

Modulation of Visual Stimulus Discrimination by Sustained Focal Attention: An MEG Study

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PURPOSE. Visual attention, normally focused on the center of the visual field, can be shifted to a location in the periphery. This process facilitates the recognition of objects in the attended region. The present experiment was designed to investigate the time course of sustained attention that is known to augment stimulus perception in normal subjects.

METHODS. Cortical activity of the human brain related to shifts of the attentional focus was examined with magnetoencephalography. Subjects had to identify a stimulus presented on a screen at one of two locations in the periphery of their visual fields. Sustained attention was either deployed toward the target by a preceding cue or not.

RESULTS. Results confirmed a reaction time advantage on recognizing objects in the part of the visual field where attention had been deployed. A stronger magnetic brain response was detected for noncued targets at a latency of 260 to 380 ms after target onset. Source localization revealed a neuronal generator of the attention-related component in the parietal cortex.

CONCLUSIONS. Sustained attention facilitates target detection. The component that is localized in the parieto-occipital cortex in the noncued condition is thought to reflect a transient shift of attention toward the target location. (*Invest Ophthalmol Vis Sci.* 2006;47:1225–1229) DOI:10.1167/iov.04-1338

Focal attention^{1,2} enables humans to select a specific location in the visual field and preferentially process information in that location. Targets in an attended location in the visual field are detected faster³ and more accurately^{4,5} and are easier to discriminate than those occurring outside that focus of attention.⁶ This effect is independent of whether the attended object is presented in the center of the visual field (i.e., the fovea, or the periphery).

Covert attention is the ability to select information at a cued location without moving the eyes. Two components of covert attention—*sustained* and *transient*—have been described so

far.² Transient attention is fast and automatic. It is controlled by the sudden onset of an exogenous peripheral cue and cannot be controlled volitionally.^{2,7} It guides saccadic eye movements and improves performance in spatial resolution tasks.^{8,9} Transient attention is mediated by a ventral network that is strongly lateralized to the right hemisphere.¹⁰

Sustained attention, in contrast, is a volitional process, by which the foveated and the attended region of the visual field are split.^{2,8} The result is that recognition of targets in the attended part of the visual field is facilitated, which lowers discrimination threshold² and reduces reaction times.¹¹ It has been found that the mechanism that allocates and maintains sustained attention involves a part of the parietal cortex and a dorsal network.^{10,12}

Experiments have shown with electroencephalography (EEG) that sustained attention has modulatory effects on attentional components such as P1 or N1.¹³ Earlier studies that were conducted to investigate sustained attention used a block design, in which subjects had to deploy their attention to a given location throughout the entire block of trials. In this study, we changed not only the procedure, but also the method used to investigate neural correlates of sustained attention: First, instead of using a block design, in which subjects have to deploy their attention to a given location throughout an entire block of trials, we used a randomized design, in which subjects have to readjust their attention in each trial. Second, instead of using EEG or functional (f)MRI, we use magnetoencephalography (MEG) to investigate the magnetic correlates of sustained attention. MEG is a very sensitive noninvasive method to study neuronal processes underlying behavior.¹⁴ In contrast to EEG, which measures electrical potentials due to neuronal activity, MEG measures magnetic fields generated by electric currents. It has very good temporal resolution of up to 1 ms. Therefore, this method is especially suitable for assessing the time course of activation. MEG also provides a good spatial resolution of several millimeters, which makes it possible to estimate intracranial localization of the generator source of a given signal.^{14–16}

The importance of studying sustained attention lies in the fact that it relates to an aspect of advanced maculopathies. When these patients lose foveal vision in both eyes, they have to optimize the use of their remaining vision by using an eccentric retinal area instead (eccentric viewing). Such a preferred retinal locus (PRL)^{17,18} is a point in the near periphery of the retina that can become a new center of the visual field.¹⁹ It has been hypothesized that sustained attention is an important mechanism in this impairment, because it facilitates detection and recognition of targets at the PRL.²⁰ In summary, voluntary control of sustained attention can be useful for patients with maculopathies, to improve their visual capabilities. Studying this mechanism in normally sighted subjects is a valid model for those with maculopathies.²¹

METHODS

Subjects

Twelve healthy subjects aged 20 to 33 years (mean, 24.3) participated in this study (five women, seven men). The subjects had no history of

