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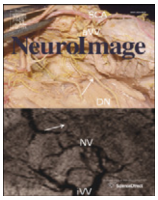

Spatiotemporal dynamics of early spatial and category-specific attentional modulations

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ABSTRACT

Different attention types select and focus brain resources on relevant sensory information. However, key questions remain unresolved: when and where cortical visual processing is first modulated by different types of attention? How do such modulatory effects spread thereafter? Here, we address these issues for spatial and category-specific types of attention using magnetoencephalography (MEG). First we identified the dynamics of visual attention-independent sensory processing to serve as a baseline framework for the attentional modulations of interest. We found that visual information is processed through the entire hierarchy of visual areas in at least two phases, in the 40–130 ms and 130–230 ms periods respectively. Spatial attention modulations were identified from the beginning of the initial stimulus-evoked response in the primary visual cortex ~70 ms post-stimulus. Category-specific attention modulated face processing beginning from the first face-specific response in high-level object-related areas ~100 ms post-stimulus, substantially earlier than previously reported for face-directed attention. Thus both attention types modulated responses during the first processing phase, beginning at the earliest brain area capable of coding the attentional target. Thereafter attentional effects propagated through the visual cortex together with the stimulus-evoked activity. Category-specific attention did not affect the first-phase responses in low-level strongly retinotopic visual areas, while the second-phase responses were enhanced when the stimulus was the response target and reduced when it was a distractor. Responses during both phases in high-level object-related areas were enhanced by category-specific attention independent of their target/distractor status. Spatial attention effects were stronger in low-level areas, whereas category-specific attention effects were stronger in high-level object-related areas.

Introduction

Attention is a cognitive process that selects and focuses brain resources on the relevant sensory information. Functional magnetic resonance imaging (fMRI) studies of attention have identified networks of frontoparietal brain regions that control the deployment of attention (Corbetta and Shulman, 2002; Corbetta et al., 2000; Kincade et al., 2005) and found modulatory influences of attention in nearly all visual cortical areas (Kanwisher and Wojciulik, 2000; Kastner and Ungerleider, 2000). However, fundamental unresolved questions remain concerning when and where in the visual pathway the stimulus processing is first modulated by different types of selective attention and how does each such modulatory effect spread thereafter?

The question of the first modulation of the routine visual processing by different attention types has been extensively studied with conflicting results. Spatial attention has long been assumed to first modulate the sensory-evoked responses in the extrastriate visual cortex (Clark and Hillyard, 1996; Di Russo et al., 2003; Gonzalez et al., 1994; Heinze et al., 1994; Hillyard and Anllo-Vento, 1998; Mangun et al., 2001; Martinez et al., 1999, 2001b; Noesselt et al., 2002; Woldorff et al., 1997, 2002) and affect activity in V1 at longer latencies (after 100 ms post-stimulus) by means of delayed feedback from higher level areas (Di Russo et al., 2003; Martinez et al., 2001b; Noesselt et al., 2002). Recent studies however have contradicted this view showing that spatial attention enhances stimulus-evoked cortical activity beginning at the initial feedforward response in V1 at ~55 ms post-stimulus (Kelly et al., 2008; Poghosyan and Ioannides, 2008).

Likewise, the earlier studies of non-spatial feature-based attention have claimed that the earliest attentional effect occurs after 100 ms post-stimulus in the extrastriate visual cortex, circumventing the initial evoked response in V1 (AnlloVento and Hillyard, 1996; Anllo-Vento et al., 1998; Baas et al., 2002; Eimer, 1995; Hillyard and Anllo-Vento, 1998; Hillyard and Munte, 1984; Hillyard et al., 1998; Martinez et al., 2001a; Schoenfeld et al., 2007; Zhang and Luck, 2009). Furthermore,

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Abbreviations: MFT, magnetic field tomography; RAC, regional activation curve; LO, lateral occipital; pFus, posterior fusiform; AI, attentional index.

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until recently it was widely believed that non-spatial attention affects stimulus processing at later stages than spatial attention, and is contingent upon spatial selection (Hillyard and Anllo-Vento, 1998). However, most recent studies (Proverbio et al., 2010; Zani and Proverbio, 2009) have found that non-spatial feature-based attention directed to spatial frequency modulates the initial V1 response as early as 40–60 ms post-stimulus, in contrast to past claims (Baas et al., 2002; Martinez et al., 2001a).

The null results regarding the modulation of initial evoked response in V1 by spatial attention and spatial frequency feature-based non-spatial attention in earlier studies can be attributed to a range of methodological issues, including inter-individual variability and excessive filtering (Kelly et al., 2008; Poghosyan and Ioannides, 2008; Proverbio et al., 2007). Modulations of visual event related potentials by intermodal selective attention with signal topography and latencies (early phase of event-related potential (ERP) C1 component) consistent with that of the initial V1 response have also been found (Karns and Knight, 2009).

Attending to faces is known to strongly modulate the face-related patterns of hemodynamic activity measured with fMRI (O'Craven et al., 1999; Serences et al., 2004; Wojciulik et al., 1998). Electroencephalography (EEG) and MEG measurements have been used to determine when and where in the visual pathway the first face-directed attentional effects are encountered, without reaching converging conclusions. While some studies reported modulations of the 170-ms face specific electromagnetic response (Downing et al., 2001; Eimer, 2000; Holmes et al., 2003; Sreenivasan et al., 2009), others found modulations only at later latencies (Carmel and Bentin, 2002; Cauquil et al., 2000; Furey et al., 2006; Lueschow et al., 2004). Notwithstanding these differences, the earliest face-directed attentional effect reported so far is the modulation of the 170-ms face-specific brain response by object-based attention (Downing et al., 2001; Eimer, 2000; Holmes et al., 2003). Note, that in all these studies the subject's attention was directed to specific faces rather than to the face category per se, and the attentional effects are found during the second, identification phase of face processing (Itier and Taylor, 2002, 2004a, 2004b; Itier et al., 2006; Linkenkaer-Hansen et al., 1998; Liu et al., 2002; Sugase et al., 1999).

Recently Latinus et al. (2010), using a gender discrimination task with bimodal, face and voice stimuli, have reported attention-related enhancement of stimulus-evoked ERP P1 component at ~100 ms. However, their experimental design did not differentiate between the effects of intramodal face-directed attention and attention directed to an entire sensory modality, or between the modulations of auditorily and visually evoked neural responses. Thus, to the best of our knowledge no study so far has unambiguously determined the effect of face-directed attention on the first category-related neural response at ~100 ms post-stimulus (Herrmann et al., 2005; Itier and Taylor, 2002, 2004a, 2004b; Itier et al., 2006; Linkenkaer-Hansen et al., 1998; Liu et al., 2002; Meeren et al., 2008; VanRullen and Thorpe, 2001).

Based on the reported evidence regarding the first modulation of the visual processing by different attention types (Downing et al., 2001; Eimer, 2000; Holmes et al., 2003; Karns and Knight, 2009; Kelly et al., 2008; Poghosyan and Ioannides, 2008; Proverbio et al., 2010; Zani and Proverbio, 2009) we hypothesize that the visual stimulus processing is first affected by attention at the earliest processing level capable of coding/discriminating the attentional target. In addition, we hypothesize that attention may affect differently the low- and high-level visual cortical areas.

Here we define as low-level the visual areas that show a strongly retinotopic spatial organization, and are more sensitive to low-level visual features such as stimulus contrast than to high-level features such as stimulus category. We define as high-level the areas that are more sensitive to high- than low-level visual features, and show no or loosely retinotopic spatial organization, such as eccentricity bias (Levy et al., 2001). According to our definition, low-level areas respond almost exclusively to contralateral stimuli and high-level visual areas respond strongly to ipsilaterally as well as contralaterally presented stimuli.

Here we test our hypotheses for two important types of attention, spatial attention and non-spatial category-specific attention. We used an experimental protocol that allowed us to study within the same framework the effects of both attention types together with the stimulus-evoked activity. We used MEG together with a robust distributed source model (Ioannides et al., 1990; Moradi et al., 2003; Papadelis et al., 2009; Poghosyan and Ioannides, 2007, 2008; Taylor et al., 1999) to estimate neural activity in each visual area with millisecond accuracy. We were thus able to document in detail what are the effects of spatial and non-spatial category-specific attention in individual cortical areas and how they evolve in time, and compare their spread through the visual hierarchy with that of the stimulus-evoked response.

Materials and methods

Subjects

Five right-handed, male subjects with normal hearing and normal or corrected-to-normal visual acuity participated in the experiment. RIKEN's (the institution where the experiment was conducted) ethics committee approved the study, and all the subjects gave their informed written consent after all procedures were explained to them before the experiment.

Rationale of the experimental design

The following section (Stimuli and experimental design) describes in detail the stimuli and experimental protocol used in the current study. Here we briefly provide a rationale for some of the choices made in their design. To test our hypotheses we needed first to trace the progression of the attention-independent visually evoked responses from the first cortical response in V1 to higher level visual areas, and in this context identify and compare the modulatory effects of different types of attention.

