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Spatial Attention Modulates Initial Afferent Activity in Human Primary Visual Cortex

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It is well established that spatially directed attention enhances visual perceptual processing. However, the earliest level at which processing can be affected remains unknown. To date, there has been no report of modulation of the earliest visual event-related potential component "C1" in humans, which indexes initial afference in primary visual cortex (V1). Thus it has been suggested that initial V1 activity is impenetrable, and that the earliest modulations occur in extrastriate cortex. However, the C1 is highly variable across individuals, to the extent that uniform measurement across a group may poorly reflect the dynamics of V1 activity. In the present study we employed an individualized mapping procedure to control for such variability. Parameters for optimal C1 measurement were determined in an independent, preliminary "probe" session and later applied in a follow-up session involving a spatial cueing task. In the spatial task, subjects were cued on each trial to direct attention toward 1 of 2 locations in anticipation of an imperative Gabor stimulus and were required to detect a region of lower luminance appearing within the Gabor pattern 30% of the time at the cued location only. Our data show robust spatial attentional enhancement of the C1, beginning as early as its point of onset (57 ms). Source analysis of the attentional modulations points to generation in striate cortex. This finding demonstrates that at the very moment that visual information first arrives in cortex, it is already being shaped by the brain's attentional biases.

Keywords: C1, ERP, spatial attention, V1, visual

Inroduction

Voluntarily directing one's attention to a specific location in visual space results in improved detection and discrimination of stimuli appearing at that location (Posner 1980; Hillyard et al. 1998). Functional magnetic resonance imaging (fMRI) studies have demonstrated that modulations of cortical processing accompanying this improvement can extend to the lowest hierarchical level, primary visual cortex (V1; e.g., Gandhi et al. 1999; Kastner et al. 1999). However, whether V1 modulation occurs during initial sensory afference cannot be determined using fMRI due to inadequate temporal resolution, and so remains a matter of considerable controversy. Despite findings of V1 response modulations in nonhuman primates (Motter 1993; McAdams and Reid 2005), and of modulated anticipatory activity in V1 (Kastner et al. 1999; Silver et al. 2007), there has been no report of spatial attentional modulation of the "C1" component of the human event-related potential (ERP) (see Martinez et al. 1999). This has led to the prevailing view that attention only influences V1 activity during delayed re-entrant feedback (Noesselt et al. 2002).

That the C1 component (peaking between 65–90 ms) reflects mainly activity of V1 has been shown by ERP studies using topographic and source localization techniques (Gomez Gonzalez et al. 1994; Clark et al. 1995; Di Russo et al. 2002). This was already a widely held tenet, based on the observation that the scalp distribution of the C1 is highly dependent on retinal location, in a way that is consistent with retinal representation within V1 (Jeffreys and Axford 1972; Butler et al. 1987). Lying along the banks and within the depths of the calcarine fissure, which itself takes a convoluted path along the medial occipital cortical surface, V1 has been said to show "almost an infinity of individual variation" (Polyak 1957). It has been found to vary widely in shape, size, and areal extent relative to anatomical landmarks in histological studies (Rademacher et al. 1993). Although major consistent features enable characterization of a "typical" C1 topography (e.g., upper-field projects to lower calcarine banks, leading to negative scalp potential), subject-by-subject analysis of the C1 strongly reflects such anatomical variability (Jeffreys and Axford 1972; Clark et al. 1995; Foxe and Simpson 2002; Proverbio et al. 2007). This motivates the question whether measures of initial afferent V1 activity in earlier ERP studies have been sufficiently reliable to make the claim that initial V1 activity cannot be influenced by attention (see Mangun et al. 1993; Gomez Gonzalez et al. 1994; Clark and Hillyard 1996).

We would argue that in a typical ERP study sample (N= 10–20), much fewer individuals are likely to exhibit a robust C1 for a single selected location than would be the case for later, larger components generated on the lateral cortical surface such as the P1 or N1. Hence, uniform measurement of the C1 across the sample may not offer sufficient power for detecting what may be subtle modulations thereof. To control for intersubject variability in the present study, we employed a simple individualized mapping procedure, whereby both the optimal spatial locations for stimulation and the optimal electrode locations for derivation were determined in an independent preliminary "probe" session, and were applied subsequently in a follow-up session involving a spatial attention task.

Though ERP studies have provided the ultimate support for early, perceptual-stage attentional selection as opposed to postperceptual selection (Hillyard et al. 1998), theoretical arguments for early selection have often been made solely on the basis of behavioral findings. In particular, that attention can influence the detection of simple luminance increments (e.g., Luck et al. 1994) and increase the contrast sensitivity of stimuli, thus altering appearance (Carrasco et al. 2004), strongly points to selection in early processing stages (Vogel et al. 2005). However, tasks placing demands on such elementary, low-level information processing have not been employed in ERP studies addressing the modulation of the earliest components. It has been shown that attention can operate flexibly so that the

locus of selection varies according to the processing stages most overloaded by a particular task (Lavie 1995; Vogel et al. 2005). Along these lines, we reasoned that selection at the lowest level may be contingent on the task heavily relying on low-level information. Accordingly, we employ a novel task in the present study that involves detection of low-contrast luminance decrements within high-contrast pattern stimuli.

