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Effects of attention and arousal on early responses in striate cortex

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Abstract

Humans employ attention to facilitate perception of relevant stimuli. Visual attention can bias the selection of a location in the visual field, a whole visual object or any visual feature of an object. Attention draws on both current behavioral goals and/or the saliency of physical attributes of a stimulus, and it influences activity of different brain regions at different latencies. Attentional effect in the striate and extrastriate cortices has been the subject of intense research interest in many recent studies. The consensus emerging from them places the first attentional effects in extrastriate areas, which in turn modulate activity of V1 at later latencies. In this view attention influences activity in striate cortex some 150 ms after stimulus onset. Here we use magnetoencephalography to compare brain responses to foveally presented identical stimuli under the conditions of passive viewing, when the stimuli are irrelevant to the subject and under an active GO/NOGO task, when the stimuli are cues instructing the subject to make or inhibit movement of his/her left or right index finger. The earliest striate activity was identified 40–45 ms after stimulus onset, and it was identical in passive and active conditions. Later striate response starting at about 70 ms and reaching a peak at about 100 ms showed a strong attentional modulation. Even before the striate cortex, activity of the right inferior parietal lobule was modulated by attention, suggesting this region as a candidate for mediating attentional signals to the striate cortex.

Introduction

In everyday situations, attention is employed to facilitate perception of stimuli relevant to the current behavioral goal. For example, a driver pays attention to traffic lights to travel safe and to avoid the heavy fine, while a passenger sitting next to him and gazing at the same traffic light might not even notice it. Attention affects processing of the relevant visual stimulus primarily by enhancing its neural responses at different levels of the visual information-processing pathways of the brain (Kanwisher & Wojciulik, 2000; Kastner & Ungerleider, 2000). Moreover, it can modulate neural responses to selected location of visual field (Heinze *et al*., 1994; Mangun *et al*., 1997, 2001; Woldorff *et al*., 1997; Tootell *et al*., 1998; Muller & Kleinschmidt, 2003), as well as responses to whole visual objects (Kanwisher & Driver, 1992; OCraven *et al*., 1999; Muller & Kleinschmidt, 2003) and to visual features, such as color, motion or shape (Corbetta *et al*., 1990; Anllo-Vento & Hillyard, 1996; Beauchamp *et al*., 1997; Clark *et al*., 1997; OCraven *et al*., 1997; Chawla *et al*., 1999; Bartels & Zeki, 2000; Saenz *et al*., 2002; Liu *et al*., 2003). These modulations are strongest in extrastriate visual areas. However, activity of striate cortex as well can be affected by different aspects of selective attention (Watanabe *et al*., 1998a,b; Brefczynski & DeYoe, 1999; Gandhi *et al*., 1999; Kastner *et al*., 1999; Somers *et al*., 1999; Saenz *et al*., 2002).

Event-related potentials (ERP) (Hillyard & Anllo-Vento, 1998; Martinez *et al*., 1999; Fu *et al*., 2001; Mangun *et al*., 2001) and magnetoencephalography (MEG) were used to determine precise latencies of various attentional effects in the visual cortex. All the studies agree that the C1 (onset at 50 ms) component of the ERP is not modulated by attention, but the following components – P1 (70–130 ms) and N1 (160–200 ms) (Martinez *et al*., 1999; Torriente *et al*., 1999), PD130 (100–140 ms) and SN (160–250 ms) (AnlloVento & Hillyard, 1996; Anllo-Vento *et al*., 1998; Hillyard & Anllo-Vento, 1998), N2pc (180–290 ms) and its magnetic equivalent (Hopf *et al*., 2000), and face-specific M170 (Downing *et al*., 2001) are modulated. In spite of evidence from human functional magnetic resonance imaging (fMRI; Watanabe *et al*., 1998a,b; Saenz *et al*., 2002) and single neuron recordings in monkeys (Roelfsema *et al*., 1998), ERP and MEG studies did not find evidence of object- or feature-based attentional effects in V1. However, several studies investigating the effects of spatial attention (Martinez *et al*., 2001; Noesselt *et al*., 2002; Di Russo *et al*., 2003) identified modulation of striate activity at later latencies, ascribing it to feedback signals from higher areas (Martinez *et al*., 2001). The earliest attentional effect in striate cortex was identified by Noesselt *et al*. (2002), between 140 and 250 ms.

In the present study we used MEG to investigate the effect of foveally directed attention to shape and color on early brain responses, and most importantly to identify the earliest response in V1 affected by attention.

Materials and methods

Subjects

Six healthy right-handed subjects (one female, age range 23–36 years) with no history of psychiatric disorders participated in the MEG experiment. All experimental procedures were undertaken with the understanding and written consent of each subject, and conformed to The Code of Ethics of the World Medical Association (Declaration of Helsinki), and were approved by the ethical committee of the host institution (RIKEN).

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Stimuli and task

The subject was seated in a magnetically shielded room and instructed to fixate on a small cross at the center of the screen placed 60 cm ahead. The fixation cross was displayed throughout the run, including the presentation of the stimuli as shown in Fig. 1. Six types of visual stimuli (red and green arrows, pointing to left, right or both directions) were back-projected on the screen by a video projector placed outside the shielded room (Fig. 1). Stimuli were presented at the center of the screen. In each run, 60 stimuli for each type were presented in random order (i.e. 360 stimuli per run), with the inter-stimulus interval randomized between 1.2 and 2.0 s. Each stimulus was displayed for 32 ms. In the active runs, the subject was required to extend the index finger(s) indicated by green arrow(s) (GO trials), and to withhold the movement after the appearance of red arrow(s) (NOGO trials). In this way the subject had to attend to the stimuli during the whole run in order to be able to respond quickly and correctly. In the control runs the subject just watched the same stimuli without discrimination or any finger movement; therefore there was no need to attend the stimuli. The experiment started with a control run, followed by two active runs and ended with a second control run.

MEG recording and pre-processing

The MEG signal was collected using 151-channels whole-head system (CTF Systems, Vancouver, Canada) at a sampling rate of 1250 Hz. In addition and in synchrony with the MEG signal, vertical and horizontal electrooculogram (EOG) and the electromyogram from the left and right arms were recorded. Optical switches measured the responses of both fingers.

The MEG signal was converted to third-order synthetic gradient and resampled offline at 625 Hz. Trials with wrong responses, or contaminated with eye movements, measured by EOG, were removed. Independent component analysis was used to remove the artefacts due to eye blinks and heartbeat. The processed signal was averaged for each condition and stimulus type separately with respect to the stimulus onset (−400 to +600 ms), thus giving 12 averaged trials for each condition (2 runs × 6 stimulus types).

The subject's head location was recorded at the beginning and the end of each run, which lasted about 10 min. Active or first control runs during which head movement exceeded 0.5 cm were repeated. Subject's head movement slightly exceeded 0.5 cm in the second control run in two of the six subjects. Table 1 provides the head movement information for each run and subject.

Virtual signal

The early peaks in the MEG signal elicited by our stimuli, particularly at about 100 ms after stimulus onset, had predominantly dipolar distribution (Fig. 2A). The five sensors (p_1–p_5) that produced the most clear positive deflections and five sensors (n_1–n_5) that produced the most clear negative deflections at about 100 ms after stimulus onset were selected to construct the composite virtual signal (*VS*) defined by:

$$VS(t) = \frac{1}{5}\left[\sum_{i=1}^{5} S_{p_i}(t) - \sum_{i=1}^{5} S_{n_i}(t)\right]$$

VS does not reflect activity of one cortical source, rather it reflects a pattern of neural activity in a relatively large area of cortex situated between the two sets of selected sensors. The choice of sensors was made directly from the field map of the activity over the occipital sensors for each subject and run independently. The spatial sensitivity profile of *VS* is broadly, but not exclusively, focused on the visual cortex, but it is considerably sharper than the very poor spatial sensitivity profile of each sensor (Liu *et al*., 1998). Using five (rather than one) sensors in each of the two subsets ensures that the compound signal from generators between the two sets of sensors is picked up evenly and limits the influence of large random fluctuations in any one sensor. It also makes the computed values less sensitive than the measurements from a single sensor to small changes in head localization from run to run. *VS* generated for each of six subjects were at first normalized, then averaged together to produce grand average *VS*.