Auditory attention condition

We added an auditory attention condition in our experimental design to provide a proper baseline for identifying the visual stimulus-evoked responses independent of visual attention. The use of passive viewing condition for this purpose is not very appropriate since in such conditions the general arousal level of the subjects is different and hence any identified effect may be attributed to non-specific arousal.

Visual stimuli

Because of the nature of the retinotopic organization of the early visual cortex (V1–V4), it is very difficult to disentangle neural sources in V1 and in the following early visual areas using foveally presented stimuli. Therefore, we presented our stimuli in the lower quadrants of the visual field, which enabled us to accurately trace the visually evoked responses beginning from the initial afferent response in V1. Such a design produces detailed results regarding the spatiotemporal dynamics of the early visual processing as we have demonstrated in a number of recent studies (Moradi et al., 2003; Poghosyan and Ioannides, 2007, 2008).

We used high-contrast checkerboard stimuli for unambiguous and reliable identification of neural sources in the low-level visual areas. The high-contrast edges of checkerboard patterns elicit strong responses in these areas and allow accurate identification of their neural sources. Moreover, similar sized checkerboard stimuli presented at similar locations in visual field quadrants have been used successfully before together with the same data analysis methods as in the current study for accurate mapping of early visual areas (Moradi et al., 2003; Poghosyan and Ioannides, 2007, 2008).

We used face stimuli to study the effects of category-specific attention, because face is a rather archetypal category showing robust category-specific processing in terms of both behavioral measures and brain responses. Furthermore, it is the most studied object category and provides clear predictions about the overall localization and temporal dynamics of the corresponding brain sources.

Stimuli and experimental design

Auditory and visual stimuli were delivered to subjects, while they were seated in a dimly lit magnetically shielded room. Two categories of stimuli were used in each sensory modality: Sound stimuli were low (at 475 Hz, 500 Hz and 525 Hz) and high (at 1900 Hz, 2000 Hz and 2100 Hz) frequency tones (Fig. 1A) with rise/fall times of 0 ms and intensity of 78 dB SPL. Visual stimuli were ellipse-shaped images of high-contrast checkerboards and faces (mean luminance 92 cd m^{-2}) with 8.5° × 6.5° dimensions (Fig. 1A). Checkerboards had a check size of 0.85° × 0.85° and were oriented vertically, tilted at 18° or −18° angles. Faces were of a Caucasian male with neutral, happy and angry expressions. Visual stimuli were back-projected on the screen, placed 60 cm ahead of the subject, with a high-luminance projector (NEC HIGHlite 8000Dsx+, modified for luminance uniformity control), which was located outside the shielded room.

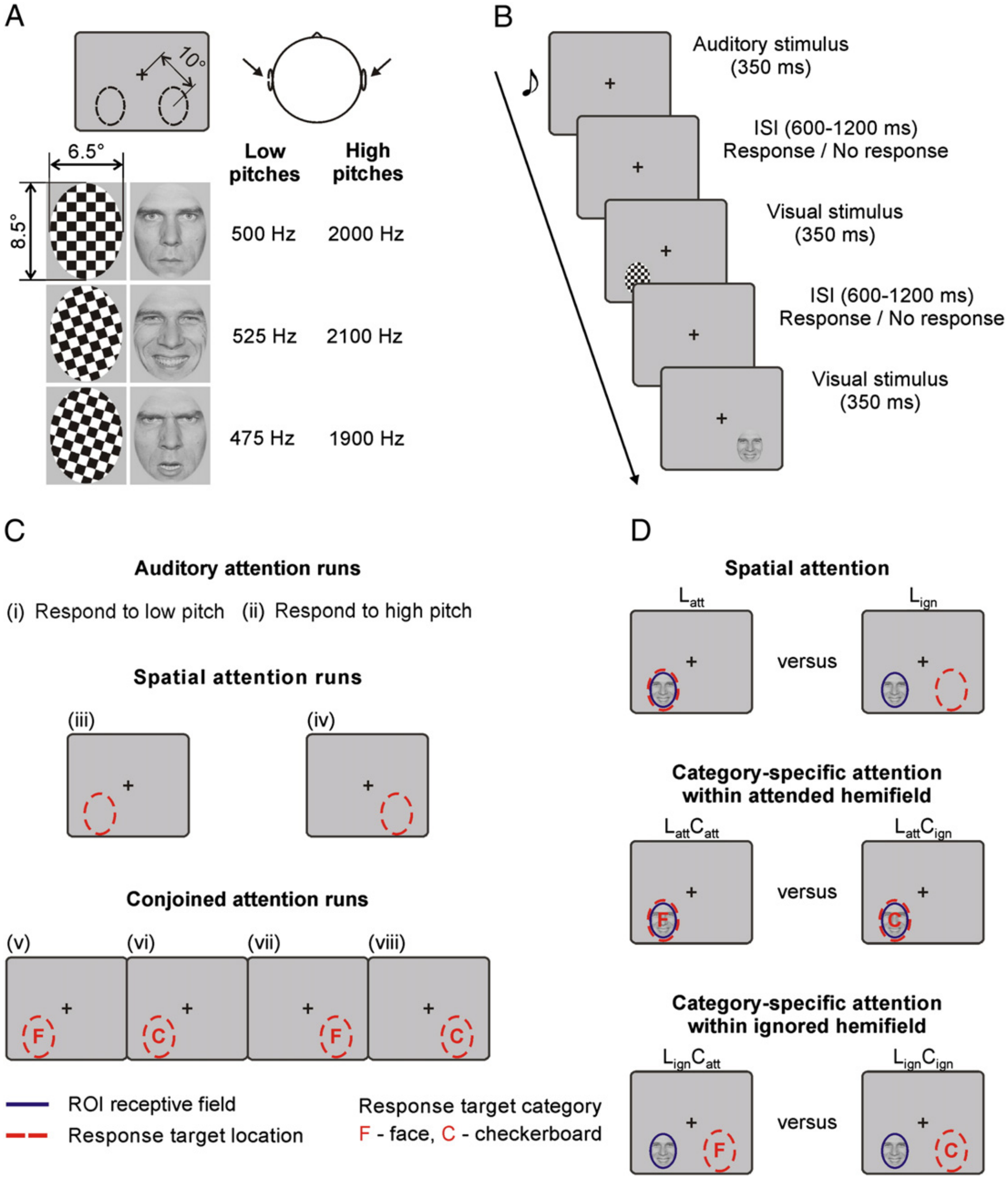

Fig. 1. Experimental design. *A*, Auditory and visual stimuli, 350 ms in duration, were presented either in the left or right ear, or the lower left or right visual field in random order. Subjects were required to respond to target stimuli during interstimulus interval (ISI), which was randomized between 600 and 1200 ms. *B*, Four categories of stimuli (checkerboards, faces, low and high frequency tones), each with three exemplars, were used. Dimensions and presented locations of visual stimuli are shown above the images. *C*, Data from eight runs are reported here: two auditory attention runs (i and ii), where subjects responded to low or high pitch; two visual spatial attention runs (iii and iv), where subjects responded to any visual stimuli appearing in the left or right visual hemifield; and four visual conjoint attention runs (v-viii), where subjects responded to combination of visual hemifield and stimulus category. The red dashed oval shows the response target location (i.e. attended location), while the red letters F and C indicate target category (i.e. attended category), face and checkerboard respectively. *D*, Spatial attention was studied by comparing responses to each stimulus category when the stimulated visual hemifield was attended versus ignored (top row). Category-specific attention was studied using trials from the conjoint attention condition separately for stimuli presented within the attended (middle row) and ignored (bottom row) hemifields. In each case the comparison was made between runs where stimuli belonged to target (i.e. attended) versus non-target (i.e. ignored) category. The examples in the figure illustrate comparisons for face stimulus category.

All stimuli were 350 ms in duration. Auditory stimuli were presented to subjects via air-tube headphones in the left or right ear. Visual stimuli were presented at 10° eccentricity along the 45° diagonals in lower left or right hemifield (Fig. 1A). In each run stimuli were presented in random order, independent of sensory modality, with interstimulus interval varied randomly between 600 and 1200 ms (Fig. 1B). The experiment for each subject included eight runs of ~3 min each. During a run, each stimulus in each side was presented for six times, thus total of 144 presentations were completed in each run (2 sensory modalities × 2 stimulus categories in each sensory modality × 3 exemplars in each category × 6 repetitions of each exemplar × 2 presentation sides, left and right).

Subjects were instructed to avoid any kind of eye or body movement, maintain fixation on a central cross and respond to the target stimuli as accurately and quickly as possible by lifting the right index finger from the optical button device. The response target was indicated to subjects before the beginning of each run by a written cue on the screen, which in different runs was: (i) “Low pitch”, (ii) “High pitch”; (iii) “Left visual filed”, (iv) “Right visual field”; (v) “Left face”, (vi) “Left checkerboard”, (vii) “Right face”, or (viii) “Right checkerboard” (Fig. 1C).

