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Cortical and subcortical coordination of visual spatial attention revealed by simultaneous EEG-fMRI recording

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Running Head: CORTICAL-SUBCORTICAL COORDINATION OF ATTENTION

Cortical and subcortical coordination of visual spatial attention revealed by simultaneous EEG-fMRI recording

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Abstract

Visual spatial attention has been studied in humans with both electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) individually. However, due to the intrinsic limitations of each of these methods used alone, our understanding of the systems-level mechanisms underlying attentional control remains limited. Here, we examined trial-to-trial covariations of concurrently recorded EEG and fMRI in a cued visual spatial-attention task in humans, which allowed delineation of both the generators and modulators of the cue-triggered event-related oscillatory brain activity underlying attentional-control function. The fMRI activity in visual cortical regions contralateral to the cued direction of attention covaried positively with occipital gamma-band EEG, consistent with activation of cortical regions representing attended locations in space. In contrast, fMRI activity in ipsilateral visual cortical regions covaried inversely with occipital alpha-band oscillations, consistent with attention-related suppression of the irrelevant hemispace. Moreover, the pulvinar nucleus of the thalamus covaried with both of these spatially specific, attention-related, oscillatory EEG modulations. As the pulvinar's neuroanatomical geometry makes it unlikely to be a direct generator of the scalp-recorded EEG, these covariational patterns appear to reflect the pulvinar's role as a regulatory control structure, sending spatially specific signals to proactively modulate visual cortex excitability. Together, these combined EEG/fMRI results illuminate the dynamically interacting cortical and subcortical processes underlying spatial attention, providing important insight not realizable using either method alone.

Keywords: attentional control; pulvinar; visual cortex; EEG; fMRI.

Significance Statement

Non-invasive recordings of changes in the brain's blood flow (fMRI) and electrical activity (EEG) in humans have individually shown that shifting attention to a location in space produces spatially-specific changes in visual-cortex activity in anticipation of a stimulus. The mechanisms controlling these attention-related modulations of sensory cortex, however, are poorly understood. Here, we recorded these two complementary measures of brain activity simultaneously and examined their trial-to-trial covariations to gain insight into these attentional control mechanisms. This multi-methodological approach revealed the attention-related coordination of visual-cortex modulation by the subcortical pulvinar nucleus of the thalamus, while also disentangling the mechanisms underlying the attentional enhancement of relevant stimulus input and those underlying the concurrent suppression of irrelevant input.

A key function of spatial attention is to select for further scrutiny the most relevant parts of the vast sensory input we experience continuously in life, thereby enhancing detection and discrimination of items occurring at an attended location (Posner, 1980). This enhanced processing is thought to rely on top-down signals from frontal and parietal cortex, which bias and, ultimately, amplify sensory processing of stimuli presented at the attended location relative to those at unattended locations (Corbetta and Shulman, 2002). To understand the neural mechanisms underlying spatial attention, human electrophysiology and neuroimaging have largely focused on cortical regions; however animal electrophysiology, clinical observations, and theoretical models have implicated the involvement of subcortical areas such as the superior colliculus and the pulvinar nucleus of the thalamus in the orienting of visual-spatial attention (LaBerge & Buchsbaum, 1990; Petersen et al., 1987; Karnath et al., 2002; Shipp, 2004; Saalmann and Kastner, 2011).

Here, we examined the cortical and subcortical mechanisms of anticipatory modulation of sensory cortex during voluntarily directed spatial attention. During cue-triggered visuospatial shifts of attention, spatially specific modulations are observed in occipital cortex; in particular, the effects in the two hemispheres depend on where in space one is attending. Studies utilizing fMRI have consistently shown relative blood-oxygenation-level-dependent (BOLD) signal increases in visual cortex contralateral to the direction of attention, interpreted as the enhancement of processing for the attended location of space. Likewise, event-related potential (ERP) (Harter et al., 1989; Hopf and Mangun, 2000) and event-related gamma-band (> 30 Hz) EEG oscillations (Ward, 2003; Jensen et al., 2007; Doesburg et al., 2008) over occipital scalp have been linked to