Table 1. Head movement during each run (cm)

Subject	Control run before test	Active test run 1	Active test run 2	Control run after test
1	0.30	0.14	0.24	0.38
2	0.29	0.33	0.23	0.52
3	0.36	0.50	0.37	0.30
4	0.47	0.16	0.16	0.64
5	0.34	0.35	0.37	0.31
6	0.15	0.23	0.11	0.14

Source analysis

For source analysis, four separate, partially overlapping, source spaces (17 × 17 × 11 grid points each) completely covering the left and right hemispheres and back and top of the brain were used. Magnetic field tomography (MFT; Ioannides *et al*., 1990) was used to obtain three-dimensional distribution of the primary current density at each grid point of each source space. The solutions from all four source spaces were combined together into one big source space, which covered the whole brain, using the values of the solutions and the sensitivity profile of the sensors from nearby points in separate source spaces (Ioannides, 2002). The borders between V1 and V2 visual areas for two of the subjects were obtained in a separate fMRI experiment.

For each subject, regions of interest (ROI) with the radius of 1 cm and centered in left and right V1 were defined. The loci that showed the strongest response in occipital region for at least 5 ms between 70 and 120 ms in all four runs (two active and two control) and were anatomically located on, or slightly above or below calcarine fissure were designated as centers of ROIs. The main direction for the ROIs was defined from the current density direction in V1 at about 100 ms after stimulus onset.

For each subject, voxel-by-voxel statistical parametric maps (SPM) were generated using Student's *t*-test. SPMs were constructed by comparing different conditions (active and control), and post- and prestimulus periods of both conditions pooled together. In comparison between different conditions, 16 ms windows (10 samples) from each of six averaged trials were put together to form a distribution for each condition separately. After comparing these distributions, the center of the window was moved by 1.6 ms (1 sample) to form new distributions. In comparison between post- and prestimulus periods (active and control conditions pooled together), 300 ms windows from the prestimulus period (from −400 to −100 ms) of each averaged trial were put together to form the baseline distribution, then each 6.4 ms window (active window) from the post-stimulus period was compared with that at baseline. After each comparison the center of the active window was moved by 1.6 ms for the next comparison with the same

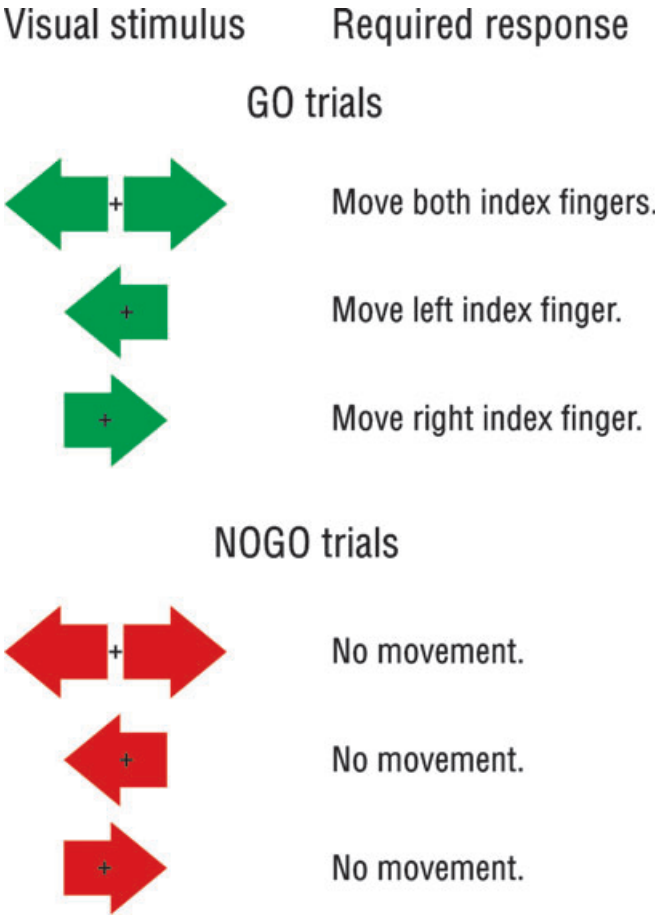

FIG. 1. Stimuli and task. Six types of visual stimulus (red and green arrows, pointing to left, right or both directions) were used. In each run, 60 stimuli of each type were randomly presented for 32 ms. Interstimulus interval was randomized between 1.2 and 2.0 s. Two conditions were used: active and control. In active condition the subject was required to respond by moving the specified index finger(s) in response to green arrows and not to move in response to red arrows. In control condition the subject had to fixate and passively watch the stimuli.

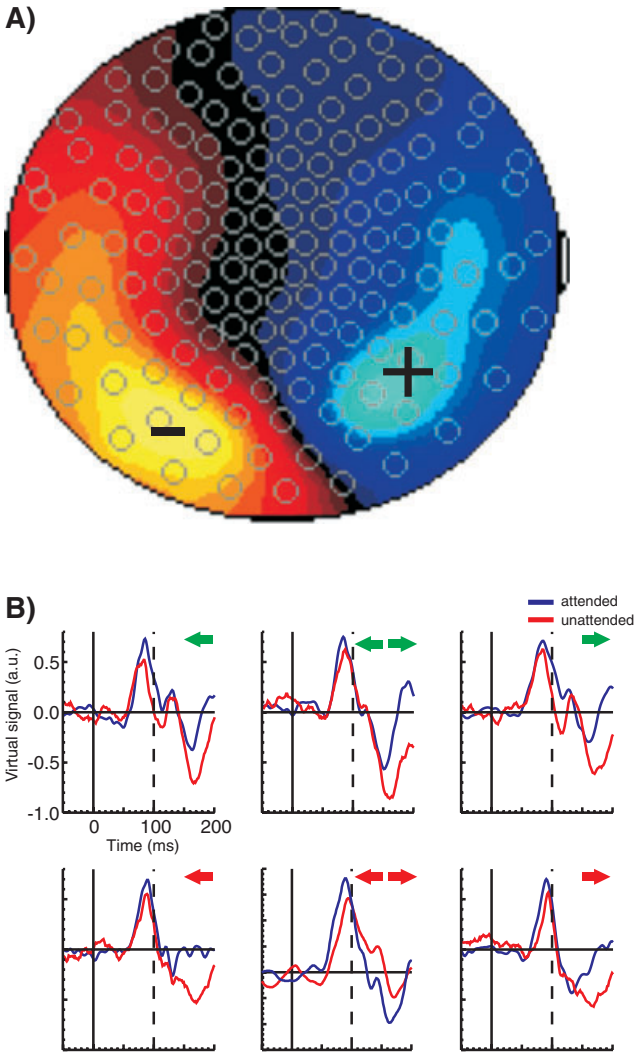

FIG. 2. Attentional effect in average *VS*. (A) Distribution of the magnetic flux over the MEG sensors in response to the green left arrow at about 100 ms for subject 1. Blue contours indicate magnetic flux going into the head, it is defined as positive direction and red contours indicate magnetic flux going outside of head and is defined as negative direction. Very similar field maps were identified in each one of the subjects. (B) Grand average *VS* generated from the average MEG signals over the occipital region in active and control conditions in response to green (upper row) and red (lower row), left (left column), right (right column) and both (middle column) directions pointing arrows. On each graph *VS* under active (blue) and control (red) conditions are plotted together. Arrows on each graph indicate the stimulus type.

baseline. These SPMs generated for each subject separately were transformed to common Talairach space (Talairach & Tournoux, 1988). For each voxel at each latency window, the number of subjects showing statistically significant change in activity (in the same direction) was computed. Statistical significance was set at $P < 0.005$ (corrected for multiple comparisons). For display purposes the results were projected on the MR image of one of the subjects. More details on source reconstruction method and post-reconstruction statistical analysis can be found elsewhere (Ioannides *et al*., 2004).

Regional activation curve (RAC)

The instantaneous regional activation was computed for each V1 ROI at each time slice (1.6 ms) by averaging the projections (on the main direction) of the current density vector of all the source space points inside of the ROI. The RAC was composed for each ROI by the sequence of instantaneous regional activations. RACs were generated separately for left and right V1 ROIs. RACs define the time course of the activation of the particular brain region along its main direction. RACs of left and right V1 were generated from −50 to +200 ms after stimulus onset. Grand average RACs of left V1 and right V1 for each condition were produced by averaging corresponding RACs of individual subjects together. In addition, grand average RACs were generated for each of four runs separately.

