempted to isolate executive control processes associated with the allocation of attention by manipulating the extent to which attentional resources were dynamically allocated across a set of trials (comparing different attention switching frequencies). They found a broadly distributed set of frontal and posterior regions that showed sensitivity to the executive processes demanded by their attention switching task. It is likely that this broad distributed network overlaps with the orienting (frontal eye fields, inferior and superior parietal areas) and executive control (anterior cingulate gyrus and lateral prefrontal areas with strong connections to parietal lobes) attentional networks described by Posner and colleagues (Bush et al., 2000; Posner and Petersen, 1990; Posner et al., 2006). The nature of the frontoparietal network is described by Corbetta (1998) as a mediator of the allocation of attention (covert control) and control of eye movements (overt control) to bias sensory processing. The claim is that the frontoparietal network is the source of the selection (the control), not the site of the modulation. More recently, Corbetta and Shulman (2002) distinguish between the dorsal frontoparietal control network (goal or cue directed selection) and the ventral frontoparietal system (stimulus driven attention) which can modulate the dorsal system.

It is critical to distinguish the top-down attentional control signals from the neural activity that is modulated in response to those signals (Corbetta and Shulman, 2002). An analogy can be made with verbal working memory. It may be important to distinguish between executive control (CE) which manipulates information in working memory and maintenance (PL) of information in working memory, and this idea makes an assumption that these are two functionally different processes that are reflected in the processing of distributed and connected networks. As illustrated in an extensive survey (Cabeza and Nyberg, 2000), published cerebral activations during verbal WM tasks span much of the frontal and parietal cortices, as well as commonly involving cingulate and cerebellar areas. The widespread and bilateral distribution of verbal WM sites (Cabeza and Nyberg, 2000) requires explanation beyond vague claims of a widely distributed network, particularly in light of the longstanding association between verbal memory and the left hemisphere. Uncertainty regarding the left hemisphere/verbal WM association is clarified somewhat through the fMRI work of Gruber and Von Cramon (2003). They used classic articulatory and non-articulatory (visual) suppression tasks that interfere with maintenance of verbal and visuospatial information respectively. They demonstrated predominantly left lateralization of PL activity (Broca's area, precentral gyrus and left inferior prefrontal regions) and bilateral activation (superior frontal and intraparietal sulcal regions) for visuospatial sketchpad activity (the postulated short-term store for visuospatial information). In addition, verbal working memory activations became bilateral under articulatory suppression. While the authors suggest that articulatory suppression requires subjects to use "non-articulatory maintenance", it is equally plausible that articu-

latory maintenance continues but requires increased effort. Since these studies involved predominantly storage/maintenance functions, lack of activations attributable to the CE is not surprising.

A recent event-related fMRI study involving maintenance of letters in WM (Narayan et al., 2005) also provided evidence of left lateralization involving dorsolateral prefrontal-parietal circuitry. Predominant left lateralization was also noted during maintenance of visuospatial information (Corbetta et al., 2002). The possibility of verbal encoding of required information is suggested by the authors.

While regional activation varies considerably across functional neuroimaging studies, the main brain regions generally considered to subservise WM subcomponents are well represented by Smith and Jonides' (1999) review, which suggests that storage/maintenance aspects of WM are associated with activation in ventrolateral prefrontal (Broca's area) and supplementary motor and premotor cortical areas, and that process control and manipulation are associated with dorsolateral prefrontal (DLPFC) and superior parietal activation. As we discuss below, neuroimaging-based evidence associating neuroanatomy with subsystems of verbal WM is sometimes hard to evaluate because often the tasks do not effectively dissociate CE processing from PL processing.

Earlier neuroimaging investigations of verbal WM tended to utilize either a verbal item recognition task or a verbal "n-back" task (see Smith and Jonides, 1999 for a review). Item recognition tasks often employ visual presentation of an array of letters followed by a single letter probe after a variable delay. While the PL may be required to retain array items in WM during the delay period, this procedure is unlikely to make major demands upon the CE, rendering it less useful for studies of CE-related regional activation. One such study (Prabhakaran et al., 2000) used this type of task incorporating letter identification, letter location and combined identification/location probes. This study did not show clear lateralization of fMRI activation for verbal versus spatial demands. Combined identification requirements tended to predominantly engage prefrontal whereas single modality conditions resulted in stronger posterior activation. While it may be that greater CE engagement is required for the combined task, memory load effects may also explain these results.

During n-back tasks, participants may view letters presented one at a time and must at all times be prepared to report the presented *n* items prior to the current item. This task likely engages both CE and PL, however, dissociation of these WM components has proved to be problematic using n-back studies because both processes are engaged concurrently. A running sequence of items must be maintained in memory (PL) and there is difficult manipulation of the items (CE) as new ones are added to the sequence and old ones that are no longer necessary are discarded. Ideally, n-back task performance could be compared against a control task that selectively tapped only PL or CE processes, but this has been harder to do in practice. A number of imaging studies present the same problem, in that it is difficult to design a task that involves both PL and CE and then to successfully dissociate the two processes so that, in many cases, even after the subtraction of the control conditions, the activation likely reflects both PL and CE (Awh et al., 1996; Tsukiura et al., 2001).

Several event-related fMRI studies (D'Esposito et al., 1999; Postle et al., 1999) compared retention and alphabetic re-arrangement of letter strings, such that storage/rehearsal and manipulation-related activations could be reasonably differentiated. These studies demonstrated differential sensitivity of brain regions to memory load and mental manipulation, suggesting prefrontal involvement in CE (manipulation) processes and more posterior load-sensitive (PL-related) sites. However, there was some variance in the localization across subjects so that a clear dissociation of PL and CE functions was not obtained. DLPFC effects related to memory load were found in 2 of 5 subjects, and manipulation-associated cerebral activation involved both dorsolateral and ventrolateral prefrontal cortex in 4 of 5 subjects and was not clearly lateralized. In a review of these event-related fMRI studies, D'Esposito et al. (2000) suggested that the lateral prefrontal cortex may be generally involved in multiple working memory subprocesses including PL and CE functions, with greater activation of the lateral PFC when manipulation of information is required in addition to maintenance. This is supported by a recent PET study (Collette et al., 2007) which showed common areas in left frontopolar, bilateral DLPFC and premotor cortex, bilateral intraparietal sulcus, right inferior parietal lobule and cerebellum activity for three different types of working memory tasks (single characters, words and auditory tones). While there is some indication of more dorsal involvement for control processes, PFC process-specific fractionation for PL and CE-related activity is not well substantiated. It is not yet clear the degree to which our model of the PFC should be fractionated into content specific control, verbal and attention related areas or whether it is more useful to consider a more general model of PFC function (see Stuss, 2006).

Nyberg et al. (2002) provide fMRI evidence to support common frontoparietal substrates for several WM tasks with dorsolateral prefrontal engagement associated with likely increased CE activity. That is, dorsolateral prefrontal activation was minimal for a 1-back task and clearly present for 2-back and random number generation tasks. Bilateral parietal and dorsal frontal (premotor) activations were common to all three, suggesting a role for this network in storage/maintenance. However, these differences in activation can also be explained by differences in task difficulty with respect to storage/maintenance. That is, engagement of DLPFC may be required to support the increased storage/maintenance activities in the 2-back and random number tasks compared to the 1-back task. Another fMRI study that attempted to activate control (executive) aspects of working memory compared activations on two verbal tasks performed separately versus concurrently (Bunge et al., 2000). The left inferior prefrontal activation was involved regardless. The authors argued that the combined task increased utilization of a general resource and that the results do not support the idea that there is a particular substrate specific to control. However, interpretation is clouded by the fact that the individual tasks (sentence reading, word recall) each potentially involved aspects of both storage and control. In addition, although the same general region was activated in the combined as compared to the individual conditions, the volume of activation in the combined condition exceeded the combined volume for the two single conditions so that it is possible that there was recruitment of additional control areas.