anticipatory enhancement in the contralateral visual cortex. In contrast, alpha-band EEG (~8-12 Hz) has a negative relationship with the BOLD signal, with increased alpha being linked to decreased BOLD activity and decreased cortical excitability (Goldman et al., 2002; Laufs et al., 2003; Scheeringa et al., 2012). Although earlier studies suggested that alpha-power decreases contralateral to the attended location lead to enhanced processing at that location (Yamagishi et al., 2005), subsequent studies have linked the underlying hemispheric asymmetry to alpha-power *increases* contralateral to the *to-be-ignored* location of space (Kelly et al., 2006; Rihs et al., 2007), supporting a role of alpha oscillations in relative suppression of irrelevant information in the environment.

Although it is clear that attending to a location in space produces spatially specific modulations of activity in visual cortex, it remains unclear whether the effects observed with fMRI and those observed with EEG reflect the same underlying neural mechanisms. Moreover, activity in subcortical structures is generally inaccessible with scalp EEG, due to their neuroanatomical structure (Nunez and Srinivasan, 2006). The modulatory effects of subcortical structures on cortical EEG, however, can be ascertained when EEG is recorded concurrently with fMRI (Huster et al., 2012) by examining the trial-to-trial covariations of the activity measured with the two methods. Here, we simultaneously recorded EEG and fMRI during a cued spatial attention task to link these EEG and fMRI modulations.

On each trial, a centrally presented directional cue predicted where a pair of to-be-discriminated target stimuli would appear (**Fig. 1**). Periods of cue-elicited spatially-specific modulations of occipital scalp EEG were identified and extracted in the alpha (8-12 Hz) and gamma (38-42 Hz) frequency bands on each trial. These single-trial

amplitudes were then covaried with the fMRI responses for the corresponding trials, revealing coordinated interactions between cortical and subcortical brain regions for the control of visual spatial attention.

--- Insert **Fig. 1** about here ---

Materials and Methods

Participants

Twenty-five participants took part in the study after providing informed consent. Data from 8 participants were unusable due to excessive movement artifacts in the fMRI (3 participants) or ocular artifacts in the EEG (5 participants). Data from the remaining 17 participants (12 female, mean age = 24.4 ± 3.5 years, all right handed with normal or corrected-to-normal vision) were used for analysis. All experimental protocols were approved by the Duke University Institutional Review Board.

Stimuli & Paradigm

Throughout the task a small fixation spot remained on the screen, along with rectangular box outlines in the left and right visual fields, approximately 7° from fixation, that served as attentional landmarks within which the target stimuli could be presented (**Fig. 1**). Participants were instructed to maintain fixation, and eye-movements were monitored to ensure proper fixation. Each trial started with an arrow cue presented at fixation for 250 ms. Left and right arrows served as attention-directing cues (Attend Cues) and were 100% predictive of the potential target location. On two-thirds of Attend-Cue trials a target display was presented for 50 ms, either at 750 ms (short-SOA) or

1500 ms (long-SOA) after cue onset. On one-third of trials no target display was presented (cue-only condition (Woldorff et al., 2004)). Target displays consisted of two shapes selected from a stimulus set of five shapes (box outlines of a "+", a "C", a "Z", and a mirror-reversed "C" and "Z"; see (Boehler et al., 2011)), presented within the cued landmark box. Participants indicated if the two shapes were identical (50% of target trials) or different (50% of target trials) by pressing a button with the right index or middle finger, respectively. An upward pointing arrow cue indicated that no target would appear on that trial (Interpret-Cue trial), thus serving as a control cue requiring the same sensory and meaning-interpretation as the Attend Cues but not engaging attentional orienting.

