The Timing of Neural Activity during Shifts of Spatial Attention

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Abstract

■ We developed a new experimental task to investigate the relative timing of neural activity during shifts of spatial attention with event-related potentials. The task enabled the investigation of nonlateralized as well as lateralized neural activity associated with spatial shifts. Participants detected target stimuli within one of two peripheral streams of visual letters. Colored letters embedded within the streams indicated which stream was to be used for target detection, signaling that participants should "hold" or "shift" their current focus of spatial attention. A behavioral experiment comparing performance in these focused-attention conditions with performance in a divided-attention condition confirmed the efficacy of the spatial cues. Another behavioral experiment showed that overt shifts of spatial attention were mainly complete by around 400 msec, placing an upper boundary for isolating neural activity that was instrumental in controlling spatial shifts. Event-related potentials recorded during a covert version of the focused-attention task showed a large amount of nonlateralized neural activity associated with spatial shifts, with significant effects starting around 330 msec. The effects started over posterior scalp regions, where they remained pronounced. Transient effects were also observed over frontal scalp regions. The results are compatible with a pivotal role of posterior parietal areas in initiating shifts of spatial attention. ■

INTRODUCTION

Convergent findings from neuropsychology, neuroimaging, neural stimulation, and single-unit recordings have established that a cortical fronto-parietal network closely associated with oculomotor function plays a critical role in controlling the orienting of spatial attention (Gottlieb, 2007; Taylor, Nobre, & Rushworth, 2007; Awh, Armstrong, & Moore, 2006; Thompson & Bichot, 2005; Moore, Armstrong, & Fallah, 2003; Yantis & Serences, 2003; Corbetta & Shulman, 2002; Hopfinger, Woldorff, Fletcher, & Mangun, 2001; Nobre, 2001; Kastner & Ungerleider, 2000; Mesulam, 1999). However, within this spatial orienting network, the functional interactions of parietal and frontal areas have remained difficult to determine. Parietal and frontal areas involved in spatial attention and oculomotor control, lateral intraparietal sulcus (LIP) and FEF respectively, are anatomically interconnected (Stanton, Bruce, & Goldberg, 1995; Cavada & Goldman-Rakic, 1989; Andersen, Asanuma, & Cowan, 1985; Petrides & Pandya, 1984), contain cells with similar activation profiles (Goldberg, Bisley, Powell, & Gottlieb, 2006; Thompson & Bichot, 2005), and show similar patterns of modulation during attention tasks (Pessoa, Kastner, & Ungerleider, 2003; Chafee & Goldman-Rakic, 2000).

An important first step toward revealing the specific contributions of parietal and frontal areas is to determine the relative timing of their activation. This requires applying a method with high temporal resolution to measure activity in parietal and frontal neurons during the performance of the same task since we now recognize that the timing of neural modulation can be influenced by the specific intervals used between stimuli and the temporal expectations that these engender (Anderson & Sheinberg, 2008; Buschman & Miller, 2007; Nobre, Correa, & Coull, 2007; Janssen & Shadlen, 2005; Ghose & Maunsell, 2002; Nobre, 2001). Buschman and Miller (2007) recently used such an approach to investigate the relative timing and synchronization of activity in LIP, FEF, and lateral prefrontal cortex during visual search tasks. By recording single-unit activity simultaneously from the three areas, they were able to show that the sequence of activation between parietal and frontal areas differed according to whether identification of the target within a stimulus array was driven by bottom–up, perceptually driven factors or top–down, mnemonically driven factors. These findings imply that the chain of command between parietal and frontal areas need not be fixed, but is determined flexibly by the specific perceptual context and task demands. Whereas the findings by Buschman and Miller mark a milestone

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in investigating the neural interactions between parietal and frontal areas during search behavior, they do not specifically address the problem of spatial shifts of attention. Target identification during search involves several other functions, such as comparing the target to the memorized template, ignoring distracters, and making decisions. Furthermore, the role of spatial shifts during bottom–up and top–down visual search remains debated, and at least some of the time-consuming search during top–down conditions may be mediated by slowly resolving nonspatial parallel mechanisms for stimulus comparison and identification (e.g., Nobre, Coull, Walsh, & Frith, 2003; Chelazzi, 1999; Desimone & Duncan, 1995; Wolfe, 1994).

The aim of the present study was to chart the temporal pattern of changes in functional brain activity during shifts of spatial attention in the human brain. The study capitalized on the high temporal resolution of noninvasive electrophysiological recording methods and introduced a new experimental task. The advantages of event-related potentials (ERPs) for investigating temporal processes during spatial orienting have long been recognized (Yamaguchi, Tsuchiya, & Kobayashi, 1994; Harter, Aine, & Schroeder, 1982; Eason, Harter, & White, 1969). However, research has been constrained by the sensitivity of ERPs to differences in cognitive state between experimental conditions (Hillyard & Picton, 1979; Näätänen, 1975) and in the perceptual attributes of cueing stimuli. If the level of difficulty across the "attention" tasks differs, the ERPs elicited by the targets or by predictive cues preceding them may differentially engage neural activity related to arousal or other executive control functions (e.g., Handy & Mangun, 2000). To overcome systematic contributions of differential psychological states between conditions, ERP studies have mainly been limited to contrasting brain activity during shifts to different spatial locations (Van Velzen & Eimer, 2003; Hopf & Mangun, 2000; Nobre, Sebestyen, & Miniussi, 2000; Yamaguchi et al., 1994; Harter, Miller, Price, LaLonde, & Keyes, 1989). In this case, the tasks performed are identical, and only the location of the target stimulus to be detected or discriminated is varied. Physical differences between stimuli, even when very subtle, may also have a large impact on the ERP waveform morphology. For example, arrow cues pointing rightward versus leftward are physically different, and will therefore generate a different pattern of response within visual areas, which in turn leads to a different pattern of potential over the scalp. Under such conditions, it is impossible to determine where the activity related to the differential visual processing or selection of the cue ends and the activity related to shifting attention begins. In order to avoid confounding effects related to the physical attributes of cues, compound or arbitrary cueing stimuli have been adopted, with a significance for spatial orienting that was dependent on task instruction and/or balanced across participants (Hopf & Mangun, 2000; Nobre et al., 2000). These studies suggested that posterior ERP changes preceded frontal ones, and were consistent with parietal cortex exerting a pivotal role in spatial shifts. However, even the perceptual aspects of compound cues were found capable of influencing the earlier ERP markers of spatial orienting (Van Velzen & Eimer, 2003). As a result, the sequencing of neural events underlying shifts of spatial attention remains unclear.

Grent-'t-Jong and Woldorff (2007) have recently reported an experiment with a similar aim to ours, in which they recorded ERPs elicited by cues signaling spatial shifts for target detection versus cues signaling that no task was required on a given trial. They reported changes in neural activity starting around 400 msec after presentation of the cue and suggested that activity in frontal cortex preceded that in parietal cortex. This estimate was surprisingly late given the rapid time course for the expression of behavioral validity effects in spatial orienting tasks (Gibson & Bryant, 2005; Tipples, 2002; Langton & Bruce, 1999; Posner, 1978, 1980). Furthermore, Grent-'t-Jong and Woldorff compared neural activity elicited by two conditions which differed not only in the spatial shifts of attention, but also in the level of task difficulty. Consequently, using their approach, it is difficult to separate activity specifically related to spatial shifts of attention from that related to the different task sets signaled by spatial versus no-task cues. We were compelled, therefore, to revisit this question and test the generality and reliability of their findings.