Materials and Methods

Subjects

Sixteen healthy paid volunteers (4 females), aged 20–34 years participated in this study, carried out in accordance with the principles laid down in the Declaration of Helsinki and approved by the Institutional Review Board of the Nathan Kline Institute. All subjects provided written informed consent, and reported normal or corrected-to-normal vision. Each subject underwent 2 recording sessions, the first to "probe" 8 spatial locations and characterize the C1 response independent of spatially directed attention (Fig. 1*a*), and the second to apply a priori chosen optimal stimulus locations in a spatial attention task (Fig. 2).

Stimuli and Tasks

Standard stimuli in both tasks consisted of a Gabor patch with a spatial frequency of 6 cycles/degree, a diameter of 1° at half-contrast, and duration of 100 ms. The patch could be oriented at 45° or 135° with equal probability so that subjects had no prior knowledge of orientation. Data were collapsed across orientation for all analyses. Subjects fixated on a white central cross on a gray background for the duration of both tasks.

In the probe task, Gabor stimuli were presented in random sequence at 8 locations in an annulus of 4° eccentricity, with 1 location lying in each visual octant. The locations were numbered as on a clock-face such that the (x, y) coordinates of locations 1 and 2 in degrees of visual angle were, respectively (2.33, 3.1) and (3.55, 1.7), location 3 was at (3.55, -1.7), and so on (at polar angles of 25.6° or 53.1° from the horizontal meridian; see Fig. 1*a*). Subjects responded with a left mouse button press to targets, consisting of the standard Gabor patch with a superimposed black ring of diameter 1.7° and thickness 0.07°, appearing at any location 11% of the time. This task, which was performed at >99% accuracy for all subjects, ensured that subjects maintained fixation and spread attention evenly among the 8 locations at all times. The stimulus onset asynchrony (SOA) was fixed at 833 ms. At least 18 blocks (mean 22) of 180 stimuli were run per subject (20 standards at each location plus 20 targets).

In the visuospatial attention task of the second session 2 diagonally opposite optimal locations determined in the preliminary session for the subject (see below) were each marked by 4 white dots outlining a 2.75° × 2.75° square centered on the location. A central cue instructed the subject on each trial to covertly attend to 1 of the 2 marked locations, in anticipation of an imperative stimulus ("S2") appearing 733 ms later (Fig. 2*b*). Cue stimuli (duration 100 ms) consisted of a small rotated L-shape whose corner pointed in the direction attention was to be deployed, and appeared at a distance of 0.4° from the center of the fixation cross. Cue direction was randomized, with equal probability. Standard stimuli were identical to those in the probe task. Target stimuli, which appeared randomly on 30% of trials, consisted of the standard Gabor pattern with a ring of reduced luminance of diameter 0.8° and thickness 0.11° superimposed (see Fig. 2*a*), also lasting 100 ms. Subjects were instructed to respond to targets presented at the cued location but to ignore stimuli presented at the uncued location. The cue-S2 SOA was fixed at 833 ms. The intertrial interval was fixed at 1533 ms. Each subject underwent at least 20 blocks (mean 24), each composed of 100 trials (~4.1 min).

The difficulty of target detection, defined by the drop in luminance of the ring region in targets (Fig. 2*a*), was varied adaptively across 11 levels based on online performance. The targets at each level were created simply by multiplying grayscale brightness values within the ring region by a factor of 0.4–0.9, increasing in steps of 0.05. Each block began at level 7. Thereafter difficulty dropped a level in the event of either a single *miss* or 2 *false alarms* in a row and increased a level in the event of 2 *hits* in a row. As a result, all subjects achieved an average hit rate of ~80%. Feedback on the average and maximum level reached was given at the end of each block. Subjects were encouraged to achieve and maintain performance at as high a difficulty level as possible.

Data Acquisition

Continuous electroencephalographic (EEG) data, digitized at 512 Hz, were acquired from 164 scalp electrodes and 4 electrooculographic (EOG) electrodes with a pass-band of 0.05–100 Hz and low-pass filtered up to 45 Hz offline. Noisy channels, identified by taking the standard deviation over the block and checking whether it is more than 50% greater than that of at least 2 of the 4 closest surrounding channels, were interpolated. During the attention task, eye movement was recorded using an ISCAN infrared eye-tracker (120 Hz sample rate; 0.03° resolution), the output of which was both monitored online to ensure fixation and also analyzed offline Preliminary calibration runs were carried out to ensure precise mapping of eye-position data to visual angle, wherein subjects performed 10 brief, randomly cued eye movements to each of 16 locations corresponding to the 8 probe