A total of 360 Attend Cue trials (60 for each of short-SOA, long-SOA, and cue-only for each of left and right cues) and 132 Interpret-Cue trials were presented. These trials were separated into three functional runs of 15 min each, with three 10-sec breaks within each run. The sequence of conditions was varied pseudo-randomly with discrete inter-trial intervals that varied between 4, 6, and 8 sec, with a mean of 5 sec. An additional 0-200 ms jitter was added to each trial to de-correlate the cue onsets from the onsets of the fMRI volume acquisitions.

fMRI acquisition and preprocessing

MRI data were acquired on a 3-Tesla GE MR750 system. A 3d spoiled-GRE sequence (EFGRE3D) without inversion-recovery preparation was used to acquire structural T1 images (0.9375 mm in-plane resolution, 1.2 mm slice thickness; field of view: 24cm*24cm*20cm; TR = 5.848, TE = 1.932, flip angle = 12°) for each participant.

Functional images were acquired with a customized inward spiral imaging sequence (TR = 2000 ms; TE = 30 ms; flip angle = 60°; slew rate = 120; 40 slices with 3 x 3 x 3 mm resolution; AC-PC orientation) that was modified to prevent saturation of the EEG amplifier during simultaneous recording. Each run consisted of 456 functional images, with the first five discarded to allow for reaching steady-state magnetization. No task was presented during the last eight volumes in order to fully sample the hemodynamic response to the last event.

All image preprocessing and analysis was performed using SPM8 (RRID: SCR_007037). Functional images were slice-time corrected, spatially realigned, and spatially normalized to the SPM template using the co-registered individual T1 images. Functional images were then resampled to a voxel size of 2x2x2 mm and smoothed with a 6mm full-width half-maximum Gaussian kernel.

Concurrent EEG acquisition and preprocessing

EEG data were acquired from 64 electrodes set in a custom electrode cap with extended scalp coverage (Woldorff et al., 2002), including 62 scalp recording sites, an electrode under the left eye for monitoring blinks and vertical eye movements, and an electrode on the upper back for recording the electrocardiogram (BrainAmp MR Plus, Brain Products GmbH, RRID: SCR_009443). Horizontal eye movements were detected using electrodes lateral to the left and right eyes. All signals were recorded with a band-pass of 0.016 – 250 Hz and digitized at 5000 Hz, referenced during recording to scalp-site Cz. Electrode impedances were lowered to below 5 kΩ prior to recording.

Removal of the MR gradient artifact and cardiac-pulse detection for ballistocardiogram (BCG) correction were performed in Brain Vision Analyzer 2 (Brain Products GmbH, RRID: SCR_009443). MR gradient artifacts were removed using an average template-subtraction method (Allen et al., 2000). An fMRI slice-based template of the artifact was created from a sliding average of 191 50-ms epochs, which was then subtracted from the EEG segment time-locked to each slice acquisition. The EEG was then low-pass filtered to 100 Hz and downsampled to 500 Hz. Pulse-detection using the ECG channel was then performed using a semi-automatic template-matching procedure. The resulting markers were manually reviewed and adjusted, and the EEG exported for subsequent analysis in MATLAB (RRID: SCR_001622). Removal of the BCG artifact was performed using the Optimal Basis Set procedure implemented in the FMRIB plugin for EEGLAB (Niazy et al., 2005), using the top 4 principal components for correction.

The artifact-corrected EEG was then segmented into 3.5 sec epochs (1 sec pre-stimulus to 2.5 sec post stimulus) time-locked to cue onsets and manually inspected to detect any trials containing blinks, eye-movements, or excessive noise. All participants used in the analysis had at least 70% of trials retained after artifact rejection. Data were then digitally re-referenced to the average of all scalp channels.

EEG-fMRI covariation

Because low-amplitude ERP components can be difficult to detect in single-trial data (Jung et al., 2001), we focused specifically on time-frequency effects to improve signal-to-noise in our single-trial measurements and home in on the attentional