In this experimental design, the physical stimuli remained unchanged across the runs, but the subjects were required to employ different form of attention to accurately respond to the targets (Fig. 1C). Thus, the same visual stimulus in different runs could be: in (iii and iv, visual spatial attention runs) - (a) at the attended spatial location (L_{att}), or (b) at the ignored spatial location (L_{ign}); in (v–viii, visual conjoint attention runs)–(c) at the attended spatial location and belong to attended category ($L_{att}C_{att}$), (d) at the attended spatial location, but belong to ignored category ($L_{att}C_{ign}$), (e) at the ignored spatial location, but belong to attended category ($L_{ign}C_{att}$), or (f) at the ignored spatial location and belong to ignored category ($L_{ign}C_{ign}$); in (i and ii, auditory non-spatial attention runs)–(g) altogether ignored. In this way the different attention types were studied based on the following contrasts (Fig. 1D): L_{att} versus L_{ign} for spatial attention; $L_{att}C_{att}$ versus $L_{att}C_{ign}$ for non-spatial category-specific attention within the attended hemifield; and $L_{ign}C_{att}$ versus $L_{ign}C_{ign}$ for non-spatial category-specific attention within the ignored hemifield. Auditory non-spatial attention runs were used to identify the visually evoked brain responses independent of visual attention. Accordingly, four attentional conditions were distinguished: (1) spatial attention, (2) non-spatial category-specific attention within the attended hemifield, (3) category-specific attention within the ignored hemifield, and (4) auditory attention condition.

Rationale for the conjoint attention runs

The aim of the conjoint attention runs in our experimental design was to enable us to study the effect of non-spatial category-specific attention without confounds of spatial attention. Our design allows explicit control over deployment of spatial and category-specific attention within the same run. We presented stimuli at two different visual field locations and explicitly controlled the deployment of both attention types in each experimental run. In this way by examining the effect of the category-specific attention when the stimuli were both within the “spotlight” of spatial attention ($L_{att}C_{att}$ versus $L_{att}C_{ign}$) and outside the “spotlight” of spatial attention ($L_{ign}C_{att}$ versus $L_{ign}C_{ign}$) we can probe the category-specific attentional effects without confounds of spatial attention.

Data acquisition and pre-processing

MEG was recorded using a 151 gradiometer whole-head system (CTF/VSM Omega Systems, Canada) at a sampling rate of 2500 Hz and bandpass of 0–800 Hz. In synchrony with the MEG, vertical and horizontal electrooculogram (EOG) and electrocardiogram (ECG) were recorded. EOG was used to control the subjects' fixation during the experiment. See Supplemental Data in Poghosyan and Ioannides (2008) for a detailed description of the employed procedure. In summary, the average eye movement in each run was less than 0.3° and in the interval from −100 to 100 ms relative to stimulus onset there were no eye movements exceeding the 1° threshold.

The subject's head location relative to MEG sensors was recorded at the beginning and end of each run, using head localization coils attached to the subject's head. Average head movement of each subject during a run was around 1–2 mm. Runs in which movement exceeded 4 mm were repeated. Co-registration of the MEG sensors with the individual high-resolution anatomical MRIs was accomplished using a procedure described in Poghosyan and Ioannides (2007), which provides a co-registration accuracy of 1 mm (Hironaga and Ioannides, 2002).

Offline, the MEG signals were converted to a 3rd order synthetic gradient and high-pass filtered at 1 Hz. Independent component analysis in conjunction with vertical EOG and ECG data was used to remove the eye blink and cardiac artifacts respectively. The processed MEG signals were divided into 900 ms trials, from −300 to 600 ms with respect to stimulus onset.

Supplementary Fig. 1 shows the mean global field power of 10 left hemisphere occipital MEG sensors in different attentional conditions for a representative subject and the grand average across all subjects.

Data analysis

Source analysis

Source analysis of MEG signals for each single trial was performed using magnetic field tomography (MFT) (Ioannides et al., 1990; Taylor et al., 1999) followed by statistical parametric mapping: a robust and accurate methodology (Ioannides et al., 2005; Moradi et al., 2003; Papadelis et al., 2009; Poghosyan and Ioannides, 2007, 2008) that has been routinely and successfully used in many prior studies for identifying neural responses elicited by checkerboards (Moradi et al., 2003; Poghosyan and Ioannides, 2007, 2008) and faces (Liu and Ioannides, 2006, 2010; Okazaki et al., 2008, 2010; Poghosyan and Ioannides, 2008). MFT was applied independently to every time point (0.4 ms) of each trial to estimate the three-dimensional distribution of current sources throughout the brain. The single trial MFT estimates (current density vectors) from the auditory attention condition were then used to generate statistical parametric maps (SPM).

Prior to SPM generation, MFT estimates were smoothed by integrating them over 2.4 ms (6 time points) successive windows and the moduli of the resulting integrated vectors were used to construct distributions for the SPM analysis. The basic distribution for each latency (−300 to 200), visual stimulus category (checkerboard and face) and visual hemifield (left and right) consisted of 36 such elements (2 runs × 3 exemplars × 6 repetitions). Two types of SPMs were constructed using *t*-test comparisons: post- versus pre-stimulus and face versus checkerboard.

Regions of interest and regional time courses

All SPMs were visually inspected and brain regions that exhibited distinct statistically significant (*t*-test, two-tailed, Bonferroni corrected $P<0.005$) activations consistently across subjects were identified. For each subject the centroids of such activations were designated as centers of spherical regions of interest (ROI) with a radius of 1 cm. A detailed description of how the ROIs were selected is provided in Supplementary methods. In summary eight ROIs were defined: in bilateral V1, V4, and lateral occipital (LO) and posterior fusiform (pFus) cortices (Fig. 2 and Supplementary Fig. 2). The low-level ROIs (i.e. V1 and V4) were significantly active for both face and checkerboard stimuli at similar latencies. They responded only to stimuli presented in the contralateral hemifield. The high-level ROIs (i.e. LO and pFus) were significantly stronger activated for face than checkerboard stimuli, and responded to ipsilaterally as well as contralaterally presented stimuli. Thus stimuli presented in one visual hemifield produced significant activations in six of the ROIs: contralateral V1, V4, LO and pFus, and ipsilateral LO and pFus. The principle direction for each ROI was

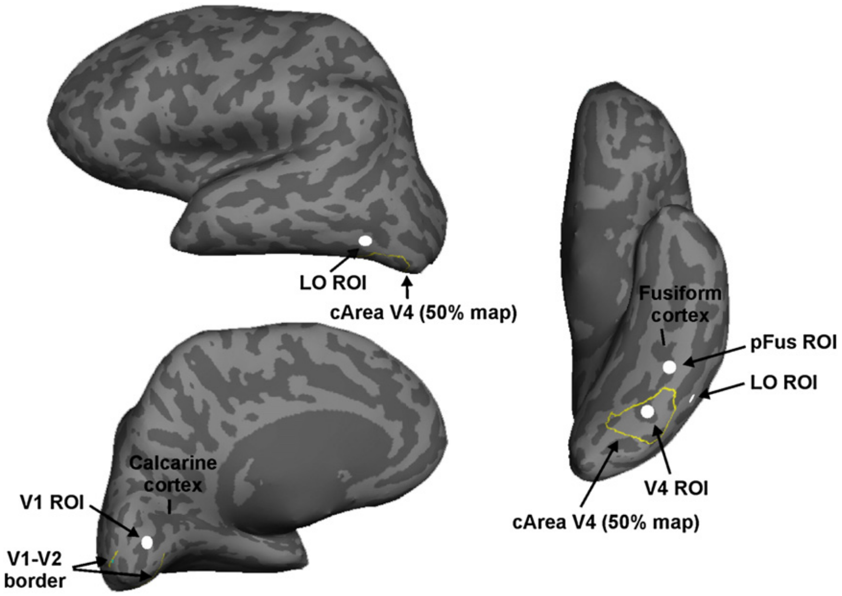

Fig. 2. ROIs in a typical subject. Lateral, medial and bottom views of an inflated left hemisphere are shown. White circles show the ROI locations. Yellow lines indicate either the V1-V2 borders (medial view, representation of vertical meridian obtained in a separate fMRI experiment) or the putative V4 area (bottom view, obtained from the 50% cytoarchitectonic probabilistic map). cArea, cytoarchitectonic area.

calculated using circular statistics (Fisher, 1993), which is an established framework for identification of statistically significant distributions based on both magnitude and direction of vectors (Ioannides et al., 2005; Poghosyan and Ioannides, 2007, 2008).