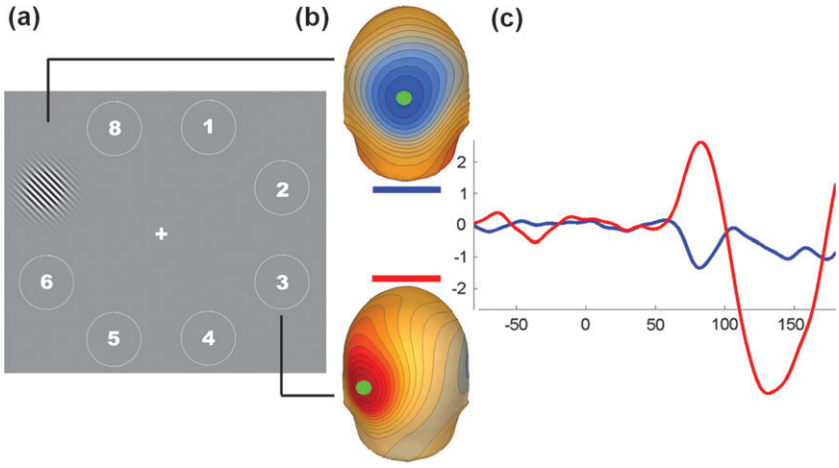

Figure 1. Probe task and procedure carried out in the preliminary session, independent of spatially directed attention. Data from a single subject (S#6) are shown. (*a*) Gabor stimuli were presented to 8 locations in a randomized sequence. Based on the resulting waveforms, we identified the pair of diagonally opposite locations from which the highest amplitude response within the C1 interval (50–80 ms) was elicited. (*b*) For these optimal locations, the negative and positive foci were identified in the scalp topography in the same C1 time frame for upper- and lower-field locations, respectively. (*c*) Average-reference waveforms were extracted from electrodes lying at the center of these foci.

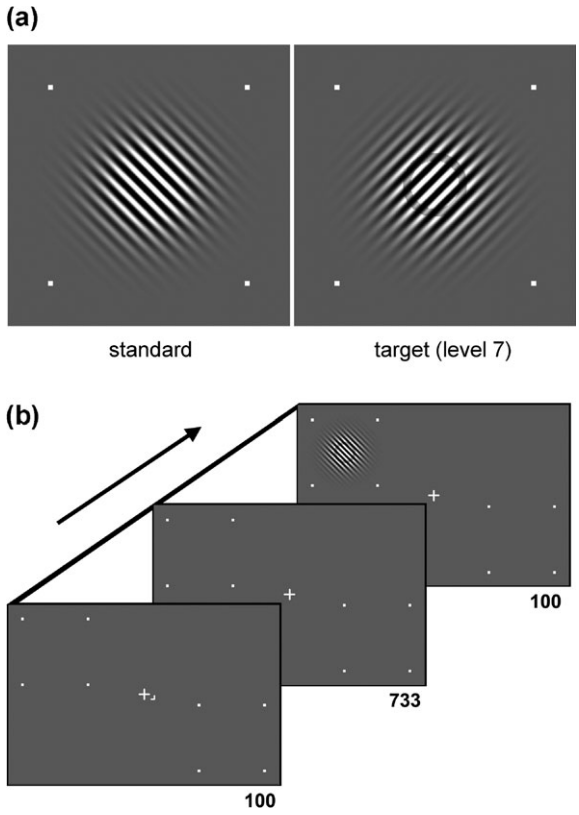

Figure 2. Spatial cueing task of the second session, incorporating the optimal pair of locations determined in session 1. (*a*) standard Gabor stimulus and target stimulus at difficulty level 7. (*b*) Task structure. In this example an invalid (uncued) target is presented, which is to be ignored.

locations and the half-way point of each relative to the fixation cross. Attention task trials were rejected offline if eye gaze deviated by more than 0.5°. Horizontal EOG data recorded from the outer canthi were also calibrated in this run, and the same rejection criterion was applied to EOG data of 3 subjects for whom eye-tracker data were not available.

Data Analysis

For both tasks, average-reference data were epoched from –80 ms before to 200 ms after stimulus onset, and baseline-corrected relative to the interval –80 to 0 ms, with an artifact rejection threshold of 60 μV applied.

Probe Data

The purpose of the probe task was to provide an unbiased estimate of C1 amplitude for each stimulus location, when attention is not directed to any one point in space, but is presumably spread equally among all locations. For each individual, ERP waveforms were derived for each of the 8 locations and examined both in terms of morphology and the evolution of topographic maps over the time frame of the C1 (50–80 ms). Timing was emphasized as the principal criterion for C1 identification, such that only initial components with an early onset of 50–60 ms, and whose amplitude rose to a level well above baseline fluctuations by 80 ms, were considered. Topographical characteristics established in previous studies additionally guided the identification, referring in particular to studies that sampled from many stimulus locations (e.g., Jeffreys and Axford 1972; Clark et al. 1995). (Because the majority of ERP studies of spatial attention have used a small number of locations lying close to or on the horizontal meridian, the C1 is often regarded as having a strictly dorsal-midline distribution. However, studies such as these that more fully covered the visual field show that C1 topography is much more sensitive to stimulus location, having distinctly lateralized distributions for stimuli located closer to the vertical meridian.) A pair of diagonally opposite locations (e.g., upper-left location 7 and lower-right location 3) was then selected on the basis that each elicited a robust C1. Pairing diagonally opposite locations ensured that the distance between attended and unattended locations in the attention task was constant across subjects, and the fixation point lay always on a line joining the locations. In 2 cases, a reliable C1 could not be measured for any probe location; therefore these subjects were excluded from further analysis.

Having selected stimulus locations, electrode sites of maximal C1 amplitude were then identified so that a single trace could be derived for each location for a given subject. In order to collapse data across subjects, it was necessary to group responses of like polarity. To this end, we identified the earliest onsetting negative focus in the scalp topographies for upper-field stimuli and the positive focus for lower-field stimuli (Fig. 1*b*,*c*). Although this is in line with the property of polarity inversion for upper- versus lower-field stimuli for locations close to the horizontal meridian (Di Russo et al. 2002), we applied this constraint here merely as a convention to group responses, providing reliability through having 2 separate observations of modulation in the attention task data.