Analysis of variance

Amplitudes and latencies of '100 ms' response were extracted from *VS* and RAC of left and right V1. Analysis of variance (ANOVA) with stimulus type (green left, green right, green both, red left, red right and red both) and condition (control and active) as fixed, and subject (six subjects) as random factors was performed on these values to identify any statistically significant effect of stimulus type or condition. For application of ANOVA, SPSS (SPSS, Chicago, IL, USA) statistical software package was used.

TABLE 2. The '100 ms' response in *VS* (Signal) and V1 (MFT)

	Latencies of the '100 ms' response (ms)		
Stimulus	*VS*	Left V1	Right V1
Green			
Left arrow	91 ± 12	95 ± 12	94 ± 13
Right arrow	90 ± 11	94 ± 11	92 ± 11
Both arrows	91 ± 11	96 ± 14	92 ± 11
Red			
Left arrow	91 ± 11	97 ± 11	100 ± 8
Right arrow	95 ± 13	99 ± 10	97 ± 11
Both arrows	94 ± 12	93 ± 15	98 ± 8
Condition			
Active	91 ± 12	94 ± 12	95 ± 11
Control	93 ± 12	97 ± 12	97 ± 11

Values are mean ± SD of peak latencies across subjects.

Results

Virtual signal

VS from the MEG signals over the occipital region was first constructed. The MEG sensors for constructing *VS* were selected directly from the field map of the activity over the occipital sensors, for each subject and run independently. The waveform of constructed *VS* reflects the activity of occipital region in broad, including striate and extrastriate visual areas. Grand average (across all six subjects) *VS* of both active and control conditions for each of six stimulus types (green left, green right, green both, red left, red right and red both) were characterized by a prominent peak at about 100 ms (Fig. 2B). Neither the latencies nor the power of the response was modulated by the type of stimulus. Consistent with previous reports (Martinez *et al.*, 1999, 2001; Torriente *et al.*, 1999; Noesselt *et al.*, 2002; Di Russo *et al.*, 2003) for all six types of stimuli, response was stronger in the active condition compared with the control condition. This attentional effect was present in the *VS* of each individual subject. ANOVA performed on the amplitudes of 100 ms response, with stimulus type and condition as fixed and subject as random factors, revealed significant effect of condition ($F = 12$, $P < 0.02$), but not stimulus type ($F = 1$, $P > 0.4$). ANOVA revealed no statistically significant differences in response latencies related to condition ($F = 2.1$, $P > 0.2$) or stimulus type ($F = 0.9$, $P > 0.5$). Table 2 shows the mean latency and standard deviation across subjects of the 100 ms response.

Tomographic source analysis

MFT (Ioannides *et al.*, 1990) was used to identify, for each subject, the generators of MEG signals within the whole brain independently for each time slice (1.6 ms). In both conditions and in response to each stimulus type, at about 100 ms, activity in V1 ROI was at the expected location (on or close to calcarine fissure) and with the expected current direction (perpendicular to the fissure). Figure 3 shows the current density vector in right V1 at about 100 ms in response to the green left arrow for all six subjects. Talairach coordinates of left and right V1 ROIs for all six subjects are given in Table 3A.

To identify brain regions that, independent of stimulus type showed differential activation between active and control conditions, SPMs were constructed using responses to all six types of stimuli in each condition pooled together. Student's *t*-tests were used to compare responses in active and control conditions for each subject separately. SPMs of each subject were then transformed to common Talairach space (Talairach & Tournoux, 1988), and the voxels that had the value of $P < 0.005$ for a period of at least 5 ms in all six subjects were identified. Several areas throughout the brain showed differential activation between active and control conditions. Their Talairach coordinates and the latencies at which they were differentially activated are reported in Table 3B.

TABLE 3A. Talairach coordinates of left and right V1 ROIs

	Left V1			Right V1		
Subject	*x*	*y*	*z*	*x*	*y*	*z*
1	−11	−97	−7	14	−98	2
2	−13	−73	6	3	−70	17
3	−10	−76	−2	11	−78	−3
4	−15	−83	7	6	−90	5
5	−10	−72	5	11	−70	13
6	−9	−89	3	11	−88	3

TABLE 3B. Brain regions and latencies showing significant attention-related activations

Area	*x*	*y*	*z*	Latencies
R IPL	50	−30	32	38–50, 182–198
R postCG	42	−19	36	126–131, 144–155
	52	−11	19	112–128, 141–157
	50	−17	49	113–133, 138–158
R IFG	48	3	23	139–155, 171–174
R MFG	15	13	43	139–152
	31	0	41	153–166
R preCG	49	−3	41	140–158
R STG	55	−32	13	150–155
R MTG	60	−14	−7	153–158
	31	−57	24	136–149
	49	−48	3	132–152
R FG (V4α)	39	−52	−20	105–132
R cingulate gyrus	20	17	32	132–158
R insula	34	12	22	163–195
R cerebellum (declive)	42	−61	−19	110–125, 153–157
L postCG	−49	−31	36	124–141, 165–187
	51	−16	28	112–140, 149–200
L preCG	−43	−15	55	128–141
	50	−11	12	131–147, 195–200
L MFG	−24	4	41	137–150
L FG	−45	−29	−12	166–192
L FG (V4α)	−31	−44	−19	164–181
L AC	−9	27	0	177–200

Talairach coordinates of the areas that showed statistically significant ($P < 0.005$) differences between active and control conditions in all six subjects and the latencies at which they show attentional modulation in milliseconds. ACC, anterior cingulate; FG, fusiform gyrus; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; L, left; MFG, middle frontal gyrus; MTG, middle temporal gyrus; postCG, postcentral gyrus; preCG, precentral gyrus; R, right; STG, superior temporal gyrus.

RACs

RACs for left and right V1 ROIs were generated from the MFT reconstructions of all subjects from −50 to +200 ms. V1 RACs were dominated by a strong response that started just after 50 ms and peaked at about 100 ms.

Grand average RACs generated from the responses to each of the six types of stimulus show that in the active conditions, in response to unilateral arrows there is a clear enhancement of the 100 ms response (starting at about 70 ms) in the V1 contralateral to the arrow's

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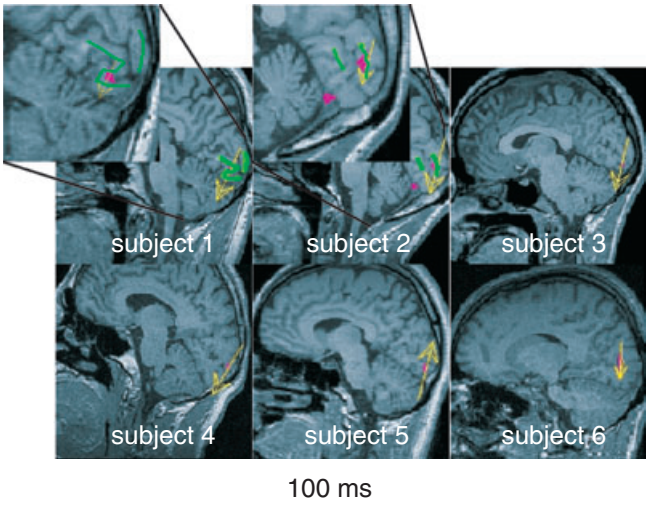

FIG. 3. V1 definition for all subjects. Sagittal views of right V1 activity at 100 ms in response to green left arrows for all six subjects. Yellow arrows show the instantaneous MFT solutions thresholded above 90% of maximum current density. Green lines on the MR image of subject 1 and subject 2 indicate the V1/V2 border identified in a separate fMRI experiment.