Regional activation curves (RAC) for each ROI were then generated from each single trial MFT estimate by integrating, for each time point of 0.4 ms, the projections of the current density vectors along the principle direction in the ROI (Poghosyan and Ioannides, 2007, 2008). RAC describes the activation time course of an ROI along its principal direction. To quantify the signal content in an ensemble of single trial RACs we computed their signal-to-noise ratio (SNR) (Laskaris and Ioannides, 2001; Raz et al., 1988) using a 10 ms moving window. The SNR can be thought of as the ratio of the "energy" in the reproducible part of the signal divided by the "energy" of the residual signal across single trials. SNR time courses were generated for each ROI (eight ROIs), stimulus category (faces and checkerboards), attentional condition (auditory attention, spatial attention, and category-specific attention within attended and ignored hemifields) and subject (five subjects). In addition to SNR time courses average RACs were also generated by averaging together the corresponding single trial RACs (shown in Supplementary figures).

Analysis of response properties (peak latencies and peak magnitudes)

Magnitudes and latencies of peaks in the intervals of 40 – 130 and 130 – 230 were extracted from each single trial RAC (eight ROIs) for further detailed statistical analysis.

Preliminary analysis of response properties

Before embarking on the main analysis of response properties, two preliminary statistical tests were performed with a primary aim to reduce the number of independent factors to be considered during the main analysis. The purpose of the first statistical test was to determine if there were significant differences between the response properties of corresponding left and right hemisphere ROIs. If the differences were not significant then we could collapse the response properties of corresponding ROIs across the cerebral hemispheres. The second test was performed to determine if attention affects the response latencies. If the latencies were not significantly affected by attention then the attentional effects could be studied only in terms of the magnitude change, and the modulation latencies for each type of attention could be examined by pooling together the response latencies from all the trials of the corresponding attentional condition.

First preliminary statistical test: left versus right hemisphere ROIs. Full factorial mixed-model analysis of variance (ANOVA) was applied separately to the extracted peak latencies and peak magnitudes, with cerebral hemisphere (left and right), ROI (eight ROIs), stimulus category (face and checkerboard), attentional condition (auditory attention, spatial attention, conjoint attention) and response phase (peaks in the 40–130 and 130–230 intervals) as fixed factors, and subject (five subjects) as random factor. There was no main effect of hemisphere ($F_{(1,4)}<3$, $P>0.1$) and no two-way interactions of hemisphere by other factors ($P>0.1$), therefore in subsequent analyses the peak magnitudes and latencies of corresponding left and right hemisphere ROIs were collapsed across the stimulated visual hemifields. Because each stimulated hemifield produced significant activations in six ROIs, after collapsing the data we ended up with the six ROIs (contralateral V1, V4, LO and pFus; and ipsilateral LO and pFus).

Second preliminary statistical test: effect of attention on response latencies. Application of ANOVA to peak response latencies separately for each attentional condition and response phase, with ROI (six ROIs), stimulus category and experimental run (eight runs) as fixed factors and subject as random factor showed no significant main effect of experimental run or significant two-way interaction of experimental run by stimulus category (in six separate ANOVAs $P>0.1$), meaning that the response latencies are not significantly affected by attention. The mean and SD of ROI peak latencies for four different attentional conditions (auditory attention, spatial attention, category-specific attention within the attended hemifield and category-specific attention within the ignored hemifield) were then calculated by pooling together the extracted latencies from both runs of each condition – 720 elements (5 subjects × 2 runs × 2 hemifields × 2 categories × 3 exemplars × 6 repetitions).

Main analysis of response properties

The response magnitudes of the six ROIs in different attentional conditions were analyzed using full factorial mixed-model ANOVA where subject factor was treated as random factor and other factors as fixed.

Stimulus-evoked responses. Stimulus evoked responses obtained from the auditory attention condition were analyzed separately for low- (V1 and V4) and high-level (contralateral and ipsilateral LO and pFus) ROIs. To this end four-way ANOVA was performed with the following factors: stimulus category, ROI, response phase and subject.

Spatial attention. The spatial attentional effect was analyzed by means of five-way ANOVA, factors: attention (attended versus ignored hemifield), stimulus category, ROI (all six ROIs), response phase and subject.

Category-specific attention. The effect of category-specific attention was assessed from the conjoint attention runs, separately for stimuli presented in the attended and ignored hemifields, and in each case separately for low- and high-level ROIs. To this end five-way ANOVAs were used with the following factors: attention (attended versus ignored category), stimulus category, ROI, response phase and subject.

Attentional index. To quantify the effects of different types of attention in our ROIs we calculated the attentional index (AI) from the extracted peak response magnitudes. First, the mean peak response magnitude was calculated for each stimulus category by averaging values across 36 trials (2 hemifields × 3 exemplars × 6 repetitions). Then these mean values were used to calculate the AI for each subject, attentional condition, stimulus category, ROI and response phase, as follows: $AI = (attended - ignored)/(attended + ignored)$.

The interactions between attention types (spatial versus category-specific) and ROI levels (low versus high) were assessed by means of five-way ANOVA with the factors attention type, stimulus category, ROI level, response phase and subject, and AI as dependent variable.

Behavioral performance. Hit rates and reaction times were also analyzed using full factorial mixed-model two-way ANOVA with attentional condition fixed and subject as random factors. In all cases, SPSS (IBM Inc., USA) statistical software package was used for ANOVA.

Results

Performance

The behavioral performance of subjects was assessed based on hit rates and mean reaction times in each run. The hit rates in different attentional conditions were similar ($F_{(2,40)} = 0.2$, $P = 0.85$; auditory attention—91%, spatial attention—91%, conjoint attention—89%), but the mean reaction times were significantly different ($F_{(2,40)} = 4.6$, $P = 0.022$; auditory attention—491 ms, spatial attention—400 ms, conjoint attention—419 ms). Scheffe's post-hoc test showed that this difference is due to slower reaction times in auditory attention condition (spatial versus conjoint attention $P = 0.811$; visual spatial versus auditory attention $P = 0.05$; visual conjoint versus auditory attention $P = 0.076$).

Stimulus-evoked responses

We use the SNR time courses obtained from the auditory attention condition (i.e. independent of visual attention) as exemplars of stimulus-evoked responses. For each one of our ROIs this stimulus-evoked activity was characterized by two distinct responses: one in the 40–130 ms and the other in the 130–230 ms latency ranges (Fig. 3A). Such responses were evident in the SNR time courses obtained from the spatial and conjoint attention conditions as well. There was virtually no overlap in the peak latencies extracted from these two responses, thus dividing the neural processing into two distinct phases corresponding to two distinct passes of activity through the hierarchy of visual areas (Fig. 4).

As expected, the low-level visual areas (V1 and V4) responded only to stimuli presented in the contralateral hemifield and the response magnitudes were significantly higher for checkerboards than faces (Fig. 3A, solid blue versus green lines; Fig. 3B and Table 2). ANOVA revealed also significant two-way ordinal interactions of stimulus category by ROI and stimulus category by response phase (Supplementary Fig. 3). The follow-up ANOVAs for each ROI and response phase showed that both responses in both low-level ROIs were significantly higher for checkerboards than faces. The responses occurred earlier in V1 than V4, with mean peak latencies of 72 and 124 ms for V1, and 91 and 147 ms for V4 respectively. In contrast to low-level areas, the high-level visual areas (LO and pFus) responded strongly to faces, while the activity elicited by checkerboards was comparatively very small (Fig. 3A, green versus blue lines; Fig. 3B and Table 2). No significant two-way interactions of stimulus category by ROI or stimulus category by response phase were found. Strong activity in these areas was evident for the faces presented in the ipsilateral hemifield as well, albeit with slightly lower magnitude and a delay of ~20 ms as compared to responses to contralaterally presented faces. The contralateral hemisphere responses in both areas peaked around 100 and 170 ms, with LO peaking on average 10 ms earlier. In both ROIs the earlier response (at ~100 ms) was smaller in magnitude.

Attentional effects

Spatial attention

The effect of visual spatial attention was assessed based on trials from the spatial attention condition. Specifically, responses to each stimulus category were compared when the stimulated visual hemifield was attended versus ignored (Fig. 1D, top row, L_{att} versus L_{ign}). Spatial attention enhanced stimulus-evoked activity in all ROIs, including responses in the LO and pFus in the hemisphere ipsilateral to the stimulated hemifield (Fig. 5, solid versus dotted lines; Fig. 6, khaki bars and Table 3). In addition to significant main effect of attention ANOVA revealed a significant two-way ordinal interaction of attention by ROI (Supplementary Fig. 4). Application of separate ANOVAs for each ROI showed that the spatial attentional modulations were statistically significant in all ROIs. In all these tests the two-way interaction effect between attention and response phase was not significant, indicating that the effect of spatial attention was significant during both responses. The effect, as evidenced by the AI was stronger in the low-level areas (Fig. 6 and Table 4). No significant interactions of ROI level by stimulus category, or ROI level by response phase were found. In all ROIs the modulation latencies were similar to those of the corresponding stimulus-evoked responses (Fig. 4).