Attention Task Data

For the attention task data, ERPs to the upper- and lower-field stimuli were derived for the conditions of attention toward and away from each location. Trials containing deviations of gaze from central fixation of greater than 0.5° during the cue-S2 interval were rejected. Three subjects who made such deviations on more than 30% of trials were excluded from further analysis. Only nontarget stimuli were analyzed in both sessions, excluding false alarm trials, resulting in an average sweep count of 350 per condition for the probe data and 330 per condition for the attention task data.

To test for attentional modulation of the C1, we first took as the dependent variable the average amplitude over the interval 50–80 ms, measured from waveforms at the optimal electrodes determined independently in the first session. An analysis of variance (ANOVA) with the factors of attention (toward vs. away) and field of S2 (upper vs. lower) was then carried out. It was necessary to invert the upper-field values for this test so that polarity was all positive, enabling comparison of the strength of effects across fields.

To follow up early attention effects found in the initial ANOVA, a second analysis was conducted to estimate both the onset of the unbiased "probe" C1 and the onset of attentional modulation in the cueing task for comparison. For both the probe and attention task data, upper- and lower-field waveforms were combined by subtraction, giving a single waveform for each of the probe, attended, and unattended conditions. To estimate the onset of cortical activity in the absence of biased attention, we computed running t-tests comparing probe waveform amplitude at each sample point to zero. The onset was defined as the point at which the difference reached significance at the 0.05 level for 10 or more consecutive points (>20 ms) beginning at that point (see Foxe and Simpson 2002; Molholm et al. 2002). To determine modulation onset in the attention data, we computed running *t*-tests comparing the attended to the unattended waveform at each point, with the same constraints applied.

Effects of attention on the later P1 component were also investigated for the purposes of comparison with previous studies. Though more consistently observed across subjects, the P1 has been found to vary also as a function of stimulus location, albeit to a lesser degree than the C1 (e.g., Clark et al. 1995). Thus, electrodes for P1 amplitude measurement were determined on the basis of grand average probe data for each of the 8 locations, and applied in the attention task data to test for modulation effects. In line with many studies distinguishing an earlier contralateral P1 phase from a later ipsilateral phase (e.g., Di Russo et al. 2002), we measured and tested early (90–110 ms; contralateral electrodes for all locations) and late (110–140 ms; ipsilateral electrodes for all locations but 1 and 8) phases of the P1 separately. As for the C1, an ANOVA with the factors attention and field was carried out for each P1 phase in the attention task data.

Source Analysis

We estimated intracranial sources of attentional modulation using a distributed linear inverse solution based on a Local Auto-Regressive

Average (LAURA) model of the unknown current density in the brain (Grave de Peralta et al. 2001), implemented in the Cartool analysis package. LAURA uses a realistic head model with a solution space of 4024 nodes, where voxels are restricted to the gray matter of the Montreal Neurological Institute's (MNI's) average brain divided into a regular grid with 6-mm spacing. For each subject the inverse solution was estimated for the difference waveforms (attended minus unattended) in the attention task data. We then found the maximally activated node within the set of all nodes lying within Brodmann areas 17 (57 nodes across hemispheres), 18 (259) or 19 (290) over the interval 50–70 ms, that is, just shy of the typical onset of the earliest P1 (Martinez et al. 1999; Di Russo et al. 2002).

Results

Probe Task and Mapping Procedure

Attesting the utility of the mapping procedure, optimal locations selected on the basis of the probe data varied considerably across the 11 included subjects (see Fig. 4). In the majority of cases a reliable C1 was observed for less than half of the probed locations, such that the selection of location pairs was guided most often by the presence or absence of the C1, rather than a comparison of relative amplitudes. For 9 of the 11 subjects, the timing and topography of the C1 for selected locations closely matched those demonstrated in previous studies (e.g., Clark et al. 1995; Di Russo et al. 2002). Consistent with the cruciform model of V1 (Jeffreys and Axford 1972; Butler et al. 1987), subjects with optimal locations lying close to the vertical meridian (subjects 1, 2, 7, 9, 11) exhibited bipolar C1 distributions reflecting the projection of these locations onto parts of V1 lying furthest outside the calcarine sulcus. Of the 6 subjects whose optimal locations lay close to the horizontal meridian, 4 (subjects 3, 6, 8, 10) exhibited a distinct midline dorsal distribution for upper-field stimuli, matching the "classic" C1 topography observed in many studies (e.g., Martinez et al. 1999; Di Russo et al. 2003). The more lateral negative foci observed for the remaining 2 subjects (4, 5) were strong exceptions to the classic pattern, highlighting the extent of variability accounted for by the mapping procedure.

Behavioral Results of Spatial Cueing Task

As stimuli appearing at the uncued location were to be ignored, we cannot derive a behavioral measure of attentional modulation as is often done for traditional Posner tasks involving probabilistic cues. However, the effectiveness of the adaptive difficulty manipulation in maintaining task difficulty at a high level, and thus keeping subjects highly engaged, is demonstrated in a mean ± SD hit rate of 80.7 ± 3.3% and d' of 2.36 ± 0.34.