direction (arrowhead) and in response to bilateral arrows – in both V1 areas (Fig. 4A). In contrast, there is no substantial difference in amplitude of 100 ms response to unilateral arrows in V1 ipsilateral to arrowhead (Fig. 4B). In addition, for each subject, the difference between corresponding RACs in active and control conditions was computed. These differential RACs were then averaged across subjects to produce grand average differential activation curves, which are provided as supplemental Fig. 1. In five out of six subjects, each unilateral arrow produced attentional modulation of the 100 ms response in the V1 area contralateral to the arrowhead. Four of these five subjects showed no modulation of ipsilateral V1. The other one of these five subjects showed, in addition, modulation in left V1 in response to ipsilateral (left) pointing arrows. In the sixth subject modulation was present only in the right V1 independent of the arrow's direction. For the same period, bilateral arrows produced modulation in a little over than 50% of V1 responses across subjects and trial types. Application of ANOVA to the amplitudes of 100 ms responses showed significant effect of condition in V1 contralateral to arrowhead (left V1, in response to both and right arrows: $F = 5$, $P < 0.04$; right V1, in response to both and left arrows: $F = 8.6$, $P < 0.03$). Effect of condition in ipsilateral V1 was not significant (left V1, in response to left arrows: $F = 0.08$, $P > 0.8$; right V1, in response to right arrows: $F = 1$, $P > 0.3$). In all of the cases, differences in response amplitude related to stimulus type were not significant (left V1, in response to both and right arrows: $F = 3$, $P > 0.06$, in response to left arrows: $F = 0.7$, $P > 0.4$; right V1, in response to both and left arrows: $F = 0.1$, $P > 0.9$, in response to right arrows: $F = 0.02$, $P > 0.9$). As in the case of *VS*, ANOVA revealed no statistically significant differences in response latencies related to condition (left V1, in response to both and right arrows: $F = 4$, $P > 0.08$, in response to left arrows: $F = 1$, $P > 0.3$; right V1, in response to both and left arrows: $F = 3$, $P > 0.1$, in response to right arrows: $F = 0.08$, $P > 0.8$) or stimulus type (left V1, in response to both and right arrows: $F = 0.7$, $P > 0.6$, in response to left arrows: $F = 0.2$, $P > 0.7$; right V1, in response to both and left arrows: $F = 1$, $P > 0.2$, in response to right arrows: $F = 0.4$, $P > 0.5$). The mean latencies and standard deviations across subjects of 100 ms response in V1 are summarized in Table 2.

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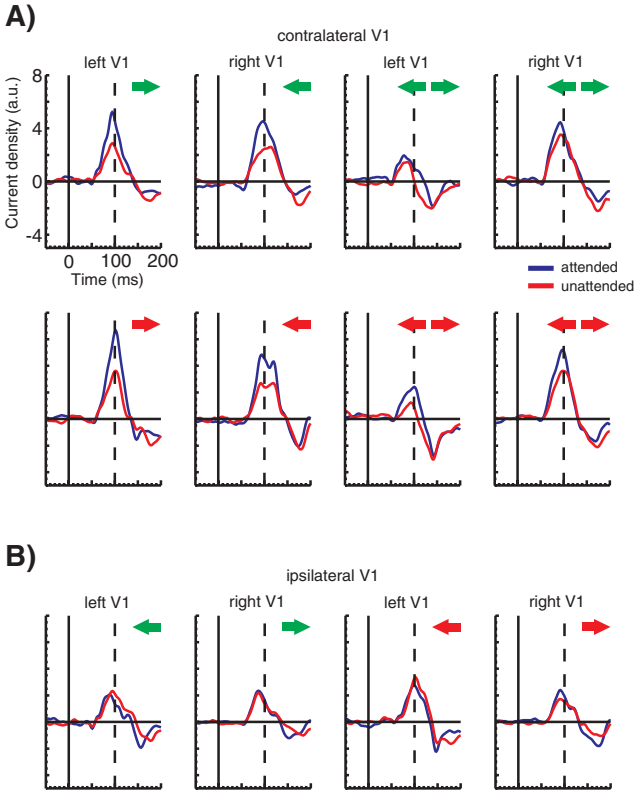

FIG. 4. Attentional effects in V1. On each graph the arrows indicate the stimulus type, and the blue and red curves the grand averaged responses in active and control conditions, respectively. The current density values are given in arbitrary units. (A) Grand average RACs of left (first and third columns) and right (second and fourth columns) V1 generated from the responses to green (upper row) and red (lower row), right (first column), left (second column) and both (third and fourth columns) directions pointing arrows. For unilateral arrows each graph shows V1, in the hemisphere contralateral to the arrowhead. For bilateral arrows the responses in both V1s are shown. (B) Grand average RACs of green (upper row) and red (lower row), left (left column) and right (right column) V1 generated from the responses to unilateral arrows pointing to ipsilateral direction.

Grand average RACs generated for each of four runs separately show an enhancement of V1 responses in the second runs of each condition relative to the first ones, in both contralateral (Fig. 5A) and ipsilateral (Fig. 5B) to arrowhead's V1s. Enhancement is slightly more in control condition; however, ANOVA computations show that it does not reach the level of significance (left V1: $F = 5$, $P > 0.08$; right V1: $F = 0.05$, $P > 0.8$). Responses in both active runs are stronger than responses in both of control runs.

Earliest striate response

Early striate responses that were common in active and control conditions, and were not modulated by attention, were sought by SPMs between post- and prestimulus periods. In these comparisons, separate SPMs were computed for each subject after pooling together MFT reconstructions of all averaged trials in active and control conditions. After the SPMs of individual subjects were transformed to common Talairach coordinates, a common striate cortex area on the calcarine was identified corresponding to statistically significant activations (at $P < 0.005$ after multiple comparison correction) between 40 and 45 ms in four out of six subjects. Figure 6A shows this common area with V1/V2 border projected on the MR image of

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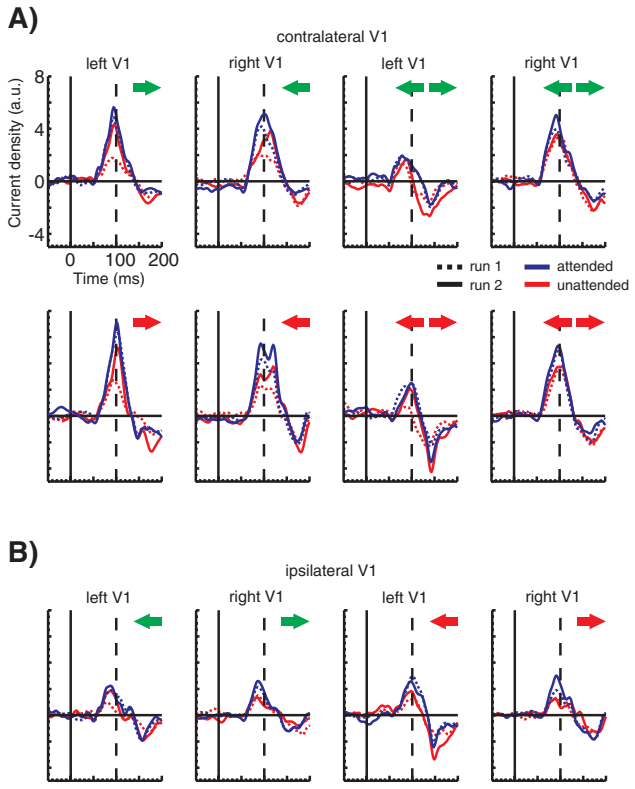

FIG. 5. Order effect in V1. Same as Fig. 4, except grand averaged responses in each run of each condition are plotted separately. Dotted and solid curves indicate run 1 and run 2, respectively.

subject 1. Figure 6B shows the same activation projected on 3D image of the calcarine.

Discussion

Using the broad sensitivity of *VS* constructed from MEG signals from the occipital sensors, we found clear evidence for attentional modulation with a peak at 100 ms after stimulus onset (Fig. 2B). Application of ANOVA demonstrated that this modulation is statistically significant, and that there is no significant difference in the latency of the peak in different conditions. This latency corresponds to the electrical P1 (70–130 ms) component, which has previously been shown to be enhanced by attention (Mangun, 1995; Anllo-Vento *et al.*, 1998; Hillyard & Anllo-Vento, 1998; Martinez *et al.*, 1999, 2001; Torriente *et al.*, 1999; Noesselt *et al.*, 2002; Di Russo *et al.*, 2003). We emphasize here that the waveforms of *VS* and that of MEG signal are not necessarily due to activity in a single cortical region. Therefore, the neural mechanism underlying the modulation of *VS* amplitude is ambiguous. Changes in *VS* could arise from a modulation of few discrete cortical areas or from a change of neural activity pattern in the occipital region in general. In a recent study, we have demonstrated that much of the signal variation elicited by visual stimuli reflects activity in polymodal areas. The activity in the polymodal areas is linked to V1 in a non-linear way (Laskaris *et al.*, 2003).