We developed a new experimental approach to chart both nonlateralized and lateralized brain activity linked to spatial shifts of attention, whereas previous ERP studies primarily investigated lateralized activity only. Our task involved high levels of selection requirements throughout performance and introduced several controls in order to isolate neural activity specifically related to spatial shifts of attention. The paradigm built upon design features of tasks used previously by Rushworth, Passingham, and Nobre (2005) and Yantis et al. (2002). Throughout an experimental block, participants viewed peripheral streams of visual stimuli covertly. They focused attention upon one stream at a time to detect predesignated target stimuli. Cueing stimuli embedded within the streams signaled participants to continue to attend to the current stream (hold cues) or to shift attention to the stream in the complementary location of the other visual field (shift cues). In this way, participants always remained in an alert state and maintained or shifted focused spatial attention away from fixation at all times. The physical attributes of "stay" and "shift" cues were completely equated, and both cues required equivalent symbolic decoding. Cueing stimuli were always followed by at least three standard (nontarget) arrays. This enabled us to isolate neural activity related to shifting the focus of spatial attention triggered by the cue from neural activity related to target identification and response selection related to the target. By analyzing the ERPs elicited by the standard arrays, it was also possible to measure the consequences of focused spatial attention upon visual processing and to chart the time course of visual modulation following spatial shifts of attention.

To establish the validity of our experimental task and to confirm that participants used the instructions of the spatial cues to focus their attention, we first conducted a behavioral study (Experiment 1), in which performance measures in the focused-attention spatial cueing task were compared to performance measures in a divided-attention condition, where participants were required to monitor both peripheral streams simultaneously in order to detect targets in either visual field. If participants were able to benefit from the spatial cues to focus attention effectively on one peripheral stream, their performance should be more accurate in the focused-attention condition with spatial cues than in the divided-attention condition (Van Voorhis & Hillyard, 1977; Hillyard & Galambos, 1967).

Once the face validity of the task was established, we conducted an ERP experiment, in which we measured neural activity elicited by cues and targets in the focused-attention task using spatial shift or stay cues (Experiment 3). We had two main predictions regarding cue-related neural activity related to shifting attention. We expected that the leading frontal activity reported by Grent-'t-Jong and Woldorff (2007) reflected engaging the differential task sets and setting the control functions associated with the differential task difficulty across cueing conditions, functions which typically engage frontal activity (e.g., Stuss & Knight, 2002). After equating for the task sets across experimental conditions, we predicted that activity over the posterior scalp, reflecting activity in parietal cortex, would become more pronounced during spatial shifts and would possibly lead activity recorded over the frontal scalp. Our prediction was based on the fMRI findings showing the dominant role of posterior parietal cortex during shifts of spatial attention (Kelley, Serences, Giesbrecht, & Yantis, 2008; Serences & Yantis, 2007; Yantis et al., 2002; Vandenberghe, Gitelman, Parrish, & Mesulam, 2001). Our second prediction was that activity related to spatial shifts should be observable earlier than 400 msec, preceding the time it takes to implement an overt shift of spatial attention by moving the eyes. In order to establish the time required to implement an overt shift of attention within the context of our specific experimental task, we also tested some participants on an overt version of the ERP experiment and recorded the latencies of saccades using the horizontal electrooculogram (Experiment 2).

The visual responses elicited by the standard arrays enabled us to test whether and when visual processing was biased by the focus of attention after a spatial shift. The ERPs elicited by standard arrays were also free from any neural activity related to target identification or response selection and execution. Based on results from previous experiments that have investigated visual modulation during focused spatial attention, we used the contralateral enhancement of the visual P1 potential as a marker of effective spatial modulation of visual processing (Luck, Heinze, Mangun, & Hillyard, 1990).

EXPERIMENT 1: BEHAVIORAL TASK VALIDATION

An initial behavioral experiment was used to validate the manipulation of spatial attention to the rapid serial visual presentation (RSVP) streams within the context of our experimental paradigm.

Methods

Participants

Fifteen healthy volunteers took part in the behavioral experiment (10 women, mean age = 26 years, range = 19–47 years). In this and in all the following experiments, the experimental methods were noninvasive and had the approval of the Ethics Committee of the University of Oxford. Informed consent was obtained from all participants.

Behavioral Task

Figure 1A illustrates schematically the behavioral task. We compared the behavioral measures across two conditions with equivalent visual stimulation and motor requirements, but differing in instructions about the allocation of spatial attention. In all cases, the display consisted of a central fixation box (subtending 0.5° visual angle from a distance of 80 cm) and a set of four RSVP streams on each side. The streams were temporally synchronized. Their presentation lasted 50 msec and they changed identity with a stimulus onset asynchrony (SOA) randomized between 300 and 500 msec. Across conditions, participants were instructed to detect targets embedded within the RSVP streams using focused attention or divided attention.

In the "focused-attention" condition, participants detected targets in only one of two peripheral streams, while ignoring targets in the other visual field. Spatial cues indicated the relevant location for target detection. Participants were instructed to maintain visual fixation on the central box and to press the space bar whenever an "X" or an "O" appeared on the instructed side (attended), while ignoring their appearance on the other side (ignored). At the beginning of each experimental block, a small tick mark appeared to one side of the fixation box for 3 sec, indicating the initial relevant side for target detection. Subsequently, colored letters appearing within the RSVP stream indicated the relevant side, prompting participants either to maintain the spatial focus of attention (hold cue) or to shift the focus of attention to the other side (shift cue). Cues and targets