Electrophysiological Results of Spatial Cueing Task

Figure 3*a* shows the ERP responses averaged over all 11 subjects, contrasting the conditions of attention toward and away from each location, with waveforms to upper- and lower-field stimuli superimposed. The ANOVA testing the C1 component revealed a significant main effect of attention ($F_{1,10}$ = 20.25, P < 0.001). There was no effect of field or interaction between factors. Follow-up t-tests in each field revealed a significant attention effect for both the upper-field stimuli ($t(10)$ = 4.10, P < 0.002) and lower-field stimuli ($t(10)$ = 4.28, P < 0.002). The ANOVA testing P1 amplitude revealed

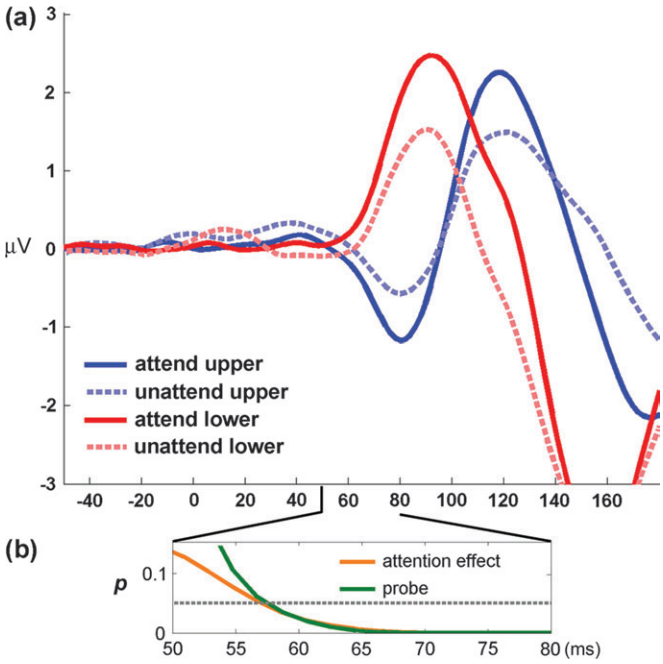

Figure 3. (*a*) Grand average waveforms for attention toward and away from upper- and lower-field stimuli. (*b*) P-values derived from running t-tests to determine the onset of the probe C1 from session 1 and the onset of the attention effect in session 2.

a significant effect of attention for both the early ($F_{1,10}$ = 23.02, P < 0.001) and the late phase ($F_{1,10}$ = 15.58, P < 0.005).

The timing of attentional modulation with reference to the onset of the unbiased probe C1 onset represents a crucial indicator of striate cortex generation. Figure 3*b* plots the series of P-values resulting from point-wise t-tests in the time frame of C1 onset for the deviation of probe amplitude from baseline, and for the difference in amplitude between the attended and unattended conditions. As the figure indicates, the point at which significance is reached for the probe C1 coincides precisely with that of the attention effect, at 57 ms.

Figure 4 displays the data of each individual subject, illustrating the selected optimal measurement points on the probe topographies at 80 ms and the waveforms derived at these electrodes in the attention task data. Also shown are the probe ERP topographies at 100 ms, the peak latency of the contralateral P1, for the lower-field locations. As both the lower-field C1 and early phase P1 manifest as contralateral positivities, their topographies tend to overlap. This overlap has not yet been quantified systematically, possibly due to inadequate electrode density in earlier studies (Jeffreys and Axford 1972; Clark et al. 1995). In addition, differences in exact stimulus locations across studies make direct comparison difficult. Nevertheless, it can be seen from Figure 4 that the majority of subjects show a marked shift in the positive contralateral focus from 80 to 100 ms, indicating that the 2 components are well dissociated. It is worth noting, for example, that all 3 subjects having location 5 as their lower-field location exhibit a lateral shift in topography from the C1 to the P1, which is highly similar to that seen in 2 recent studies wherein stimulus locations were ~0.5° from this location (Di Russo et al. 2002, 2003). The average absolute shift in the focus of positive potential across subjects was measured as 2.8 ± 1.8 cm—almost twice the average interelectrode distance on the 160-channel electrode cap used.