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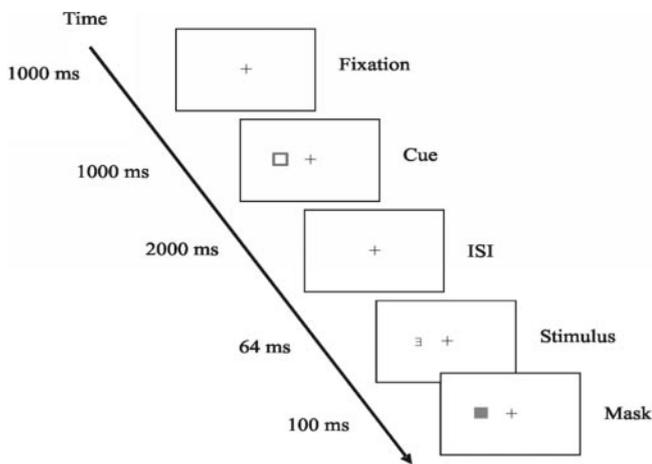


FIGURE 1. Sequence of presentation of each experimental trial for the cued condition. The sequence of events for the noncued condition was similar, except for the absence of the cue and an ISI of 3000 ms.

eye diseases or serious general health problems, and they described themselves as right-handed. They had normal or corrected-to-normal vision. Because of excessive eye movement artifacts, the data from two subjects had to be excluded from the analysis. One further subject was excluded from the reaction time analysis because of technical problems. All subjects gave informed consent according to the tenets of the Declaration of Helsinki.

Stimuli

Stimuli were presented by a video projector (NECGT2150, frame rate of 60 Hz; NEC London, UK) on a white screen installed 1 m in front of the subjects. Subjects were asked to fixate binocularly a cross in the middle of the screen throughout the whole experiment. Visual targets consisted of black “tumbling” Snellen E’s of 1° visual angle (size markedly above threshold), which were flashed at 12° to the left and to the right of the fixation cross. The opening of the Snellen E’s was either upward, downward, to the left or to the right. The stimulus duration was 64 ms. A red square served as the cue. It appeared for 1 second and indicated the side and location of appearance of the target on half of the trials. The interstimulus interval (ISI) between cue and target was 2 seconds. On the other half of the trials, the intervals between targets were the same; however, no cue was provided. A square filled with a random dot pattern directly followed the stimulus for 100 ms and served as mask to terminate stimulation and to avoid afterimages. See Figure 1 for a diagram of the presentation sequence.

Absolute performance levels can differ substantially between subjects, so that variable settings that make target recognition impossible for one subject may render the task easy for another.²⁰ Therefore, in the current experiment, the target luminance was adjusted for each subject individually by a one-up two-down, four-alternative, forced-choice staircase procedure that was applied directly before the start of the actual experiment.²² This was done using the experimental paradigm described in the next section. The goal was to make task difficulty comparable for all subjects. This procedure ensured that all subjects were able to discriminate at least 75% of targets correctly. The maximum difference in target-background contrast between subjects was $38\% \pm 14\%$.

Procedure

Subjects were seated in a sound-attenuating, magnetically shielded room. They were asked to fixate a central cross on a screen during the whole experiment at a viewing distance of 1 m. Subjects were instructed to indicate the orientation of a Snellen E as fast as possible by moving a joystick in the direction of its opening. The experiment consisted of 300 trials per subject. The cue appeared in only half of the

trials. Targets were distributed equally to the left and right side of the fixation cross. The order of the trials was randomized. The entire session took approximately 30 minutes to complete.

Recording

During the experiment, the magnetoencephalogram (MEG) was recorded using a whole-head system (CTF Inc., Vancouver, BC, Canada) with 151 sensors picking up the magnetic field of the brain. In addition, vertical and horizontal electrooculogram (EOG) was recorded (type E230X-2J Biopotential Skin Electrodes; InVivoMetric, Healdsburg, CA), to detect eye movements throughout the experiment. To record vertical eye movements, two electrodes were placed above and below the right eye. An additional electrode was placed on the outer canthus of the left eye, to control for horizontal eye movements. Electrode impedance was kept below 5 k Ω . EOG signals were amplified and recorded by additional bipolar electrical channels of the MEG electronics.

Both, magnetic brain responses and EOG were digitized with a sampling rate of 625 Hz. With a sampling rate of 625 Hz, only signals with frequencies lower than the half of the sampling frequency can be correctly recorded. Therefore, the magnetic brain activity was filtered using a fourth-order low-pass filter with a cutoff frequency of 208 Hz. No high-pass filter was used.