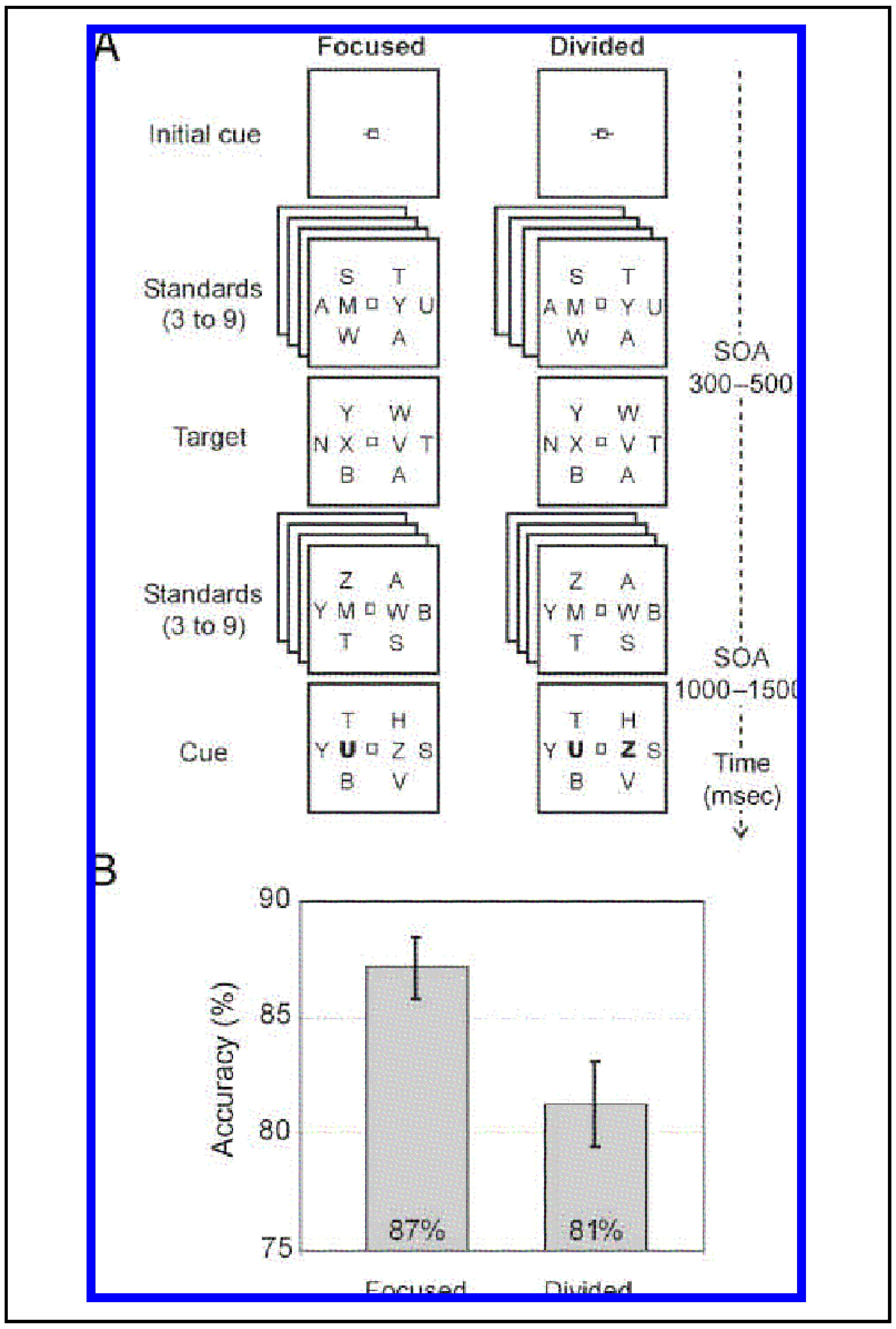

Figure 1. (A) Schematic illustration of the task in the focused-attention (left) and in the divided-attention condition (right). Participants had to press the space bar whenever a target letter "X" or "O" appeared on the attended side in the focused-attention condition, or in either side in the divided-attention condition. In the focused-attention condition, the attended side was indicated at the beginning of each block by an initial cue and, subsequently, by colored cue letters. All visual stimuli were rendered in light grey on a black background. Cue letters are in bold here, but were presented in red and green during the experiment. Each color prompted participants either to maintain the spatial focus of attention (hold cue) or to shift the focus of attention to the other side (shift cue). In the divided-attention condition, both sides were attended at the same time and colored letters were irrelevant for the task. Cues and targets appeared within streams of standard letters in a random order, with the constraint that they were separated by at least three and at most nine standard items. The initial cue was presented for 3 sec, whereas all the following arrays were presented for 50 msec. They changed identity with an SOA randomized between 300 and 500 msec. A longer SOA preceded cue stimuli, randomized between 1000 and 1500 msec. The letters A–B–H–M–N–S–T–U–V–W–Y–Z were used as distracters, and the letters X–O as targets. (B) Accuracy results in the behavioral experiment as a function of attention condition. Results from all 15 participants are reported. Bars correspond to the standard error of mean.

were embedded within streams of standard letter stimuli in a random order, with the constraint that they were separated by at least three and at most nine standard items (1200–5000 msec). Moreover, shift and hold cues appeared with equal probability and in a randomized and unpredictable order. Participants had to maintain a high level of focused attention throughout the entire experimental block in order to detect the imperative target stimuli and the instructive cues.

The cue and target letters appeared only within the two peripheral streams that were closest to fixation, centered at 4.2° to the left and right of the central fixation box along the horizontal meridian. Colored cue letters appeared only in the attended side, whereas target letters could appear in either side, although not at the same time. The other streams, surrounding the two central streams on three sides with an edge-to-edge separation of 1.05°, were distracters. The letters A–B–H–M–N–S–T–U–V–W–Y–Z were used as distracters, and the letters X–O were used as targets, each one subtended approximately 0.56° horizontally and 0.7° vertically. All visual stimuli, except cue letters, were rendered in light gray on a black background. For half the participants, a green letter instructed them to maintain attention at the currently attended location, whereas a red letter instructed them to shift attention to the currently unattended side. For the other half of the participants, the color association was reversed.

In the "divided-attention" condition, participants were required to monitor for targets in both peripheral streams simultaneously. At the start of an experimental block, two small tick marks appeared at either side of the fixation box, instructing participants to attend simultaneously to both sides for the length of the run (see Figure 1A). Colored letters appeared with the same frequency as in the focused-attention condition, but they were not relevant to the task: Participants were instructed to ignore them. In the divided-attention condition, colored letters appeared at the same time in both sides to avoid any effect of lateralized attentional capture (Yantis & Jonides, 1984). The parameters for the presentation of cues, targets, and standard arrays were equivalent to those in the focused-attention condition.

In both conditions, the colored letters serving as cues were preceded by a longer SOA, randomized between 1000 and 1500 msec. Extensive pilot testing indicated the importance of providing these longer intervals preceding the cue. At short intervals, there is significant dual-task interference between the task of searching for targets at the relevant location and the task of decoding spatial cues and implementing the instructed shift. Participants could still perform the target-detection task adequately when cues appeared at short intervals, but they were not able to use the spatial cues reliably to focus their attention effectively. Under these circumstances, participants showed no reliable benefit in focused- versus divided-attention conditions, and therefore appeared to perform both conditions of the task by dividing their attention between the locations of the two RSVP streams. Our observations stress the importance of obtaining corroborating behavioral and/or neural evidence of the effective allocation of focused spatial attention in tasks investigating attentional shifts.

Procedures

Participants sat in a dimly illuminated room at 80-cm distance from a computer screen. A chin rest ensured that they were centered with respect to the monitor and keyboard. They were instructed to maintain visual fixation on the central box and to avoid making eye movements during the experimental blocks. Eye position was monitored with an ISCAN RK-464 eye-tracker (ISCAN, Burlington, MA). Participants used their right and left hands alternately for half of the task. The starting hand was counterbalanced across participants.

Participants performed eight blocks of each of the focused-attention and divided-attention conditions. Blocks contained approximately 10 colored cue arrays and 10 targets, which appeared, randomly and unpredictably, separated by three to nine standard arrays. In each block, a total of 10 cues was presented. In the focused-attention condition, cues were approximately equally divided among the different types of cues (hold right: RR; hold left: LL; shift right-to-left: RL; shift left-to-right: LR). Both attention conditions required the same number of responses. The order of attention condition was counterbalanced across participants. The experiment lasted about 90 min, including short breaks after each block of trials.

Data Processing

Behavioral performance was evaluated in terms of accuracy (i.e., percent correct responses) and RTs. In the focused-attention condition, experimental blocks in which the participants lost track of the correct task-relevant side were excluded. Because target letters (i.e., X and O) appeared both on the attended and unattended side, but participants were instructed to respond only when they appeared on the attended side, a concomitant severe drop in accuracy (i.e., no response at attended targets) and surge of false alarms (i.e., responses at unattended targets) indicated that participants had lost the correct relevant side for target detection.

Results and Discussion

Data from all 15 participants were analyzed, excluding the blocks in which the correct attended side was lost (5 blocks in all). Accuracy (percent correct) and RTs were analyzed with separate repeated-measures ANOVAs, which tested for the effects of attention condition (focused, divided) and target side (right, left).

The accuracy analysis revealed a main effect of attention condition [$F(1, 14) = 5.39$, $p = .036$]. Participants were more accurate in identifying peripheral targets under conditions of focused attention (87%) compared to divided attention (81%) (Figure 1B). Neither the main effect of target side nor the interaction between attention condition and target side reached significance. The RT analysis revealed only a significant main effect of target side [$F(1, 14) = 9.44$, $p = .008$], indicating that participants were faster at identifying targets on the right (624 msec) than on the left (655 msec) side. The factor of attention condition was not significant and the two factors did not interact.

These results confirmed the ability of participants to shift spatial attention effectively according to the cue instructions and to benefit from using focused spatial attention. The use of spatial cues enables participants to focus their attention effectively on the task-relevant side to detect target stimuli with greater accuracy. The validation of the use of spatial cues within the context of the focused-attention condition enabled us to apply the experimental paradigm to investigate the timing of neural activity related to the control of shifts of spatial attention.

The RT results also indicated greater fluency for identifying targets appearing in the right visual field. This pattern of results is common in spatial attention tasks requiring the discrimination of target stimuli (e.g., Nobre et al., 2000), and may be related to how visual processing is biased across the visual environment by the right-hemisphere dominant function of spatial attention (McCourt & Olafson, 1997; Mesulam, 1981).

EXPERIMENT 2: OVERT SHIFTS OF SPATIAL ATTENTION

An overt, oculomotor version of the "focused-attention" condition was performed in order to place an upper bound for the timing of the neural activity that may be involved in generating shifts of visual spatial attention, and therefore to guide interpretation of the ERP experiment (Experiment 3).

Methods

Participants

Three additional volunteers participated in an overt eye-movement version of the focused-attention task (3 women, mean age = 27.6 years, range = 25–30 years).