Category-specific attention

Category-specific attention within the attended hemifield. The effect of category-specific attention on visual processing was probed using trials from the conjoint attention runs. First, the responses to stimuli presented in the attended hemifield were compared when the stimuli belonged to target (i.e. attended) versus non-target (i.e. ignored) category (Fig. 1D, middle row, $L_{att}C_{att}$ versus $L_{att}C_{ign}$). SNR time courses showed that the responses to faces in LO and pFus in both hemispheres (ipsilateral and contralateral to stimuli) were enhanced by face-directed attention (Fig. 7 and Supplementary Fig. 5, solid red versus blue lines, and Fig. 6, blue bars). Importantly, both responses at ~100 and ~170 ms were affected by the task. Activity in the same areas elicited by checkerboards was very small, as found also in the auditory attention condition, and did not show any substantial attentional effect (not shown). Application of ANOVA (using only the four high-level ROIs) revealed a significant two-way interaction of attention by stimulus category (Supplementary Fig. 6 and Table 5). The follow-up separate ANOVAs for each stimulus category showed that responses to faces were significantly enhanced by face-directed category-specific attention, whereas responses to checkerboards

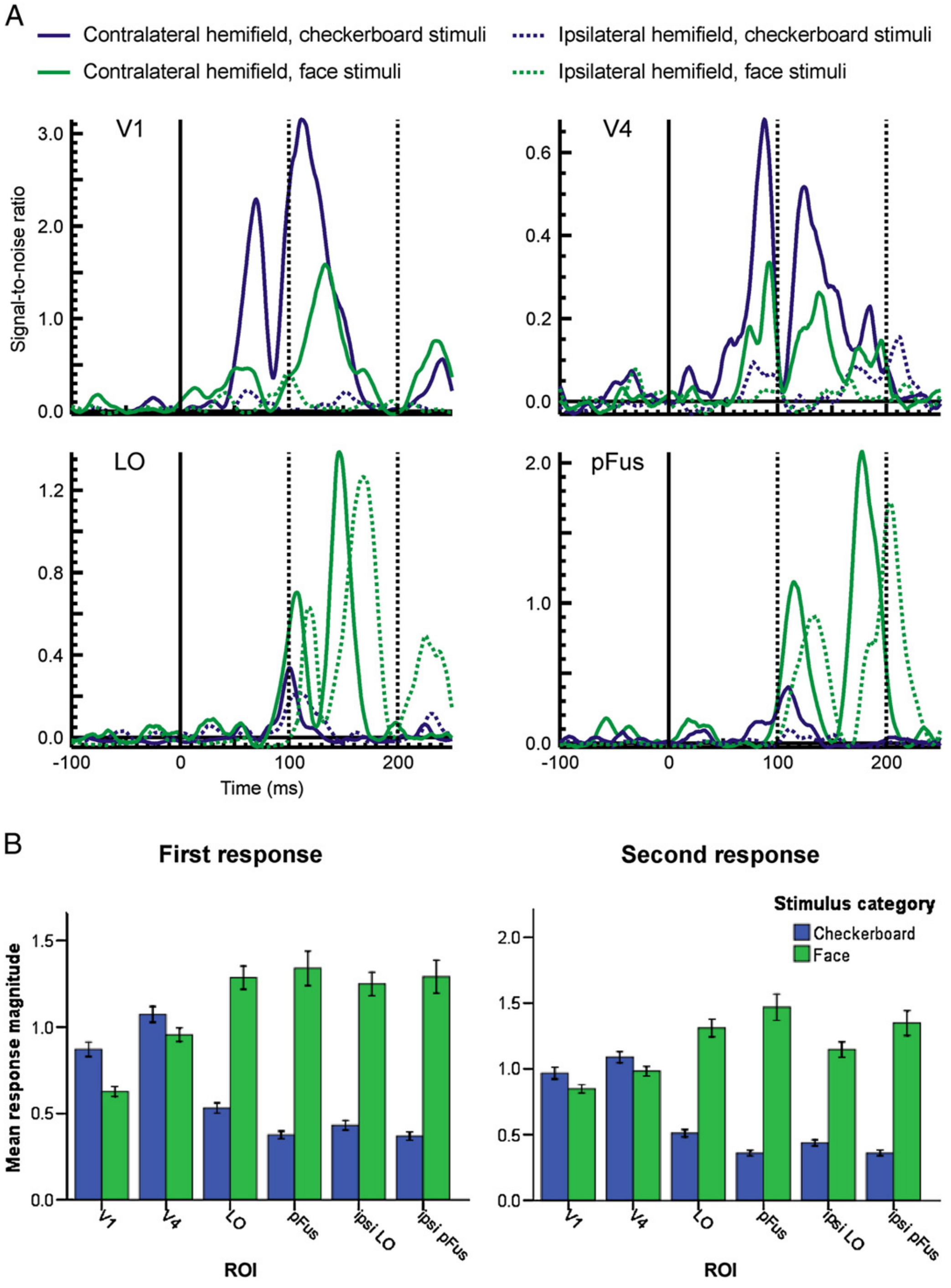

Fig. 3. Stimulus evoked responses obtained from auditory attention condition. *A*, SNR time courses of left hemisphere ROIs in a typical subject. Responses to checkerboard (blue lines) and face (green lines) stimuli presented in the right (contralateral; solid lines) and left (ipsilateral; dotted lines) hemispheres are shown. *B*, Response magnitudes. Mean peak response magnitudes (in arbitrary units) in all ROIs (left and right hemisphere responses collapsed) during the first (upper) and second (lower) processing phases. ipsi, ipsilateral. Error bars, ± SEM.

were affected by checkerboard-directed category-specific attention only marginally. In both tests the two-way interaction effects between attention and response phase, and attention and ROI (four high-level ROIs) were not significant ($P > 0.1$). This result demonstrates that the category-specific attention to faces facilitates face processing in high-level object-related areas beginning as early as ~100 ms post-stimulus (see also later).

The activity in the low-level visual areas showed different pattern of modulations (Fig. 7 and Supplementary Fig. 5, solid lines, and Fig. 6, blue bars). There was a significant two-way disordinal interaction of attention by response phase (Supplementary Fig. 7 and Table 5). The follow-up tests showed that this interaction reflects the fact that the first response was unaffected by the target category, while the second response was stronger when the stimulus category was attended. No significant interaction of attention by stimulus category, or attention by ROI (V1 and V4) was found for either response ($P > 0.1$). The effects of the category-specific attention just described relate to stimuli that were the response targets and appeared within attended hemifield, hence we cannot fully exclude the involvement of response selection (Hommel and Schneider, 2002) and spatial attention mechanisms.

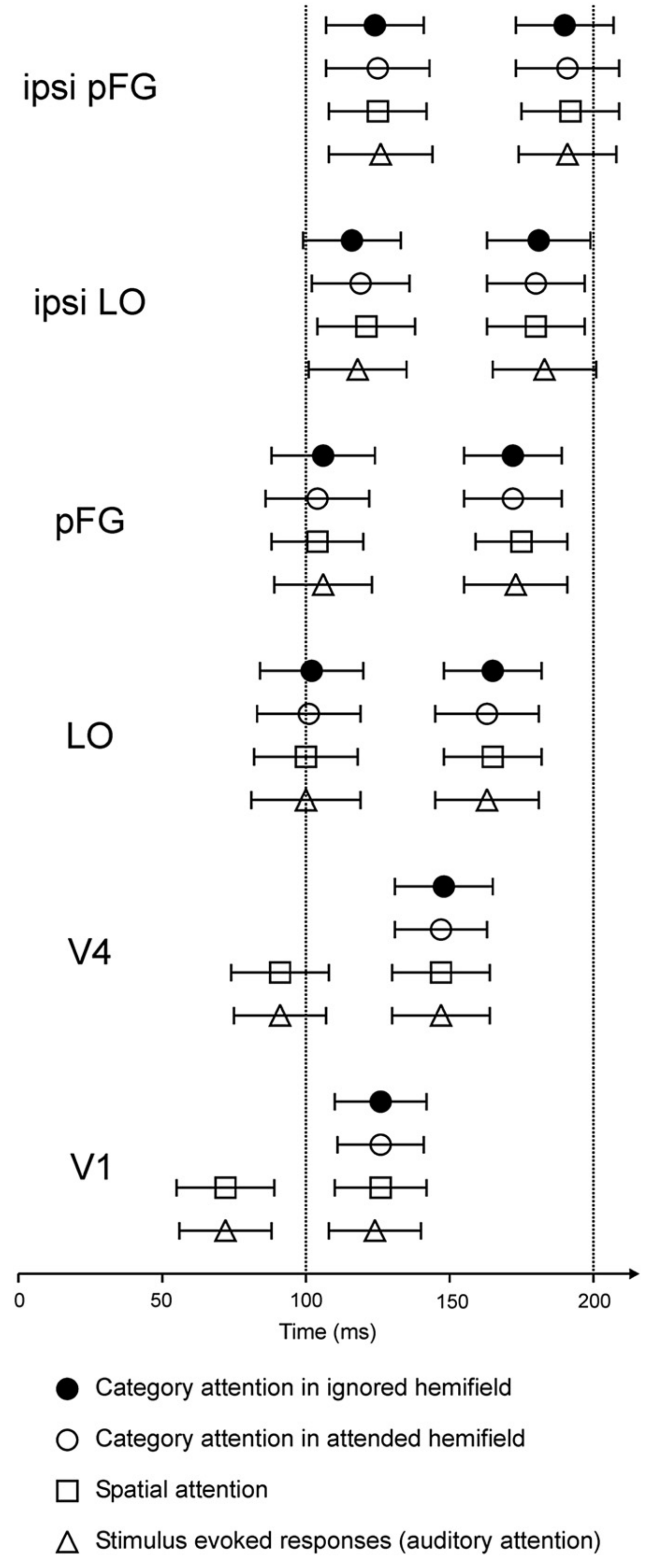

Fig. 4. Processing stages. The mean peak latencies of stimulus evoked responses in all ROIs (left and right hemisphere responses collapsed), in the first 200 ms, from auditory attention (triangle), spatial attention (square) and category-specific conditions within the attended (open circle) and ignored (filled circle) hemifields. Only the latencies of the statistically significant effects are shown. ipsi, ipsilateral. Error bars, ± SD.