Tomographic analysis showed that the earliest attentional modulation in V1 started at about 70–80 ms and reached its peak at about 100 ms after stimulus onset (Fig. 4). ANOVA demonstrated that this modulation was statistically significant in all cases, but only for the V1 on the contralateral side to the arrowhead. As in a case of *VS*, there

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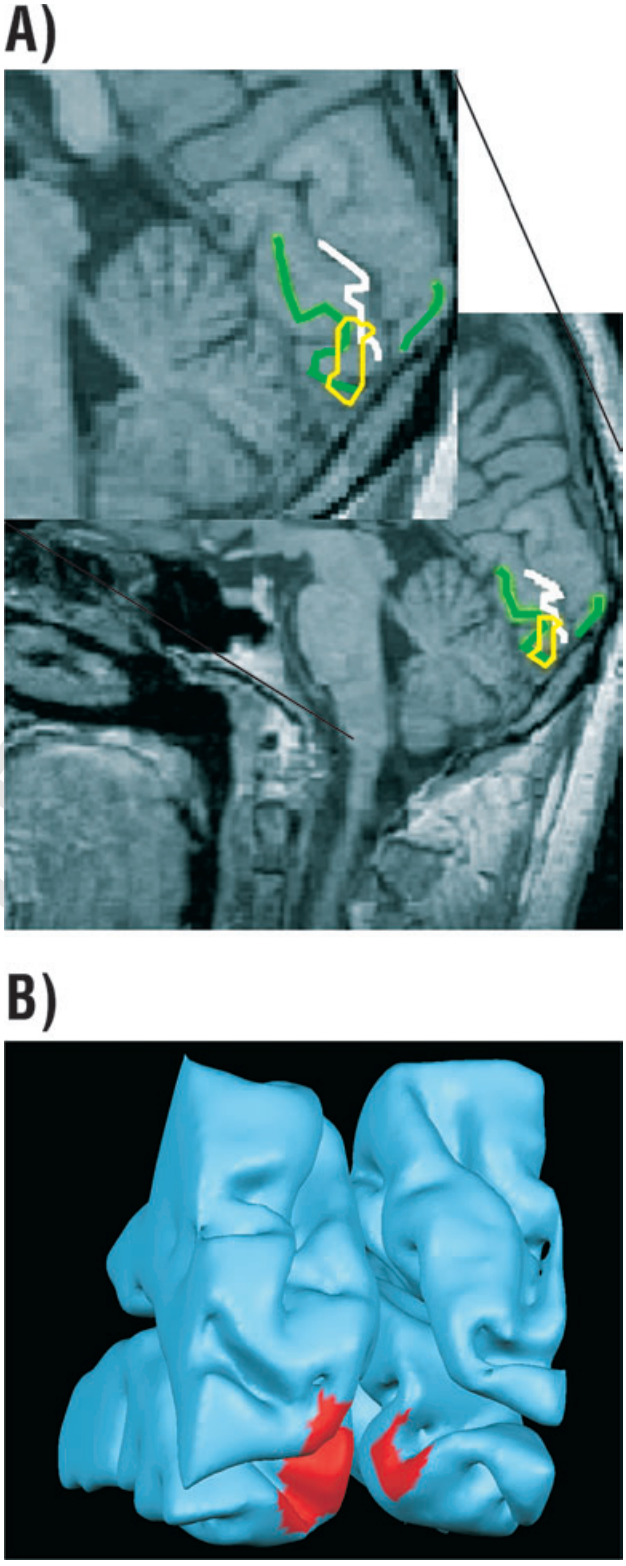

FIG. 6. Very early V1 activity, not affected by attention. V1 activity, combined across subjects, between 40 and 45 ms, identified from the SPMs generated from the comparison of post- and prestimulus periods. (A) Yellow contour encompasses the region where statistically significant ($P < 0.005$) differences were identified in four out of six subjects. Green lines indicate representation of vertical meridian (V1/V2 border), white line – representation of horizontal meridian. (B) The same activation as in (A) (area in red) displayed on the 3D image of calcarine fissure of subject 1.

were no statistically significant differences in response latency in either V1.

V1 responses in the same experimental condition were enhanced after subjects used them in their task performance (Fig. 5). This suggests that sensitivity to a stimulus in V1 increases as the subject becomes more familiar with the stimulus and/or when the stimulus acquires special contextual saliency for the subject. Nevertheless, the differences between amplitudes of responses in the same conditions were not significant. Responses in V1 were smaller in each one of the control runs than in the active runs.

Because the level of arousal in active and control conditions was not controlled in our experimental design, it is impossible to completely exclude the effect of arousal on enhancement of V1 responses. However, only with arousal, without involvement of mechanisms of selective attention, it is difficult to explain our results. Arousal is the state of physiological reactivity (Broadbent, 1971; Kahneman, 1973; Eysenck, 1982; Robbins & Everitt, 1995), ranging from sleep at one end to excitement or panic at the other (Coull, 1998). Arousal can affect activity of brain regions involved in attentional control (Robbins & Everitt, 1995; Coull, 1998; Portas *et al*., 1998; Foucher *et al*., 2004) and, hence indirectly, it can influence the activity of visual information-processing areas (Foucher *et al*., 2004). Portas *et al*. (1998) have shown that in the absence of attention, arousal does not affect responses of visual cortex. Another strong argument for involvement of selective attention in the effect found in V1 in our study is the spatial specificity of responses. Consistent and statistically significant attentional effects were found only in the contralateral to the arrowhead's V1 (Fig. 4). Arousal alone does not carry any topographic information and it would affect V1 in a spatially non-specific manner. In contrast, it has been shown that selective attention is spatially specific (Kastner *et al*., 1999; Martinez *et al*., 1999; Somers *et al*., 1999; Kastner & Ungerleider, 2000; O'Connor *et al*., 2002). Therefore, the involvement of selective attention in lateralized enhancement of V1 responses is essential.

Spatial specificity of the attentional modulation in V1 does not yet imply spatial selection. In our paradigm attention was directed to fovea. Foveally presented stimuli led to responses in both hemispheres, hence spatial selective attention would have enhanced responses of V1 in both hemispheres, contrary to the results in the current study. For the same reason involvement of object-based attention on the modulation of V1 activity in the current study can be excluded also. Another aspect of attention involved here is a feature-based selective attention. In order to respond correctly, subjects had to attend to two different features of the stimulus: color and shape. Attentional effect identified in V1 cannot be the result of attending to color, as in this case also effect had to be present in both hemispheres. However, attending to the shape of an arrow is different. According to the models of attention based on the concept of saliency map (Koch & Ullman, 1985; Itti & Koch, 2000; Treue, 2003), visual input in the brain is represented by its saliency, that is by its difference in features compared with surrounding visual input. Top-down attentional processes then modulate this bottom-up saliency by enhancing or weakening it, depending on the behavioral relevance of a particular location, feature or object. Evidence suggests that this topographic saliency map is maintained in V1 (Lee *et al*., 1998, 2002; Treue, 2003; Hopf *et al*., 2004). Arrowhead in our case, behaviorally, as well as based on its physical features, is the most salient part of an arrow. During the presentation of the stimuli it completely fell in one hemifield, thus had its neural representation only in the contralateral V1. Therefore we attribute the effect identified in V1 in our study to selective attention to shape.

In active runs the subject had to respond by finger movement, in control runs there was no motor involvement; however, any contribution of the motor component to the enhancement of the V1 response can be excluded as the effect is equally strong in response to both green (GO trials) and red (NOGO trials) arrows (during NOGO trials there was no movement).