Behavioral Task and Procedures

Except for the oculomotor instructions, the experimental task and parameters were the same as those used in the focused-attention condition of Experiment 1. Participants were instructed to look at the spatial location indicated by the cues in order to identify the target stimuli within the stream of distracters using foveal vision.

The number of experimental blocks and trials were the same as those used for the ERP experiment (Experiment 3). Participants performed 26 experimental blocks, each lasting about 90 sec. In total, there were 260 cues, 65 in each of the four cueing conditions (RR, LL, RL, LR) and 230–280 target stimuli. The experiment lasted about 1.5 hr, including short breaks after each block of trials.

EOG Recordings

Saccades were measured continuously during task performance by recording horizontal EOG with electrodes placed laterally to each eye. The signals were measured with a BrainAmp 32MRplus amplifier (BrainProducts GmbH, Munich, Germany), using a band-pass filter of 0–200 Hz at a 500-Hz sampling rate. The incidence of correct saccades after shift cues and of correct maintenance of fixation after hold cues was calculated for each participant. Saccade latencies following shift cues were visually identified on a trial-by-trial basis, as the onset of the step-function deflection of the EOG signal away from baseline. The distribution of saccade latencies following shift cues was calculated for each participant.

Results and Discussion

The number of participants performing the overt experiment was insufficient for statistical analyses, but accuracy and RTs were calculated for detecting target stimuli in the left and right visual field, in order to ensure that task performance was adequate and that the pattern of data was comparable to that obtained in the covert behavioral and ERP experiments. The three participants who performed the task overtly showed a high degree of accuracy, 98–100% overall, and without losing track of the relevant side for target discrimination. Their behavioral responses (mean RT = 545 msec) tended to be faster than that of participants who performed the task under covert conditions.

The eye movements were also highly accurate. After shift cues, participants correctly performed a saccade toward the contraversive location within 800 msec on 97% of the trials. They were also highly accurate in withholding saccades after "hold" cues (3% false alarms). Importantly, most overt shifts were complete between 300 and 400 msec (modes and medians). Because of the skewed nature of the distributions of saccade latencies, the different measures of central tendency gave different estimates. The modes occurred between 312 and 346 msec; the medians occurred between 360 and 388 msec; and the means occurred between 387 and 439 msec.

These saccade–latency results place an upper boundary for identifying ERP effects that are involved in initiating and controlling spatial shifts of attention before their overt counterparts can be implemented. The results from the overt attention task indicated that the ERP effects occurring before 350 msec were those most likely to reflect neural activity that is instrumental in controlling and guiding spatial shifts of attention.

EXPERIMENT 3: ERP STUDY

Methods

Participants

Eighteen healthy volunteers participated in the ERP experiment. Data from two participants were discarded from the analysis: one due to very low performance accuracy and another due to excessive noise in the recording. The remaining 16 participants (10 women) had a mean age of 26.7 years (range = 19 to 47). All were right-handed according to the Edinburgh Handedness Inventory test (+92) (Oldfield, 1971) and had normal or corrected-to-normal vision. Eight individuals participated in both Experiments 1 and 3.

Behavioral Task and Procedures

The task and instructions were the same as the focused-attention condition in Experiment 1. Participants covertly detected targets within only one RSVP stream, as instructed by spatial cues, and ignored targets in the irrelevant side. To ensure clean ERP recordings, participants were also requested to minimize blinking and to relax their muscles during task performance.

The numbers of blocks (26) and stimuli (65 cues for each of the conditions RR, LL, RL, LR and 230–280 targets) were the same as those used in Experiment 2. The experiment lasted about 2 hr, including the ERP setup and short breaks after each block of trials.

ERP Recordings and Data Processing

The electroencephalographic (EEG) activity was recorded continuously with active electrodes mounted on an elastic cap (www.biosemi.com) from 128 standard locations according to the 10–5 electrode system (Oostenveld & Praamstra, 2001). Two additional electrodes placed on the right and left mastoids were used as off-line reference sites, and four other electrodes were used to record the eye movements (EOG) bipolarly. Horizontal EOG was measured by electrodes placed on the left and right of the external canthi. Vertical EOG electrodes were placed above and below the left eye. EEG and EOG signals were amplified with a band-pass filter of 0–417 Hz by BioSemi Active-Two amplifier, and digitized at a sampling rate of 2048 Hz.

The continuous EEG recordings were segmented offline. Cue-related epochs started 200 msec before and ended 600 msec after cue presentation. Data were rereferenced to the mean of both mastoid electrodes and refiltered digitally with a low-pass of 40 Hz. All amplitude values were referred to the 200-msec precue baseline. Epochs with excessive drift, eye movements, blinks, or muscle artifacts were excluded from analysis. Trials were automatically eliminated if the voltage exceeded ±50 μV at either the vertical or horizontal EOG channels or if it exceeded ±100 μV at any other channel. In addition, the EOG channels were inspected visually. Trials corresponding to incorrect behavioral performance were also eliminated from the analysis. Separate averages were computed for each type of cue and for each side (RR, LL, RL, LR).

ERPs elicited by standard arrays, containing nontarget letters only, were analyzed in order to validate the manipulation of spatial attention. Specifically, we tested whether the participants' allocation of attention induced an enhancement of the early contralateral visual potential P1, shown previously to be modulated by spatial attention when bilateral stimulus arrays are used (Luck et al., 1990). In particular, we considered the standard arrays which appeared in the first, second, and third positions after the presentation of shift and hold cues. Epochs were constructed from 100 msec before to 300 msec after the onset of standard arrays. Separate averages were obtained for arrays presented while participants attended the left and right streams after shift and hold cues. The rest of the data processing was exactly the same as described for ERPs related to the cue presentation.

ERP Analysis

Cue-related potentials. Cue-related ERPs were interrogated in a systematic and exploratory way to reveal novel markers of neural activity related to the control of visual spatial shifts. The components of the ERPs elicited by cues were identified through their peaks and troughs as well as through topographical analysis delineating successive stable functional states (see below). Lateral posterior electrodes were used to compute the mean amplitude of the characteristic visual potentials P1 (110–150 msec) and N1 (160–200 msec). Specifically, we considered seven pairs of symmetrical electrodes (A8/B5, A9/B6, A10/B7, D29/B13, D30/B12, D31/B11, D32/B10) over the parietal–occipital region of the scalp. To test for later, putative shifting-related effects, six successive time windows were tested: 250–290, 290–330, 330–370, 370–410, 410–450, and 450–500 msec. The mean amplitude within each temporal interval was analyzed separately over a frontal and a parietal area, each consisting of 25 electrodes divided into five antero-posterior regions (see Figure 4). For each potential, repeated-measures ANOVAs tested for effects of the experimental factors of interest: cue side (right, left) and cue instruction (hold, shift), as well as for factors related to the position of the electrodes.

The analysis time windows were set after an exploratory analysis of the data across the entire epoch, using successive *t*-test comparisons (Murray et al., 2002; Guthrie & Buchwald, 1991), which showed no earlier effects of the experimental variables. No later time windows were analyzed because the latency results of the overt saccades experiment indicated that most spatial shifts of attention were complete before 500 msec (see Experiment 2).

The Greenhouse–Geisser epsilon correction factor was applied in all ERP analyses, where appropriate, to compensate for possible effects of nonsphericity in the measurements. Subsidiary analyses were used where necessary to clarify the pattern of significant interactions between experimental factors.

Cue-related topographies. In addition to the analysis of the amplitude effects, we applied a temporal segmentation procedure to define differences in the topographical distribution of ERPs over time and between task conditions (Pascual-Marqui, Michel, & Lehmann, 1995), using CARTOOL software (version 3.32; developed by D. Brunet, Functional Brain Mapping Laboratory, Geneva, Switzerland). In summary, we were interested in testing whether specific patterns of brain activity were associated with shifting spatial attention. The segmentation analysis identifies periods of stability in the topographical maps of the ERPs, which are thought to correspond to stable functional states during information processing corresponding to activity within a given brain region or network. Changes in the topography across different conditions may arise independently of differences in amplitude of the component, reflecting an activation of distinct neural generators rather than a modulation in the magnitude or latency of responses seen at discrete electrode positions (Lehmann & Skrandies, 1980). Such changes in the global configuration of electrical activity over time can provide important additional information about spatio-temporal dynamics of visual processing, not always available in conventional waveform measures (Michel, Seeck, & Landis, 1999).

