Article

Neuronal Synchronization along the Dorsal Visual Pathway Reflects the Focus of Spatial Attention

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SUMMARY

Oscillatory neuronal synchronization, within and between cortical areas, may mediate the selection of attended visual stimuli. However, it remains unclear at and between which processing stages visuospatial attention modulates oscillatory synchronization in the human brain. We thus combined magnetoencephalography (MEG) in a spatially cued motion discrimination task with source-reconstruction techniques and characterized attentional effects on neuronal synchronization across key stages of the human dorsal visual pathway. We found that visuospatial attention modulated oscillatory synchronization between visual, parietal, and prefrontal cortex in a spatially selective fashion. Furthermore, synchronized activity within these stages was selectively modulated by attention, but with markedly distinct spectral signatures and stimulus dependence between regions. Our data indicate that regionally specific oscillatory synchronization at most stages of the human dorsal visual pathway may enhance the processing of attended visual stimuli and suggest that attentional selection is mediated by frequency-specific synchronization between prefrontal, parietal, and early visual cortex.

INTRODUCTION

When confronted with cluttered visual scenes, visuospatial attention adaptively devotes the brain's processing capacity to the information relevant for the task at hand. It has been suggested that oscillatory synchronization of neuronal activity within and between cortical areas acts as a flexible mechanism of attentional selection by regulating the gain of information transmission between neuronal populations (Engel et al., 2001; Fries, 2005; Salinas and Sejnowski, 2001). Recent studies in monkeys and humans have provided principle support of this hypothesis (Bichot et al., 2005; Buschman and Miller, 2007; Doesburg et al., 2008; Fan et al., 2007; Fries et al., 2001; Gruber et al., 1999;

Händel et al., 2008; Saalmann et al., 2007; Taylor et al., 2005; Thut et al., 2006; Worden et al., 2000; Wyart and Tallon-Baudry, 2008). However, evidence as to the extent to which visuospatial attention modulates oscillatory synchronization in the primate brain remains sparse. Specifically, it remains unclear within and between which processing stages visuospatial attention modulates oscillatory synchronization.

On the one hand, invasive studies in monkeys typically sample activity only from small neuronal populations and thus far have demonstrated spatially selective attentional effects on synchronization only in areas V4 and LIP (Bichot et al., 2005; Fries et al., 2001; Saalmann et al., 2007; Taylor et al., 2005). On the other hand, human electroencephalography (EEG) and magnetoencephalography (MEG) studies showing spatially selective attentional effects on oscillatory activity have been restricted to the sensor level (Doesburg et al., 2008; Gruber et al., 1999; Thut et al., 2006; Worden et al., 2000; Wyart and Tallon-Baudry, 2008) and thus have provided only limited information about the cortical regions involved. As a consequence, it remains unclear whether visuospatial attention modulates oscillatory synchronization in early visual areas suggested to express the effect of top-down signals on sensory processing (Hopfinger et al., 2000; Kastner et al., 1999; Ress et al., 2000), as well as in regions commonly implicated in the control of attention such as parietal cortex and the frontal eye fields (FEF) (Corbetta and Shulman, 2002; Donner et al., 2000; Kastner and Ungerleider, 2000; Moore et al., 2003; Serences and Yantis, 2006). In particular, it is unknown whether selective attention has regionally specific effects on oscillatory synchronization within these areas, which might help to strengthen the case for their functional specialization in mediating attentional selection. Furthermore, it is currently not known whether and how selective attention modulates the rhythmic synchronization between frontal, parietal, and early visual regions in the human brain.

To address these questions, we combined MEG with novel source-reconstruction techniques. This allowed us to simultaneously investigate oscillatory activity within, and synchronization between, several well-defined cortical regions across the entire human brain. Subjects performed a spatially cued motion discrimination task (Figure 1). Correspondingly, we focused on five key regions involved in visual motion processing and spatial attention: pericalcarine cortex (V1/V2), human motion complex (MT+), ventral and posterior intraparietal sulcus (vIPS and
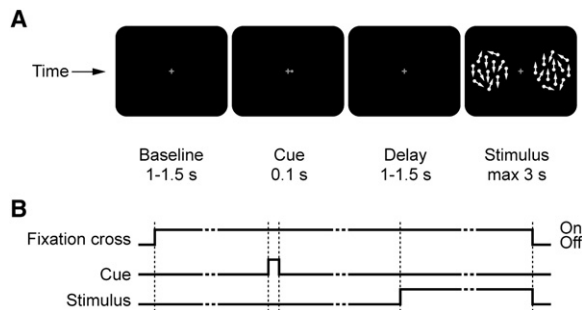
Figure 1. Spatially Cued Motion Discrimination Task

(A) Schematic illustration of the stimulus display.

(B) Time course of the fixation cross, cue, and stimulus presentation throughout one trial. Trials started with onset of a central fixation cross. After a variable delay (1–1.5 s), a small dot presented for 100 ms directly to the left or right of the fixation cross cued subjects to covertly shift attention to the left or right visual field. After another random delay (1–1.5 s), two dynamic random dot stimuli were displayed in circular apertures in the left and right visual hemifield. Subjects reported the perceived motion direction of the cued stimulus by pressing one of two response keys, while ignoring the stimulus in the other hemifield. Stimulation was terminated with the subject's response, or if no response was given within a 3 s time period.

Figure 2. Rhythmic Neuronal Activity Induced by Visual Stimulation and Spatial Attention

Time-frequency representation of the response in magnetoencephalography (MEG) amplitude averaged across three groups of anterior (A), lateral (B), and posterior (C) sensors. These sensors are marked in black dots in the topographies on the right. Responses are characterized as the percentage change in signal amplitude relative to the blank precue baseline (500 ms before cue onset). Solid white lines mark the time of cue and stimulus onset; the time of response onset is marked by the black triangle. Because of the variable delays between cue onset, stimulus onset, and response, the data were realigned to these points in time. Note that the time axis is displayed relative to these three events. The dotted white lines mark the temporal boundaries of the realigned data.

pIPS), and FEF. In all of these regions, attention modulated local oscillatory activity in a spatially selective fashion, but attentional modulations exhibited a remarkably different spectral signature and stimulus dependence between cortical areas. Importantly, the spatial selectivity of attentional modulations allowed for unequivocal dissociation of neural correlates of visuospatial attention from nonspecific processes such as arousal or task preparation. Furthermore, we found that spatial attention also selectively modulated the oscillatory synchronization between MT+, posterior IPS, and FEF in a relatively stimulus-independent fashion.

Our data suggest that oscillatory synchronization serves as a mechanism of visuospatial attention along the entire human dorsal visual pathway, including early visual processing stages as well as frontoparietal regions implicated in the control of attention. Our data indicate that the spectral profile of corresponding attentional modulations is not homogenous but varies substantially between regions. Furthermore, our data provide strong evidence that the enhanced routing of attended visual information across processing stages is mediated by frequency-specific synchronization between these regions.

RESULTS

We recorded whole-head MEG while subjects (n = 8) performed a spatially cued motion discrimination task (Figure 1). Subjects ignored a stimulus in the uncued hemifield while discriminating the motion direction of a random dot pattern in the cued hemifield. The motion coherence of stimuli was adjusted to the subjects' individual discrimination threshold. Performance was on average 78% correct (SD 3%) at 18% motion coherence (SD 5%) with a median response latency of 1.1 s (SD 0.2 s).