Statistical comparison between active and control conditions identified a network of brain areas, mostly in the right hemisphere. This same network was shown to be involved in attentional processing in previous fMRI studies (Kastner *et al*., 1999; Bartels & Zeki, 2000; Corbetta *et al*., 2000; Hopfinger *et al*., 2000). Our study adds to the 'where information' from fMRI, the 'when information', i.e. the precise timing when activity in each of these areas is modulated (Table 3B). Because the responses to all six stimulus types were pooled together, areas including V1 that exhibit spatial specificity or any other stimulus-specific effect are not seen in this statistical comparison. The brain regions identified in this comparison may be involved in aspects of selective attention, as well as in controlling attentional signals and arousal.

In contrast to the broad agreement between our study and earlier studies about localization of attentional effects, including in striate cortex, the timing of the earliest attentional modulation in V1 in our study is considerably earlier than previously reported. While we show that the modulation in V1 has already reached its peak by 100 ms, reports in many recent studies using fMRI, ERP and MEG show attentional effect in V1 considerably later, with the closest to our results reported in the study by Noesselt *et al*. (2002), where modulation of V1 activity by spatial attention was after 140 ms.

Combined fMRI/ERP studies (Mangun, 1995; Martinez *et al*., 1999, 2001; Noesselt *et al*., 2002; Di Russo *et al*., 2003) have shown attention-related enhancement of P1 and N1 ERP components. Few dipoles in extrastriate visual areas, which were co-localized with fMRI activations, were estimated for each of these components. However, this correspondence between dipolar sources of ERP components and fMRI activations cannot be definitive, as ERP and fMRI signals can arise from different underlying neural activities (Nunez & Silberstein, 2000; Arthurs & Boniface, 2002; Heeger & Ress, 2002; Di Russo *et al*., 2003; Vanni *et al*., 2004b). In addition, we have demonstrated that the use of equivalent current dipoles often fails to detect activity in striate cortex if extrastriate areas are concurrently active (Tzelepi *et al*., 2001). So, even if attentional effects were present in V1 at about 100 ms (during P1 component) they could easily be masked by the activity in extrastriate visual areas in a dipole analysis of the data. In contrast, MFT, the reconstruction method used in the current study, has repeatedly demonstrated the capability of accurate localization of V1 generators even for cases where other generators in extrastriate regions were simultaneously active (Tzelepi *et al*., 2001; Moradi *et al*., 2003). In the second of these studies we demonstrated an early ($\sim$ 40 ms after stimulus onset) and transient ($\sim$ 5 ms) activation in V1 with an accuracy of about 3 mm as compared with fMRI localization (Moradi *et al*., 2003). Figure 3 demonstrates the current density vector in V1 at about 100 ms in all six subjects. For all subjects it is localized in the correct anatomical region and has direction perpendicular to calcarine fissure, as would have been expected from V1 activation. On the same figure we also show the V1/V2 border for two subjects, one of whom participated in our previous fMRI/MEG study (Moradi *et al*., 2003). The zoomed images show that the activity is within the V1/V2 border and hence they correspond to V1 activation. As in the current study, all stimuli were presented on the horizontal meridian, it is impossible to demonstrate the inversion of current direction in V1 in response to stimuli in upper and lower visual fields.

In most of the studies that identified attentional modulations in V1 at later latencies (Martinez *et al*., 2001; Noesselt *et al*., 2002; Di Russo *et al*., 2003), attention was covertly directed to stimuli away from the fixation point. In our study the stimuli were presented at the fovea and subjects overtly attended to it. It is possible that attention acts more effectively when the stimulus is overtly attended at the fovea.

Another difference is the aspect of attention employed. In the studies mentioned above, mechanisms of spatial attention affected responses in V1, whereas in our study the modulation of V1 activity was due to attention to the shape of an object.

Electrophysiological studies of attention to color and motion with stimuli presented at the fovea (AnlloVento & Hillyard, 1996; Anllo-Vento *et al*., 1998; Hillyard & Anllo-Vento, 1998) did not find attention-related effects in V1. Moreover, they have shown that effects of attention to color and motion in extrastriate cortex occur later than those of spatial attention. Lack of attentional effect in V1 in these studies can be due to the methods and ERP waveforms used for source localization. Alternatively, this, in conjunction with our results, might suggest that attentional processing of different features of an object involves regions at different levels of visual information-processing hierarchy at different latencies, but these facts need further and more careful examination.

Our finding is still consistent with the notion that the initial response in V1 is not affected by attention. Although the stimuli used in our study did not favor a strong V1 activation, the early weak V1 activity was identified in four out of six subjects at about 40 ms (Fig. 6). It is highly unlikely that this V1 response is not a stimulus-evoked response, but is some kind of anticipatory activity, as it was identified in statistical comparison of post- vs. prestimulus periods. Anticipatory activity would have been the same in both periods and would not be evident in this comparison. In addition, interstimulus interval was randomized to avoid any expectation effects and it is very improbable that anticipatory activity will be sufficiently time-locked to stimuli that will survive the averaging. This early response was not affected by attention and was very transient $\sim$5 ms, in complete agreement with our previous study using the more effective checkerboard pattern stimuli (Moradi *et al*., 2003).

To exclude the possibility of eye movements affecting the results, stimuli were presented for a very short period (32 ms). With such a short presentation there is no advantage to be gained from eye movements. In addition, during the experiment eye movements were measured using EOG and trials with high EOG amplitude were removed. If on the other hand there was some advantage of steady fixation in the active condition, then this would affect most the very early entry into V1 at about 40 ms. The absence of any effect in the early V1 response is therefore showing that the effect we see in the next wave of V1 activation is not due to either eye movements or steady fixation.

The earliest attention-related change in brain activity was identified in right inferior parietal lobule (IPL; Table 3B), at 38 ms after stimulus onset, even before the modulation of striate responses. This is in accord with previous neuroimaging studies (Kim *et al*., 1999; Labar *et al*., 1999; Wojciulik & Kanwisher, 1999; Corbetta *et al*., 2000; Hopfinger *et al*., 2000; Yantis *et al*., 2002; Liu *et al*., 2003; Shikata *et al*., 2003), suggesting involvement of IPL in attentional control processes, and is also consistent with the top-down attentional control theory (Kastner *et al*., 1999; Hopfinger *et al*., 2000; Kastner & Ungerleider, 2000; Mehta *et al*., 2000a,b).

In addition to the shape of the stimuli, subjects attended to the color; hence, attentional effects were identified in an area in left and right frontal gyrus known to be selective for color (Bartels & Zeki, 2000). In our study, SPM analysis identified attentional modulation within a few mm of the area termed as V4α by Bartels & Zeki (2000). The attentional modulation of this area was identified first in the right hemisphere (105–132 ms) and about 60 ms later (164–181 ms) in the left hemisphere.

Striate responses to bilateral arrows showed early attentional modulation in V1, but not as consistently as unilateral arrows. This can be due to the interactions between stimuli in different hemifields (in a case of bilateral arrows) at various levels of visual processing, including V1 (Vanni *et al*., 2004a), and also because of the complex pattern of MEG responses it will produce.

In conclusion, we mapped a network of brain areas that show an early attentional modulation and identified their precise timing in the first 200 ms, i.e. the time period preceding the movement-related activations. Our results provide the first clear evidence of early attentional modulation of V1 beginning well within 100 ms, following the short attention-independent V1 activation about 30 ms earlier. These results are therefore still consistent with the top-down attentional control theory, but they suggest that under certain conditions attentional mechanisms can act with extraordinary speed to account for attentional modulation in V1 that has already reached its peak by 100 ms after stimulus onset.

Supplementary material

The following supplementary material may be found on: http://www.blackwellpublishing.com/products/journals/suppmat/EJN4181/EJN4181sm.htm

Fig. S1. Attentional effects in V1.

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Abbreviations

EOG, electrooculogram; ERP, event-related potentials; fMRI, functional magnetic resonance imaging; IPL, inferior parietal lobule; MEG, magnetoencephalography; MFT, magnetic field tomography; RAC, regional activation curve; ROI, regions of interest; SPM, statistical parametric map; *VS*, virtual signal.

References

Anllo-Vento, L. & Hillyard, S.A. (1996) Selective attention to the color and direction of moving stimuli: electrophysiological correlates of hierarchical feature selection. *Percept. Psychophys.*, **58**, 191–206.

AnlloVento, L. & Hillyard, S.A. (1996) Selective attention to the color and direction of moving stimuli: electrophysiological correlates of hierarchical feature selection. *Percept. Psychophys.*, **58**, 191–206.