We compared topographies elicited by shift versus hold cues, starting from cue onset until 500 msec (1024 time frames). For each participant, ERP waveforms elicited by cues on the left and on the right were averaged together in a manner that preserved the location of electrodes relative to the cue side (contralateral or ipsilateral), and were re-referenced to the average of all electrodes (excluding electrodes used for bipolar EOG and for mastoid references). The waveforms across individuals were then grand-averaged, normalizing for the global field power. Topographical analysis was carried out using the Atomize & Agglomerate Hierarchical Clustering approach implemented in Cartool. The optimal number of topographic maps and their times of occurrence were selected on the basis of a cross-validation criterion in which the smallest number of segment maps explaining the greatest amount of variance is retained (Pascual-Marqui et al., 1995). The results revealed that the group-averaged data could be segmented by a solution of 11 different maps (see Figure 3), explaining more than 90% of the total variance.

Standard-related potentials. The visual P1 potential elicited by standard arrays appearing in the first, second, and third positions after the presentation of shift and hold cues was also analyzed. The mean amplitude was measured over seven pairs of symmetrical electrodes placed over the lateral posterior region where the P1 was largest (A10/B7, A9/B6, A8/B5, D32/B10, D31/B11, D30/B12, D29/B13) within latency windows centered on its peak latency (90–130 msec).

Results and Discussion

Behavioral Data

Only one experimental block in one participant was excluded from the analysis due to the loss of the correct, task-relevant side. Accuracy and RTs were analyzed using two separate ANOVAs. Only the factor target side (right, left) was considered. The pattern of behavioral performance was equivalent to that in the focused-attention condition of the behavioral Experiment 1. Performance accuracy was high (94%) and unaffected by the target position. RTs showed a significant main effect of target side [$F(1, 15) = 11.32, p = .004$]. Participants were faster with targets on the right (584 msec) than on the left (606 msec) side.

ERP Data

Effects of spatial orienting on visual potentials of standard arrays. The analysis performed on the amplitude of the P1 potential elicited by the standard arrays provided a corroborative measure of the effective use of focused spatial attention according to the cue instruction. A repeated-measures ANOVA was performed on the mean amplitude of the P1 over lateral posterior electrodes with four factors: *standard position* after the cue (first, second, third), *cue instruction* (hold, shift), electrode *hemisphere* (ipsilateral, contralateral), and *electrode site* (7 levels). The results confirmed the enhancement of the early visual component over the posterior scalp contralateral to the attended side (Figure 2), as shown by the significant main effect of hemisphere [$F(1, 15) = 44.18, p < .001$]. The P1 attentional effect exhibited a different time course according to the standard position and to the instruction provided by cues preceding the standard arrays. The factor hemisphere interacted both with the standard position [$F(2, 30) = 15.36, p < .001$] and with the cue instruction [$F(1, 15) = 8.39, p = .01$]. A trend was also observed for the three-way interaction between hemisphere, standard position, and cue instruction [$F(2, 30) = 3.21, p = .07$].

Subsidiary analyses indicated that significant enhancement of the visual P1 by focused attention took some time to develop after shift cues. The typical enhancement of P1 became significant for standard arrays in the second and third position [$ps < .001$]. After hold cues, where spatial attention had already been directed to the relevant side by the previous cue(s), the P1 effect was consistently and reliably observed for standard arrays in first, second, and third positions ($ps < .03$).

Cue-related shifts of spatial attention. Using this novel experimental approach, we were able to observe nonlateralized ERP effects related to top–down shifting of spatial attention. The changes in neural activity occurred sufficiently early to play an instrumental role in controlling spatial shifts. Effects over posterior scalp region preceded and were more durable than those over the

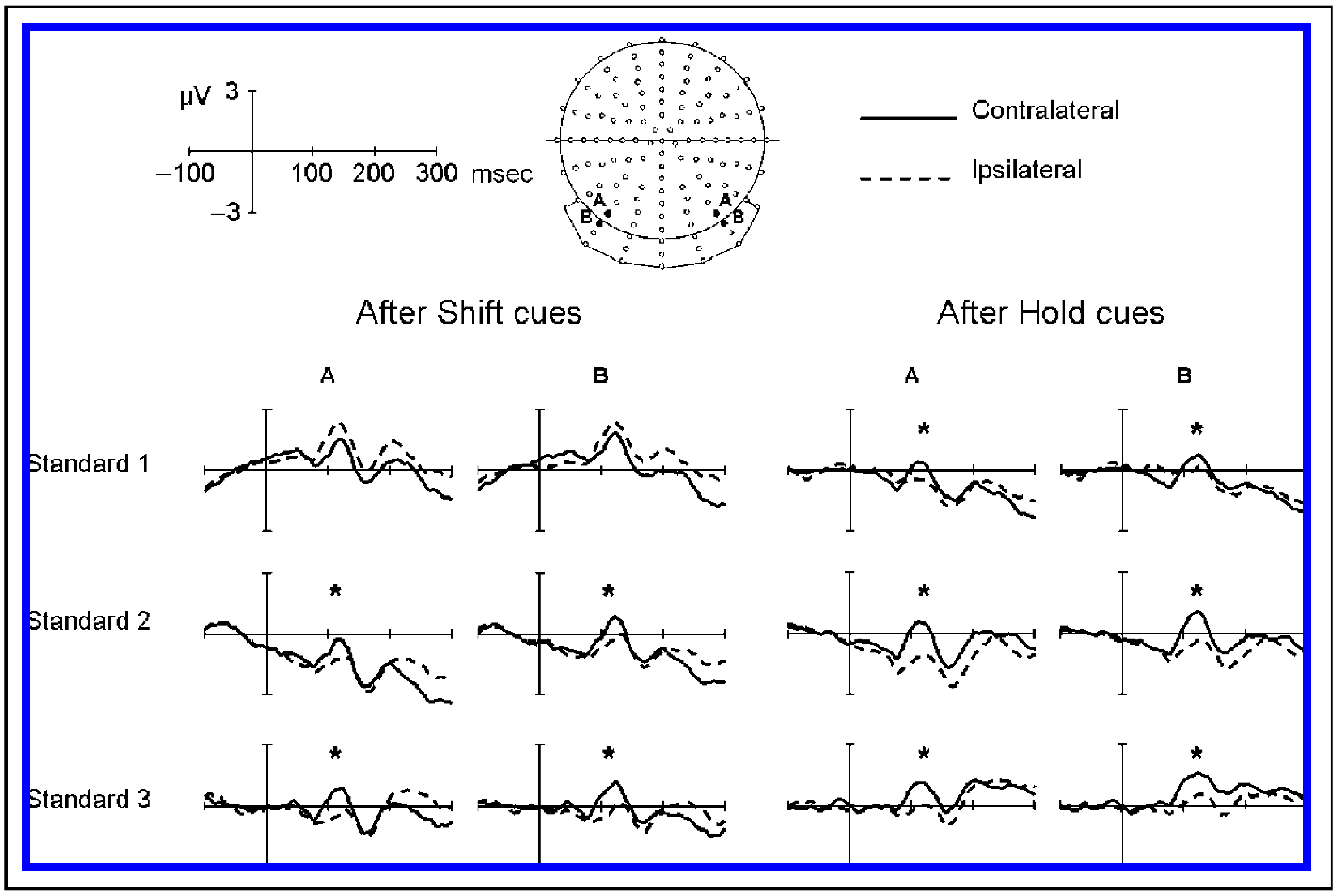

Figure 2. Grand-averaged waveforms elicited by the standard arrays appearing in the first, second, and third positions after "shift" cues (left) and "hold" cues (right), when participants were attending to the location contralateral to the electrode (solid line) or ipsilateral to the electrode (dotted line) side. An enhanced P1 can be observed over the posterior electrodes contralateral to the attended side for Standards 2 and 3 after "shift" cues and for all standards after "hold" cues. The locations of the electrode sites for the sample waveforms are shaded black. Polarity of the waveforms is plotted with positive values upward.