We characterized frequency-specific activity at the sensor level by pooling responses within anterior, lateral, and posterior
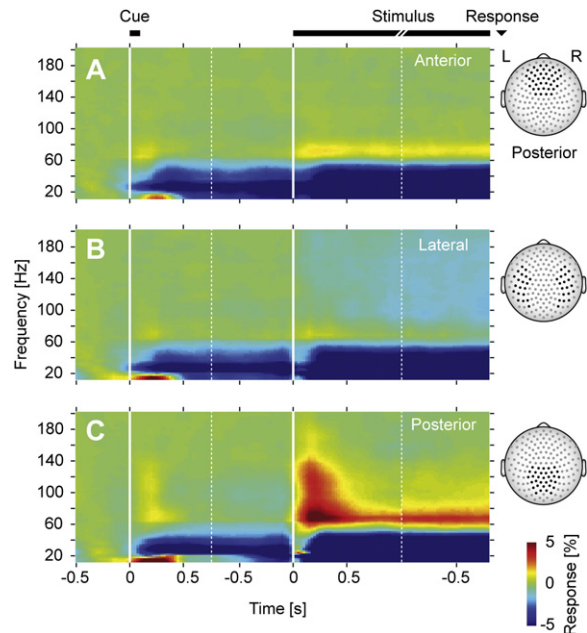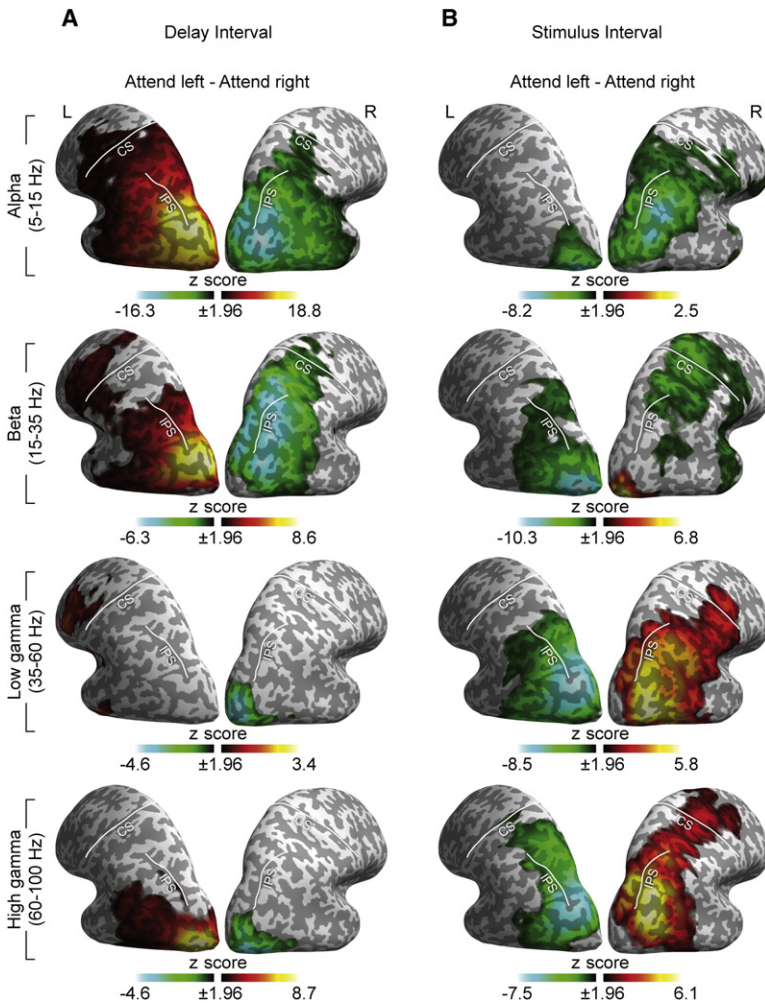
sensors (Figure 2). We observed a brief low (10–20 Hz) and high (70–140 Hz) frequency response to cue presentation followed by a tonic and widespread suppression from about 10 to 50 Hz. Onset of the dynamic random dot stimuli was followed by a transient and then tonic high-frequency response (50–100 Hz) primarily localized at posterior sensors. This high-frequency response was complemented by a strong and widespread decrease of activity below 50 Hz. This characteristic antagonistic spectral profile of responses to visual stimuli closely resembles previous MEG data employing dynamic random dot stimuli presented in the center of the visual field (Donner et al., 2007; Siegel et al., 2007).

Cortical Pattern of Attentional Modulation of Rhythmic Neuronal Activity

Before and during stimulus presentation, attention modulated population activity along the entire dorsal visual pathway in a spatially selective fashion (Figure 3). We estimated neural activity at the cortical source level using a linear spatial filtering technique ("beamforming"; see Experimental Procedures). We separately investigated the stimulation-free delay interval (750–0 ms before stimulus onset), the stimulus interval (100–500 ms after stimulus onset), and four contiguous frequency ranges roughly

Figure 3. Cortical Pattern of Spatially Selective Attentional Modulations

The images display the difference in neural activity during the delay (A) and stimulus (B) interval between trials when attention was directed to the left or right visual hemifield. Effects are separately shown for four different frequency bands (rows) and are displayed on the reconstructed and inflated cortical surface of the Montreal Neurological Institute template brain. Hemispheres are viewed from the posterior and are rotated slightly to enhance readability. Dark and light gray shadings indicate sulci and gyri, respectively. The locations of the central sulcus (CS) and intraparietal sulcus (IPS) are marked for orientation. All functional maps display pooled z scores thresholded at $p < 0.05$ (corrected; random effects).

corresponding to classical EEG bands: 5–15 Hz ("alpha"), 15–35 Hz ("beta"), 35–60 Hz ("low gamma"), and 60–100 Hz ("high gamma"). To isolate spatially selective attention from unspecific effects (such as arousal), we contrasted activity between "attend left" and "attend right" trials.

In accordance with previous reports (Thut et al., 2006; Worden et al., 2000; Wyart and Tallon-Baudry, 2008), attention induced a relative suppression of alpha band activity in the hemisphere representing the attended hemifield before stimulus onset. However, in contrast to these reports, we also found widespread attentional baseline suppressions in the beta band and, more surprisingly, in the low (right hemisphere) and high (bilateral) gamma band, specifically around the calcarine. By contrast, in the stimulus interval, we observed an attentional enhancement of low gamma band activity in extrastriate areas, which accords with previous sensor-level data (Gruber et al., 1999; Wyart and Tallon-Baudry, 2008). However, unlike these reports, during stimulation we observed further attentional modulations in the alpha, beta, and high gamma bands.

These effects were not attributable to phase-locked event-related fields (ERFs), which are also modulated by visuospatial attention (Hillyard and Anllo-Vento, 1998). We repeated the

above analyses after subtracting the average signal components phase locked to cue or stimulus onset, thus removing any ERFs. This analysis yielded results nearly identical to the data described above (see Figure S1 available online). These attentional modulations thus reflect rhythmic neuronal activity not phase locked to external events.

Dissociation between Attentional Modulations across the Dorsal Visual Pathway

Both the spectral signature and stimulus dependence of attentional modulations differed markedly between subsequent processing stages of the dorsal visual pathway. We compared spatially selective attentional effects between five key stages: V1/V2, MT+, vIPS, pIPS, and FEF. For each region of interest (ROI), we computed a predictive index of the focus of attention using receiver operating characteristic (ROC) analysis (Figure 4) (Green and Swets, 1966). Ranging between 0 and 1, this index can be interpreted as the probability of an ideal observer to predict the subject's focus of attention from the hemispheric lateralization of activity on a single trial. Values larger or smaller than 0.5 (chance level) correspond to an attentional enhancement or suppression, respectively.

We observed the strongest spectral dissociation in the beta band during stimulation (Figure 4B): while such activity was enhanced in V1/V2, it was suppressed in the FEF (direct comparison between regions: $p < 0.01$; corrected). We observed further strong regional differences: during the delay interval (Figure 4A), attention suppressed beta band activity in the IPS but not in V1/V2 (direct comparison: $p < 0.01$; corrected). By contrast, high gamma band activity was suppressed in V1/V2, but not in pIPS and FEF (direct comparisons: $p < 0.01$; corrected). During stimulus presentation (Figure 4B), we found an enhancement of beta band activity specifically in V1/V2, while vIPS and pIPS showed predominantly an increase of gamma band activity (direct comparisons: $p < 0.01$; corrected). Furthermore, alpha band activity was suppressed in pIPS, but not in FEF and V1/V2 (direct comparisons: $p < 0.01$; corrected).
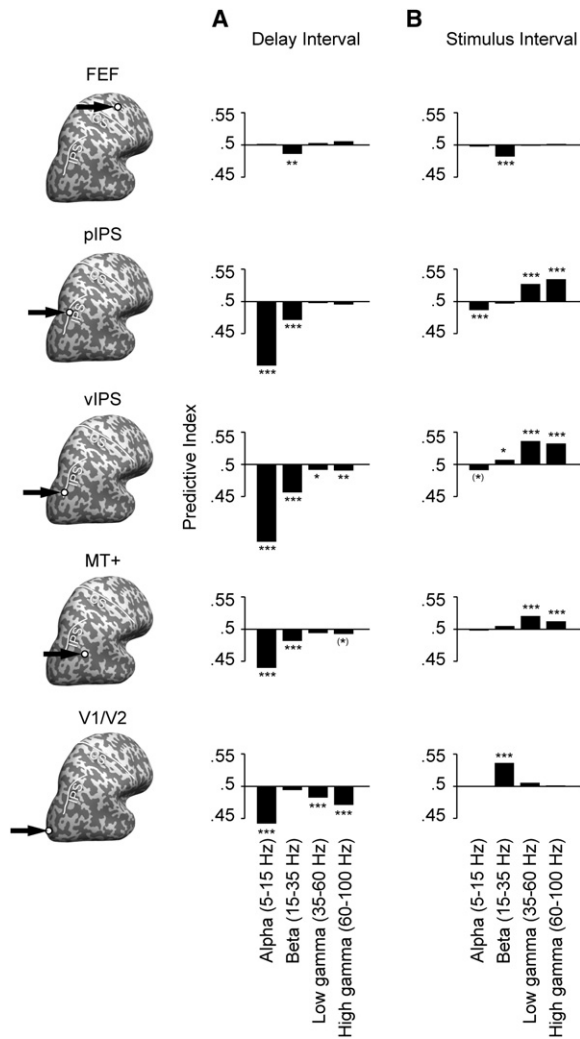
Figure 4. Strength of Attentional Modulations