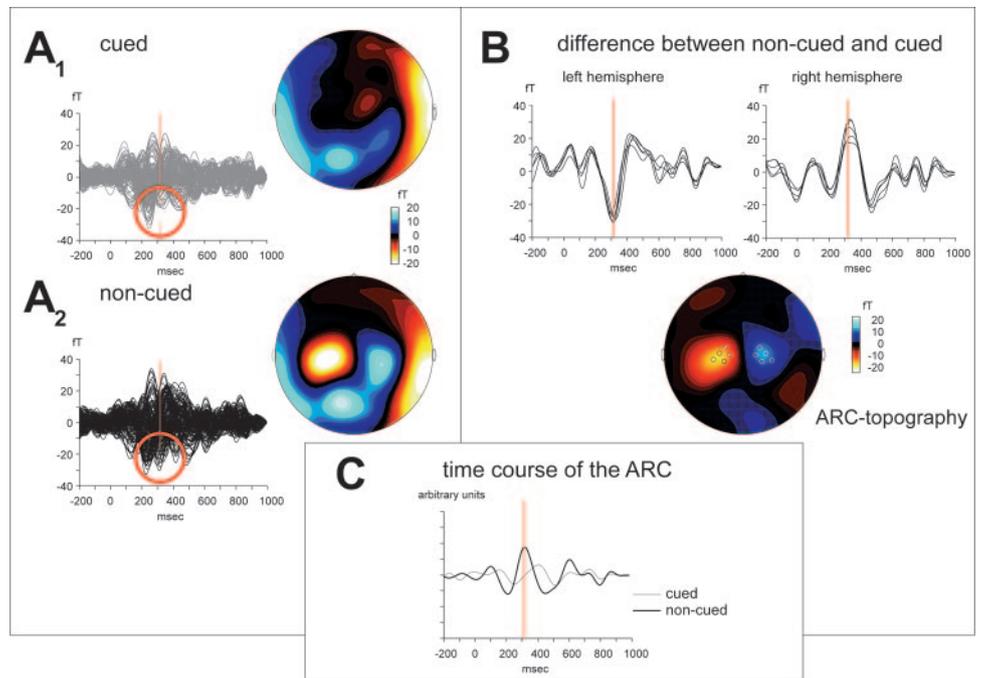
Analysis

Trials during which EOG indicated a shift in eye position or an eye blink in the interval between cue onset and 1 second after target presentation, as revealed by an activity greater than 70 μ V, were discarded from further analysis. An additional criterion to detect eye movements and blinks was activity greater than 1 pT in frontolateral MEG channels. For each subject, single trials of evoked responses were averaged according to whether the target appeared to the left or to the right side of the fixation cross and whether a cue appeared before or not (cue left, cue right, noncued left, noncued right). In addition, for each of the four conditions, the evoked magnetic fields were averaged across all subjects and trials (grand average). Data were filtered with a digital band pass with cutoff frequencies of 2 and 10 Hz. Filtering this specified frequency range allowed for the optimal recording of the observed magnetic activity.

To quantify magnetic activity, the global field activity, defined as the root mean square of the magnetic amplitudes across channels $G_b(t) = \sqrt{\sum b_{ib}^2(t)/n_b}$ for each point in time t and each hemisphere b was calculated. $b_{ib}(t)$ denotes the magnetic activity at channel i of n_b channels at time t at either the left ($b = l$) or right ($b = r$) hemisphere. To characterize the time course of activity before target presentation, the average activity was calculated within seven time windows of 500 ms each, overlapping by 50%. Statistical comparisons between the cued and the noncued condition were done by analyses of variance (ANOVAs) with repeated measurement factors for *hemisphere* (levels: activity on left and right hemisphere), *side* (levels: stimulation in left and right visual field), and *condition* (levels: cued and noncued).