suppression and enhancement processes previously associated with the alpha and gamma bands, respectively. EEG epochs were transformed into the time-frequency domain in EEGLAB (RRID: SCR_007292) using an FFT approach with Hanning window tapering. Because we were interested in how the change in alpha and gamma power on each trial related to changes in the fMRI BOLD signal, single-trial data were normalized using the 200-ms pre-stimulus baseline period for each epoch. Mean event-related spectral perturbations across all participants were calculated for occipital electrodes (TO1/2, P3i/4i, O1'/2', PO1/2) ipsilateral and contralateral to the to-be-attended direction in two frequency ranges of interest, alpha (8-12 Hz) and gamma (38-42 Hz), and used to identify time windows of interest for further analysis. However, averaging of individually-baselined epochs of power, which are necessarily positive, produces an overall positive shift in mean power (Grandchamp and Delorme, 2011). Although this positive shift changes the overall morphology of the average ERSP waveform, it does not impact the timing or frequency of the significant contralateral vs. ipsilateral differences, which were our main focus here. For display purposes and to facilitate comparison with previous studies (e.g., Kelly et al., 2006; Rihs et al., 2007; Yamagishi et al., 2005), we also calculated mean event-related spectral perturbation (ERSP) responses with baseline correction performed after averaging across trials (see Fig. 3). Three time-frequency windows were chosen for covariational analysis as they showed significant (all p's < .05) contralateral vs. ipsilateral differences in occipital scalp activity -- 800-1200 ms post-cue for the alpha band, and 400-600 ms and 1200-1400 ms for the gamma band.

The single-trial values were then extracted for each time-frequency window for both ipsilateral and contralateral electrode sites and included as parametric modulators in the SPM regression analyses. For each cueing condition (Right Short-SOA, Long-SOA, and Cue-Only; Left Short-SOA, Long-SOA, and Cue-Only; Interpret Cues), fMRI BOLD responses were modeled by a canonical hemodynamic response function with temporal and dispersion derivatives. Parametric modulators were included for Right and Left Long-SOA and Cue-Only trials. The short-SOA trials were included in the design to encourage participants to shift attention to the cued location as quickly as possible but were not included in the covariation analyses. Rest breaks were also modeled as regressors of no interest. These regressors were then entered into a general linear model along with the six realignment parameters for each run.

Separate GLMs were constructed to model covariation for each time-frequency component (contralateral and ipsilateral for early gamma, alpha, and late gamma). For each analysis, we created contrasts to examine covariation for leftward and rightward shifts of attention separately in order to evaluate activity that varied with the direction of attention, as well as collapsed across leftward and rightward shifts to evaluate activity common to all attentional shifts. The analyses utilized a voxel-wise threshold of $p < .001$ (uncorrected), with an extent threshold of $k > 25$ contiguous voxels. We also examined the results of the combined analyses using a smaller extent threshold of $k > 10$ due to the possibility of observing non-lateralized activations in the small thalamic and midbrain structures that would not be visible with larger extent thresholds, but no additional subcortical activations were identified with this lower threshold.

Attention control regions were identified by contrasting Attend Cue vs. Interpret Cue BOLD activity. Spatially-specific activation of occipital cortex was assessed by contrasting BOLD activity on Left-Cue Attend trials with Right-Cue Attend trials (Long-SOA and Cue-Only). For BOLD-only contrasts a threshold of $p < .01$ (FDR corrected) and an extent threshold of $k > 25$ were applied. Significant clusters of activity from the Attend Cue vs. Interpret Cue contrast were used to create functional ROIs in occipital and parietal cortex using MarsBaR (Brett et al., 2002; RRID: SCR_009605)(see Table 1).

--- Insert Table 1 about here ---

Results

Standard fMRI analysis confirmed greater activation of the typical attention network in response to Attend Cues relative to Interpret Cues (**Fig. 2**), including increased BOLD signal in occipital and parietal cortices, inferior and superior frontal cortex, anterior insula, and the thalamus. Contrasts of responses to the Attend-Left and Attend-Right Cues yielded expected relative increases in BOLD signal in the visual cortex contralateral to the direction of attention.