The question remains whether the CE and PL functions share neural substrates within the limits of fMRI resolution or whether previous fMRI approaches at dissociation have been ineffective for reasons including ones articulated above. While recent perspectives suggest dynamic relations between WM processes and widely distributed cortical regions (Carpenter et al., 2000), convergent evidence from multiple levels of analysis supports some degree of structure/function localization including left-lateralized verbal processing. Lack of sufficient constraint of cognitive processes in experimental designs may limit neuroimaging evidence regarding dissociation of WM subprocesses and may explain the general lack of left-lateralized distribution of activation attributed to verbal WM in neuroimaging studies. If the baseline and main activation tasks are incompletely matched with respect to stimulus or temporal parameters, or if tasks insufficiently engage the desired set of processes, then subtraction results are more likely to produce bilateral non-specific activation.

The goal of the current paper is to examine whether PL and CE processes are functionally distinct. High density event-related potentials (ERP) are useful as a methodology to dissociate PL and CE processes. They provide measures of cognitive processing with excellent temporal resolution. Scalp distribution maps of this activity provide some limited spatial information, which may support dissociation, albeit not necessarily specific anatomical localization of underlying substrates. For example, McCollough et al. (2007) examined electrophysiological correlates of visual working memory in a task designed to minimize the ability to use verbal memory processes. They identified an early negative component (CDA, contralateral delay activation; a broad component measured over posterior sites beginning 200–300 ms) that was sensitive to both retinal location of the visual memory items, memory load and accuracy, indicating that this component is an electrophysiological index of visual working memory representations (McCollough et al., 2007). The graded effects of visual working memory load on the amplitude of the CDA are interesting and suggest that we might find graded effects on verbal working memory components due to memory load.

A high density array (124 channel) ERP study by Clark and co-workers (2001) utilized a verbal working memory task. Topographic and source localization methods indicated primarily left hemisphere involvement for a series of component latency ranges, including a later component (~830 ms) involving bilateral portions of prefrontal and parietal cortex. While their task involved storage and control aspects, there was no means of separating them with respect to effects on ERP. However, the results do support the involvement of the left hemisphere in verbal working memory processes.

1.1. Dissociation of WM subcomponents: the running memory procedure

In general, the design of fairly pure PL tasks is straightforward, while CE processes in verbal WM rarely if ever take place in the absence of storage and PL processes. Removal of activation due to storage and PL processes in WM tasks that engage CE to obtain "isolation" of CE activity has proved to be a challenge. The running memory procedure was developed as an experimental method to distinguish control from storage/maintenance processes.

Variants of the *running memory task* (Morris and Jones, 1990; Kiss et al., 1998, 2001; Kusak et al., 2000; Salmon et al., 1996) provide means of more fully dissociating storage/rehearsal and CE contributions to WM. For instance, one can present varying length series of two or more individual numerals, such that the length of a given numerical series is unpredictable for the participant. Each series is followed by a two-digit numerical probe. The research participant is asked to *remember the last two numbers* in each series and to indicate whether their memory set matches the two-digit probe. In terms of Baddeley's WM model, participants must retain (store/rehearse) a two-item memory set, hypothetically requiring the PL. The CE is engaged as they mentally manipulate or *update* PL contents as subsequent individual numerals are presented. The two-digit probe tests whether participants retain the correct identity and order of memory set items.

Studies by Kiss and co-workers (1998, 2001) used this method to provide evidence for an event-related potential (ERP) component that may be specific for CE activity. They found an increase in the amplitude of this central parietal component (positive difference wave for WM updating minus control, peak latency of approximately 560 ms) when updating was required for both auditory and visual material. Frontocentral positivities within a similar timeframe in a running memory task using visually presented verbal material were also reported by Kusak and co-workers (2000).

A small modification of the instructions for this running memory task utilized in the present study provides a means of specifically engaging PL processes, without alteration of stimuli or response requirements. As a separate task, participants are instructed to *remember the first two numbers* in each series, requiring retention and rehearsal of only the initial items in anticipation of an eventual probe, permitting observation of brain activity primarily reflecting PL processes as

participants monitor the remaining digits in the series to detect the probe while they are rehearsing the first 2 digits. We included two-item and three-item memory set conditions so that we could compare the effects of memory load and identify processing changes across serial positions in both memory load conditions. For example, similar processes should occur at the second serial position in the two-item condition as at the third serial position in the three-item condition. Finally, a third control condition simply required participants to monitor the digit series waiting for a probe which they classified as target (if it included only numbers) or non-target (if included a letter).

This approach was employed to attempt to electrophysiologically distinguish between PL and CE processes. We hypothesized that PL and CE processes may be observable as temporally and topographically dissociable electrophysiological effects. Because rehearsal load per se is unaffected by serial position (rehearsal is required for the preceding two (or three) items regardless of the number of single digits presented), the magnitude of rehearsal (PL) effects, as indicated by ERP amplitude for example, should be unchanged with serial position. We expected that storage/rehearsal of the verbal stimuli would be left-lateralized. For the updating task our previous studies suggested increases in magnitude/amplitude with increasing serial position in central parietal regions, perhaps due to cumulative effects of proactive interference resulting in progressively greater CE involvement. This magnitude dissociation was suggested but not convincingly demonstrated by previous studies (Kiss et al., 1998, 2001) because both storage/maintenance and process control (required for updating) were hypothetically required for the updating task and no separate storage/maintenance task was available for comparison.

The present study utilized 128 recording channels to explore spatiotemporal patterns of PL and CE-associated voltage changes. The main purpose of this study was to

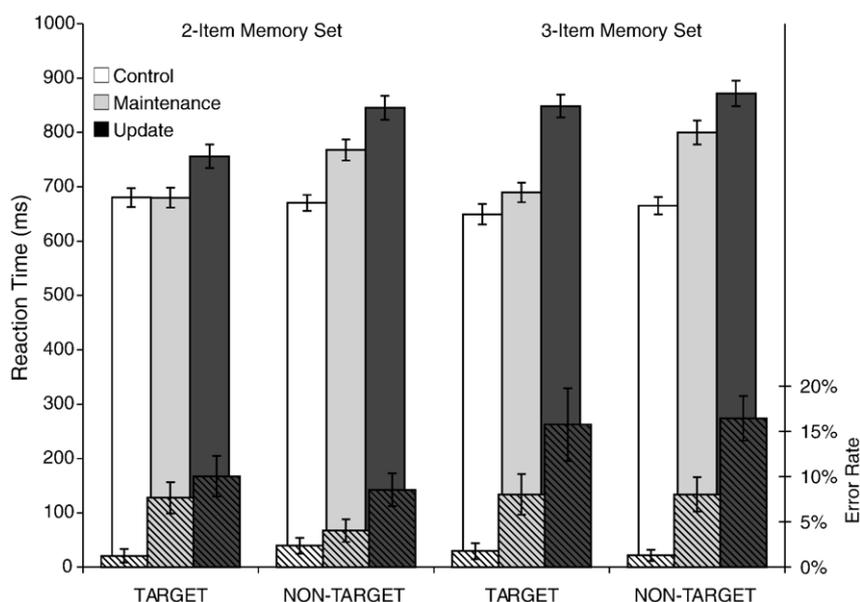


Fig. 1 – Mean reaction times (left axis) and error rates (right axis) for probe trials. Data are divided by memory set size (2 or 3 items), probe type (target or non-target), and task type (control, maintenance or update). Error bars represent standard errors.

attempt to dissociate the storage/maintenance and control processing aspects of working memory and potentially gain some insight regarding neuroanatomical correlates. Based on prior work, we hypothesized that maintenance tasks should show similar serial position effects (i.e., enhanced amplitudes) relative to the last position for which stimuli needed to be encoded for WM, versus subsequent trials requiring only basic rehearsal. In contrast, updating tasks should show increasing CE activity with increasing serial stimulus position. We expected to observe spatially dissociable effects of WM between frontal and parietal regions of interest, with the most basic prediction being that frontal effects would likely be better correlated with proposed CE processes.