Anllo-Vento, L., Luck, S.J. & Hillyard, S.A. (1998) Spatio-temporal dynamics of attention to color: evidence from human electrophysiology. *Hum. Brain Mapp.*, **6**, 216–238.

Arthurs, O.J. & Boniface, S. (2002) How well do we understand the neural origins of the fMRI BOLD signal? *Trends Neurosci.*, **25**, 27–31.

Bartels, A. & Zeki, S. (2000) The architecture of the colour centre in the human visual brain: new results and a review. *Eur. J. Neurosci.*, **12**, 172–190.

Beauchamp, M.S., Cox, R.W. & DeYoe, E.A. (1997) Graded effects of spatial and featural attention on human area MT and associated motion processing areas. *J. Neurophysiol.*, **78**, 516–520.

Brefczynski, J.A. & DeYoe, E.A. (1999) A physiological correlate of the 'spotlight' of visual attention. *Nat. Neurosci.*, **2**, 370–374.

Broadbent, D.E. (1971) *Decision and Stress*. Academic Press, London.

Chawla, D., Rees, G. & Friston, K.J. (1999) The physiological basis of attentional modulation in extrastriate visual areas. *Nat. Neurosci.*, **2**, 671–676.

Clark, V.P., Parasuraman, R., Keil, K., Kulansky, R., Fannon, S., Maisog, J.M., Ungerleider, L.G. & Haxby, J.V. (1997) Selective attention to face identity and color studied with fMRI. *Hum. Brain Mapp.*, **5**, 293–297.
Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P. & Shulman, G.L. (2000) Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nat. Neurosci.*, **3**, 292–297.
Corbetta, M., Miezin, F.M., Dobmeyer, S., Shulman, G.L. & Petersen, S.E. (1990) Attentional modulation of neural processing of shape, color, and velocity in humans. *Science*, **248**, 1556–1559.
Coull, J.T. (1998) Neural correlates of attention and arousal: insights from electrophysiology, functional neuroimaging and psychopharmacology. *Prog. Neurobiol.*, **55**, 343–361.
Di Russo, F., Martinez, A. & Hillyard, S.A. (2003) Source analysis of event-related cortical activity during visuo-spatial attention. *Cereb. Cortex*, **13**, 486–499.
Downing, P., Liu, J. & Kanwisher, N. (2001) Testing cognitive models of visual attention with fMRI and MEG. *Neuropsychologia*, **39**, 1329–1342.
Eysenck, M.W. (1982) *Attention and Arousal, Cognition and Performance*. Springer, Berlin.
Foucher, J.R., Otzenberger, H. & Gounot, D. (2004) Where arousal meets attention: a simultaneous fMRI and EEG recording study. *Neuroimage*, **22**, 688–697.
Fu, S.M., Fan, S.L., Chen, L. & Zhuo, Y. (2001) The attentional effects of peripheral cueing as revealed by two event-related potential studies. *Clin. Neurophysiol.*, **112**, 172–185.
Gandhi, S.P., Heeger, D.J. & Boynton, G.M. (1999) Spatial attention affects brain activity in human primary visual cortex. *Proc. Natl. Acad. Sci. USA*, **96**, 3314–3319.
Heeger, D.J. & Ress, D. (2002) What does fMRI tell us about neuronal activity? *Nat. Rev. Neurosci.*, **3**, 142–151.
Heinze, H.J., Mangun, G.R., Burchert, W., Hinrichs, H., Scholz, M., Munte, T.F., Gos, A., Scherg, M., Johannes, S., Hundeshagen, H., Gazzaniga, M.S. & Hillyard, S.A. (1994) Combined spatial and temporal imaging of brain activity during visual selective attention in humans. *Nature*, **372**, 543–546.
Hillyard, S.A. & Anllo-Vento, L. (1998) Event-related brain potentials in the study of visual selective attention. *Proc. Natl. Acad. Sci. USA*, **95**, 781–787.
Hopf, J.M., Luck, S.J., Girelli, M., Hagner, T., Mangun, G.R., Scheich, H. & Heinze, H.J. (2000) Neural sources of focused attention in visual search. *Cereb. Cortex*, **10**, 1233–1241.
Hopf, J.M., Noesselt, T., Tempelmann, C., Braun, J., Schoenfeld, M.A. & Heinze, H.J. (2004) Popout modulates focal attention in the primary visual cortex. *Neuroimage*, **22**, 574–582.
Hopfinger, J.B., Buonocore, M.H. & Mangun, G.R. (2000) The neural mechanisms of top-down attentional control. *Nat. Neurosci.*, **3**, 284–291.
Ioannides, A.A. (2002) Magnetic field tomography: theory, applications and examples from the visual system. In Hirata, K., Kotani, M., Koga, Y., Nagata, K. & Yamazaki, K. (Eds), *Recent Advances in Human Brain Mapping*. Elsevier, Amsterdam, pp. 261–270.
Ioannides, A.A., Bolton, J.P.R. & Clarke, C.J.S. (1990) Continuous probabilistic solutions to the biomagnetic inverse problem. *Inverse Problem*, **6**, 523–542.
Ioannides, A.A., Corsi-Cabrera, M., Fenwick, P.B., del Rio, P.Y., Laskaris, N.A., Khurshudyan, A., Theofilou, D., Shibata, T., Uchida, S., Nakabayashi, T. & Kostopoulos, G.K. (2004) MEG tomography of human cortex and brainstem activity in waking and REM sleep saccades. *Cereb. Cortex*, **14**, 56–72.
Itti, L. & Koch, C. (2000) A saliency-based search mechanism for overt and covert shifts of visual attention. *Vision Res.*, **40**, 1489–1506.
Kahneman, D. (1973) *Attention and Effort*. Prentice Hall, Englewood Cliffs, N.J.
Kanwisher, N. & Driver, J. (1992) Objects, attributes, and visual attention. *Curr. Dir. Psychol. Sci.*, **1**, 26–31.
Kanwisher, N. & Wojciulik, E. (2000) Visual attention: insight from brain imaging. *Nature Rev.*, **1**, 91–100.
Kastner, S., Pinsk, M.A., De Weerd, P., Desimone, R. & Ungerleider, L.G. (1999) Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron*, **22**, 751–761.
Kastner, S. & Ungerleider, L.G. (2000) Mechanisms of visual attention in the human cortex. *Annu. Rev. Neurosci.*, **23**, 315–341.
Kim, Y.H., Gitelman, D.R., Nobre, A.C., Parrish, T.B., Labar, K.S. & Mesulam, M.M. (1999) The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. *Neuroimage*, **9**, 269–277.
Koch, C. & Ullman, S. (1985) Shifts in selective visual attention: towards the underlying neural circuitry. *Hum. Neurobiol.*, **4**, 219–227.
Labar, K.S., Gitelman, D.R., Parrish, T.B. & Mesulam, M.M. (1999) Neuroanatomic overlap of working memory and spatial attention networks: a functional MRI comparison within subjects. *Neuroimage*, **10**, 695–704.
Laskaris, N.A., Liu, L.C. & Ioannides, A.A. (2003) Single-trial variability in early visual neuromagnetic responses: an explorative study based on the regional activation contributing to the N70m peak. *Neuroimage.*, **20**, 765–783.
Lee, T.S., Mumford, D., Romero, R. & Lamme, V.A. (1998) The role of the primary visual cortex in higher level vision. *Vision Res.*, **38**, 2429–2454.
Lee, T.S., Yang, C.F., Romero, R.D. & Mumford, D. (2002) Neural activity in early visual cortex reflects behavioral experience and higher-order perceptual saliency. *Nat. Neurosci.*, **5**, 589–597.
Liu, L.C., Ioannides, A.A. & Muller-Gartner, H.W. (1998) Bi-hemispheric study of single trial MEG signals of the human auditory cortex. *Electroencephalogr. Clin. Neurophysiol.*, **106**, 64–78.
Liu, T.S., Slotnick, S.D., Serences, J.T. & Yantis, S. (2003) Cortical mechanisms of feature-based attentional control. *Cereb. Cortex*, **13**, 1334–1343.
Mangun, G.R. (1995) Neural mechanisms of visual selective attention. *Psychophysiology*, **32**, 4–18.
Mangun, G.R., Hinrichs, H., Scholz, M., Mueller-Gaertner, H.W., Herzog, H., Krause, B.J., Tellman, L., Kemna, L. & Heinze, H.J. (2001) Integrating electrophysiology and neuroimaging of spatial selective attention to simple isolated visual stimuli. *Vision Res.*, **41**, 1423–1435.
Mangun, G.R., Hopfinger, J.B., Kussmaul, C.L., Fletcher, E.M. & Heinze, H.J. (1997) Covariations in ERP and PET measures of spatial selective attention in human extrastriate visual cortex. *Hum. Brain Mapp.*, **5**, 273–279.
Martinez, A., Anllo-Vento, L., Sereno, M.I., Frank, L.R., Buxton, R.B., Dubowitz, D.J., Wong, E.C., Hinrichs, H., Heinze, H.J. & Hillyard, S.A. (1999) Involvement of striate and extrastriate visual cortical areas in spatial attention. *Nat. Neurosci.*, **2**, 364–369.
Martinez, A., Di Russo, F., Anllo-Vento, L., Sereno, M.I., Buxton, R.B. & Hillyard, S.A. (2001) Putting spatial attention on the map: timing and localization of stimulus selection processes in striate and extrastriate visual areas. *Vision Res.*, **41**, 1437–1457.
Mehta, A.D., Ulbert, I. & Schroeder, C.E. (2000a) Intermodal selective attention in monkeys. I: distribution and timing of effects across visual areas. *Cereb. Cortex*, **10**, 343–358.
Mehta, A.D., Ulbert, I. & Schroeder, C.E. (2000b) Intermodal selective attention in monkeys. II: physiological mechanisms of modulation. *Cereb. Cortex*, **10**, 359–370.
Moradi, F., Liu, L.C., Cheng, K., Waggoner, R.A., Tanaka, K. & Ioannides, A.A. (2003) Consistent and precise localization of brain activity in human primary visual cortex by MEG and fMRI. *Neuroimage*, **18**, 595–609.
Muller, N.G. & Kleinschmidt, A. (2003) Dynamic interaction of object- and space-based attention in retinotopic visual areas. *J. Neurosci.*, **23**, 9812–9816.
Noesselt, T., Hillyard, S.A., Woldorff, M.G., Schoenfeld, A., Hagner, T., Jancke, L., Tempelmann, C., Hinrichs, H. & Heinze, H.J. (2002) Delayed striate cortical activation during spatial attention. *Neuron*, **35**, 575–587.
Nunez, P.L. & Silberstein, R.B. (2000) On the relationship of synaptic activity to macroscopic measurements: does co-registration of EEG with fMRI make sense? *Brain Topogr.*, **13**, 79–96.
O'Connor, D.H., Fukui, M.M., Pinsk, M.A. & Kastner, S. (2002) Attention modulates responses in the human lateral geniculate nucleus. *Nat. Neurosci.*, **5**, 1203–1209.
OCraven, K.M., Downing, P. & Kanwisher, N. (1999) fMRI evidence for objects as the units of attentional selection. *Nature*, **401**, 584–587.
OCraven, K.M., Rosen, B.R., Kwong, K.K., Treisman, A. & Savoy, R.L. (1997) Voluntary attention modulates fMRI activity in human MT-MST. *Neuron*, **18**, 591–598.
Portas, C.M., Rees, G., Howseman, A.M., Josephs, O., Turner, R. & Frith, C.D. (1998) A specific role for the thalamus in mediating the interaction of attention and arousal in humans. *J. Neurosci.*, **18**, 8979–8989.
Robbins, T.W. & Everitt, B.J. (1995) Arousal systems and attention. In Gazzaniga, M.S. (Ed.), *The Cognitive Neurosciences*. MIT Press, Cambridge, MA, pp. 703–720.
Roelfsema, P.R., Lamme, V.A. & Spekreijse, H. (1998) Object-based attention in the primary visual cortex of the macaque monkey. *Nature*, **395**, 376–381.
Saenz, M., Buracas, G.T. & Boynton, G.M. (2002) Global effects of feature-based attention in human visual cortex. *Nat. Neurosci.*, **5**, 631–632.
Shikata, E., Hamzei, F., Glauche, V., Koch, M., Weiller, C., Binkofski, F. & Buchel, C. (2003) Functional properties and interaction of the anterior and posterior intraparietal areas in humans. *Eur. J. Neurosci.*, **17**, 1105–1110.
Somers, D.C., Dale, A.M., Seiffert, A.E. & Tootell, R.B. (1999) Functional MRI reveals spatially specific attentional modulation in human primary visual cortex. *Proc. Natl. Acad. Sci. USA*, **96**, 1663–1668.