Attentional modulations are displayed separately for the delay (A) and stimulus (B) interval. Each row corresponds to one region of interest (ROI), the location of which is marked on the inflated right hemisphere displayed in the left column (FEF, frontal eye field; pIPS, posterior intraparietal sulcus; vIPS, ventral intraparietal sulcus; MT+, human motion complex; V1/V2, pericalcarine cortex). For each ROI, frequency band, and temporal interval, the predictive index displays the probability with which an ideal observer can predict the direction of attention from the lateralization of the respective response between the left and right hemispheres. Predictive indices larger or smaller than chance level (0.5) correspond to an attentional enhancement or suppression of activity, respectively, in the hemisphere contralateral to the attended hemifield. Asterisks indicate the level of significance: */**/***p < 0.05/0.01/0.001 (corrected); (*)p < 0.05 (uncorrected).

The comparison of attentional effects between the delay and stimulus intervals revealed a remarkable difference in the stimulus dependence of these effects between posterior and frontal regions. V1/V2, MT+, vIPS, and pIPS showed a strong stimulus dependence with even opposite significant attentional modulations before and during stimulation (direct comparisons between intervals: p < 0.01 for all of these regions and bands; corrected). By contrast, in the FEF we found no stimulus dependence with
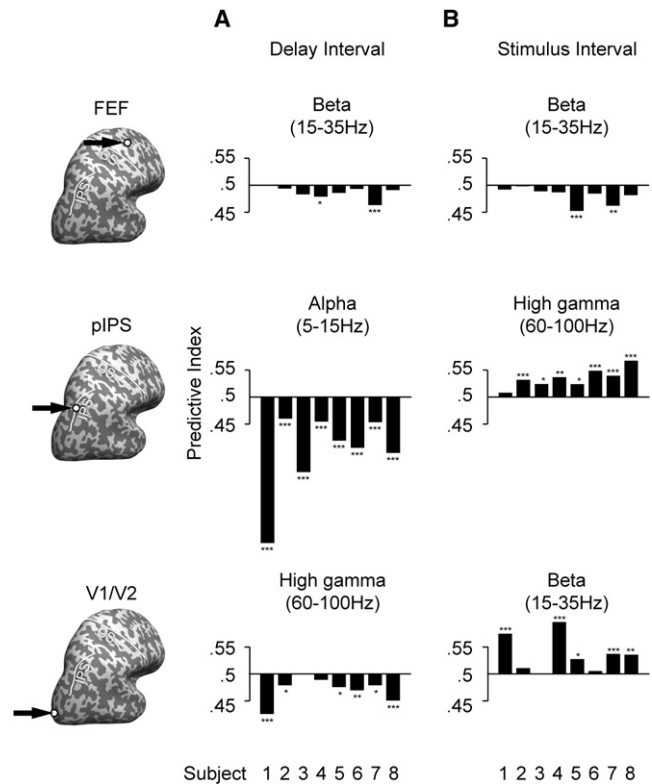

Figure 5. Strength of Attentional Modulations in Single Subjects

Receiver operating characteristic (ROC) analysis of attentional modulations during the delay (A) and stimulus (B) interval for all individual subjects. Bar plots display for each subject the predictive index of attentional lateralization for the strongest attention effects in the low- and high-frequency range in each temporal interval and beta band activity in FEF. Asterisks indicate the level of significance: */**/***p < 0.05/0.01/0.001 (uncorrected).

the same attentional beta band suppression in both intervals (direct comparisons: p > 0.1 for all bands). A direct comparison revealed significantly lower stimulus dependence in FEF than in the four posterior regions (p < 0.001; corrected). Thus, attentional modulation was strongly stimulus dependent in V1/V2, MT+, and the IPS, as predicted for brain areas expressing the effect of attention. By contrast, attentional modulation was stimulus independent in the FEF, as predicted for a region controlling the deployment of attention.

Consistency across Individual Subjects

These effects were remarkably consistent across individuals. We repeated the above ROC analysis for the two strongest attentional modulations in the high- and low-frequency range during the delay (alpha band: pIPS; gamma band: V1/V2) and stimulus (beta band: V1/V2; gamma band: pIPS) interval as well as the stimulus-independent beta band effect in FEF (Figure 5). All of these effects were consistently observed in individual subjects, with many effects being statistically significant even on the single-subject level.

We also consistently observed the dissociation of the spectral pattern and stimulus dependence of attentional modulations in individual subjects. For the spectral dissociation, 86% of the
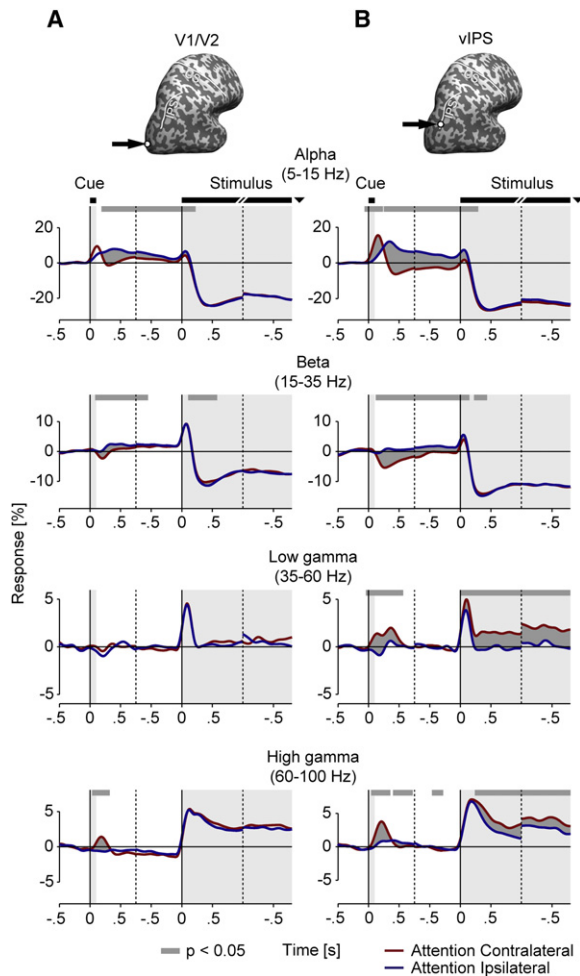
Figure 6. Time Course of Attentional Modulations

The red and blue traces display the time course of population activity in V1/V2 (A) and vIPS (B) in the cortical hemisphere contralateral (red) and ipsilateral (blue) to the attended hemifield. Rows correspond to activity in the four investigated frequency bands. Responses are measured in percent signal amplitude change relative to the 500 ms blank precue baseline. Solid vertical black lines mark cue and stimulus onset. Light gray regions mark the temporal interval of cue and stimulus presentation. Significant differences between contralateral and ipsilateral activity are marked by dark gray shadings and bars above traces (p < 0.05; corrected; random effects). The data were realigned to cue onset, stimulus onset, and response, and the time axis is displayed relative to these three events. The dotted vertical black lines mark the temporal boundaries of the realigned data.

single-subject comparisons between regions showed the same sign of difference as the group-level comparison. 46% of these consistent interregional differences were statistically significant (p < 0.05) even on the single-subject level. The stimulus dependence showed a similar consistency: 86% of the temporal comparisons that showed a significant stimulus dependence on the group level (V1/V2, MT+, vIPS, and pIPS) displayed the same sign of difference for single subjects. 62% of these differences were statistically significant (p < 0.05) for individual subjects. Furthermore, we found a significantly lower stimulus dependence in FEF compared to the posterior regions in 63%

of the direct comparisons on the single-subject level (p < 0.05). In sum, most of the effects observed at the group level were also statistically significant on the single-subject level.