Table 1
ROI coordinates.

	Coordinates (mm)		
	X	Y	Z
Right hemisphere			
V1	8 ± 3	− 82 ± 8	8 ± 5
V4	37 ± 6	− 74 ± 2	− 12 ± 6
LO	39 ± 5	− 74 ± 1	− 2 ± 4
pFus	44 ± 3	− 61 ± 3	− 14 ± 5
Left hemisphere			
V1	− 9 ± 2	− 80 ± 6	8 ± 5
V4	− 30 ± 5	− 80 ± 4	− 13 ± 6
LO	− 45 ± 3	− 70 ± 4	− 7 ± 6
pFus	− 41 ± 7	− 56 ± 3	− 16 ± 4

LO, lateral occipital; pFus, posterior fusiform. Mean ± SD Talairach coordinates.

Category-specific attention within the ignored hemifield. To unambiguously disentangle the effect of category-specific attention from other influences, we considered brain responses to non-target stimuli that appeared outside the focus of spatial attention. To this end, we performed the same comparison as before that is between responses in trials where stimulus belonged to target category versus non-target category, but now for stimuli presented in the ignored hemifield (Fig. 1D, bottom row, $L_{ign}C_{att}$ versus $L_{ign}C_{ign}$). Critically, for the high-level object-related areas this comparison revealed the same effect as found before, namely an enhancement of both, 100- and 170-ms face-elicited responses in both hemispheres (ipsilateral and contralateral to stimuli) when faces were attended (Fig. 7 and Supplementary Fig. 5, dotted red versus dotted blue lines; Fig. 6, green bars and Table 6). No such effect was found for checkerboard-elicited responses. Furthermore, as before the two-way interaction effects between attention and response phase, and attention and ROI were not significant ($P > 0.1$). In sum, these results convincingly show that the face-directed category-specific attention boosts the face-induced neural activity in LO and pFus at ~100 and ~170 ms, independent of response target and demands of spatial attention.

A different pattern of attentional influences was identified in the low-level areas (V1 and V4, Fig. 7 and Supplementary Fig. 5, dotted red versus dotted blue lines, and Fig. 6, green bars). In these areas the first response was unaffected by the category-specific attention, just as in the earlier comparison (Table 6). However, the second response in both ROIs was significantly reduced by it, with no significant interaction of attention by stimulus category, or attention by ROI ($P > 0.1$). Furthermore, the first response was affected by the target hemifield that is by the spatial component of the conjoint attention (Fig. 7 and Supplementary Fig. 5, dotted red versus dotted blue lines). The interaction effect of attention by stimulus category was not significant.

Interaction of attention types with ROI levels

Next we used AI to examine the interaction of attention types (spatial versus category-specific) with ROI levels (low versus high, Supplementary Fig. 8) – ANOVA revealed a highly significant two-way disordinal interaction (Table 4). Follow-up ANOVAs were performed separately for low- and high-level ROIs. In low-level ROIs the AI of

Table 2
ANOVA summary: stimulus-evoked responses.

Source	d.f.	F	P
Low-level ROIs			
Category	1,4	113.68	0.0004
Category*ROI	1,4	27	0.007
Category*Phase	1,4	46.2	0.002
Follow-up tests for each ROI and response phase			
Category	1,4	> 31	< 0.002
High-level ROIs			
Category	1,4	266.6	0.00008
Category*ROI	1,4	1.1	0.39
Category*Phase	1,4	1	0.37

ANOVA Factors: stimulus category, ROI, response phase and subject. * Indicates interaction of factors. d.f., degrees of freedom: hypothesis, error.

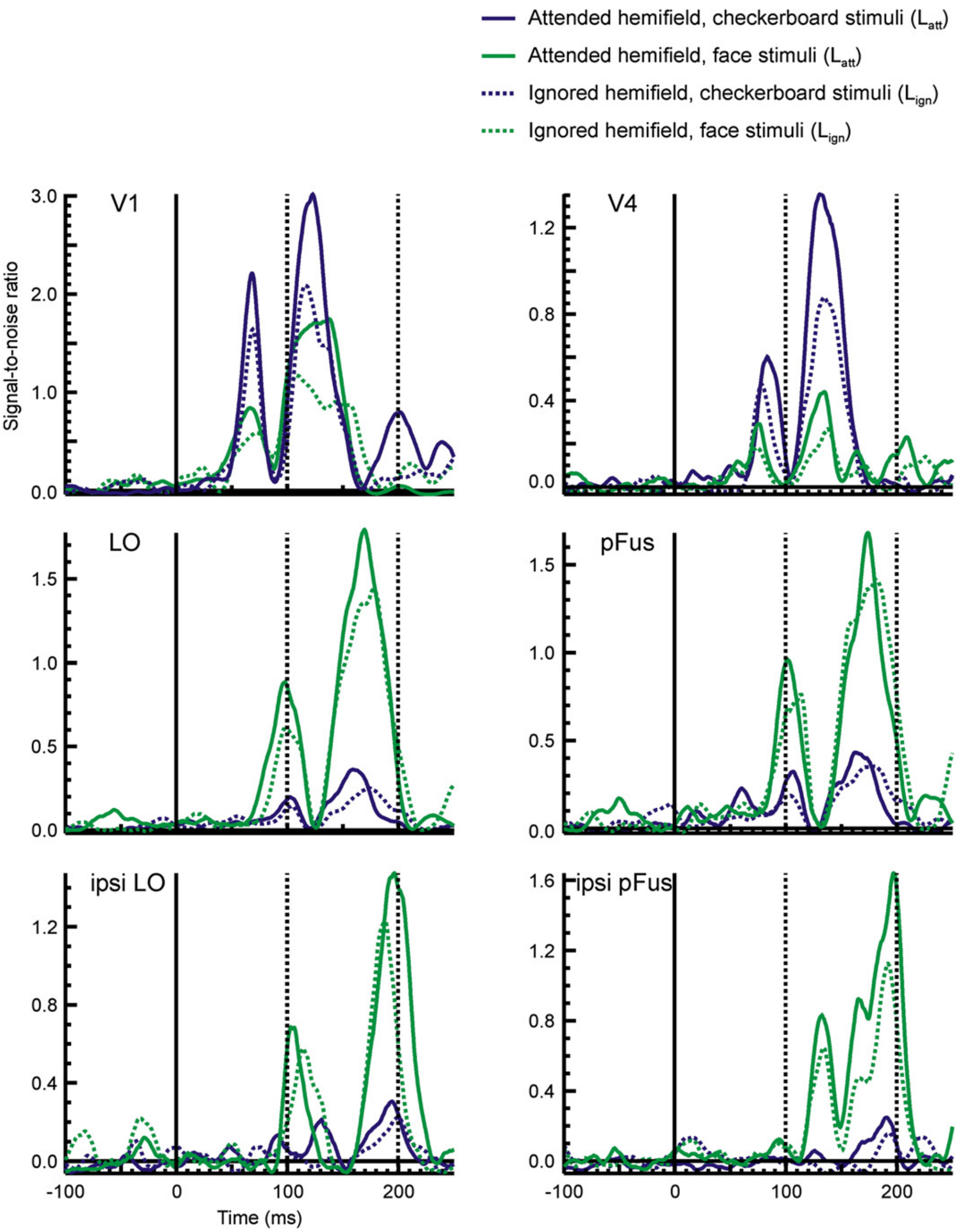

Fig. 5. Spatial attentional modulations. SNR time courses of left hemisphere V1, V4, LO and pFus ROIs and right hemisphere LO and pFus ROIs in a typical subject. Responses to checkerboard (blue lines) and face (green lines) stimuli presented in the right hemisphere are shown. Solid lines, stimulated hemifield (right) was attended; dotted lines, stimulated hemifield was ignored (attention was directed toward left hemifield). ipsi, ipsilateral.

only the second response for both checkerboard and face stimuli were examined; in high-level areas both responses for only face stimuli were examined. We found that in low-level ROIs the effect of spatial attention was stronger (Fig. 6), whereas both responses in high-level areas were affected more by the face-directed category-specific attention (Fig. 6), including in cases where faces appeared in the ignored hemifield.