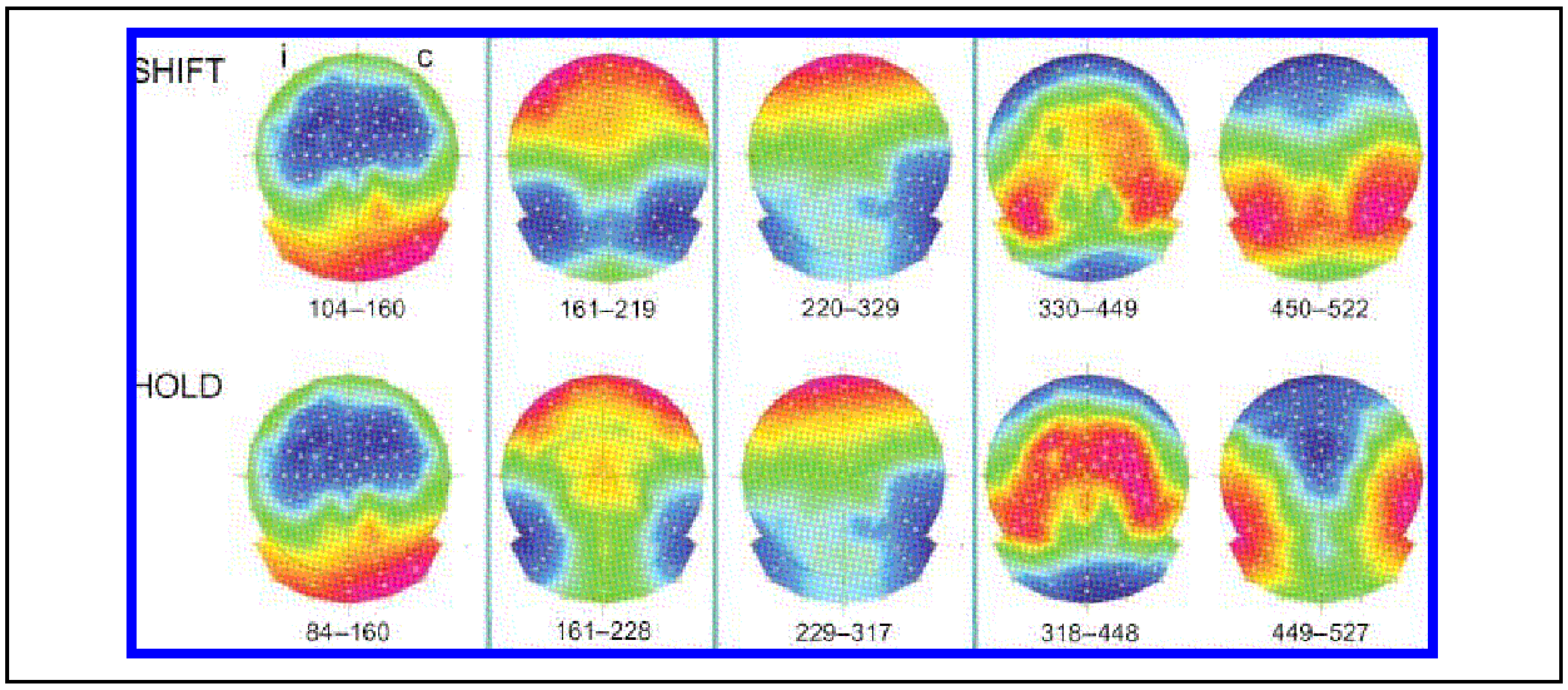

Figure 3. The results of the topographic analysis performed on ERP waveforms elicited by "shift" versus "hold" cues. Axial views of the electric field configuration, using the average voltage across all electrodes as reference, are scaled to unitary strength by dividing the voltage at each electrode by the global field power. Electrode locations ipsilateral to the cue location are plotted on the left, and electrodes contralateral to the cue are plotted on the right. Blue boxes indicate windows in which "shift" and "hold" cues elicited different topographies.

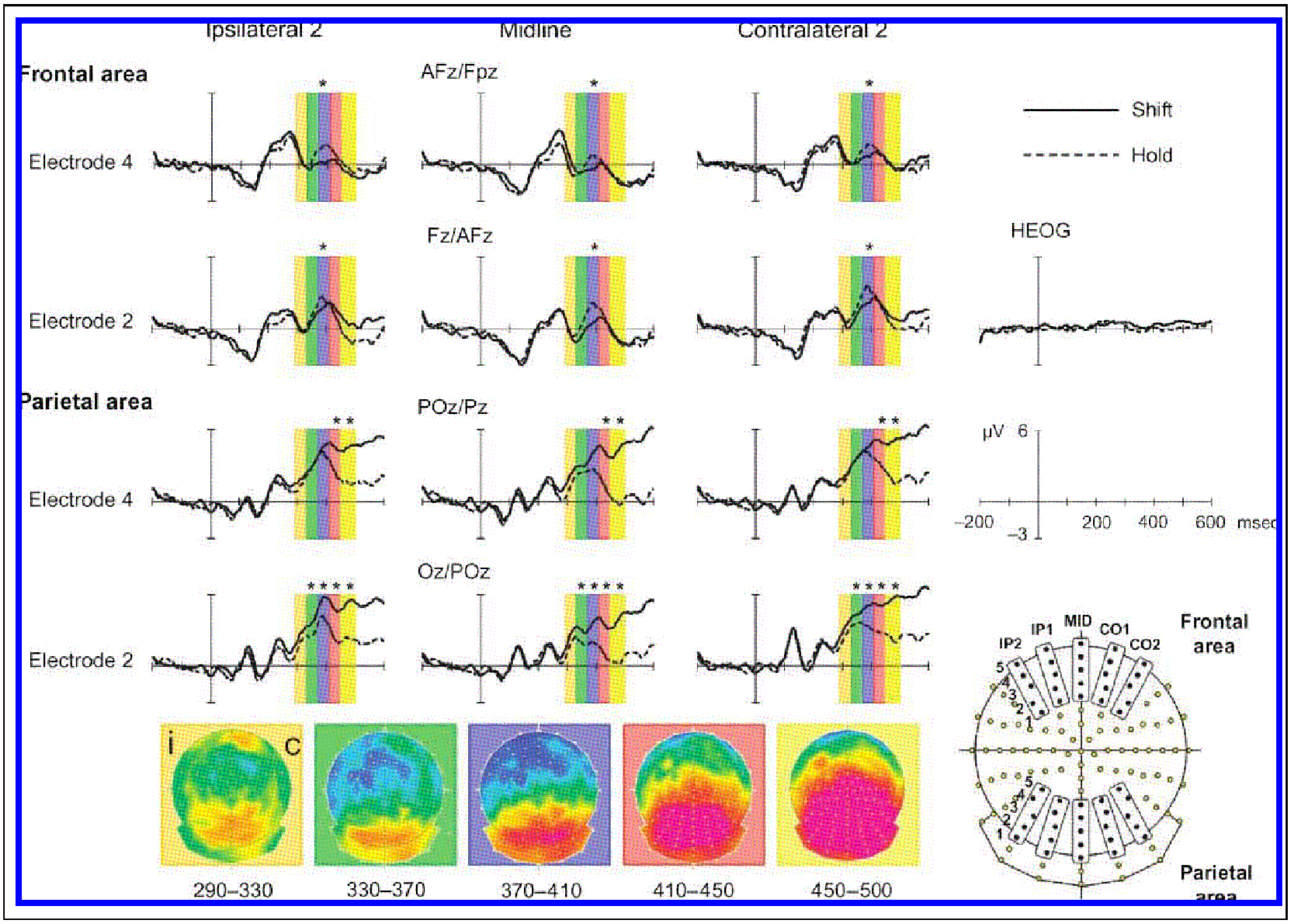

Figure 4. Grand-averaged waveforms elicited by "hold" (dotted line) and "shift" (solid line) conditions in the frontal and parietal areas. Because ERP amplitudes did not show any difference relative to the cue side, data in this figure are collapsed for "hold-left" and "hold-right" and for "shift-left" and "shift-right." For each area, the second and the fourth electrodes of the ipsilateral 2, midline, and contralateral 2 regions are shown. Each time window analyzed is indicated with a colored box and significant differences are marked with asterisks. Scalp topographies of the amplitude difference between the two conditions are shown for each time window, within the corresponding color. The topographies use data referenced to the average of the mastoids, as used for the ERP analysis. The anterior scalp is shown on the top and the contralateral scalp on the right side. The electrode montage is shown at the bottom right. The locations of the electrode sites used in the component analyses are shaded black. Frontal and parietal areas were divided in five antero-posterior regions (ipsilateral 1, ipsilateral 2, midline, contralateral 1, contralateral 2), each one consisting of five electrodes. Contralateral and ipsilateral refer to the cue side.