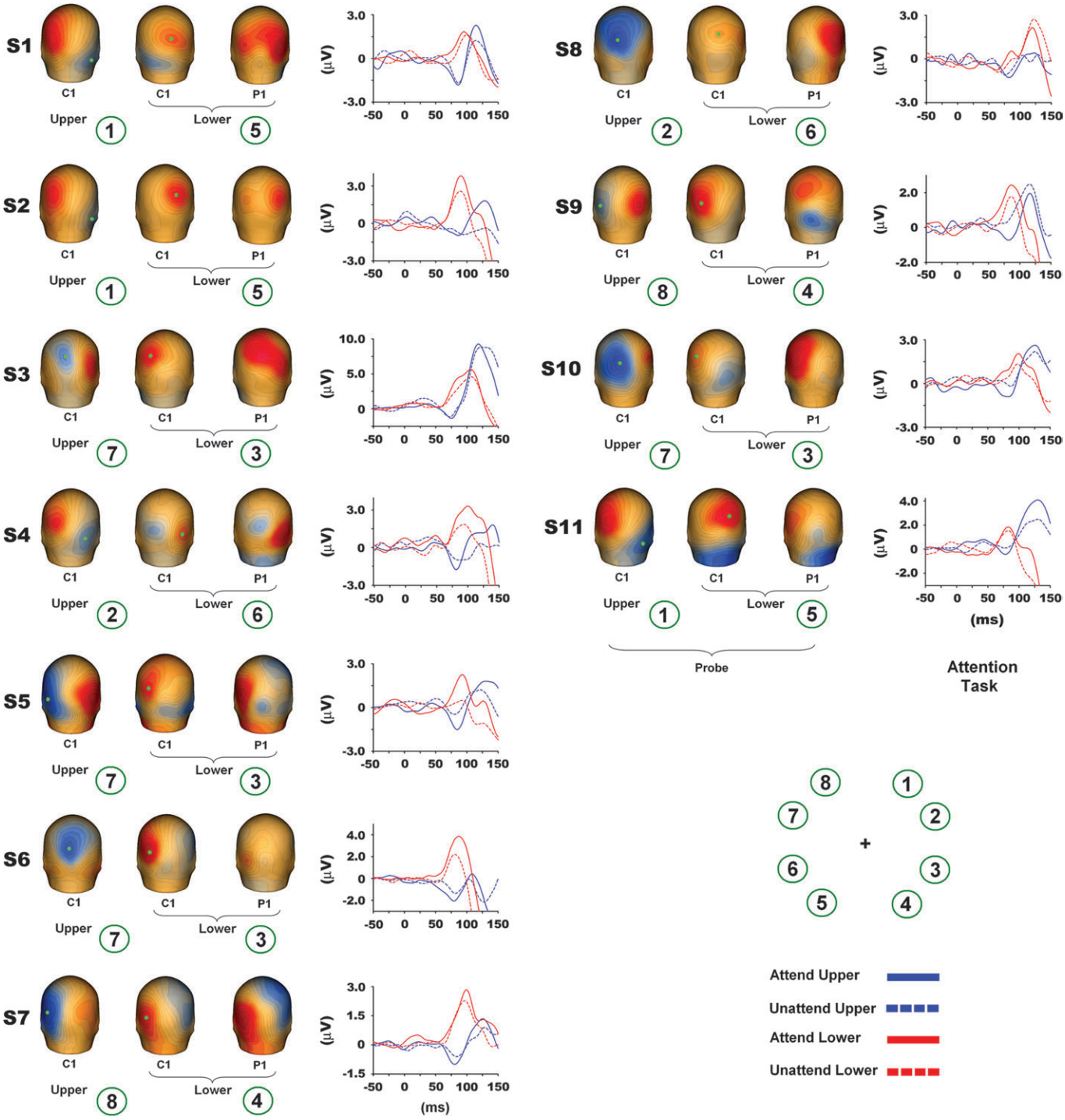

Figure 4. Individual subject scalp topographies at the 80-ms time point for upper-field locations and at 80 and 100 ms for lower-field locations from the probe data, and attended and unattended waveforms (average reference) from the attention task data for the pair of diagonally opposite locations selected for each individual. Scalp electrodes selected to measure individual C1s on the basis of probe topographies are shown as green circles. C1 (80 ms) and P1 (100 ms) topographies for lower-field locations are shown on the same scale for each subject to highlight changes in amplitude as well as topographical focus.

We estimated the intracranial sources of attentional modulation of the C1 using a distributed inverse solution (LAURA). Specifically, the site of maximum modulation in visual cortex in the time range of C1 onset (50–70 ms), was determined for each subject. Following the procedure of Martinez et al. (1999) we averaged Talairach coordinates of the source sites across subjects, which revealed coordinates of (x = 24, y = –80, z = 3) and (x = –23, y = –78, z = 10) for left and right hemifield stimuli respectively, consistent with striate cortex generators (note again that only 9% of included nodes in MNI space were from area 17). Offline analysis of eye-tracking data for the accepted trials in the attention task revealed an average absolute gaze deviation in any direction across subjects of 0.09° ± 0.05° (mean ± SD), illustrated in Figure 5°.

Discussion

In the present study intersubject variability of the C1 component of the human ERP was controlled for in a simple individualized mapping procedure, resulting in robust measurement of initial V1 activity. We applied this procedure to data recorded during a spatial attention task involving elementary luminance decrement detection, and observed significant modulation of the C1. Further, a fine-grained timing analysis showed that the onset of attentional modulation precisely coincided with the onset of the "probe" C1 measured without spatially focused attention. Source localization results provide further support for a striate source of the modulation. These findings count against the theory that V1 activity is impenetrable during initial afference and may only modulate during delayed re-entrant feedback, which has emerged on the basis of combined ERP and fMRI studies showing V1 modulations in fMRI data but not modulation of the C1 (Martinez et al. 1999; Noesselt et al. 2002; Di Russo et al. 2003). Conversely, our results are consistent with the interpretations of previous fMRI studies finding attentional modulation in V1 (Gandhi et al. 1999; Somers et al. 1999) and also with single-unit studies in nonhuman primates (Motter 1993; Ito and Gilbert 1999; McAdams and Reid 2005).