Time Course of Attentional Modulations Reflects Sustained Deployment of Attention

The temporal evolution of attentional modulations resembled the sustained maintenance of covert attention on the peripheral target location. We focused on V1/V2 and vIPS, which showed the strongest effects of attention. During the cue interval, there was a transient but strongly lateralized response from about 100–400 ms post cue onset (Figure 6). This transient could reflect lateralized stimulus responses to the cue (presented at 0.4 deg to the right or left from fixation), the attention shift, or both. This transient was followed by tonic attentional modulations up to stimulus onset that matched those effects observed for the fixed delay interval analyzed above. These tonic baseline modulations were statistically significant (p < 0.05; corrected) in the alpha band for V1/V2 and vIPS and in the beta band for vIPS. During stimulus presentation, we found that attentional modulations evolved about 100 ms post stimulus onset and were again tonically sustained up to the behavioral response. For the stimulus interval, we found statistically significant tonic modulations in the low and high gamma band in vIPS (p < 0.05; corrected).

Attentional Modulations Predict Behavioral Discrimination Performance

If the reported modulations of oscillatory activity are functionally relevant for the enhanced processing of attended visual information, their strength should be correlated with behavioral performance. We thus tested, for those intervals, ROIs, and frequency bands that showed significant attentional modulations (see Figure 4), whether these were stronger before correct than before incorrect behavioral responses. Indeed, we found a significant behavioral effect for several attentional modulations: the strength of alpha band suppression in MT+, vIPS, and pIPS during the delay interval as well as the strength of high gamma band enhancement in pIPS during the stimulus interval significantly predicted the correctness of the behavioral response (p < 0.01). In other words, the stronger these spatially selective attentional modulations were on a given trial, the more likely the subjects would successfully complete that trial. Thus, in support of a functional relevance, the lateralization of oscillatory activity along the dorsal stream allowed for predicting not only the focus of attention but also the subjects' behavioral discrimination performance.

Attention Modulates Interregional Coherence in the Dorsal Visual Pathway

It has been proposed that attention flexibly routes relevant sensory signals through the cortical hierarchy by selectively modulating the synchronization between the corresponding neuronal groups across different cortical processing stages (Fries, 2005). We predicted that this should be reflected in a spatially selective modulation of the interregional phase coherence (see Experimental Procedures), specifically between areas MT+, pIPS, and the FEF. Selecting these relatively distant (>37 mm) regions allowed for probing synchronization between
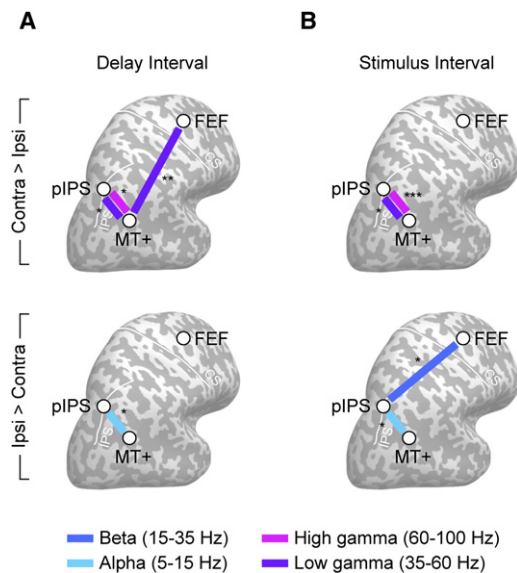
Figure 7. Attentional Modulation of Interregional Synchronization

Attentional modulations are displayed separately for the delay (A) and stimulus (B) interval. Panels in the upper row indicate cortical regions between which attention significantly enhanced synchronization in the hemisphere contralateral as compared to ipsilateral to the attended visual hemifield (i.e., a spatially selective modulation of coherence). Panels in the lower row depict corresponding attentional reductions of synchronization. Colors indicate the frequency band of a significant modulation. Asterisks mark the level of significance: */**/***p < 0.05/0.01/0.001 (uncorrected).

the key processing stages involved in the spatially cued motion discrimination task (Sapir et al., 2005) while minimizing confounding effects of volume conduction between nearby areas. We estimated the coherence between these regions at the cortical source level (see Experimental Procedures) and isolated spatially selective effects of attention by contrasting coherence in the hemispheres ipsilateral and contralateral to the attended hemifield.

Across all bands and both intervals, we found significant spatially selective attentional modulations of interregional synchronization between each pair of ROIs (Figure 7). Attention enhanced high-frequency synchronization (35–100 Hz) in the hemisphere contralateral to the attended hemifield, while in the low frequency range (5–35 Hz), we found a relative decrease of synchronization. Importantly, this antagonistic pattern was expressed both in the absence and in the presence of the visual stimulus, closely resembling an attentional control mechanism. Overall, 6 out of the 8 significant modulations were consistent across intervals. In particular, synchronization between MT+ and pIPS showed the most significant attentional effects that were all consistent across intervals. These effects were spatially specific and could not be explained by a spatial distance confound. For each ROI pair, we performed a control analysis testing for an attentional effect between these two ROIs and a third control ROI placed at equal mutual distance (see Experimental Procedures). There was no significant attentional effect on interregional synchronization for any of these control analyses (p > 0.05). Taken together, these results show that visuospatial

attention modulates frequency-specific neuronal synchronization between MT+, pIPS, and FEF in a spatially selective fashion.

DISCUSSION

We have characterized the modulation of local population activity and interregional synchronization by visuospatial attention in the human dorsal visual pathway during a spatially cued motion discrimination task. Before and during visual stimulation, attention modulated local population activity along the entire dorsal visual pathway in a spatially selective manner. Attentional effects were tonically sustained throughout the delay and stimulus intervals and were consistently observed in individual subjects, and their strength predicted subjects' behavioral performance on single trials. The spectral signature and stimulus dependence of attentional effects differed markedly between visual, parietal, and frontal cortex. While attentional modulations were strongly stimulus dependent in V1/V2, MT+, and IPS, they were relatively stimulus independent in the FEF. Spatial attention also selectively modulated the coherence between areas MT+, pIPS, and the FEF in different frequency ranges in a relatively stimulus-independent fashion.

Attentional Modulation of Rhythmic Population Activity

The present data show at which processing stages of the human dorsal visual pathway visuospatial attention modulates the rhythmic patterning of neuronal activity. Previous studies have shown enhancement of gamma band activity and suppression of alpha band activity by visuospatial attention in macaque areas V4 and LIP (Fries et al., 2001; Saalmann et al., 2007; Taylor et al., 2005), in human scalp EEG/MEG (Gruber et al., 1999; Thut et al., 2006; Worden et al., 2000; Wyart and Tallon-Baudry, 2008), and for feature-based attention in human EEG (Müller and Keil, 2004). However, the processing stages at which visuospatial attention modulates rhythmic activity along the human sensorimotor pathway remained unclear. By combining MEG and source-reconstruction techniques, we have demonstrated that such modulations are expressed across the entire dorsal pathway, from low-level areas such as V1/V2, through MT+ and parietal cortex, up to premotor stages (FEF). Thus, spatially selective oscillatory activity is linked to the focus of visuospatial attention not only at mid-level processing stages but also at the earliest processing stages (V1/V2) as well as in frontal regions implicated in the control of attentional signals. Furthermore, our data demonstrate that the spectral profile of these modulations is not homogenous but varies strongly between regions, a finding that has important functional implications to be discussed below.

Our present results are based on hemifield-selective attentional modulations. Thus, the magnitude of the reported effects depends on both the strength of the attentional modulation itself and the hemifield selectivity of each region under study. Although selectivity decreases at higher levels of the visual pathway such as the IPS and the FEF (Hagler and Sereno, 2006; Koyama et al., 2004; Silver et al., 2005; Wandell et al., 2007), we found robust hemifield-selective attentional effects in these regions. This suggests that, in accordance with single-unit results (Colby and Goldberg, 1999; Schall and Thompson,

1999), attentional modulations are particularly strong in these areas. Our findings on oscillatory activity accord well with recent functional magnetic resonance imaging (fMRI) data that show spatially selective attentional modulations of the blood oxygenation level-dependent (BOLD) signal in early visual areas as well as in the IPS and FEF (Sylvester et al., 2007).