frontal scalp region, suggesting that the posterior parietal nodes of the fronto-parietal network play a pivotal role in initiating and controlling top–down shifts of spatial attention.

Topographical segmentation of the ERPs elicited by shift and hold cues separated the waveforms into distinguishable stages of neural processing during perception and decoding of the cue, and subsequent shift or maintenance of spatial focus; and pointed toward differences in neural mechanisms engaged by shift versus hold cues (Figure 3). The first identifiable topography in the waveforms was associated with the visual P1, in which lateral posterior positivity was accentuated over electrodes that were contralateral to the salient cue stimulus in the array. Concomitant negative potentials were observed over fronto-central electrodes. Subtle differences in distribution were observed for the next stage, during which the N1 potential occurred. In both cases, the N1 showed a characteristic lateral posterior negative distribution, with concomitant positive potentials over frontal regions. However, for shift cues, the distribution of the potential extended more medially over parietal electrodes. After the N1 stage, a common stage of processing occurred, which was characterized by a pronounced negative potential over electrodes contralateral to the cue. This topography was interpreted as reflecting the N2PC potential (Luck & Hillyard, 1994), related to the identification and focused processing of either shift or hold cue stimuli. The topographies diverged again after this stage. Between approximately 320 and 450 msec, the topographies showed relative positivity over lateral parietal and fronto-central regions, accompanied by a negative focus over occipital electrodes, which was more pronounced after hold cues. ERPs then showed positive potentials over occipital–parietal areas accompanied by negative potentials over frontal regions. For shift cues, the positive parietal potentials were more medially distributed and became increasingly medial over time. For hold cues, the parietal potentials were distributed laterally and were accompanied by more posterior medial frontal negativity.

Repeated-measures ANOVAs comparing mean amplitudes of the successive potentials between shift and hold conditions were used to reveal shift-related activity. Visual P1 and N1 potentials were analyzed over lateral posterior electrodes, where the potentials were largest, testing for the effects of cue instruction (hold, shift), cue side (right, left), hemisphere (ipsilateral, contralateral), and electrode site (7 levels). Mean amplitudes during later, successive stages of neural processing were analyzed over extensive parietal and frontal portions of the scalp, testing for effects of cue instruction, cue side, electrode region within the parietal or frontal cluster (contralateral 1, contralateral 2, midline, ipsilateral 1, ipsilateral 2), and electrode site within each region (5 levels).

Analysis of potentials elicited by shift and hold cues showed the effects of spatial orienting to become significant from 330 to 370 msec and to start over parietal sites (Figure 4). No effects involving cue instruction were found in the early visual potentials (P1, N1) or during the next two successive time windows (i.e., 250–290 and 290–330 msec). Between 330 and 370 msec, cue instruction interacted with electrode site [$F(4, 60) = 7.67$, $p = .004$]. This interaction showed that ERPs elicited by "shift" cues tended to be more positive than those elicited by "hold" cues, especially over the second electrodes of all regions (A9, A16, A22, A29, B6) ($p = .08$). The factor of cue instruction did not interact with cue side or region, suggesting no significant lateralization of the effect. No effects involving cue instruction were found over frontal electrodes during this time window ($ps \geq .15$).

Effects of cue instruction remained evident throughout the remainder of the waveforms. During the next temporal window, 370–410 msec, effects became significant over frontal electrodes. ERPs elicited by shift cues were more negative than ERPs by hold cues, as revealed by a main effect of cue instruction [$F(1, 15) = 4.81$, $p = .04$]. There were no interactions with region, cue side, or electrode site, suggesting the effect to be similarly distributed over the frontal electrodes tested. The frontal effects were short-lived, and no effects involving cue instruction occurred over later temporal windows ($ps \geq .20$).

Over parietal electrodes, effects of cue instruction remained significant throughout all temporal windows tested. Between 370 and 410 msec, cue instruction continued to interact with electrode site [$F(4, 60) = 4.73$, $p = .024$]. The nature of the effect was similar to that observed during the preceding temporal window (shift-related positivity), but subsidiary analyses showed the effect to extend over a wider region, being significant over the first (A10, A15, A23, A28, B7) ($p = .05$) and second (A9, A16, A22, A29, B6) ($p = .03$) electrodes, and tending toward significance over the third electrodes (A8, A17, A21, A30, B5) ($p = .08$). The effect continued to spread over the parietal electrodes, and main effects of cue instruction were observed between 410–450 and 450–500 msec [all $Fs(1, 15) > 8.94$, $p < .009$]. During these times, the shift-related positivity was significant over all parietal electrode sites ($p \leq .005$). Effects of cue instruction over the parietal electrodes did not interact with region or cue side during any temporal window tested, showing that the parietal effect was not significantly lateralized.

GENERAL DISCUSSION

Our new experimental task enabled us to investigate nonlateralized as well as lateralized neural activity related to spatial shifts, while still equating for the participants' state of arousal during task performance. Looking only at lateralized brain activity may greatly underestimate effects related to spatial shifts because neurons in the relevant posterior parietal and frontal areas have very large receptive fields, which often extend into the ipsilateral visual field (Wandell, Dumoulin, & Brewer, 2007; Barash, Bracewell, Fogassi, Gnadt, & Andersen, 1991). The physical appearance of the cues and the need to decode their symbolic meaning ("hold" or "shift") were equated across conditions. The requirement to maintain or shift attention between two peripheral streams also ruled out factors associated with switching the spatial focus of attention between central versus peripheral locations on a trial-by-trial basis, as occurs in Posner-like designs. Effects related to continual suppression of saccades toward peripheral locations were also equated between hold and shift conditions. The operations of shifting and holding attention both occurred within the context of a highly alert state of focused spatial attention and required continued active detection of targets. These controls enabled us to ascribe ERP differences to the spatial-shifting instructions indicated by the cues. Moreover, the clear separation between cue and target stimuli enabled us to identify the activity related to the spatial shifts of attention (hold vs. shift cues) uncontaminated by activity related to stimulus detection, decision-making, and responding related to targets (see also Rushworth et al., 2005; Rushworth, Passingham, & Nobre, 2002).

The efficacy of the attentional orienting cues in our paradigm was confirmed by the results of the behavioral experiment (Experiment 1) and by the visual potentials evoked by the standard arrays in the ERP experiment (Experiment 3). These measures were necessary to ensure that participants followed the spatial cues appropriately and performed the task under focused-attention condition, rather than using divided attention. In the behavioral experiment, participants were more accurate in identifying peripheral targets under conditions of focused compared to divided attention. In the ERP experiment, the early visual P1 potential elicited by the bilateral arrays was significantly enhanced contralaterally to the cued side immediately following the "hold" cues, confirming the spatial biasing of visual processing according to focused attention. The presence of attentional modulation of visual excitability immediately after "hold" cues further showed that cue identification and decoding did not disrupt the already-established spatial attentional bias toward that location. Modulation of visual processing took some time to develop after "shift" cues.