Although the C1, measured in the same latency interval (e.g., Clark et al. 1995; Martinez et al. 1999) or even later (e.g., Di Russo et al. 2002, 2003), has consistently been shown to originate in striate cortex, and is here observed to modulate with attention, we must still rule out the possibility that an overlapping P1 modulation, which has been seen to onset as early as 70 ms (Martinez et al. 1999), contributed to the effect. First of all, we found equally strong modulations for negative upper-field C1s as positive lower-field C1s. As in every other study on the subject, the P1 modulation found here was a relative enhancement with attention, resulting in a positive shift. If there were contributions from an overlapping P1 effect, we would have found greater modulations for positive than negative C1s, or might not have observed modulation of the negative C1 at all. Secondly, the point of onset of the attention effect, calculated as 57 ms, is a good deal earlier than the earliest observed modulations of the P1, and not only coincides with the unbiased probe C1 onset calculated here, but coincides with or even precedes C1 onset latencies expressed in the vast majority of previous studies relating to the issue (e.g., Gomez Gonzalez et al. 1994; Clark et al. 1995; Clark and Hillyard 1996; Martinez et al. 1999; Di Russo et al. 2002, 2003; Pourtois et al. 2004; Stolarova et al. 2006; Proverbio et al. 2007). Finally, the average distance on the scalp by which the contralateral positive focus shifted between 80 and 100 ms for lower-field stimuli is large enough to render a common generator for the C1 and P1 extremely unlikely. Moreover, where valid comparison is possible, the temporal and spatial characteristics of the C1 and P1 measured here match those in previous studies where separate generators in striate and extrastriate cortex, respectively, has been convincingly asserted (e.g., Di Russo et al. 2002, 2003).

It is worth pointing out again that it was by convention that we selected electrodes lying within the negative topographical focus for measurement of upper-field C1s and within the positive focus for lower-field C1s. Polarity inversion of the C1 at midline sites has become a routine indicator of a striate cortical source. This is because the majority of studies have used stimulus locations near or on the horizontal meridian, which project to parts of V1 lying well inside the calcarine fissure (e.g., Martinez et al. 1999; Di Russo et al. 2002, 2003; Noesselt et al. 2002). However, it is well known that locations close to the vertical meridian project to the part of V1 lying on the outer banks of the calcarine cortex (see Clark et al. 1995). Approximate dipolar sources for upper- and lower-field locations near the vertical meridian would thus have roughly the same orientation. This anatomical feature, along with its assured variability across individuals (see Stensaas et al. 1974), casts doubt on whether polarity inversion can be used as a valid diagnostic of V1 generation that can be generalized to all spatial locations. We would thus emphasize here that it is the timing of attentional modulation with respect to the probe activity onset that we have considered the crucial indicator of the earliest striate source activity.

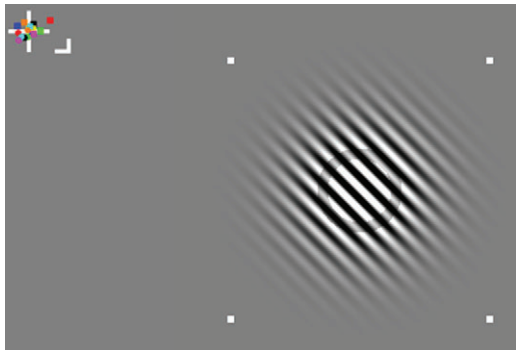

Figure 5. Average gaze deviations for trials accepted to the ERP analysis, superimposed on the stimulus display. Both upper and lower locations are shown for each subject in different colors. The stimulus is a level 7 target.

Many recent studies have focused on demonstrating the flexibility of selective attention and its expression in visual cortex. For instance, the locus of attentional selection has been shown to vary among hierarchical levels of processing according to perceptual load (Lavie 1995), the spatial scale of attended items (Hopf et al. 2006), and the involvement of perceptual versus memory systems (Vogel et al. 2005). Given these dramatic manifestations of flexibility, it seems somewhat arbitrary that gating could occur early in the visual system, but never reach down to the very first stage. It is certainly not the case that the pattern of feedback inputs to V1 from higher regions is any sparser than in later regions of extrastriate cortex (see Sincich and Horton 2005). The C1 component is not invulnerable to contextual influences, such as the motivational relevance of aversive stimuli (Pourtois et al. 2004; Stolarova et al. 2006), or indeed to concurrent auditory input (Molholm et al. 2002). Moreover, spatially specific increases in V1 baseline activity with attention in the absence of stimulation have been found in human fMRI studies (Kastner et al. 1999; Silver et al. 2007), suggestive of anticipatory priming of V1 neurons. In human EEG studies, anticipatory changes in alpha-band oscillatory power have been found to be retinotopically specific (Worden et al. 2000; Kelly et al. 2006), consistent with priming of the very earliest cortical stages. It seems paradoxical then that there has been no report of modulation of the C1—why would anticipatory priming of V1 neurons affect processing not in the first volley but only during later rounds of feedback?

Though it is clear that increased sensitivity has been afforded by the mapping procedure, it is unlikely that this factor alone

fully accounts for our detecting a C1 modulation, and why many other studies have not. Indeed, without controlling for variability as we have done here, several studies have measured relatively high-amplitude C1s that were not observed to modulate (e.g., Martinez et al. 1999; Di Russo et al. 2003). Recently, Proverbio et al. (2007) also found large individual variability in the C1, with only half of subjects showing a negative C1, which would be expected for stimuli centered on the horizontal meridian (see Clark et al. 1995; Martinez et al. 1999). Even for this subgroup of subjects, there was no effect of spatial attention on the C1. It is therefore of interest to consider differing experimental parameters, which, individually or together, may have further contributed to the outcome.