2. Results

2.1. Overt behavior

Participants' overall mean reaction time and mean error rate data are shown in Fig. 1. Mean error rate was smaller for 2-item (6.6%) versus 3-item conditions (8.5%), $F(1,19)=7.33$, $p<0.05$. Mean error rate also differed between the control (1.6%), maintenance (6.9%) and updating tasks (12.7%), $F(2,38)=35.13$, $p<0.001$. Differences in mean error rate between task types were more pronounced for 3-item than 2-item memory conditions, supported by an interaction of memory condition and trial

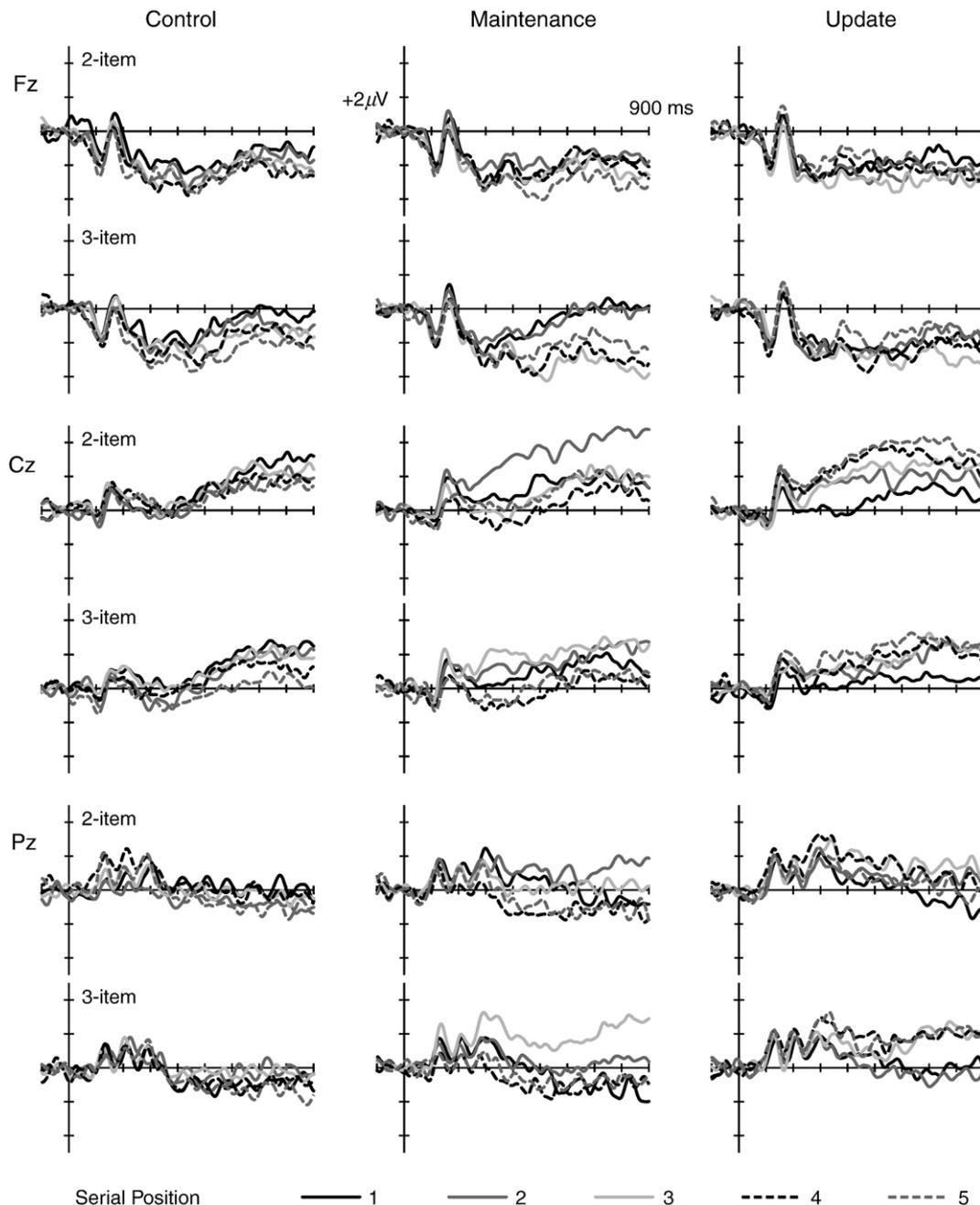


Fig. 2 – Grand average stimulus-locked ERP waveforms at electrode Fz, Cz and Pz for memory item (non-probe) trials. Data are divided by memory set size (2 or 3 items), task type (control, maintenance or update), and serial position (1 to 5).

type, $F(2,38)=4.90$, $p<0.05$. Error rate was not substantially affected by responding to target versus non-target trials.

Mean reaction times were shortest for the control task (666 ms) followed by maintenance (734 ms) and updating tasks (830 ms), $F(2,38)=81.00$, $p<0.001$. Mean reaction time was faster overall for target (717 ms) than for non-target trials (770 ms), $F(1,19)=34.763$, $p<0.001$. While performance on the control task was equivalent for both target and non-target trials across 2-item and 3-item conditions, 2-item maintenance and updating

tasks were faster than 3-item maintenance and updating tasks respectively, supported by a significant interaction between memory condition and task type, $F(2,38)=10.213$, $p<0.001$.

The interaction of task type and probe type, $F(2,38)=29.552$, $p<0.001$, modulated by the 3-way interaction of these factors and memory set size, $F(2,38)=5.697$, $p<0.05$, supported the observation that, on target trials, participants' performance for the maintenance task was relatively fast, approaching that of the control task, but was relatively slower when the probe

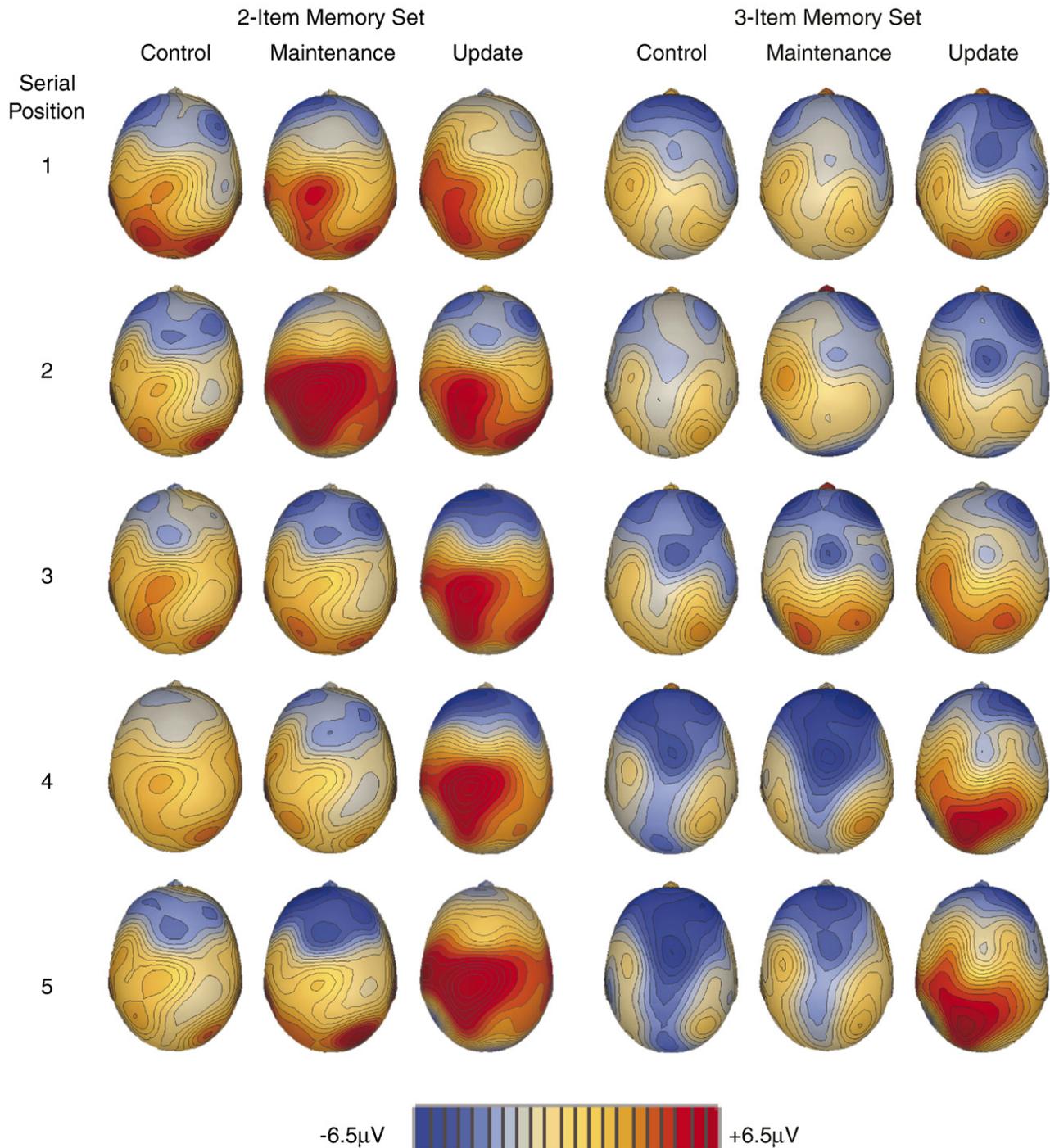


Fig. 3 – Scalp voltage topography at 500 ms post-stimulus for 2-item and 3-item memory set. Data are further divided by task type (control, maintenance or update) and serial position (1 to 5). Current source density data corresponding to these voltage topographies are shown in [Fig. 4](#).

stimulus was a non-target, compared to substantial slowing for both target and non-target trials in the updating condition.