Discussion

We used MEG with MFT, a robust analysis method (Ioannides et al., 1990; Moradi et al., 2003; Papadelis et al., 2009; Poghosyan and Ioannides, 2007, 2008; Taylor et al., 1999) to examine the effects of spatial and category-specific attention on visual information processing within key low- (V1 and V4) and high-level (LO and pFus) areas. In support of our first hypothesis we found that the earliest effect of both types of attention appeared during the first pass through the visual hierarchy at the earliest processing level capable of coding/discriminating the attentional target. Specifically, we confirm the earlier finding (Kelly et al., 2008; Poghosyan and Ioannides, 2008) that spatial attention enhances the initial feedforward response in V1, the earliest cortical level capable of adjusting the precise location and size of spatial attention spotlight. We show for the first time that the face-directed category-specific attention modulates the first face-category-related neural response at ~100 ms post-stimulus in the high-level object-related visual areas LO and pFus. In addition we found that beginning from the respective initial modulations,

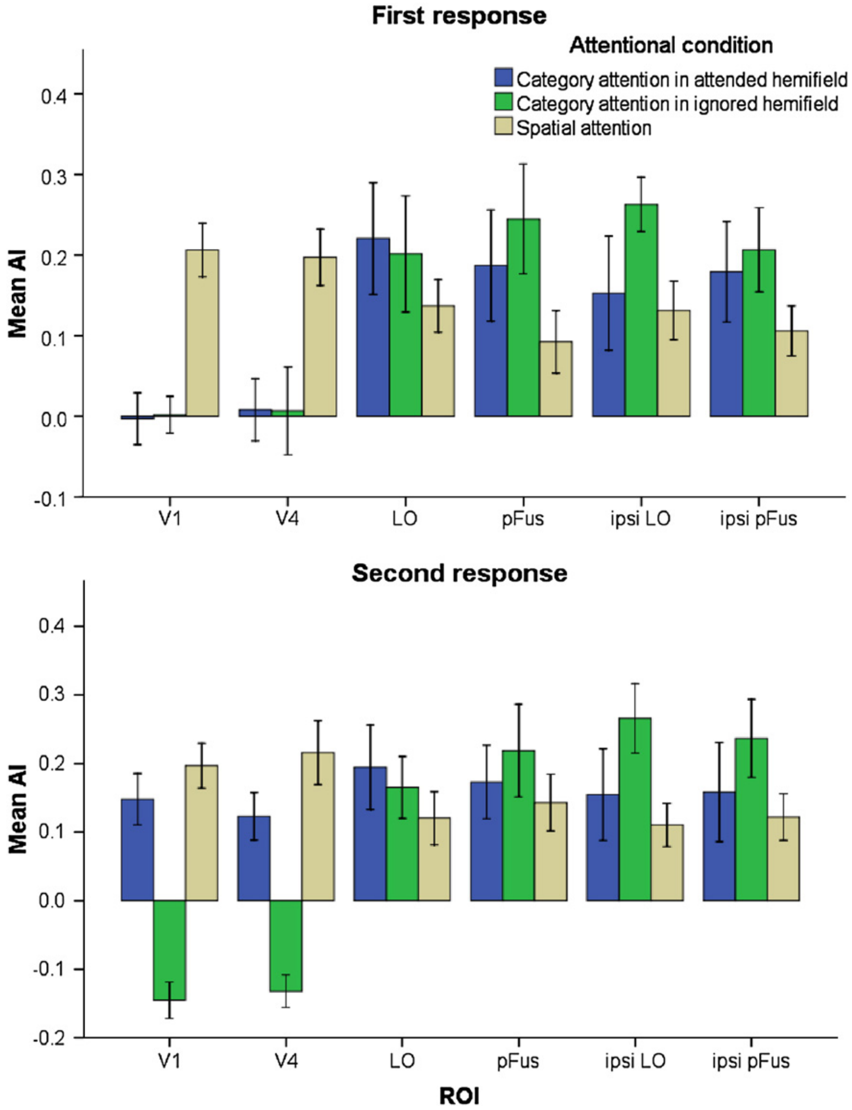

Fig. 6. Magnitudes of attentional modulations. Mean (across subjects) AI in all ROIs (left and right hemisphere responses collapsed) during the first (upper) and second (lower) processing phases. AI = (attended − ignored) / (attended + ignored) provides a normalized quantitative measure of attentional effects in different ROIs. khaki, spatial attentional effect; blue, category-specific attentional effect in the attended hemifield; green, category-specific attentional effect in the ignored hemifield. ipsi, ipsilateral. AI, attentional index; Error bars, ±2 SEM.

both types of attention affected all the following stimulus-evoked responses throughout the visual cortex.

Our results show that face-directed attention can facilitate face processing beginning within 100 ms after stimulus onset, substantially earlier than previously suggested (Downing et al., 2001; Eimer, 2000; Furey et al., 2006; Holmes et al., 2003; Lueschow et al., 2004; Sreenivasan et al., 2009). The next response in the same areas (at ~170 ms) was also enhanced by attention. This latter result (modulation of 170-ms face-related response) agrees with some earlier reports (Downing et al., 2001; Eimer, 2000; Holmes et al., 2003; Sreenivasan et al., 2009), but disagrees with others (Carmel and Bentin, 2002; Cauquil et al., 2000; Furey et al., 2006; Lueschow et al., 2004).

The lack of attentional effect on the 100-ms face-selective electrophysiological response in the previous literature can be explained by the type of attentional manipulations employed. Such studies have

Table 3
ANOVA summary: spatial attention.

Source	d.f.	F	P
Attention	1,4	142.9	0.0003
Attention*ROI	5,20	7.1	0.0006
Follow-up tests for each ROI			
Attention	1,4	> 29	< 0.006
Attention*Phase	1,4	> 1	> 0.3

ANOVA Factors: attention, stimulus category, ROI (six ROIs), response phase and subject. * Indicates interaction of factors. d.f., degrees of freedom: hypothesis, error.

Table 4
ANOVA summary: attentional index.

Source	d.f.	F	P
ROI level	1,4	26.4	0.007
ROI level*Category	1,4	1.7	0.27
ROI level*Phase	1,4	0.04	0.85
ROI level*attention type	1,4	326.3	0.00005
Follow-up tests for each ROI level			
Low-level ROIs, second phase			
Attention type	1,4	43.4	0.003
High-level ROIs, face category			
Attention type	1,4	114.5	0.0004

ANOVA Factors: attention type, stimulus category, ROI level, response phase and subject. * Indicates interaction of factors. d.f., degrees of freedom: hypothesis, error.