Role of Rhythmic Population Activity in Attentive Visual Processing

Cortical activity engages in rhythmic population activity over a broad range of spectral scales (Buzsaki and Draguhn, 2004; Steriade, 2000), but the functional role of this rhythmic patterning of activity remains debated. In the visual system, population activity in the gamma band has been linked to stimulus properties (Gray et al., 1989; Liu and Newsome, 2006; Siegel et al., 2007; Siegel and König, 2003), selective attention (Fries et al., 2001; Gruber et al., 1999; Müller and Keil, 2004; Taylor et al., 2005), working memory (Pesaran et al., 2002), and visual awareness (Rodriguez et al., 1999; Wyart and Tallon-Baudry, 2008). Gamma band activity has also been attributed to selective attention in the auditory and somatosensory domain (Bauer et al., 2006; Ray et al., 2008). The gamma power of population measures such as the local field potential (LFP) seems tightly correlated with synaptic drive and average firing in a neuronal population (Henrie and Shapley, 2005) and presumably reflects local neuronal synchronization, which has been suggested to enhance the functional impact of spiking activity on postsynaptic processing stages (Engel et al., 2001; König et al., 1996; Salinas and Sejnowski, 2001). By contrast, population activity in the alpha band has traditionally been thought to reflect reduced thalamo-cortical transmission (Steriade, 2000) and cortical "deactivation" (Pfurtscheller et al., 1996; Thut et al., 2006; Worden et al., 2000). Our observations of an attentional gamma band enhancement in extrastriate and parietal cortex during stimulus presentation and a widespread baseline suppression of alpha band activity are in line with these hypotheses. The strength of these modulations was positively correlated with perceptual discrimination performance, ensuring that subjects maintained attention on the peripheral target throughout the trial and that the reported modulations reflect this shift. More importantly, and in accordance with previous reports (Thut et al., 2006; Wyart and Tallon-Baudry, 2008), this behavioral correlation provides strong evidence that the demonstrated modulations of rhythmic activity play a functional role in the preferential processing of the attended stimulus.

Gamma Band Suppression and Beta Band Enhancement with Attention

In light of the above concept of the functional role of gamma band activity, it is surprising that spatial attention consistently suppressed gamma band activity in V1/V2 before stimulus onset. However, this counterintuitive finding accords with single-unit data demonstrating a relative suppression of spiking activity by visuospatial attention in macaque area V4 before stimulus onset (Ghose and Maunsell, 2002). The gamma band suppression may thus reflect a gain regulation at the first cortical processing stage that reduces baseline firing in the absence of sensory drive. Surprisingly, this prestimulus gamma band

suppression and the beta band enhancement during stimulation in V1/V2 (see below) were observed not only at the ROI location corresponding to the stimulated peripheral visual field but also at the foveal representation near the occipital pole (see Figure 3). Thus, further invasive studies are needed to investigate the exact spatial extent and profile of these attentional modulations relative to the focus of visuospatial attention.

We found dissociated attentional modulations of beta band activity between early visual and premotor areas. During stimulus processing, attention specifically enhances such activity in primary visual cortex. This adds to a recent body of evidence pointing toward a positive correlation between beta band activity and active processing in the visual system. Beta band activity in macaque V1 correlates with perceptual dominance during binocular rivalry (Gail et al., 2004) and generalized flash suppression (Wilke et al., 2006). Beta band activity in ventral (Tallon-Baudry et al., 2001) and dorsal (Donner et al., 2007; Gross et al., 2004; Pesaran et al., 2002) extrastriate areas correlates with behavioral performance in various visual tasks requiring visual attention and/or short-term memory. In accordance with these findings, our data suggest that in primary visual cortex, beta band activity serves to facilitate processing of attended visual locations. By contrast, in the FEF we observed an attentional suppression of beta band activity. This suppression accords well with the contralateral beta band suppression observed in primary motor cortex preceding voluntary limb movements (Crone et al., 1998). Beta band suppression may thus be a common spectral signature of neural activation in the primary motor cortex and FEF.

Taken together, these observations challenge a simple antagonistic concept of the role of low- and high-frequency population activity in visual attention. The dissociated spectral profile of attentional modulations along the dorsal pathway suggests that the mechanisms and the functional role of such rhythmic activity may differ between cortical areas.

Attentional Modulation of Interregional Synchronization

Interregional synchronization may control the communication between cortical areas (Womelsdorf et al., 2007). Top-down visual attention is thought to be mediated by large-scale neural interactions between frontoparietal and visual cortex (Corbetta and Shulman, 2002; Kastner and Ungerleider, 2000; Serences and Yantis, 2006). It has been proposed that attention routes selected sensory information through the cortical hierarchy by dynamically altering the coherence between neuronal groups across distant cortical areas (Buzsaki and Draguhn, 2004; Fries, 2005). Recent monkey (Buschman and Miller, 2007; Saalmann et al., 2007) and human (Doesburg et al., 2008; Gross et al., 2004) MEG/EEG studies support this hypothesis but did not simultaneously investigate spatially selective attentional effects on synchronization between early visual, parietal, and prefrontal areas. The present data show that before and during stimulus presentation, synchronization between these processing stages is modulated by attention in a spatially selective fashion. Furthermore, in contrast to local population activity, the attentional modulation of interregional coherence showed little stimulus dependence. In particular, attention enhanced the coherence between MT+ and LIP in the gamma band and suppressed it in

the alpha band both before and during visual stimulation. Comparison of the power and coherence effects observed here clearly suggests that the attentional effects on coherence do not simply reflect modulations of local oscillatory activity but rather reflect genuine changes of interregional synchronization. For instance, during the delay interval, gamma band coherence between MT+ and LIP shows an attention enhancement, while local gamma band activity in these regions shows no modulation or even an attentional reduction. This also indicates that distinct mechanisms might underlie local, as compared to interregional, neuronal communication. In summary, the present data suggest that frequency-specific synchronization of extrastriate, parietal, and frontal regions subserves the selective routing of attended visual information in the human brain.

Control and Effects of Attention

Invasive and noninvasive studies suggest dissociated substrates for the control and effect of attentional signals in frontoparietal and visual cortex, respectively. Human imaging studies have identified a frontoparietal network of regions along the IPS and the FEF as a potential attentional control network (Corbetta et al., 1993; Corbetta and Shulman, 2002; Kastner and Ungerleider, 2000; Serences and Yantis, 2006). More recently, this hypothesis has received further support from invasive studies in monkeys (Buschman and Miller, 2007; Moore et al., 2003). However, direct physiological evidence for a strict dissociation of attentional control and effects remained sparse. Prestimulus enhancements of the BOLD signal were observed not only in frontoparietal regions (Corbetta et al., 2000; Hopfinger et al., 2000; Kastner et al., 1999; Sapir et al., 2005) but also, albeit more weakly, in early visual areas (Hopfinger et al., 2000; Kastner et al., 1999; Ress et al., 2000; Sapir et al., 2005). Furthermore, attention effects in the firing rates of frontoparietal regions are not stimulus independent but are modulated by visual input (Colby and Goldberg, 1999; Schall and Thompson, 1999).

The present data provide two new lines of evidence in support of a functional dissociation. First, we demonstrate that the spectral signature of attentional effects differs widely between frontal, parietal, and early visual areas. This dissociation may reflect distinct neuronal mechanisms underlying the control and effect of attention within these regions. Second, we show differences in the stimulus dependence of attentional effects between areas. While many attentional modulations even reversed between the delay and stimulus intervals in V1/V2, MT+, and the IPS, this stimulus dependence was absent in FEF. In other words, the stimulus independence in FEF matches precisely the type of effect predicted for an attentional control region. By contrast, the stimulus dependence of effects in posterior cortex suggests that it expresses the effects of attentional top-down signals on incoming sensory signals. Moreover, a purely additive model of bottom-up and top-down factors would predict attentional effects to be independent of the sensory input. Thus, rhythmic population activity in early visual and parietal cortex likely reflects a complex nonadditive interaction between bottom-up and top-down signals. These effects on rhythmic population activity accord well with fMRI evidence demonstrating stimulus dependence and independence of attentional BOLD modulations in IPS and FEF, respectively (Shulman et al., 2003).