--- Insert **Fig. 2** about here ---

Event-related spectral perturbation (ERSP) values for the alpha (8-12 Hz) and gamma (38-42 Hz) activity time-locked to the cue onsets were extracted from four posterior scalp electrodes over each hemisphere. A comparison between electrodes ipsilateral and contralateral to the cued direction was used to identify time windows of the oscillatory EEG for covariation analyses with the BOLD signal. Alpha power was greater ipsilateral to the cued direction beginning ~600 ms after cue onset and lasting

until the end of the cue period (i.e., until target onset on trials with long cue-target intervals; **Fig. 3**). Gamma power was greater contralateral to the cued direction in the two time intervals: 400-600 ms and 1200-1400 ms (**Fig. 3**). Thus, for covariation analysis we selected three non-overlapping time-frequency periods: Early Gamma (38-42 Hz; 400-600 ms), Alpha (8-12 Hz; 800-1200 ms), and Late Gamma (38-42 Hz; 1200-1400 ms). Single-trial power values in these windows contralateral and ipsilateral to the direction of attention were then included as parametric modulators in the general-linear-model (GLM) analyses to identify voxels in the brain where the fMRI BOLD signal covaried with the EEG power on a trial-to-trial basis.

--- Insert **Fig. 3** about here ---

Pulvinar modulates attention-related changes in occipital EEG

In the early time interval (400-600 ms post cue onset), gamma activity over occipital scalp contralateral to the direction of attention showed a positive covariation with BOLD signal in low-level visual cortex, left insula, and bilateral pulvinar (**Fig. 4**), regardless of the direction of attention. In contrast to the clear contralateral-vs-ipsilateral differences in the early gamma-band occipital EEG on the scalp (**Fig. 3**), no significant lateralizations for the early gamma-band / fMRI covariations with respect to the direction of attention were seen in occipital cortex.

The covariation observed in the pulvinar was particularly interesting, as this subcortical structure, due to its anatomical geometry, does not produce an open field that can be picked up at the scalp, thereby making it inaccessible to direct EEG measures (Nunez and Srinivasan, 2006). Thus, the observed covariation in the pulvinar likely results from it modulating cortical activity that is then picked up by EEG. The

pulvinar has been previously implicated in shifting spatial attention (Petersen et al., 1987; LaBerge and Buchsbaum, 1990) and the suppression of irrelevant information (Strumpf et al., 2012). Moreover, the pulvinar has been linked to the regulation of alpha oscillations and alpha-gamma cross-frequency coupling in visual cortex in monkeys (Saalmann et al., 2012), and to the generation of resting-state occipital alpha oscillations in human EEG-fMRI studies (Liu et al., 2012). Yet, given the lack of a direct scalp-level activity measure, the attentional modulation of occipital alpha is often attributed to frontal and parietal cortical structures without reference to the thalamus at all (Corbetta and Shulman, 2002; but see Shipp, 2004).

To further examine the role of the pulvinar in attentional control, we created functional ROIs for the left and right pulvinar derived from the early-latency gamma-covariation results (see **Fig. 4**) and examined the alpha and late-gamma covariations within these ROIs. Unlike early gamma, where covariation was present bilaterally in the pulvinar for both left and right cues, significant cue-direction X hemisphere interactions were found for both ipsilateral alpha ($F = 7.44$, $p = .015$) and late contralateral gamma ($F = 4.51$, $p = .05$) covariations (main effects of cue direction and hemisphere were all non-significant, p's > .49). These alpha and late-gamma covariation effects, however, were in opposite hemispheres. Alpha power over occipital scalp ipsilateral to the direction of attention covaried positively with the BOLD signal in the ipsilateral pulvinar, whereas gamma power over contralateral occipital scalp covaried positively with the BOLD signal in the contralateral pulvinar. Notably, EEG from the opposite scalp sites (contralateral scalp for alpha and ipsilateral scalp for gamma) showed no significant covariation in the pulvinar (all p's > .63).

--- Insert **Fig. 4** about here ---

Alpha and gamma reflect distinct mechanisms for anticipatory modulation of visual cortical activity

Alpha and late-Gamma activity covaried with BOLD signal in occipital cortex, but the lateralization with respect to the direction of attention was reversed for the two frequency bands (**Fig. 5**). Ipsilateral increases in alpha power on the scalp were related to decreased BOLD signals in ipsilateral visual and parietal cortices. Conversely, contralateral increases in late gamma power on the scalp were related to increased BOLD signals in contralateral visual cortex. Neither contralateral alpha nor ipsilateral gamma significantly covaried with BOLD responses.