2.2. Initial ERP analyses

Grand average ERP waveforms from the Pz, Cz and Fz electrodes are presented in Fig. 2. These data show ERP responses for 2- and 3-item control, maintenance and updating tasks, for stimuli presented in serial positions one through

five. Based upon previous studies (Kiss et al., 1998, 2001), and visual inspection of the present mean ERP amplitude effects, a 450 ms to 650 ms time window was chosen to statistically characterize the central parietal slow wave activity observed on inspection of grand mean waveforms and initially compare effects between parietal and frontal regions of interest. To this end, repeated-measures analysis of variance (ANOVA) with Greenhouse–Geisser correction was performed with factors of region (Parietal, Frontal), memory set size (2-item, 3-item),

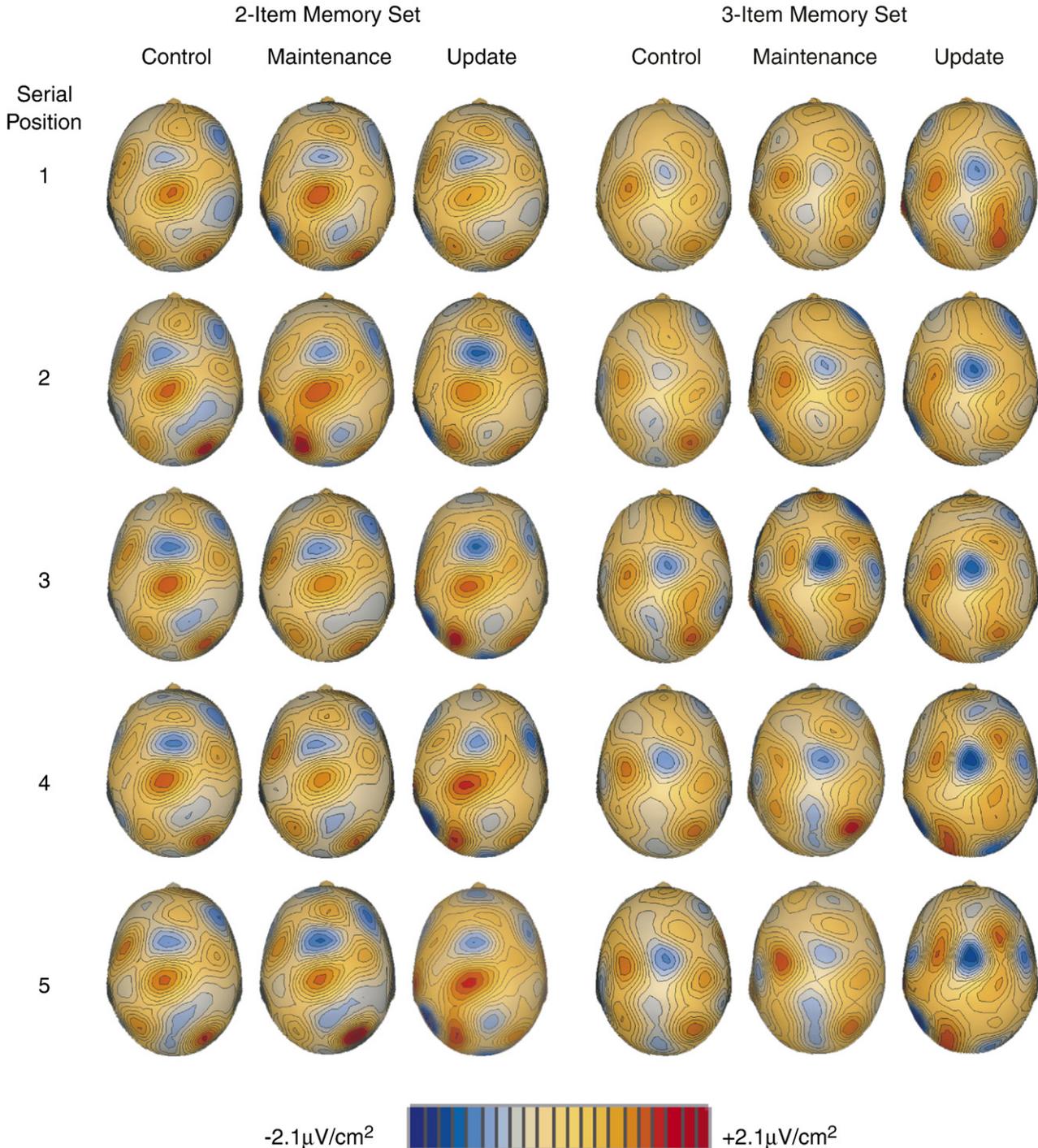


Fig. 4 – Scalp current source density at 500 ms post-stimulus for 2-item and 3-item memory set. Data are further divided by task type (control, maintenance or update) and serial position (1 to 5). Current source density data in this figure correspond directly to topographic voltage data shown in Fig. 3.

serial position (1, 2, 3, 4, 5) and task type (control, maintenance, updating), using average amplitudes from electrodes within our regions of interest. A main effect of region supported the observation of more positive amplitudes over the parietal region of interest, $F(1,19)=12.91$, $p<0.01$. Systematic differences in mean amplitudes were observed over varying levels of run position and memory set size for different task types, with different patterns of effects apparent between frontal and parietal regions of interest. These initial observations were supported by the 2-way interaction of region with task type, $F(2,38)=37.84$, $\epsilon=0.78$, $p<0.001$, the 3-way interaction of region with task type and serial position, $F(8,152)=9.14$, $\epsilon=0.63$, $p<0.001$, and the 4-way interaction of region with task type, serial position and memory set size, $F(8,152)=6.35$, $\epsilon=0.67$, $p<0.01$. These effects were further modified by an interaction of serial position and task type, $F(8,152)$, $\epsilon=0.59$, $p<0.001$, with generally smaller differences over run positions observed for the control task compared with maintenance and updating tasks. In order to better characterize and investigate these effects, we examined data from parietal and frontal regions of interest separately.

2.3. ERPs over parietal regions

The Cz and Pz waveforms shown in Fig. 2 are representative of the general pattern of ERPs observed at electrodes across our bilateral central parietal region of interest. Mean amplitude differences were observed between control, maintenance and updating tasks, $F(2,38)=17.89$, $\epsilon=0.78$, $p<0.001$, with additional effects on mean amplitudes between task types across serial position, $F(8,152)=12.17$, $\epsilon=0.66$, $p<0.001$, with other differences suggested by a marginal interaction of memory set size, task type and serial position, $F(8,152)=2.06$, $\epsilon=0.64$, $p=0.076$.

To better investigate the influence of task type on parietal slow wave amplitudes, repeated-measures ANOVAs with factors of memory set size (2-item, 3-item) and serial position (1, 2, 3, 4, 5) were performed separately for control, maintenance and updating tasks. In the control task, mean amplitudes did not differ across serial positions, $F(4,76)=1.21$, $\epsilon=0.78$, $p>0.3$, and there was no interaction between memory load and serial position, $F(4,76)=0.86$, $\epsilon=0.80$, $p>0.4$.