Together, these data indicate that attentional effects along the IPS are incompatible with pure attentional control but suggest that rather than being strictly segregated, control and effects of attention are implemented in a functional continuum along the fronto-occipital axis (Serences and Yantis, 2006; Silver et al., 2005). However, it should be noted that MEG, like fMRI, cannot separate different neuronal populations or layer-specific effects within the same region. Thus, invasive studies are required to investigate the microstructure of attentional effects and test the possibility that in regions like the IPS, stimulus-driven signals are locally segregated from endogenous attentional signals.

In contrast to locally synchronized oscillatory activity, visuospatial attention established a selective pattern of interregional coherence in the dorsal visual pathway that was only weakly influenced by the visual input. Thus, interregional synchronization across multiple stages of the cortical hierarchy might specifically reflect the top-down control of attention.

Conclusions

We have demonstrated in humans that, in the presence and absence of visual stimuli, visuospatial attention profoundly modulates locally synchronized oscillatory activity as well as interregional synchronization along the entire dorsal visual pathway from early visual up to prefrontal regions. Importantly, we found an unanticipated dissociation of the spectral signatures and stimulus dependencies of attentional effects between different processing stages. Our data indicate that regionally and spectrally specific synchronization within most stages of the human dorsal visual pathway may underlie the enhanced processing of attended visual stimuli. Furthermore, our results provide strong evidence for the hypothesis that attentional selection is mediated by frequency-specific synchronization between prefrontal, parietal, and early visual cortex.

EXPERIMENTAL PROCEDURES

Subjects and Experimental Design

Eight subjects (7 male, 1 female; age range 23–32 years; 2 authors, 6 naive) participated in the study, which was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (CMO Regio Arnhem-Nijmegen). Informed consent was obtained from all subjects prior to the measurements. All subjects were in good health, had no past history of psychiatric or neurological illness, and had normal or corrected-to-normal vision.

We used a spatially cued two-alternative forced-choice motion discrimination paradigm. Each trial was started by the onset of a red fixation cross on a uniform black background. After a random baseline (1000–1500 ms), a visual cue instructed subjects to covertly shift their visual attention to either the left or right visual hemifield. A small green dot of 0.1 deg diameter presented randomly for 100 ms at 0.4 deg eccentricity to the left or right of the fixation cross served as the cue. Cue presentation was followed by a variable (1000–1500 ms) delay interval during which only the fixation cross was presented. Then, two dynamic random dot patterns were simultaneously displayed in circular apertures in the left and right visual hemifield (22.4 deg diameter; 14.4 deg eccentricity). In each trial, the coherent fraction of dots in each aperture independently moved either upward or downward with equal probability. For each frame, the level of motion coherence determined the fraction of dots that was displaced according to a common motion vector, while all other dots were displaced randomly (dot diameter ~0.2 deg; dot density 1.7 deg^{-2}; motion speed 11.5 deg/s; local dot contrast 100%). The

coherently moving dots were randomly selected anew on each frame. Subjects were instructed to covertly shift their attention to the cued visual hemifield directly following cue presentation and to report the perceived direction of motion in the cued aperture by button press with either the left or right index finger. Stimulus response mapping was counterbalanced across subjects. Stimuli were turned off immediately after the subject's response, or 3 s after onset if no response had been delivered by then. Auditory feedback (a beep) was provided after each incorrect response via plastic tubes and earpieces. Following the response, subjects were allowed to make eye movements or blinks during an intertrial interval of 1500 ms duration. Each of the eight subjects participated in six recording sessions with 480 trials, resulting in a total number of 23,040 recorded trials.

The level of motion coherence was adjusted to each subject's individual motion discrimination threshold based on a psychophysical recording session prior to the MEG recording: subjects performed the task in the MEG setup at six constant levels of motion coherence, and thresholds were determined by fitting a Weibull function to the psychophysical data.

All stimuli were constructed offline using MATLAB (The MathWorks, Inc.), and stimulus presentation was controlled using Presentation software (NeuroBehavioral Systems). All stimuli were presented via a mirror system on a back-projection screen using a calibrated LCD projector (60 Hz refresh rate).

Data Acquisition and Preprocessing

MEG was recorded using a 151-channel whole-head system (Omega 2000, CTF Systems Inc.) in a magnetically shielded room. The electrooculogram (EOG) was recorded simultaneously for offline artifact rejection. Head position relative to the MEG sensors was measured before and after each recording session. For all analyzed data sets, head displacements were below 5 mm. MEG signals were low-pass filtered online (cutoff 300 Hz) and sampled at 1200 Hz.

Trials containing eye blinks, eye movements, muscle artifacts, or signal jumps were rejected offline from further analysis using semiautomatic procedures. Line noise removal was performed by selecting data segments of 10 s length with the epochs of interest in the center. These segments were Fourier transformed; the 50, 100, 150, and 200 Hz components of the spectra were zeroed; the time courses were reconstructed by inverse Fourier transformation; and epochs of interest were cut out of these denoised 10 s data segments.

T1-weighted structural MRIs were recorded for all subjects. For source reconstruction, individual single-shell models (Nolte, 2003) were derived from the segmentation of these structural MRIs.

Data Analyses

All analyses were performed in MATLAB using the "FieldTrip" open-source toolbox (http://www.ru.nl/fcdonders/fieldtrip) and custom software. Cortical segmentation and surface reconstruction were performed using BrainVoyager QX (Brain Innovation B.V.) and SPM2 (http://www.fil.ion.ucl.ac.uk/spm). Spatial alignment of structural MRIs and functional maps was performed using SPM2.

Spectral Analyses and Response Quantification

Spectral analyses of the MEG data were performed using "multitaper" spectral estimates based on discrete prolate spheroidal sequences. Transformations to the frequency domain were performed on the single-trial level before averaging across trials. We characterized oscillatory responses as the percentage change R in signal amplitude (square root of power) relative to the blank prestimulus baseline.

Time-frequency transformation was performed by a sliding-window multitaper analysis (250 ms length; 25 ms step size; ±12 Hz spectral smoothing; 5 Slepian tapers) after realigning all data to cue onset, stimulus onset, and the behavioral response.

Source Reconstruction

To estimate the spectral amplitude of responses at the cortical source level, we used the "beamforming" adaptive linear spatial filtering technique (Gross et al., 2001; Van Veen et al., 1997) as described previously (Donner et al., 2007; Siegel et al., 2007). In short, for each frequency and source location, a linear filter was computed that passes activity from that location with unit gain while maximally suppressing activity from other sources. All source-level analyses were independently performed for four frequency bands: 5–15 Hz, 15–25 Hz, 35–60 Hz, and 60–100 Hz. For each recording session, forward models were computed using individual single-shell volume conductor models and the measured head positions. Whole-brain source reconstructions were performed on a regular 3D grid of 6 mm resolution and linearly interpolated to 1 mm resolution.

For each subject and session, differences of source-level activity across conditions were quantified as z scores in the individual head space. These z score maps were nonlinearly aligned to a template brain (Montreal Neurological Institute) based on the individual structural MRIs and pooled across subjects by taking their sum normalized by the square root of the number of subjects. To test the resulting statistical map for a significant deviation from zero across subjects (random effects), we applied a nonparametric permutation test based on spatial clustering: The sign of each subject's statistical maps was randomly flipped, resulting in a set of 256 permuted statistical maps that approximated the distribution of measured z score maps under the null hypothesis. For each of these permuted maps as well as the measured map, spatial clusters were defined as continuous volumes of absolute pooled z scores > 1.96. z scores were summed within each cluster, and the p value of each cluster of the measured map was computed as the probability of obtaining a cluster with a larger summed z score in the distribution of the maximum summed z scores across the permuted maps. This procedure conservatively accounts for multiple comparisons across space. All statistical maps were thresholded at p < 0.05 (corrected) and displayed on the reconstructed and inflated cortical surface of the template brain.