--- Insert **Fig. 5** about here ---

These alpha and gamma covariations also appeared to occur in distinct regions of visual cortex, with the alpha covariations occurring in more medial and posterior regions of occipital cortex and the gamma covariations in more lateral and anterior regions. This pattern suggests a hierarchical distinction in attentional suppression vs. enhancement. For example, suppression of irrelevant information could take place at lower levels of processing, reducing processing of information from the to-be-ignored visual field earlier in the processing stream, whereas efficient target enhancement could

happen at higher levels of visual processing specific to the relevant features of the target (Slagter et al., 2015).

It is possible, however, that BOLD-EEG covariation in the occipital lobes actually does occur in the same locations for both the alpha and gamma frequencies, but appears distinct in the whole-brain analyses due to individual variability, along with sensitivity limitations in such analyses. Thus, we examined covariational activity for early contralateral gamma, ipsilateral alpha, and late contralateral gamma within functional ROIs constructed from significant clusters observed in the alpha covariation analysis, and in occipital and parietal ROIs delineated in the Attend Cue vs. Interpret Cue fMRI BOLD contrast (**Fig. 6**). If the distinct alpha and gamma covariations are the result of poor sensitivity in the whole-brain analysis, then spatially-specific covariations should be observed for both the alpha and late gamma within the two sets of occipital ROIs. In contrast, if alpha and gamma activity recorded at the scalp indeed reflects the targeting of distinct visual areas for attentional suppression versus for attentional enhancement, respectively, then spatially-specific alpha and gamma covariations should occur in distinct ROIs.

As can be seen in **Fig 6**, no spatially specific activity (i.e., no cue-direction X hemisphere interaction) was apparent for either the early or late gamma covariation within the alpha-derived ROIs. Within the occipital BOLD ROIs, however, spatially-specific activity was observed, but only for the late contralateral gamma covariation. Within the parietal BOLD ROIs, significant covariations with early gamma were observed in both hemispheres for both left and right cues, but the activity was not spatially specific, mirroring the spatially non-specific activity observed in the pulvinar

during this same time-frequency window. Together, these results demonstrate that spatially-specific attentional modulations in the alpha and late gamma EEG are related to distinct BOLD modulations in different areas of visual cortex. More specifically, scalp-measured changes in contralateral gamma are most closely related to the increased BOLD observed contralateral to the to-be-attended location in space. Alpha, on the other hand, shows an inverse relationship with BOLD signal in early visual cortex ipsilateral to the to-be-attended location in space, providing further evidence that increases in alpha specifically reflect a mechanism for suppressing neural activity for to-be-ignored locations.

--- Insert **Fig. 6** about here ---

Discussion

For both the alpha-band and late gamma-band EEG observed on the scalp, spatially-specific modulations of activity in anticipation of an upcoming stimulus were related to modulations of the BOLD signal in the pulvinar and occipital cortex. The fact that the pulvinar does not have the neuroanatomical geometry to be a primary generator of the scalp EEG activity itself (Nunez and Srinivasan, 2006) suggests that the covariational activity pattern in this subcortical structure reflects its possible role as a regulatory control structure, sending spatially specific signals to modulate the excitability of visual cortex. It is possible that these covariations arise due to the pulvinar maintaining a condensed representation of visual cortex activity (Shipp, 2001). However, given recent evidence that the pulvinar is involved in filtering distracting information (Fischer & Whitney, 2012; Strumpf et al., 2012) and regulates cortical alpha oscillations

as well as alpha-gamma cross-frequency coupling in visual cortex (Saalman et al., 2012), we suggest it is more likely that the pulvinar is involved in directly modulating visual cortical activity.