In a subsequent analysis, difference waves between the cued and noncued conditions were computed on the basis of the grand average, to detect physiological correlates of attentional shifts. Difference waves revealed a marked attention-related component (ARC) peaking in the latency range between 280 and 360 ms after target onset. To quantify the contribution of this component to the evoked responses of individual subjects and conditions, subspace projection, a type of linear regression analysis, was used.^{23,24} We assumed that the contribution of the attention-related component $C = (c_i)$ varies over time according to the function $a(t)$, with c_i being the magnetic amplitude at channel i , to the evoked magnetic field $B(t) = bi(t)$ at channel i and instant t . Based on the linear superposition of magnetic fields, the measured magnetic field can then be written as $B(t) = a(t) \cdot C + R(t)$. $R(t)$ represents additional activity not related to the attention-related

FIGURE 2. Steps of data analysis. (A) *Left:* grand averages of the magnetic field evoked by the target stimuli presented in the right hemifield are displayed for the cued (A_1) and non-cued (A_2) condition. The time course of all 151 channels of the MEG system (in milliseconds) are superimposed to detect time ranges of differing activities between both conditions. As indicated by the red ring and the cursor, main differences can be seen at a latency of 315 ms. *Right:* the corresponding magnetic field distribution. Positive polarity of magnetic activity correspond to magnetic fields leaving the surface of the head (outgoing flux), negative polarity indicates ingoing flux. The magnetic flux density is given in femtoTesla (fT). (B) To identify the attention-related component difference, waveforms were calculated between the cued and the noncued condition for each channel. For reasons of clarity only the wave forms of a subset of the channels in the centroparietal region of the left and right hemisphere (circles in the maps) are depicted (B, top). It is assumed that the difference map (B, bottom) reflects the topography of the ARC. (C) The contribution of the ARC component to the total magnetic activity is estimated using regression analysis. The time course of the ARC component is shown for the cued (gray trace) and the noncued (black trace) condition. At 315 ms, an amplitude peak was detected for the noncued condition.



component. Using regression analysis the contribution $a(t)$ of the ARC to the total magnetic field was calculated for any time point.²³ In the present experiment, different topographies of the attention-related component were chosen for left and right presentation of the stimuli. In both conditions, the topography of the ARC was derived from the difference waves of the grand averages at a latency of 315 ms after target onset. Note that in contrast to the earlier procedure designed to detect waveform differences between the four conditions on the basis of the grand averages, here the contribution of the topography of the ARC to the evoked magnetic fields of the *individual* subjects was calculated using regression analysis. Consequently, an activation function of the ARC component was obtained. Interestingly, the peak of the activation function was found at 315 ms for left and right visual field stimulation. To obtain a parameter for statistical analysis, we selected the activity at 315 ms. The shift in latency is possibly a result of the temporal overlapping of multiple components involved in processing the target stimuli.

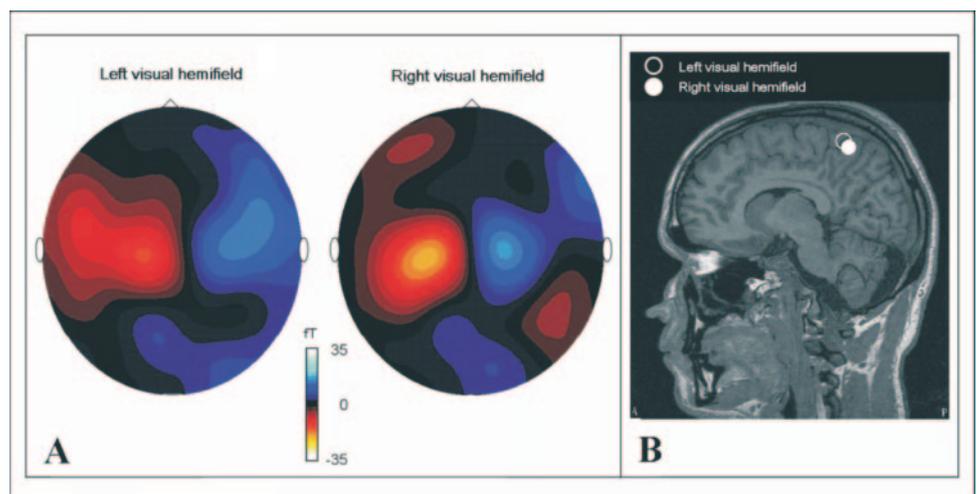
Figure 2 presents the different steps of the analysis in more detail. Applying the subspace approach to the evoked responses of individual subjects and conditions, four waveforms were obtained for each subject and one for each condition. To quantify the contribution of the ARC, the maximum activity and its corresponding latency were determined. Statistical comparison between the four conditions (cued left, cued right, noncued left, noncued right) was performed by using ANOVA with the repeated measurement factors *side* and *condition*. Finally, the localization of the component visible in the difference wave was estimated with an equivalent dipole model.^{15,16}