Region of Interest Analyses

We defined the following ROIs based on anatomical criteria on the template brain and nonlinearly aligned their position to the individual subjects' anatomical MRIs. The V1/V2 position was defined at the calcarine representation of the stimulated peripheral visual field halfway between the occipital pole and the parieto-occipital sulcus (Wandell et al., 2007). The MT+ position was defined at the junction of the inferior temporal sulcus and the lateral occipital sulcus (Dumoulin et al., 2000). Functional definitions of MT+ obtained from standard fMRI localizers were available for four subjects and were in close correspondence with the anatomical criteria. The vIPS position was defined at the junction of the intraparietal sulcus with the transverse occipital sulcus. When tracing the horizontal ramus of the IPS in the posterior-anterior direction, one typically encounters a sharp transition from a deep and poorly truncated segment to a shallower and more extensively truncated segment. The pIPS position was defined halfway between this transition and the vIPS location. The FEF position was defined at the junction of the precentral sulcus and the superior frontal sulcus.

We used beamforming to reconstruct single-trial responses for each ROI and computed a lateralization index L by subtracting the response in the right hemisphere from the response in the left hemisphere. We then used receiver operating characteristic (ROC) analysis to compute a "predictive index" I that approximates the probability with which an ideal observer can predict the direction of attention from the hemispheric lateralization of the neural response on a single trial (Green and Swets, 1966). I was estimated as the area under the ROC curve for the distributions of L for "attend right" and "attend left" trials. For data pooled across subjects, L was independently z-transformed for each subject and session. We tested for a significant deviation of I from chance level (0.5) using a nonparametric permutation test (Efron and Tibshirani, 1998) with 10^6 permutations randomly shuffling trials between attentional conditions. p values were false discovery rate (FDR) corrected for multiple comparisons across regions, bands, and intervals.

To compare attentional modulations between intervals and regions, we computed an attentional index M for each trial as the average difference in response R between the hemispheres contralateral and ipsilateral to the focus of attention. In analogy to the above analysis, we used ROC analysis to test for a difference in M between regions and temporal intervals. p values for these comparisons were FDR corrected. To compare the stimulus dependence of attentional modulations between regions, we computed, for each trial, band, and region, the difference of M between the stimulus and delay intervals. We then computed, for each region, the normalized stimulus dependence by averaging the absolute values of the z-transformed differences of M across

bands. To test for differences in normalized stimulus dependence between regions, we performed a permutation test (10^6 permutations) randomly shuffling M between regions. The resulting p values were FDR corrected.

Time Course of Band-Limited Source-Level Activity

For each frequency band, the sensor-level data were band-pass filtered using a 4th-order zero-phase forward-reverse digital Butterworth filter, and source-level time courses of these band-limited signals were reconstructed using the time-domain implementation of the beamforming technique (Van Veen et al., 1997). Time courses were derived along the dominant dipole direction, and the band-limited activity was computed as the absolute of the Hilbert transform, smoothed with a Hanning window of 150 ms full width at half maximum. The difference between time courses contralateral and ipsilateral to attention was tested across subjects (random effects) in analogy to the analysis in the spatial domain based on a temporally clustered permutation test. Temporal clusters of significant differences were thresholded at p < 0.05 (corrected).

Source-Level Coherence

For the standard beamforming technique, highly coherent sources that are relatively distant or closely separated can cancel out or merge, respectively (Van Veen et al., 1997). We thus estimated source-level coherence with a two-dipole beamformer that explicitly models the leadfields of two sources. This technique allows the reliably estimation of source-level coherence even under conditions of very high source correlation (Schoffelen et al., 2008). For the two-dipole beamformer, the spatial filter was computed using a combined leadfield $L_c = [L(r_1);L(r_2)]$, with r_1 and r_2 as the locations between which coherence was estimated. We used singular-value decomposition to project estimated dipole moments for both locations in their dominant spatial direction. From the resulting two-by-two source-level cross-spectral density matrix S', we derived the source-level coherence for each condition (attend left or right) according to the equation

$$Coh(r_1, r_2) = \frac{\left| S'_{1,2} \right|}{\sqrt{S'_{1,1}\, S'_{2,2}}}.$$

Coherence is biased by degrees of freedom. We thus stratified the data to the same number of tapers for both conditions. We then tested across all recording sessions (n = 48) for a significant difference between coherence in the hemispheres contralateral and ipsilateral to the focus of attention using paired t statistics. To rule out a simple distance confound, for each of the three pairs of ROIs, we placed a control ROI with the same distance to both ROIs as between the original two ROIs ventrally within the gray matter at the same cortical depth as the original pair of ROIs. The control ROIs were located near the dorsal superior temporal sulcus (control for MT-pIPS interaction), in the ventrolateral prefrontal cortex (control for MT-FEF interaction), and in the lateral temporal cortex (control for pIPS-FEF interaction).

SUPPLEMENTAL DATA

Supplemental Data include one figure and can be found online at http://www.neuron.org/supplemental/S0896-6273(08)00757-5.

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REFERENCES

Bauer, M., Oostenveld, R., Peeters, M., and Fries, P. (2006). Tactile spatial attention enhances gamma-band activity in somatosensory cortex and reduces low-frequency activity in parieto-occipital areas. J. Neurosci. 26, 490–501.

Bichot, N.P., Rossi, A.F., and Desimone, R. (2005). Parallel and serial neural mechanisms for visual search in macaque area V4. Science 308, 529–534.

Buschman, T.J., and Miller, E.K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. Science 315, 1860–1862.

Buzsaki, G., and Draguhn, A. (2004). Neuronal oscillations in cortical networks. Science 304, 1926–1929.

Colby, C.L., and Goldberg, M.E. (1999). Space and attention in parietal cortex. Annu. Rev. Neurosci. 22, 319–349.

Corbetta, M., and Shulman, G.L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. Neurosci. 3, 201–215.

Corbetta, M., Miezin, F.M., Shulman, G.L., and Petersen, S.E. (1993). A PET study of visuospatial attention. J. Neurosci. 13, 1202–1226.

Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P., and Shulman, G.L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nat. Neurosci. 3, 292–297.

Crone, N.E., Miglioretti, D.L., Gordon, B., Sieracki, J.M., Wilson, M.T., Uematsu, S., and Lesser, R.P. (1998). Functional mapping of human sensori-motor cortex with electrocorticographic spectral analysis. I. Alpha and beta event-related desynchronization. Brain 121, 2271–2299.

Doesburg, S.M., Roggeveen, A.B., Kitajo, K., and Ward, L.M. (2008). Large-scale gamma-band phase synchronization and selective attention. Cereb. Cortex 18, 386–396.

Donner, T., Kettermann, A., Diesch, E., Ostendorf, F., Villringer, A., and Brandt, S.A. (2000). Involvement of the human frontal eye field and multiple parietal areas in covert visual selection during conjunction search. Eur. J. Neurosci. 12, 3407–3414.

Donner, T.H., Siegel, M., Oostenveld, R., Fries, P., Bauer, M., and Engel, A.K. (2007). Population activity in the human dorsal pathway predicts the accuracy of visual motion detection. J. Neurophysiol. 98, 345–359.

Dumoulin, S.O., Bittar, R.G., Kabani, N.J., Baker, C.L., Jr., Le Goualher, G., Bruce Pike, G., and Evans, A.C. (2000). A new anatomical landmark for reliable identification of human area V5/MT: a quantitative analysis of sulcal patterning. Cereb. Cortex 10, 454–463.

Efron, B., and Tibshirani, R. (1998). An Introduction to the Bootstrap, 1st CRC Press Reprint (Boca Raton, FL, USA: Chapman & Hall/CRC).

Engel, A.K., Fries, P., and Singer, W. (2001). Dynamic predictions: oscillations and synchrony in top-down processing. Nat. Rev. Neurosci. 2, 704–716.

Fan, J., Byrne, J., Worden, M.S., Guise, K.G., McCandliss, B.D., Fossella, J., and Posner, M.I. (2007). The relation of brain oscillations to attentional networks. J. Neurosci. 27, 6197–6206.

Fries, P. (2005). A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends Cogn. Sci. 9, 474–480.

Fries, P., Reynolds, J.H., Rorie, A.E., and Desimone, R. (2001). Modulation of oscillatory neuronal synchronization by selective visual attention. Science 291, 1560–1563.

Gail, A., Brinksmeyer, H.J., and Eckhorn, R. (2004). Perception-related modulations of local field potential power and coherence in primary visual cortex of awake monkey during binocular rivalry. Cereb. Cortex 14, 300–313.

Ghose, G.M., and Maunsell, J.H. (2002). Attentional modulation in visual cortex depends on task timing. Nature 419, 616–620.