Talairach, J. & Tournoux, P. (1988) *Co-planar Stereotaxic Atlas of the Human Brain: 3-Dimensional Proportional System: An Approach to Cerebral Imaging*. Thieme, New York.

Tootell, R.B., Hadjikhani, N., Hall, E.K., Marrett, S., Vanduffel, W., Vaughan, J.T. & Dale, A.M. (1998) The retinotopy of visual spatial attention. *Neuron*, **21**, 1409–1422.

Torriente, I., Valdes-Sosa, M., Ramirez, D. & Bobes, M.A. (1999) Visual evoked potentials related to motion-onset are modulated by attention. *Vision Res.*, **39**, 4122–4139.

Treue, S. (2003) Visual attention: the where, what, how and why of saliency. *Curr. Opin. Neurobiol.*, **13**, 428–432.

Tzelepi, A., Ioannides, A.A. & Poghosya, N.V. (2001) Early (N70m) neuromagnetic signal topography and striate and extrastriate generators following pattern onset quadrant stimulation. *Neuroimage*, **13**, 702–718.

Vanni, S., Dojat, M., Warnking, J., Delon-Martin, C., Segebarth, C. & Bullier, J. (2004a) Timing of interactions across the visual field in the human cortex. *Neuroimage*, **21**, 818–828.

Vanni, S., Warnking, J., Dojat, M., Delon-Martin, C., Bullier, J. & Segebarth, C. (2004b) Sequence of pattern onset responses in the human visual areas: an fMRI constrained VEP source analysis. *Neuroimage*, **21**, 801–817.

Watanabe, T., Harner, A.M., Miyauchi, S., Sasaki, Y., Nielsen, M., Palomo, D. & Mukai, I. (1998a) Task-dependent influences of attention on the activation of human primary visual cortex. *Proc. Natl. Acad. Sci. USA*, **95**, 11489–11492.

Watanabe, T., Sasaki, Y., Miyauchi, S., Putz, B., Fujimaki, N., Nielsen, M., Takino, R. & Miyakawa, S. (1998b) Attention-regulated activity in human primary visual cortex. *J. Neurophysiol.*, **79**, 2218–2221.

Wojciulik, E. & Kanwisher, N. (1999) The generality of parietal involvement in visual attention. *Neuron*, **23**, 747–764.

Woldorff, M.G., Fox, P.T., Matzke, M., Lancaster, J.L., Veeraswamy, S., Zamarripa, F., Seabolt, M., Glass, T., Gao, J.H., Martin, C.C. & Jerabek, P. (1997) Retinotopic organization of early visual spatial attention effects as revealed by PET and ERPs. *Hum. Brain Mapp.*, **5**, 280–286.

Yantis, S., Schwarzbach, J., Serences, J.T., Carlson, R.L., Steinmetz, M.A., Pekar, J.J. & Courtney, S.M. (2002) Transient neural activity in human parietal cortex during spatial attention shifts. *Nat. Neurosci.*, **5**, 995–1002.

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Change to lower case	Encircle matter to be changed	
Change italic to upright type	(As above)	
Insert 'superior' character	/ through character or where required	under character e.g.
Insert 'inferior' character	(As above)	over character e.g.
Insert full stop	(As above)	
Insert comma	(As above)	
Insert single quotation marks	(As above)	and/or
Insert double quotation marks	(As above)	and/or
Insert hyphen	(As above)	
Start new paragraph		
No new paragraph		
Transpose		
Close up	linking letters	
Insert space between letters	between letters affected	
Insert space between words	between words affected	
Reduce space between letters	between letters affected	
Reduce space between words	between words affected	