RESULTS

Reaction Times

A *t*-test for paired comparisons was performed on cued versus noncued conditions for reaction times from correct trials. A

FIGURE 3. (A) Magnetic field distribution across the surface of the head as seen from top (nose is upward). *Blue:* positive potential and ingoing flux, whereas *red* depicts negative potential and outgoing flux. The topography of differences between the cued and noncued conditions is shown for a latency of 315 ms after target onset for stimulus presentation in the left and right visual fields. (B) Source localization of the magnetic field distribution of the ARC shown on the left. Source localization was computed using an equivalent dipole model.¹⁴ *Filled circle:* the topography of differences between the two conditions for stimulus presentation on the right side; *open circle:* the topography of differences for stimulus presentation on the left side.



significant difference was found between the cued and noncued conditions: the mean reaction times were 807 ms (± 50.91 ms SE) for the cued and 855 ms (± 51.49 ms SE) for the noncued condition ($t_{(8)} = -3.81$; $P < 0.005$).

Magnetic Activity

No significant differences between cued and noncued conditions were found for the global field power of brain activity in the different time windows before target presentation. However, on the basis of the grand averages for the four conditions, a significant difference in magnetic brain activity for cued and noncued was found between 280 and 360 ms after target presentation (Fig. 2). The largest effect was measured at 315 ms after target onset for target presentation in the right visual field and at 280 ms after target onset for target presentation in the left visual field. Applying subspace projection techniques, the time course of the attention-related activity after target presentation was extracted for each subject. The topography of the ARC evoked by presentation of the target stimulus in the left and right hemifield is depicted in Figure 3A. By analyzing the topography of the magnetic field, it is possible to estimate the location of the neural source generating the attention-related component. Results of source localization superimposed on an MRI are depicted in Figure 3B.¹⁵

Comparing the magnitude of activity for the four conditions at 315 ms after target presentation, a significant difference between the cued and noncued conditions for target presentation in either visual field was found for the main effect *Condition* ($F_{(1,9)} = 58.649$; $P < 0.0001$). See Figure 4 for further detail. The means of the activity indicate that the attention-related component was almost absent in the cued condition (mean \pm SE: -0.005 ± 0.27 for left-side presentations and -0.066 ± 0.23 for right-side presentations), but not in the noncued condition (mean \pm SE: 0.575 ± 0.34 for left-side presentations and 0.963 ± 0.21 for right-side stimulus presentation).

DISCUSSION

In the present study, we sought to examine the neural correlates of sustained attention elicited by cues presented before a target. With respect to the clinical relevance of sustained attention, it has been hypothesized that it is an important mechanism for patients who have maculopathies. These patients have to use eccentric viewing to optimize the use of their remaining vision.²⁰ Reaction time analysis of the current data

revealed that subjects discriminated targets appearing at attended locations significantly faster than those at unattended locations, which highlights the finding that peripheral letter recognition is improved by the deployment of sustained attention at the test location.^{2,11,21}

The current experiment was designed to investigate the time course of magnetic cortical correlates of sustained attention. Although different low- and high-frequency filter settings were used to examine slow and rapid changes in magnetic activity, and despite the behavioral benefit of cued trials, no magnetic correlates of sustained attention were found in the interval between cue and target. This can have several reasons. First, it is possible that the brain response related to the emergence of sustained attention cannot be detected by MEG. This technique is exclusively susceptible to neuronal brain currents that are oriented tangentially to the surface of the brain.^{25,26} Like EEG, MEG responses are generated by dendritic currents of cortical pyramidal cells that are oriented perpendicularly to the cortical surface.²⁷ Therefore, MEG is only able to detect brain activity that is mainly generated in the walls of cortical sulci. Consequently, if the control of sustained attention occurs in superficial cortical areas, MEG is unable to identify the corresponding brain structures. Second, shifts of sustained attention to cued locations may not occur strictly time-locked to the appearance of the cue. In our experiment, the interval between cue and target presentation was fairly long. Shifts of attention may have occurred at variable times on different trials and individual subjects. Therefore, averaging individual magnetic brain responses may yield temporally smeared courses of activity that do not allow for identification of a specific component. Finally, to optimize their strategy, subjects may not only have deployed sustained attention to the target location in the cued condition, but may also have covertly attended one of the possible locations of target onset in the noncued condition. Consequently, no difference in the ISI between conditions was detectable.