In the maintenance task, differences were observed between memory load across serial positions. In the 2-item condition the

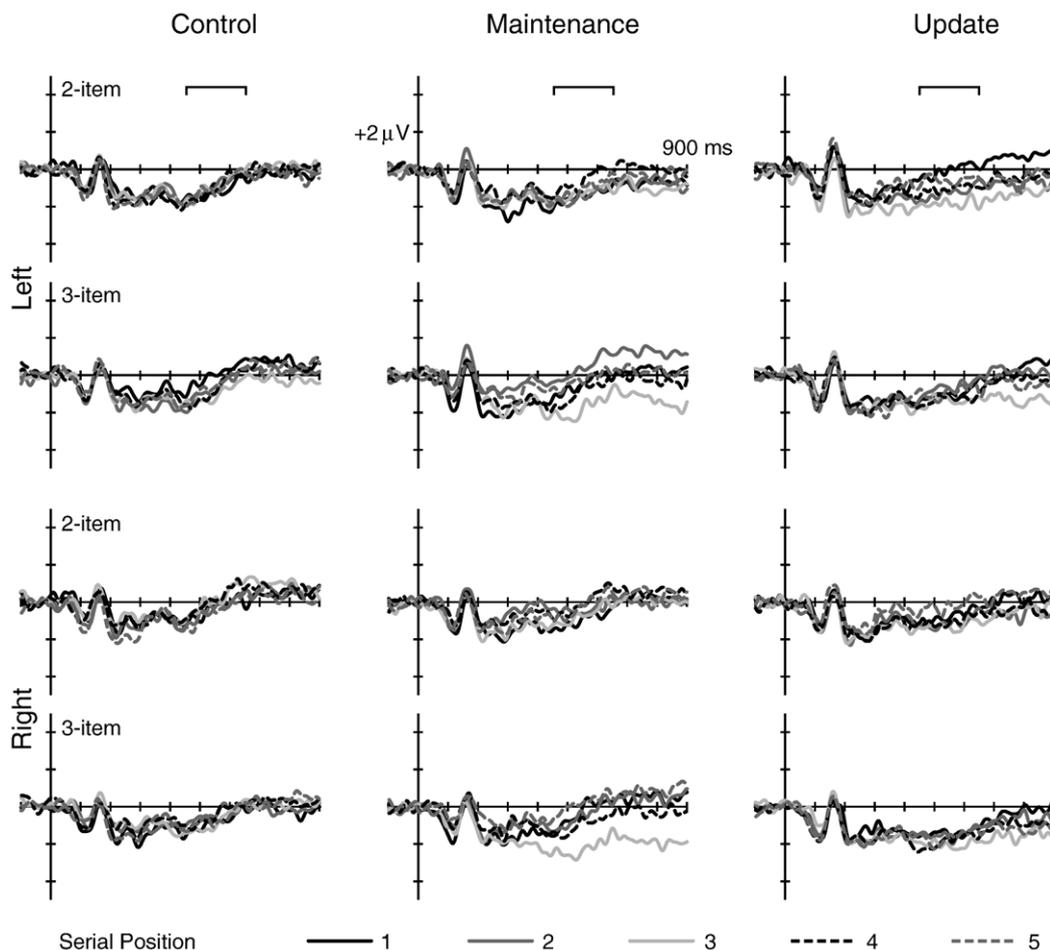


Fig. 5 – Grand-average stimulus-locked ERP waveforms for left and right frontal regions of interest. Data are further divided by memory set size (2 or 3 items), task type (control, maintenance or update), and serial position (1 to 5). The epoch for slow wave mean amplitude analyses (450–650 ms) is indicated at the top of the figure. These ERP data are shown and were assessed using a standard pre-stimulus baseline.

mean amplitude at serial position two was the largest for all serial positions, while in the 3-item condition the mean amplitude was largest for serial position three. In both conditions the mean amplitude at the remaining series positions was at or near baseline. This observation was supported by a main effect of serial position, $F(4,76)=7.90$, $\epsilon=0.67$, $p<0.001$, and a significant interaction between memory load and serial position, $F(4,76)=3.74$, $\epsilon=0.85$, $p<0.05$.

In the *updating* task, mean amplitude progressively increased for serial positions one through five for both 2-item and 3-item memory load conditions. This observation was supported by a main effect of serial position, $F(4,76)=8.99$, $\epsilon=0.78$, $p<0.001$, with a significant linear trend, $F(1,19)=30.34$, $p<0.001$, and no interaction of serial position with memory load, $F(4,76)=0.33$, $\epsilon=0.70$, $p>0.7$.

Although similar effects were present in both time periods, these amplitude effects for *maintenance* and *updating* tasks were generally more prominent in the 450–650 ms time window than the 650 ms to 900 ms epoch.

Fig. 3 shows scalp topographies for all of these conditions at 500 ms, illustrating the regional distribution of these parietal amplitude effects. Fig. 4 shows current source density

maps corresponding to the same conditions and timepoint as Fig. 3. The ERP effects described above at our central parietal region of interest appear to capture a broader parietal effect illustrated in Fig. 3, extending from central parietal to more posterior parietal areas bilaterally, with some suggestion of greater voltages over the left hemisphere. Corresponding current source density measurements of the same conditions at the same timepoint, shown in Fig. 4, reveal a distinct left posterior parietal positivity and a slightly more lateral and anterior negativity, seen at the bottom left edge of individual head pictures in the appropriate conditions. These appear to be topographically consistent across conditions, with magnitudes selectively enhanced consistent with our parietal region of interest amplitude effects and topographic patterns in Fig. 3. Inspection of Fig. 4 suggests increased current source density of this left posterior to posteriolateral parietal positivity and negativity pair, selectively for the first two serial positions of the 2-item maintenance task, the first three positions of the 3-item maintenance task and all serial positions for both 2-item and 3-item updating tasks. This distinct pattern of activity across task type, memory set size and serial position suggests a left posterior to posteriolateral