Of potential relevance is that trial-by-trial cueing was employed in the present study, whereas more continuous, rapid stimulation (1–5 stimuli per s) has been used in previous studies, with attention alternated between 2 locations every 20 s or so (e.g., Martinez et al. 1999) or directed to 1 location for an entire run of 1 minute or longer (e.g., Mangun et al. 1993). Theoretical arguments on this issue do not clearly favor either task type as being more likely to induce early modulations—the potential roles of refractory effects (such as inhibition of return) at play in rapid stimulation paradigms, or on the other hand, negative priming effects associated with trial-by-trial shifting of attention in cueing paradigms, are unknown. Such phenomena appear not to compromise the modulation of later components such as P1 and N1, as these are almost invariably observed to modulate. In previous studies looking at ERP attentional modulations for trial-by-trial cueing paradigms with instructional (not probabilistic) cues, the C1 component has not been directly tested (Eimer 1994; Hopf and Mangun 2000). Though not the most compelling explanation for the current results, a systematic investigation of C1 modulation during sustained versus trial-by-trial attention deployments may be warranted.

Another factor that distinguishes the present paradigm from most previous studies observing no C1 modulation is the spatial configuration of the attended/unattended locations, which were diagonally opposite here, rather than symmetrical about the vertical meridian. One study, however, did use a display with both types of unattended location, where subjects attended to 1 of 4 stimulus streams, 1 in each quadrant, and no effects of attention were found on the C1 (Mangun et al. 1993).

Stimulus differences are likely important, particularly in the comparison of our results with those of Martinez et al. (1999) and Noesselt et al. (2002). In the latter studies, the task involved discrimination of a symbol in the center of the stimulus among surrounding distracters, all of which were superimposed on a background checkerboard pattern. Thus, the part of the stimulus primarily responsible for evoking a strong scalp-measured C1, that is, the background, is not the part that is relevant to task performance. An important factor may be that the majority of V1 neurons whose receptive fields lie within the stimulus space actually receive input from distracter symbols—though enhancement of the entire stimulus may occur at extrastriate levels where receptive field sizes are large, enhancement of the entire stimulus at the level of V1 would be disadvantageous for task performance and therefore might not occur. In contrast, attentional enhancement of the entire stimulus pattern is required in our task and this may be a necessary condition for observing early modulation. That it is not a *sufficient* condition clearly follows from the many studies showing that C1 does not modulate during spatially cued size discrimination tasks (Mangun et al. 1993; Clark and Hillyard 1996; Di Russo et al. 2003).

An alternative explanation may lie in the further consideration of task demands. A unique feature of the present task among other ERP studies is that simple pattern detection was required, as opposed to more complex discrimination. Though strong attention effects on near-threshold detection abound in behavioral studies, the examination of ERP correlates thereof has been largely precluded by the inability to measure reliable visual ERPs to low-contrast stimuli (Luck et al. 1994). We have effectively surmounted this problem by infusing a low-contrast target pattern within a high-contrast, uniform pattern stimulus. Task performance then boils down to a simple presence–absence judgment, which, computationally, would involve a relatively direct translation from low-level features analysis to final decision.

Depending on the stimulus aspects that distinguish a target from nontarget in a given visual task, the fidelity of information in certain processing stages will be more critical to successful performance than that in other stages. In our task, crucial evidence of the low-contrast "break in context" within the otherwise uniform pattern that defines a target may be contained in feed-forward activity through V1. Indeed, it has been shown that successful figure-ground processing of this kind is strongly dependent on V1 activity (Supèr et al. 2003). Conversely, the output of low-level analyzers in V1 may be the point at which insufficient signal-to-noise most often gives rise to an erroneous response. Higher-order attentional control processes may then work to adapt the structure of cue-contingent anticipatory attentional sets such that a boost in "gain" is instantiated at this crucial stage. This targeted enhancement may be equivalent to a sharpening of contrast sensitivity similar to that shown behaviorally with transient attention (Carrasco et al. 2004). It is interesting in this context to note that a task involving near-threshold pattern detection of the kind under discussion here was used in an fMRI study showing preparatory modulations in V1 to be strongly predictive of behavioral performance (Ress et al. 2000).

The implication of this adaptive gain account is that when complex computations are crucial in the performance of a task, correspondingly complex processing stages will be favored for attentional enhancement. In other words, the level of attentional selection may follow the level of complexity of discrimination. In Proverbio et al. (2007), subjects were required to fully identify and compare animals and objects within the attended stimulus. The studies of Clark and Hillyard (1996) and Di Russo et al. (2003) employed size discrimination tasks; whereas this appears to be a simple process, size estimation may involve the interaction of levels with larger receptive fields, and the task certainly involves interaction with working memory in the comparison with a "standard" size template. On the other hand, one could reason retrospectively that the lowest levels may be targeted for enhancement in some tasks used in previous primate studies, such as the detection of a red/green color pixel within grayscale noise (McAdams and Reid 2005), and the discrimination of the orientation of small bars (fitting inside a V1 receptive field) in the presence of competing distracters (Motter 1993). Clearly, more systematic, direct investigation will be necessary to substantiate these ideas.

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