Instead of magnetic changes due to sustained attention in the cued condition, we discovered a magnetic component in the noncued condition peaking at approximately 300 ms after target presentation. Several studies using EEG already described a so-called "late positive deflection" (LPD) occurring in the time range of 200 to 500 ms after target onset.^{13,28} It has been suggested that this component is composed of a combination of the prestimuli, contingent negative variation, motor potentials and P300 components.¹³

It is questionable whether the LPD and the component we found in these experiments represent the same processes because in our experiment the deflection is temporally sharply limited. Moreover, the observed component clearly shows contralateral effects in the visual hemifield in which the target is presented. This suggests that visual rather than motor processes are involved. We therefore hypothesize that the deflection found in our experiment is related to the perception of the target. The suggestion that certain motor processes may be involved in generating the observed activity can be excluded because button presses were made 700 to 1200 ms after target onset and would therefore be much too late to have any effect on the critical component. Therefore, the component found in our study in the noncued rather than in the cued condition could constitute a signal indicating the redirection of attentional processes toward the noncued target location. Such a component could be evoked by transient focal attention, which can well be activated by the appearance of the target on the unattended side.² An ERP component in the latency range from 300 to 500 ms related to the redirection of attention has also been described in a task where a shift of visuospatial attention was induced by an arrow stimulus.^{29,30} The parietal location of the ARC in our study corresponds to a parietal source that has been found to be related to neural

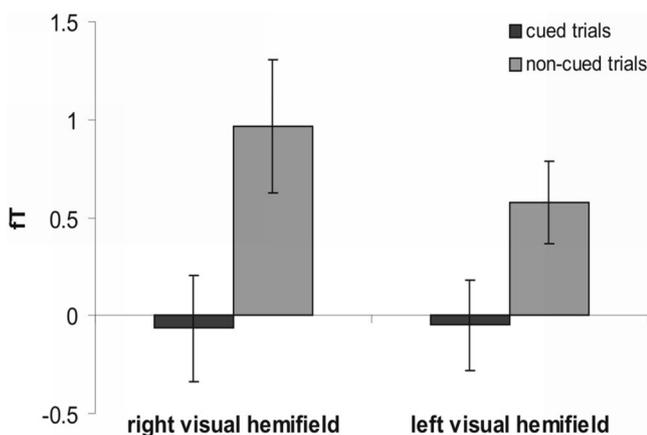


FIGURE 4. Magnetic activity determined at 315 ms after target onset for cued and noncued stimuli for stimulation of both visual hemifields. Activation at this time was stronger in the noncued trials. Error bars, SEM.

responses that ascribed the initiation of attentional shifts in an uncued visual search task.³¹ However, this source has a shorter latency of 180 to 200 ms.

A variety of EEG and MEG studies have shown that, together with performance benefits at covertly attended locations,³⁻⁶ amplitude enhancements like P1, P2, N1, or N2, occur at approximately 70 to 250 ms after target onset.^{28,32} These early components are often followed by a positivity with a latency of 240 to 700 ms, the P3, which may be related to the component found in the present study. Mainly, two distinct types of the positive deflection have been established so far, which are the novel P3 and the target P3.³³ The novel P3, evoked by novel, nontarget stimuli, has a frontocentral scalp distribution and is thought to be related to momentary shifts of attention toward an unexpected target. The target P3, in contrast, is evoked by attended target stimuli. It has a longer latency and a parietal scalp distribution.

We now assume that the component we detected in the time range of 280 to 380 ms after target onset is related to the target P3. As mentioned, subjects may have used sustained attention on both cued and noncued trials to optimize their strategy. By chance, subjects could have correctly predicted the target location in only half of the noncued trials and therefore shifted their attention to the correct location of target appearance. In the other case, a quick shift of transient attention resulted in a magnetic component peaking at around 300 ms after target presentation, which is comparable to the target P3. This component has been detected only in noncued trials because attention was already deployed at the location of target onset on cued trials and therefore facilitated the detection and recognition of targets, as confirmed by the reaction time results.

In conclusion, no neural correlates of sustained attention were detected when neuromagnetic imaging techniques were used. However, shorter reactions times for cued condition indicate facilitation of peripheral vision and therefore may benefit patients with dense central scotomas due to maculopathies. Of interest, the activity after target presentation in noncued trials appears to indicate shifts of transient attention and seems to be related to the P3 component, apparently after the occurrence of target events in EEG studies.

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