The covariations in the pulvinar were all positive, but occurred in opposite hemispheres relative to the direction of attention for the different frequency bands: Increased alpha over ipsilateral scalp was linked to increased fMRI activity in the ipsilateral pulvinar as well as to decreased fMRI activity in ipsilateral occipital cortex. Such a pattern is consistent with the hypothesis that increased alpha indexes suppression of activity in the hemisphere that processes the to-be-ignored region of space, and that this suppression is orchestrated, at least in part, by thalamocortical connections from the pulvinar (Saalmann et al., 2012). In contrast, in the hemisphere processing the to-be-attended location, increased gamma late in the cue-target interval was linked to increased fMRI activity in the contralateral pulvinar and occipital cortex, suggesting that the thalamocortical connections between the pulvinar and occipital cortex can both suppress and enhance processing.

One question that arises from these results, however, is why activity in the pulvinar is rarely observed in fMRI studies of spatial orienting, despite some early PET (LaBerge and Buchsbaum, 1990) and animal (Petersen et al., 1987; Saalmann et al., 2012) studies that have suggested the pulvinar plays a key role in shifting attention. Many fMRI studies of voluntary spatial attention have not reported thalamic activity in response to attention-directing cues, focusing instead on activations observed in attentional control regions in the frontal and parietal cortices, and for those that have reported thalamic activity the attentional modulations were either not limited to the

pulvinar part of the thalamus or did not show any spatial specificity (Kastner et al., 2004; Woldorff et al., 2004). As a result, anticipatory modulation of visual cortex is typically attributed to direct cortical input from these frontal and parietal regions (Liu et al., 2014; Marshall et al., 2015), whereas the pulvinar tends not to be included in many of the most commonly cited models of attention control (Corbetta and Shulman, 2002; Capotosto et al., 2009).

Our results provide evidence that the pulvinar does in fact play a role in the shifting of spatial attention, while also providing possible explanations for why this activity is typically not observed in traditional fMRI studies. First, the covariations with alpha occurred in the pulvinar ipsilateral to the direction of attention, while covariations with gamma occurred in the contralateral pulvinar, with both of these cortical EEG measures covarying with increases in the pulvinar BOLD signal. Without the ability to separate the signals in the two hemispheres based on EEG frequency, any pulvinar activity would thus appear to be bilateral for both leftward- and rightward-directing cues, rather than being spatially-specific (e.g., Kastner et al., 2004). Second, the covariations between the EEG and the pulvinar BOLD were time- and frequency-limited, as evidenced by the lack of spatially-specific covariations in the early gamma time window. Activity in the pulvinar may be too short-lived to produce a strong event-related BOLD signal, or activity related to different time-frequency effects could cancel each other out in the slow event-related fMRI response. Finally, it is possible that the BOLD activity in the pulvinar varies from trial-to-trial with respect to attention, but that this variation simply averages out to a near-zero (or near baseline) value and thus is not observed in the average BOLD signal difference between conditions.

These considerations point to the value of combining multiple methods to investigate the role of thalamocortical communication in controlling attention. FMRI alone has not heretofore been able to delineate the contributions of the pulvinar in this type of top-down attentional control, and scalp-recorded EEG cannot be used to directly measure neural activity in this subcortical structure (Nunez and Srinivasan, 2006). By recording the EEG concurrently with fMRI we were able to implicate the pulvinar as a control structure involved in the modulation of spatially-specific occipital oscillatory EEG and cortical activation observed during visuospatial shifts of attention, presumably in conjunction with the attentional control regions in the frontal and parietal cortices.

A second important finding from this covariational analysis is that the attentional suppression (alpha) and enhancement (gamma) effects were observed in distinct regions of visual cortex, rather than simply in homologous regions of the two hemispheres. Positive covariations between BOLD signal and occipital gamma-band EEG most closely corresponded to the task-related changes in the average BOLD signal observed with fMRI alone, consistent with previous studies relating BOLD signals and gamma-band EEG (Logothetis et al., 2001; Foucher et al., 2003; Lachaux et al., 2007). These gamma covariations occurred contralateral to the attended location, consistent with increased neuronal excitability in visual cortical regions that will process the upcoming targets**.** In contrast, the BOLD signal covaried inversely with occipital alpha-band EEG ipsilateral to the attended direction, representing decreased excitability in visual cortex processing of to-be-ignored locations, but these alpha covariational effects occurred in distinct regions from those observed in the average BOLD and

occurred earlier in time than the gamma-related enhancement of to-be-attended locations.