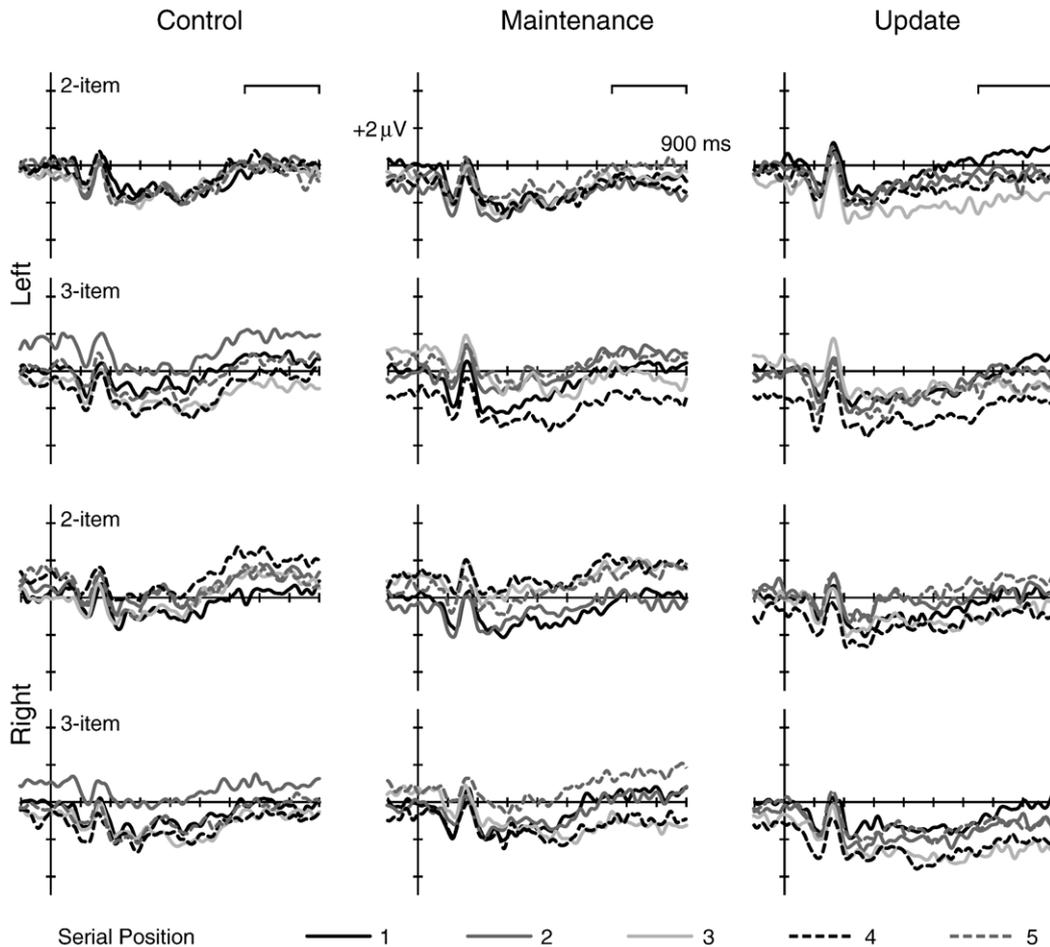


Fig. 6 – Grand-average stimulus-locked ERP waveforms for left and right frontal regions of interest. Data are further divided by memory set size (2 or 3 items), task type (control, maintenance or update) and serial position (1 to 5). The epoch for slow wave mean amplitude analyses (650–900 ms) is indicated at the top of the figure. These ERP data are shown and were assessed using a single pre-stimulus 1 (run position 1) baseline to examine extended slow wave activity.

cortical source as a likely substantial contributor to our observed ERP parietal region of interest effects.

2.4. ERPs over frontal regions

Data from frontal electrode sites were divided into left and right regions of interest, with an array of six electrodes per hemisphere centered over F3 and F4 positions, adding a factor of hemisphere (left, right) to our statistical analyses for frontal regions of interest. Grand average ERP waveforms from left and right frontal regions of interest are shown in Fig. 5. Analysis of mean amplitudes in the 450 ms to 650 ms epoch revealed a frontal effect of memory load, with greater negativity observed in the *updating* condition compared to control and maintenance conditions, more pronounced in the right hemisphere region of interest, supported by a main effect of task type, $F(2,38)=4.31$, $\epsilon=0.68$, $p<0.05$, and significant interactions of hemisphere and memory load, $F(1,19)=6.45$, $p<0.05$, and hemisphere and task type, $F(2,38)=5.97$, $\epsilon=0.85$, $p<0.05$. Right frontal amplitudes for the updating task appeared relatively unaffected by serial position, supported by an interaction of task type, serial position and memory load, $F(8,152)=2.12$, $\epsilon=0.72$, $p<0.05$, modifying a main effect of serial position, $F(4,76)=3.48$, $\epsilon=0.72$, $p<0.05$.

Grand average ERP waveforms were also constructed using a single pre-stimulus 1 (run position 1) baseline for all stimuli to better assess extended slow wave activity potentially obscured by traditional baseline methods (see Data analysis for details, below) and are shown in Fig. 6. Mean amplitude measures for the 650 ms to 900 ms epoch for left and right frontal regions of interest were assessed from this pre-stimulus 1 baseline dataset. Mean amplitudes for the updating condition generally became more negative from earlier to later serial positions, in comparison with control and maintenance tasks, supported by the interaction of task type and series position, $F(8,152)=6.06$, $\epsilon=0.61$, $p<0.001$. Memory load also appeared to have a substantial effect on frontal mean amplitudes. Differences in 2- vs. 3-item mean amplitudes were more marked in the right than left hemisphere region of interest, and serial position effects appeared more pronounced in 3-item trials. These observations were supported by interactions between memory load and hemisphere, $F(1,19)=6.70$, $p<0.05$, and between memory load and serial position, $F(4,76)=3.25$, $\epsilon=0.70$, $p<0.05$.

To test whether similar sensitivity to serial position for 2- vs. 3-item memory sets might be found in frontal activity, two additional 2×2 repeated-measures ANOVAs were conducted on data from the updating condition, with factors of memory set size (2 vs. 3) and serial position (position 3, position 4) for left vs. right hemisphere data separately. An interaction was observed between memory load and serial position over the left hemisphere region of interest, suggesting that maximal left frontal activation in the 2-item updating task occurred at serial position three, while this maximal activation occurred at serial position four in the 3-item updating task, $F(1,19)=12.31$, $p<0.01$. In contrast, right frontal activation did not show this interaction, $F(1,19)=0.31$, $p=ns$, with mean amplitudes for the updating task at serial positions 3 and 4 both numerically larger for 3-item trials than 2-item trials, although this main effect did not reach significance, $F(1,19)=2.59$, $p=0.125$.

3. Discussion

The present study employed variants of the running memory task in an attempt to dissociate executive control versus maintenance aspects of verbal working memory using ERP methods. Since performance was assessed using probes subsequent to series of stimuli requiring working-memory-related processing, we were able to minimize probe decision and response-related contributions to ERP measurements of participants' working-memory-related brain activity. In addition, stimuli were minimally varied across tasks. Accordingly, differences in ERP activity can reasonably be attributed to differential engagement of operationally defined working memory sub-processes.

3.1. Overt behavior

Participants' reaction times were slower and responding was less accurate in categorizing probe stimuli for *maintenance* compared with *control* tasks, with slowest RT and least accurate performance on the *updating* task. These results likely reflect differences in task difficulty. In addition, participants performed worse (longer RT, less accurate) for 3-item versus 2-item conditions in *updating* and *maintenance* tasks, supporting our assumption of increased difficulty with increased memory load. Equivalent performance on 2-item versus 3-item *control* tasks suggests that increased difficulty in *maintenance* and *updating* tasks can be more completely attributed to WM factors or increased difficulty in general, and not perceptual effects, particularly since there were minimal differences in stimulus attributes between 2-item and 3-item tasks.

3.2. Parietal ERPs

ERP amplitude was affected by task type, serial position and memory load. Central parietal positive slow wave activity was more prominent between 450 and 650 ms after stimulus onset, persisting until the end of our 900 ms analysis window. As illustrated in Fig. 2, *control* (non-memory) conditions showed minimal or inconsistent effects. When subjects were asked to remember the *first two* stimuli (the *maintenance* task), a central parietal positivity emerged at serial position two, with no such activity elicited for subsequently presented stimuli. When subjects were asked to remember the *first three* stimuli, the central parietal positivity was maximal following presentation of the third stimulus, again with no subsequent observed positive slow wave activity. This may reflect effortful processing required to encode and establish a coherent and sufficiently strong working memory representation once the full memory set is available, with reduced requirement for such processes on subsequent presentations of stimuli not required to be remembered. This ERP feature is probably not a reflection of rehearsal/maintenance activities *per se* since rehearsal activities would be expected to continue for stimuli presented after the emergence of this feature.

When subjects were asked to remember the *last two* or *three* individually presented stimuli with repeated, required revisions of this memory set (the *updating* task), a broad central parietal positivity was again observed, progressively increasing with each subsequent presentation of a to-be-

remembered stimulus. These results are not fully consistent with findings from Kiss and colleagues (1998, 2001). In these studies, the late parietal positivity emerged on presentation of stimulus three in a two-item updating task, *once updating was required*, and was therefore reasonably attributed to effortful CE-related processes (revision and reordering of memory set contents). In the present study under analogous 2-item updating conditions, this positive parietal feature appeared to emerge strongly after stimulus two, prior to required updating and therefore cannot be attributed to updating *per se*. One explanation for this amplitude growth is that it reflects additional, effortful processing needed to dynamically establish new working memory sets in the presence of increasing proactive interference as stimulus run position progresses.

In summary, parietal ERP effects in the *maintenance* and *updating* tasks in the present study suggest effortful, conscious (CE supervisory) activities, consistent with selection/initiation and monitoring of processes needed to establish and represent working memory set contents and potentially provide resistance to interference.

3.3. Frontal ERPs

Several electrophysiological effects were observed at frontal sites, as shown in Figs. 5 and 6. For the right frontal region of interest, and more clearly in the 450 ms to 650 ms epoch of the regular baseline ERP data in Fig. 5, a frontal slow wave was substantially more negative for the *updating* task compared to *maintenance* and *control* tasks. This negativity was more prominent for the 3-item condition. This may reflect effort or general task difficulty.