The contralateral P1 was only significantly enhanced from second array after the "shift" cues. Amplitude enhancement of the P1 potential by spatial attention within bilateral arrays replicates previous findings (Luck et al., 1990). The slower time course for effects to develop after "shift" cues is consistent with the additional cognitive operation—that of shifting attention—that had to be performed after the "shift" cue before attention could be directed appropriately. Under these conditions, the 300–500 msec interval between the onset of the "shift" cue and the onset of the first array was insufficient for a significant modulation of the visual responses. By the second array (600–1000 msec), the attentional modulation was clearly in place. These findings are in general agreement with estimates for the time it takes for symbolic cues to lead to visual modulation using the methodology of steady-state visual evoked potentials (Muller, Teder-Salejarvi, & Hillyard, 1998). Having obtained clear evidence that participants were able to shift and hold a selective focus of spatial attention as instructed, it was possible to investigate the time course of brain activity linked to the control of spatial orienting. By measuring nonlateralized changes in brain activity, earlier effects of spatial orienting were identified than could be observed by isolating only lateralized activity. The earliest effects started around 330 msec. They were not significantly lateralized and occurred over the posterior scalp. The posterior effect remained significant throughout the epoch analyzed, becoming increasingly spread over the posterior region. Effects over the frontal scalp were also observed. They followed the posterior effects and were more short lived (370–410 msec).

The absolute timing of the effects may not carry particular significance and need not generalize to spatial orienting functions in other task contexts. Identification and decoding of the cues in this task may have been particularly difficult, and the perceptual demands related to the detection of the targets were high (the mean RT, 595 msec, was relatively long). Therefore, compared to other tasks, the attention shifting dynamics may have been relatively slow. Under simpler task conditions and more intuitive or socially relevant cues, it is likely that these effects would have been brought forward in time. Furthermore, the specific time course of attention-related modulation of neural activity may be partly driven by the temporal regularities between the task-relevant stimuli and the temporal expectations these afford (Nobre et al., 2007; Janssen & Shadlen, 2005; Ghose & Maunsell, 2002). Nevertheless, importantly, the time frame of the ERP effects was consistent with the possibility that the neural processes that they indexed played an operational role in the control of spatial orienting. The neural underpinnings of spatial shifts must be in place by the combined time of the cue–target interval and the average response times in a given task. Traditionally, behavioral effects of spatial orienting based on symbolic cues were observed with cue–target intervals of 200–300 msec (Gibson & Bryant, 2005; Warner, Juola, & Koshino, 1990). More recently, even faster attentional orienting has been reported, especially with overlearned or socially relevant cues, such as arrows and eye gaze (Brignani, Guzzon, Marzi, & Miniussi, 2008; Gibson & Bryant, 2005; Tipples, 2002; Langton & Bruce, 1999). In a simple detection task with overlearned spatial cues, such observations place a limit of about 400 msec for effective shift-related mechanisms to be in operation. We used an overt orienting condition to obtain an approximate estimate of the time course of spatial shifts within the specific context of the task we used. Most saccades to shift cues occurred between 300 and 400 msec. Given that ERPs provide a conservative, upper-boundary estimate for the timing of cortical effects (Rugg & Coles, 1995), the significant effects emerging around 330 msec showed that, on average, covert shifts were initiated just earlier than or with a similar time course as overt shifts. The lack of significant modulation of the visual responses triggered by bilateral arrays immediately following "shift" cues also suggests that covert shifts were not fully implemented within 300 msec.

The relative timing of ERP effects over posterior and frontal scalp regions is an important aspect of the data. Bearing in mind the limited spatial resolution of the ERP methodology, our pattern of results is compatible with the initiation of spatial shifts occurring within parietal cortex. This interpretation is consistent with the occurrence of spatial disorders after parietal lesions (e.g., Husain & Nachev, 2007; Vallar, 2007) and with the reliable involvement of posterior parietal cortex in the superior parietal lobule and intraparietal sulcus in shifting attention between locations in similar tasks revealed by fMRI studies (Kelley et al., 2008; Serences & Yantis, 2007; Yantis et al., 2002; Vandenberghe et al., 2001). The more sustained nature of the posterior effect is also compatible with the dominance of parietal activations in direct comparisons between conditions involving shifting versus holding of spatial attention in fMRI experiments. The results do not, of course, question the involvement of frontal regions in mediating spatial shifts of attention. Indeed, stimulation studies have convincingly shown the ability of activity in the frontal eye fields to modulate activity in visual areas (Armstrong & Moore, 2007; Taylor et al., 2007; Ruff et al., 2006; Moore et al., 2003) and to influence performance in spatial attention tasks (O'Shea, Muggleton, Cowey, & Walsh, 2007; Moore & Fallah, 2004; Grosbras & Paus, 2002). Based on our findings, however, we would speculate that the critical involvement of parietal areas would precede that of frontal areas during cued endogenous spatial shifts of attention. This conclusion has been recently suggested also by Green and McDonald (2008), investigating low-frequency theta band oscillations and the relative neural sources in an attentional shift task. They found activity in both the superior and inferior parietal areas to precede that in the frontal lobe, supporting that parietal cortex provides the initial signal to shift attention. Future studies using single-pulse TMS or microstimulation to compare the time course of the effects of stimulation over parietal versus frontal regions during spatial shifts in the same task will prove particularly informative.

Our parietal-then-frontal pattern of effects differs from the sequence of frontal-then-parietal effects observed by Buschman and Miller (2007) during visual search guided by top–down working memory signals. The discrepancy is not surprising, given that visual search tasks do not isolate functions related to spatial shifts of attention. If spatial shifts do indeed occur during visual search (see Duncan & Owen, 2000; Chelazzi, 1999), they are also accompanied by functions related to comparing stimuli to the memorized template, identifying the target, ignoring the distracters, and preparing and executing a response. Notably, the timing of activity between parietal and frontal areas under top–down and bottom–up conditions of visual search were found to differ, suggesting that there is no fixed line of command between these regions (see Rossi, Bichot, Desimone, & Ungerleider, 2007). More puzzling was the divergence of our results from those by Grent-'t-Jong and Woldorff (2007), who also sought to isolate neural activity related to spatial shifts of attention using ERPs. Like us, they also reported robust nonlateralized effects linked to spatial orienting, but they reported these to start over frontal regions around 400 msec and to involve parietal sites only 700 msec after the cue presentation. The reason for the difference in the pattern of findings must lie in the experimental details. Grent-'t-Jong and Woldorff compared neural activity elicited by spatial cues and by cues that indicated that participants did not have to perform any task during that specific trial (interpret cues). Whereas both types of cues required similar identification and decoding processes, their meaning differed in more than the spatial nature of attention. The two types of cues signaled very different task sets and levels of task difficulty. The earlier frontal activity observed may have contributed to one or both of these types of processes. In contrast, in our experiment, participants maintained the same, highly challenging task set, changing only the spatial location for target detection. A few other minor points about the study of Grent-'t-Jong and Woldorff also raise some concerns. There were no behavioral or electrophysiological measures of attentional benefits, raising the possibility that participants were able to perform the task in the absence of focused attention and spatial shifts. The cues signaling leftward and rightward spatial shifts were also physically different, which may have introduced unwanted sources of variance in the resulting waveforms. Given the intuitive nature of the cues used and the ease with which they might have been detected, the attentional orienting effects they report appear extremely late. Under the considerably more challenging conditions employed in our tasks, overt shifts of spatial attention were mostly complete by 400 msec. Given the contrasting findings in our experiments compared to those by Grent-'t-Jong and Woldorff, it will be necessary to conduct additional experiments in which it is possible to measure nonlateralized ERP effects related to spatial shifts of attention in order to understand which factors affect the temporal order of activation in parietal and frontal areas participating during spatial shifts of attention.

In conclusion, by identifying activity in brain areas that participate in spatial shifts of attention, as well as lateralized activity related to the direction of attention to stimuli, our approach has made it possible to investigate the temporal ordering of neural processes that underlie spatial orienting in frontal and parietal cortex.

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