Gray, C.M., König, P., Engel, A.K., and Singer, W. (1989). Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. Nature 338, 334–337.

Green, D.M., and Swets, J.A. (1966). Signal Detection Theory and Psychophysics (New York: Wiley).

Gross, J., Kujala, J., Hamalainen, M., Timmermann, L., Schnitzler, A., and Salmelin, R. (2001). Dynamic imaging of coherent sources: Studying neural interactions in the human brain. Proc. Natl. Acad. Sci. USA *98*, 694–699.

Gross, J., Schmitz, F., Schnitzler, I., Kessler, K., Shapiro, K., Hommel, B., and Schnitzler, A. (2004). Modulation of long-range neural synchrony reflects temporal limitations of visual attention in humans. Proc. Natl. Acad. Sci. USA *101*, 13050–13055.

Gruber, T., Müller, M.M., Keil, A., and Elbert, T. (1999). Selective visual-spatial attention alters induced gamma band responses in the human EEG. Clin. Neurophysiol. *110*, 2074–2085.

Hagler, D.J., Jr., and Sereno, M.I. (2006). Spatial maps in frontal and prefrontal cortex. Neuroimage *29*, 567–577.

Händel, B., Lutzenberger, W., Thier, P., and Haarmeier, T. (2008). Selective attention increases the dependency of cortical responses on visual motion coherence in man. Cereb. Cortex. Published online April 18, 2008. 10.1093/cercor/bhn049.

Henrie, J.A., and Shapley, R. (2005). LFP power spectra in V1 cortex: the graded effect of stimulus contrast. J. Neurophysiol. *94*, 479–490.

Hillyard, S.A., and Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. Proc. Natl. Acad. Sci. USA *95*, 781–787.

Hopfinger, J.B., Buonocore, M.H., and Mangun, G.R. (2000). The neural mechanisms of top-down attentional control. Nat. Neurosci. *3*, 284–291.

Kastner, S., and Ungerleider, L.G. (2000). Mechanisms of visual attention in the human cortex. Annu. Rev. Neurosci. *23*, 315–341.

Kastner, S., Pinsk, M.A., De Weerd, P., Desimone, R., and Ungerleider, L.G. (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron *22*, 751–761.

König, P., Engel, A.K., and Singer, W. (1996). Integrator or coincidence detector? The role of the cortical neuron revisited. Trends Neurosci. *19*, 130–137.

Koyama, M., Hasegawa, I., Osada, T., Adachi, Y., Nakahara, K., and Miyashita, Y. (2004). Functional magnetic resonance imaging of macaque monkeys performing visually guided saccade tasks: comparison of cortical eye fields with humans. Neuron *41*, 795–807.

Liu, J., and Newsome, W.T. (2006). Local field potential in cortical area MT: stimulus tuning and behavioral correlations. J. Neurosci. *26*, 7779–7790.

Moore, T., Armstrong, K.M., and Fallah, M. (2003). Visuomotor origins of covert spatial attention. Neuron *40*, 671–683.

Müller, M.M., and Keil, A. (2004). Neuronal synchronization and selective color processing in the human brain. J. Cogn. Neurosci. *16*, 503–522.

Nolte, G. (2003). The magnetic lead field theorem in the quasi-static approximation and its use for magnetoencephalography forward calculation in realistic volume conductors. Phys. Med. Biol. *48*, 3637–3652.

Pesaran, B., Pezaris, J.S., Sahani, M., Mitra, P.P., and Andersen, R.A. (2002). Temporal structure in neuronal activity during working memory in macaque parietal cortex. Nat. Neurosci. *5*, 805–811.

Pfurtscheller, G., Stancak, A., Jr., and Neuper, C. (1996). Event-related synchronization (ERS) in the alpha band–an electrophysiological correlate of cortical idling: a review. Int. J. Psychophysiol. *24*, 39–46.

Ray, S., Niebur, E., Hsiao, S.S., Sinai, A., and Crone, N.E. (2008). High-frequency gamma activity (80-150Hz) is increased in human cortex during selective attention. Clin. Neurophysiol. *119*, 116–133.

Ress, D., Backus, B.T., and Heeger, D.J. (2000). Activity in primary visual cortex predicts performance in a visual detection task. Nat. Neurosci. *3*, 940–945.

Rodriguez, E., George, N., Lachaux, J.P., Martinerie, J., Renault, B., and Varela, F.J. (1999). Perception's shadow: long-distance synchronization of human brain activity. Nature *397*, 430–433.

Saalmann, Y.B., Pigarev, I.N., and Vidyasagar, T.R. (2007). Neural mechanisms of visual attention: how top-down feedback highlights relevant locations. Science *316*, 1612–1615.

Salinas, E., and Sejnowski, T.J. (2001). Correlated neuronal activity and the flow of neural information. Nat. Rev. Neurosci. *2*, 539–550.

Sapir, A., d'Avossa, G., McAvoy, M., Shulman, G.L., and Corbetta, M. (2005). Brain signals for spatial attention predict performance in a motion discrimination task. Proc. Natl. Acad. Sci. USA *102*, 17810–17815.

Schall, J.D., and Thompson, K.G. (1999). Neural selection and control of visually guided eye movements. Annu. Rev. Neurosci. *22*, 241–259.

Schoffelen, J.M., Oostenveld, R., and Fries, P. (2008). Imaging the human motor system's beta-band synchronization during isometric contraction. Neuroimage *41*, 437–447.

Serences, J.T., and Yantis, S. (2006). Selective visual attention and perceptual coherence. Trends Cogn. Sci. *10*, 38–45.

Shulman, G.L., McAvoy, M.P., Cowan, M.C., Astafiev, S.V., Tansy, A.P., d'Avossa, G., and Corbetta, M. (2003). Quantitative analysis of attention and detection signals during visual search. J. Neurophysiol. *90*, 3384–3397.

Siegel, M., and König, P. (2003). A functional gamma-band defined by stimulus-dependent synchronization in area 18 of awake behaving cats. J. Neurosci. *23*, 4251–4260.

Siegel, M., Donner, T.H., Oostenveld, R., Fries, P., and Engel, A.K. (2007). High-frequency activity in human visual cortex is modulated by visual motion strength. Cereb. Cortex *17*, 732–741.

Silver, M.A., Ress, D., and Heeger, D.J. (2005). Topographic maps of visual spatial attention in human parietal cortex. J. Neurophysiol. *94*, 1358–1371.

Steriade, M. (2000). Corticothalamic resonance, states of vigilance and mentation. Neuroscience *101*, 243–276.

Sylvester, C.M., Shulman, G.L., Jack, A.I., and Corbetta, M. (2007). Asymmetry of anticipatory activity in visual cortex predicts the locus of attention and perception. J. Neurosci. *27*, 14424–14433.

Tallon-Baudry, C., Bertrand, O., and Fischer, C. (2001). Oscillatory synchrony between human extrastriate areas during visual short-term memory maintenance. J. Neurosci. *21*, RC177.

Taylor, K., Mandon, S., Freiwald, W.A., and Kreiter, A.K. (2005). Coherent oscillatory activity in monkey area v4 predicts successful allocation of attention. Cereb. Cortex *15*, 1424–1437.

Thut, G., Nietzel, A., Brandt, S.A., and Pascual-Leone, A. (2006). Alpha-band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. J. Neurosci. *26*, 9494–9502.

Van Veen, B.D., van Drongelen, W., Yuchtman, M., and Suzuki, A. (1997). Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. IEEE Trans. Biomed. Eng. *44*, 867–880.

Wandell, B.A., Dumoulin, S.O., and Brewer, A.A. (2007). Visual field maps in human cortex. Neuron *56*, 366–383.

Wilke, M., Logothetis, N.K., and Leopold, D.A. (2006). Local field potential reflects perceptual suppression in monkey visual cortex. Proc. Natl. Acad. Sci. USA *103*, 17507–17512.

Womelsdorf, T., Schoffelen, J.M., Oostenveld, R., Singer, W., Desimone, R., Engel, A.K., and Fries, P. (2007). Modulation of neuronal interactions through neuronal synchronization. Science *316*, 1609–1612.

Worden, M.S., Foxe, J.J., Wang, N., and Simpson, G.V. (2000). Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. J. Neurosci. *20*, RC63.

Wyart, V., and Tallon-Baudry, C. (2008). Neural dissociation between visual awareness and spatial attention. J. Neurosci. *28*, 2667–2679.