Fig. 6 shows these same data calculated and assessed via a single pre-stimulus 1 (run position 1) baseline to assess extended slow wave activity. Over the left frontal region of interest, slow wave amplitude for the *updating* task in the 650 ms to 900 ms epoch was maximally negative when updating of a full memory set was first required—that is, for the first instance in a trial when partial information from a previous working memory set had to be combined with new stimulus information to establish a new working memory representation (run position 3 for 2-item updating tasks, and run position 4 for 3-item *updating* tasks, respectively). This particular position-selective activity may reflect engagement/initiation of WM updating processes. This does not appear to reflect updating processes themselves since the feature is not evident on subsequent trials requiring updating.

3.4. General discussion

While it is probable that widely distributed, dynamically combined and partially task-specific networks of brain regions subserve various working memory tasks (see Carpenter et al., 2000 for a helpful discussion) the present study provides electrophysiological evidence for likely frontal and parietal involvement in central executive functioning subserving verbal WM. The kinds of processing suggested to account for these ERP effects are consistent with Baddeley's revised model of verbal WM (Baddeley, 2000). While the CE was initially considered a general term to describe processes acting on the contents of the PL, Baddeley later utilized Norman and Shallice's (1986) notion of a supervisory attentional system,

an "attentionally limited controller" involved in the engagement (selection/initiation) of required processes as a key aspect of the CE. The view that a distributed frontoparietal network subserves WM was already well elaborated and empirically supported in the mid-1980s (Goldman-Rakic, 1987). ERP and functional neuroimaging studies have also implicated these regions in process control in humans (Brass et al., 2005). There is increasingly technologically and methodologically sophisticated neuroimaging evidence for left DLPFC involvement for verbal WM (Postle and D'Esposito, 2000) although specific lateralization remains equivocal (Gruber and Von Cramon, 2003).

A number of issues are raised by these results. Scalp ERP data are insufficient for specific neuroanatomical localization of related generators, and our current data do not allow us to conclusively localize our effects to particular cortical substrates. The purpose of this study was to examine whether effects of simple maintenance versus manipulation of information in verbal working memory could be observed and dissociated. By examining ERP correlates of differential task performance under varying memory loads, we observed enhancement of parietal ERP components selectively for situations when new verbal WM representations needed to be established, with progressively larger enhancement for successive to-be-remembered stimuli. Frontal sites revealed different patterns of activity, with right frontal sites relatively insensitive to serial position, but left frontal amplitudes maximally negative for the first event in a trial for which information from a previous memory set had to be partially combined with new stimulus information on that trial. Independent of their spatial arrangement, the distinct patterns of effects seen between parietal and left and right frontal sites suggest that activity represented by these different regions of interest is likely functionally distinct.

These ERP findings, in combination with the complementary and selective patterns of current source density shown in Fig. 4, are consistent with previous findings localizing CE functions for verbal WM to parietal and left DLPFC regions. Source localization studies may be useful for generating more focal candidates for generators of observed ERP effects. However, higher spatial resolution available through planned fMRI studies using this running memory procedure will likely provide a clearer idea of regional involvement. Preliminary studies (Gates and Kiss, 2001) have produced results compatible with our current ERP results, with focal activations predominantly in frontal and parietal regions during running memory task performance. Preliminary fMRI results did appear to suggest specific regional differences corresponding to CE and PL activities, while ERP results did show evidence consistent with *engagement* of PL activity but not PL activity itself. This may have to do with the orientation, configuration and/or location of the relevant generators and perhaps the fact that rehearsal load was insufficiently large to produce measurable electrophysiological correlates.

One potential caveat raised in regard to these results concerns participants' responding with the index vs. middle fingers of their right hands throughout this experiment and the possibility that this may have contributed to our observed left-lateralized effects. While we concede this possibility, we believe it is unlikely on several grounds. First, given that participants only responded to probe trials, and our ERP data come from

stimulus trials prior to these probe trials, direct contamination from overt responding is not present. Any partial or anticipatory response activation prior to a probe trial should be expected to increase probabilistically over run position (as the likelihood of probe presentation increases), predicting that such effects should be greater as serial position increases. There are no such hemispheric differences in our control condition data, neither left vs. right amplitude differences, nor increased trends of serial position for one side vs. the other. In addition, the left hemisphere tendency of the bilateral parietal ERP effects, evident on inspection of surface topography in Fig. 3, appears to be primarily accounted for by a posterior and posteriolateral cortical generator, observed selectively for critical WM encoding conditions in CSD data in Fig. 4. This localized activity, while in the left hemisphere, is not present at all on control or later (post-WM requirement) maintenance trials, making it very unlikely to be due to response preparation. Visual inspection of the 500 ms post-stimulus CSD maps in Fig. 4 shows several other areas of localized activity that could potentially represent left-lateralized response preparation activity, but none of these modulate systematically with respect to our critical WM findings.

It remains to be seen whether there is differential activation when maintenance and updating tasks utilize series of visuospatial stimuli with visual CE processing perhaps involving the right DLPFC or whether the CE activity is modality non-specific. A previous study (Kiss et al., 2001) did indicate a central parietal component elicited by visuospatial stimuli with similar serial position-related amplitude changes during *updating*, but the *maintenance* task was not utilized. Large array studies, utilization of source localization and fMRI would also assist in clarifying these issues and are in progress.

While the present study did not reveal a dissociable ERP correlate of pure PL maintenance activity, several functionally distinct correlates of CE processes were observed. Positive parietal ERP slow wave activity was selectively sensitive to task situations requiring the establishment, but not simple ongoing rehearsal, of new working memory sets. This pattern was notably dissociable from both left frontal activity, showing maximal negative amplitudes when partial WM contents had to be re-coded with new stimulus information for the first time, and right frontal activity which was sensitive to overall task difficulty. These findings are consistent with a left frontal-to-parietal network for process control in verbal working memory. More generally, these data suggest a functional and gross spatial fractionation of central executive processes, for which more detailed functional neuroanatomical study is required.

4. Experimental procedure

4.1. Participants

Twenty English-speaking volunteers (14 female; aged 19 to 28 years, $M=21$) with reported normal or corrected-to-normal vision were included in the study. All participants were right-handed as determined by a handedness questionnaire, consisting of a subset of questions drawn from the Edinburgh Inventory for handedness (Oldfield, 1971). Five additional subjects were excluded on the basis of technical difficulties, and two additional subjects were excluded on the basis of poor performance

(at-chance behavioral performance in several conditions). Informed consent was obtained from each participant. Eligible participants received course credit for their participation, and the remainder volunteered without compensation.

4.2. Apparatus and stimuli

Stimulus presentation and manual response measurement were performed with Presentation® experimental software (Version 0.80, www.neuro-bs.com), running on a Pentium 4 computer under the Windows XP operating system. The display used was a 17-in. color CRT monitor, at a resolution of 1024×768 pixels at a frame rate of 75 Hz. The experiment was conducted in a dimly lit room, with a chin rest used to maintain a constant viewing distance of 80 cm.

Stimuli were white digits (0 to 9) and letters (A, B, D, F, H, K, M, N, D, R) presented in 36 point Helvetica font. Individual stimulus characters were approximately 20 mm high on screen, yielding a stimulus height of approximately 1.5° of visual angle. All stimuli were presented centrally on a black background. For each trial, a variable number of single digits were presented one at a time in sequence followed by a two-item or three-item probe stimulus. Probes always consisted of a pair or triplet of digit stimuli exclusively, except for non-target probes in our control condition, where a letter stimulus was substituted for one of the probe digit stimuli.