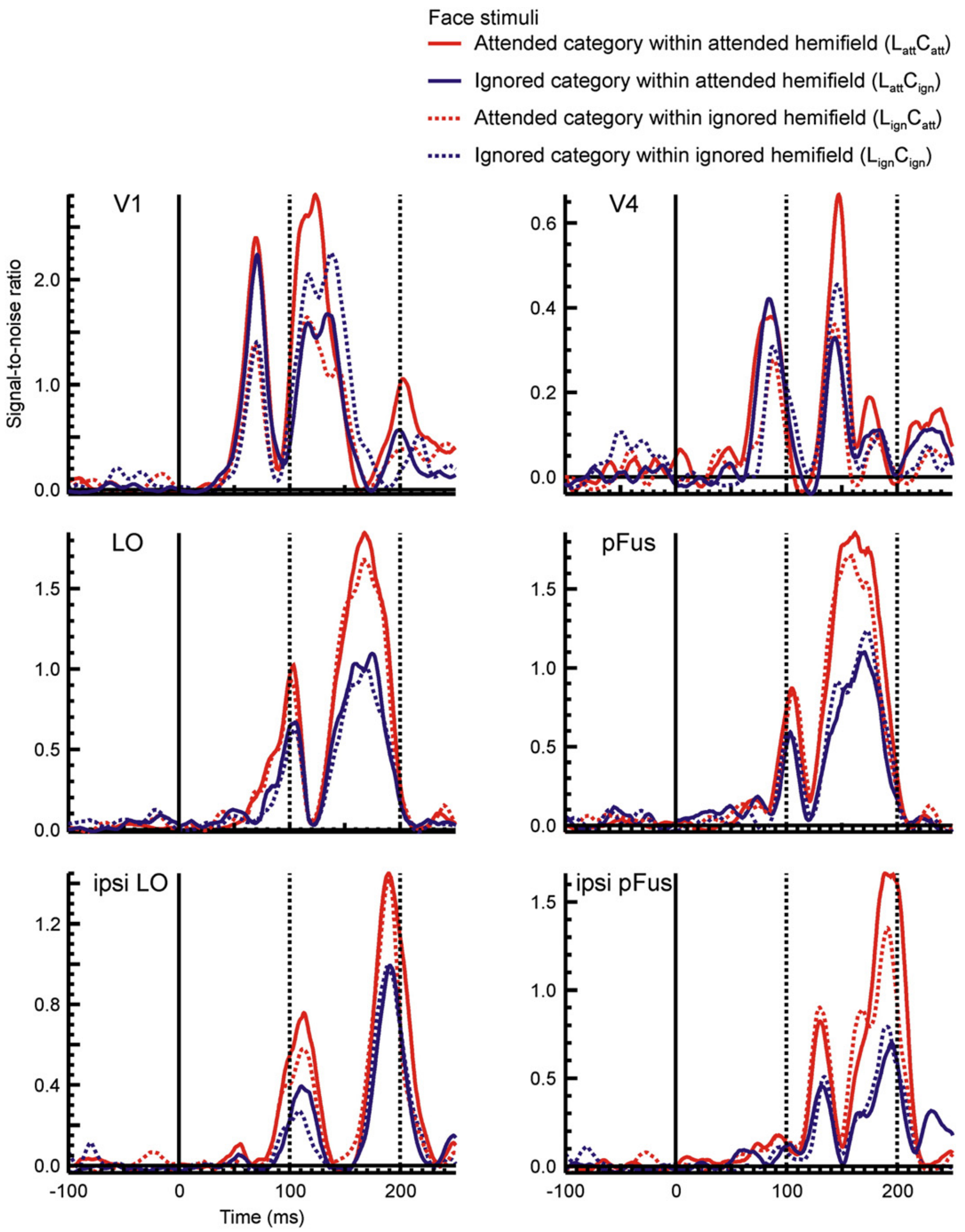

Fig. 7. Category-specific attentional modulations. SNR time courses of left hemisphere V1, V4, LO and pFus ROIs and right hemisphere LO and pFus ROIs in a typical subject. Responses to face stimuli presented in the right hemisphere are shown. Solid lines, stimulated hemifield (right) was attended; dotted lines, stimulated hemifield was ignored; red, stimulus category (face) was attended; blue, stimulus category was ignored (attention was directed toward checkerboards). ipsi, ipsilateral.

examined mainly the effect of object-based attention by requiring subjects to attend to an individual face, implicitly assuming that when subjects attend to a specific exemplar from a category (i.e. an individual face), they indirectly attend also to the basic category itself (i.e. face category). Here we examined directly the effect of category-specific attention to faces by directing attention toward the face category per se, rather than toward an exemplar from that category. Since the face category and identity are encoded in the occipitotemporal cortex around 100 and 170 ms post-stimulus respectively (Itier and Taylor, 2002, 2004a, 2004b; Itier et al., 2006; Linkenkaer-Hansen et al., 1998; Liu et al., 2002), the earliest modulation latencies found in the current and previous studies support our hypothesis that attention modulates the visual processing beginning at the first processing stage capable of representing the attentional target.

Our second hypothesis was also confirmed: we found distinct patterns of non-spatial category-specific attentional modulations in the low- and high-level visual areas. The first response in both low-level visual areas, V1 and V4 (before 100 ms), was unaffected by the manipulation of attended category, but was enhanced when the stimulated visual hemifield was attended. Whereas the second response, after 130 ms, was enhanced when both the stimulus category and location were attended, and was reduced when only one of both was attended. To the best of our knowledge this is the first report describing the effect of non-spatial category-specific attention on the responses in the low-level retinotopic visual areas.

Table 5
ANOVA summary: Category-specific attention within the attended hemifield.

Source	d.f.	F	P
Low-level ROIs			
Attention*Phase	1,4	240	0.0001
Follow-up tests for each response phase			
First phase			
Attention	1,4	0.01	0.91
Second phase			
Attention	1,4	164.5	0.0002
High-level ROIs			
Attention*Category	1,4	115.3	0.0004
Follow-up tests for each Category			
Face category			
Attention	1,4	470.7	0.00002
Checkerboard category			
Attention	1,4	5.4	0.08

ANOVA Factors: attention, stimulus category, ROI, response phase and subject. * Indicates interaction of factors. d.f., degrees of freedom: hypothesis, error.

In contrast, the corresponding responses in the high-level areas were always boosted when the stimulus belonged to the target category (even for irrelevant stimuli presented in the ignored hemifield).

Stimuli from the target category presented in the ignored hemifield or from the ignored category presented in the target location are distractors, thus we hypothesize that the reduction of the second response in the low-level areas in these cases indicates engagement of a previously unreported filtering mechanism of attention that acts globally to suppress irrelevant competing sensory inputs. This hypothesized global mechanism is different from the proposed biased competition account (Desimone and Duncan, 1995) in that here attention suppressed responses to sequentially presented and spatially distant distractors, while according to the biased competition model attention affects competitive interactions among stimuli appearing simultaneously within the receptive field of a neuron. The attended location-independent enhancement of activity in high-level visual areas by the non-spatial category-specific attention suggests engagement of a different spatially global category-specific mechanism of attention that selects all exemplars from the attended category independent of their spatial location and target/distractor status. These results show that in accord with our hypothesis even within the same task different attentional mechanisms may act in low- and high-level visual areas. Moreover, our results show for the first time a clear dissociation between attention types and ROI levels, that is the effect of spatial attention was significantly stronger in low-level retinotopic areas, whereas non-spatial category-specific attentional modulations were significantly stronger in high-level object-related areas.

The response latencies of our functionally defined ROIs are consistent with those observed in awake, behaving monkeys (Givre et al., 1994; Schroeder et al., 1991, 1998). Previous studies (Allison et al., 1999; Liu et al., 2002; Sugase et al., 1999) have shown that face processing in the high-level face-related brain areas proceeds in phases. At least two of the early phases are known to be correlated with specific cognitive processes: an early phase of face categorization, and a later phase of individual face identification (Itier and Taylor, 2002, 2004a, 2004b; Itier et al., 2006; Linkenkaer-Hansen et al., 1998; Liu et al., 2002; Sugase et al., 1999). However, until now it was not clear if this phased neural processing is a characteristic feature of few high-level visual areas or it is a reflection of distinct passes of stimulus-evoked activity through the entire hierarchy of visual areas. Our current results clarify this issue showing that at least the first two-phases correspond to a more general mode of processing across the visual hierarchy. Our results further indicate a time frame for the pass of activity in each phase. In both phases, activity began in V1 (mean peak latencies 72 and 124 ms) and appeared to spread in a feedforward manner reaching contralateral pFus at around 100 and 170 ms respectively. The activity in the contralateral LO and pFus during both passes was followed by the activity in the respective ipsilateral areas with a delay of ~20 ms.

Table 6
ANOVA summary: category-specific attention within the ignored hemifield.

Source	d.f.	F	P
Low-level ROIs			
First phase			
Attention	1,4	1.9	0.24
Second phase			
Attention	1,4	89.5	0.0007
High-level ROIs			
Face category			
Attention	1,4	436.8	0.00003
Checkerboard category			
Attention	1,4	4.5	0.1

ANOVA Factors: attention, stimulus category, ROI, response phase and subject.

The coordinates (Table 1) and response properties of our high-level ROIs suggest that they correspond to well-known face-category-selective occipitotemporal brain regions (Grill-Spector, 2003; Kanwisher et al., 1997).

The temporal sequence of evoked responses across the visual cortex identified here is consistent with a simple feedforward sweep of activity through the visual hierarchy. However the complexity of the functional (Logothetis et al., 2010; Schmid et al., 2009; Schoenfeld et al., 2002) and anatomical organization of early visual cortex with its extensive bidirectional cortico-cortical connections (Felleman and Van Essen, 1991), with key sub-cortical links (Guillery, 1995; Shipp, 2004) at every stage of neural processing makes it plain that the notion of a simple feedforward spread of stimulus-evoked responses can only be an approximation of an extremely complex web of processes, even during the first pass through the system.

Conclusions

The early visual processing through the entire hierarchy of visual areas proceeds in two temporal phases, in the 40–130 ms and 130–230 ms periods respectively. We found that in both phases spatial attentional modulations propagate largely serially from early to late visual areas, beginning from the initial stimulus-evoked response in V1. In contrast, category-specific attention bypassed the early classic retinotopic areas during the first phase of processing and affected first the late object-related areas. It thus appears that attention utilizes different mechanisms in early and late visual areas, a conclusion that is further supported by the way spatial and category-specific attention were combined in early and late visual areas during the second phase of processing. Further studies are needed to describe each of these mechanisms in detail and to investigate how failure of one or the other might relate to pathologies, including developmental difficulties associated with the control of attention and learning difficulties.

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Disclosure statement

Authors declare no conflict of interest.

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