4.3. Procedure

The experiment consisted of two sessions each lasting approximately 20 min; one involving memory sets of two items and the other involving memory sets of three items. Session order was counterbalanced between participants. Each session contained three different task types: *control*, *maintenance* and *updating*. Six blocks of each task were presented in counterbalanced order for each session. Series of two to eight or three to nine single stimuli (for 2-item or 3-item sessions respectively) were presented prior to a probe stimulus, with five such series comprising a single block. Series length was randomly assigned, with 25% probability for each of the longest three series (e.g., 75% chance that a 2-item block would have 6, 7 or 8 stimuli prior to the probe stimulus), with the likelihood of shorter series lengths evenly distributed (e.g., 6.25% chance for each of 2, 3, 4 and 5 stimulus series prior to the probe stimulus). Non-probe stimulus digits were chosen randomly, with the constraint that a given stimulus digit was different from the two preceding stimuli within a series. Probe stimuli could be either *targets* (matching) or *non-targets* (non-matching) relative to the task requirements for a given block. Each block contained three target and two non-target trials, or two target and three non-target trials, randomly determined, and in random order. There were 180 stimulus series in all, giving 30 for each combination of memory set size and task type. All stimuli were presented for 200 ms with stimulus onset asynchrony varying randomly between 1200 ms and 1500 ms.

For *maintenance* trials, subjects were asked to *remember the first two* (2-item probe) or *three* (3-item probe) stimuli in a series. When a probe stimulus appeared, subjects indicated whether the probe matched (target) or did not match (non-target) the first two/three single digit stimuli of the current series. Non-target

stimuli were constructed by changing one of the digits of what would constitute a matching target stimulus by ± 1 , randomly determined.

Procedures for *updating* trials were identical to those for *maintenance* trials, except that subjects were asked to *remember the last (most recently presented) two or three digits* in a stimulus sequence. Thus while targets for *maintenance* trials were established for subjects after the first two or three stimuli in a series, targets for *updating* trials changed with the presentation of each new digit. Target and non-target probe stimuli were constructed in the same manner as for *maintenance* trials.

In contrast to *maintenance* and *updating* trials, *control* trials did not require subjects to remember any of the digits in a stimulus sequence. Instead, subjects were instructed to respond differentially to target stimuli (sets of two or three digits) and non-targets (one or two digits, plus one letter). Letters were used only for non-targets in the control task.

Participants received a brief practice session of one block of each trial type and then completed six blocks of each trial type in the experiment proper, in counterbalanced order. In each trial, responses were made only to probes. Subjects responded with their right index and middle fingers on the “1” and “2” keys on the numeric keypad of a standard computer keyboard to denote the match or mismatch responses, with response mapping counterbalanced between participants. Subjects received instructions on-screen at the beginning of each block. For example, for 2-item tasks, participants saw “Look for sets of 2 numbers” for *control* blocks, “Remember the first 2 numbers” for *maintenance* blocks and “Remember the last 2 numbers” for *updating* blocks. Subjects were instructed to attend to the individual numbers and respond only to the multi-item probe stimuli. Speed and accuracy of performance were emphasized.

4.4. Event-related potential recording

The ActiveTwo Biosemi electrode system (BioSemi, Amsterdam, The Netherlands) was used to record continuous electroencephalographic (EEG) activity from 128 Ag/AgCl scalp electrodes plus 4 additional electrodes placed at the outer canthi and just below each eye for recording of horizontal and vertical eye movements. Two additional electrodes, common mode sense (CMS) active electrode and driven right leg (DRL) passive electrode, were also used. These electrodes replace the “ground” electrodes used in conventional systems (<http://www.biosemi.com/faq/cms&drl.htm>). Because the BioSemi system is an active electrode system there is no conventional reference electrode; a monopolar signal is stored for each active electrode and all rereferencing is done in software after acquisition. The continuous signal was acquired with an open pass-band from DC to 150 Hz and digitized at 512 Hz. The signal was bandpass filtered off-line at 0.1 to 30 Hz and rereferenced to a common average reference.

ERP averaging and analysis were performed using EEProbe software (ANT, www.ant-software.nl). EEG and EOG artifacts were removed using a $\pm 35 \mu\text{V}$ deviation over 200 ms intervals on all electrodes. Blink artifacts were selected manually and corrected by a subtraction of VEOG propagation factors via a regression algorithm on EOG components (using EEProbe signal processing software). A 1000 ms recorded EEG epoch, including 100 ms pre-stimulus baseline and 900 ms interval following

stimulus onset, was chosen for ERP averaging. ERP waveforms were then averaged separately for each electrode for each serial position and condition. Only trials followed by correct responses to probe trials were included. Topographical current source density (CSD) maps were calculated using BESA software (www.besa.de), using a reference-free spherical spline surface Laplacian (Perrin et al., 1989; approximation parameter $\Lambda = 1.0 \text{ e}^{-6}$).

Given the long duration of working memory maintenance in this experiment (1200–1500 ms between stimuli, with up to nine stimuli per trial), an additional baseline correction procedure was applied to investigate possible task-associated slow potentials which may be obscured by averaging using a per-stimulus baseline. Accordingly, all stimulus epochs within a particular series were also baseline corrected using the same pre-stimulus correction as for the first stimulus in that series to assess potential task-related long-duration slow wave activity. Data from these analyses are discussed separately to those from our primary analyses, as described below.

4.5. Data analysis

Mean reaction time for correct responses and mean accuracy were computed for all combinations of conditions: memory set size (2 items, 3 items), task type (control, maintenance, updating) and probe type (target, non-target). Repeated-measures analyses of variance (ANOVA) were conducted separately for both mean reaction time and mean accuracy with these conditions.

In contrast to the behavioral analyses' focus on overt response trials, ERP analyses focused on stimulus-locked activity elicited by individual stimuli presented during the varying length series, for which no overt responses were required. Primary ERP analyses focused on two main topographic areas: a central parietal region of interest which exhibited maximal amplitudes, comprised of a set of two electrodes, Cz and another electrode approximately 3 cm posteriorly in the midline, plus matching pairs 2 cm to the right and left of these sites (6 electrodes in total); and bilateral frontal regions of interest over dorsolateral prefrontal cortex (DLPFC), comprised of 3×2 arrays of electrodes centered over F3 and F4 positions. F3/F4 electrode sites have been shown to be a reasonable scalp approximation of underlying DLPFC location (Herwig et al., 2003). Electrode sites for the left frontal region of interest comprised an electrode pair 1 cm posterior and anterior of F3 location; a more medial pair over F1 and the mid-point of F1-AF3 positions; and a more lateral pair, 1 cm posterior to F5 (F5') and 1 cm anterior to and slightly lateral of FC3 (FC3'). The right frontal region of interest mirrored these left hemisphere sites.

For our central parietal region of interest, a broad positive component was identified via inspection of the grand average waveforms, beginning around 450 ms and continuing until the end of our 900 ms measurement epoch. This broad positivity was isolated using two time windows, from 450 ms to 650 ms, and 650 ms to 900 ms. The earlier window was emphasized in analyses since effects appear somewhat more prominent and major effects were observed in this window in our previous studies. Effects on the mean amplitude of this component were assessed via three-way repeated-measures ANOVA with Greenhouse–Geisser correction including the

following factors: memory load (set size=2, set size=3), task (control, maintenance, updating) and series position (1, 2, 3, 4, 5), using the average amplitude values from electrode sites in our regions of interest.

For bilateral frontal areas of interest, grand mean waveforms were generated using both standard baseline correction and via a single baseline prior to the first series position stimulus and visually inspected prior to statistical analysis. Frontal slow wave activity was observed to begin approximately 400 ms post-stimulus and develop throughout our observational epoch. These effects were isolated for analysis using two time windows, from 450 ms to 650 ms, and 650 ms to 900 ms, to match our parietal analysis windows. The 2-item memory set conditions did not show substantial differences using the two different baseline calculation methods. However, some effects visible in the single-baseline 3-item data, corresponding to similar effects visible in both single and standard baseline 2-item data, were either absent from the standard baseline 3-item memory set data, or only beginning to become apparent at the end of the 900 ms post-stimulus epoch. To assess these late effects, analyses of 650 ms to 900 ms epoch prefrontal ERP data were conducted using a single pre-stimulus—one (serial position one) baseline for within-series stimuli to better detect and measure late-developing slow wave activity potentially averaged away by pre-stimulus baseline correction for every stimulus. Mean amplitude effects were assessed with a four-way repeated-measures ANOVA with Greenhouse–Geisser correction including the following factors: memory load (2 item, 3 item), task (control, maintenance, updating), serial position (1, 2, 3, 4, 5) and hemisphere (left, right).

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