Lastly, an additional factor to consider here is that, given that visual placeholders were present throughout the task, it is possible that participants were specifically suppressing the placeholder as a distractor object, akin to the distractor suppression by the pulvinar that has been observed in visual search (e.g., Fischer & Whitney, 2012; Strumpf et al., 2013). Cue-elicited anticipatory modulations of alpha-band EEG are still observed in the absence of spatial landmarks (e.g., when suppressing an entire sensory modality; Fu et al., 2001), suggesting that visual landmarks may help one home in on the spatial location to be suppressed (i.e., increase precision), but are not necessary for suppression to occur. Further studies without placeholders would be required to determine if having a visible object to suppress is necessary to observe this ipsilateral pulvinar activity.

The spatial and time-frequency separation of these effects suggests that attentional suppression and enhancement happen at different points in time in the processing cascade and operate at different levels of visual processing. We suggest that these two attentional mechanisms are deployed in a flexible and adaptive manner based on the demands of the task. In the present study, the entire uncued hemifield was always task-irrelevant (i.e., a target would never appear at the uncued location), such that early visual processing for that region of space, or at least from within that visual placeholder, could be rapidly suppressed to limit any distraction from that side. Rather, our task required participants to perform a difficult discrimination of two objects at the cued location, and thus the effects may have included attentional enhancement

specifically in areas necessary for optimal target-discrimination performance. Variations in the task demands would likely lead to other patterns of modulation in occipital cortex, with the coordination of suppression and enhancement involving the thalamocortical connections from the pulvinar to the relevant occipital regions. Future studies using multimethodological approaches will be helpful for further delineation of the subcortical-cortical coordination of attentional control and influence in humans.

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606

607 **Figure Legends**

608 **Figure 1.** Schematic diagram of a target-present trial (see text for details).

609 **Figure 2.** Average BOLD signal ($p < .01$, FDR corrected, $k=25$). Attentional control
610 regions identified from the Attend Cue vs. Interpret Cue BOLD contrast (top row) and
611 spatially-specific occipital activations identified from contrasting activity for leftward-
612 directing versus rightward-directing cues.

613 **Figure 3.** Average event-related responses and scalp topographies of contralateral-
614 minus-ipsilateral differences for alpha-band (top) and gamma-band (bottom) EEG. Light
615 grey boxes denote time windows with significant ($p < .05$) differences between
616 ipsilateral and contralateral electrodes that were used for covariational analyses.

617 **Figure 4.** Covariations in the Pulvinar. Early gamma for attend cues (left and right)
618 positively covaried with BOLD signal in the pulvinar and early visual cortex ($p < .001$
619 uncorrected, $k > 25$; top panel). This contrast was then used to create functional ROIs in
620 the left and right pulvinar (bottom panel). Both ipsilateral alpha and late contralateral
621 gamma showed spatially specific positive covariations in the pulvinar ROIs (significant

cue direction X hemisphere interaction). Early gamma covariations are shown for comparative purposes only, as these regions were defined by having significant early gamma covariation activity. *= p < .05, ** = p < .01

Figure 5. Covariation between BOLD and ipsilateral alpha (top) and contralateral late gamma (bottom). Alpha was negatively correlated with occipital and parietal BOLD activity in the hemisphere ipsilateral to the cued location, whereas late gamma was positively correlated with occipital BOLD signal contralateral to the cued location. (p < .001 uncorrected, k = 25).

Figure 6. Covariations within functional ROIs based on the alpha covariation (cyan and blue bars) and occipital (red and orange bars) and parietal (purple and magenta bars) BOLD responses. Spatially-specific alpha and late-gamma covariations (significant hemisphere X cue direction interaction) occurred in distinct regions of visual cortex. Alpha covariations within the alpha-defined ROIs are shown for comparative purposes only, as these regions were defined by having significant alpha covariation activity. Some evidence of spatially-specific covariations was also seen in the parietal regions for alpha and late gamma, but these interactions did not reach significance. *= p < .05, ** = p < .01, *** = p < .001

Tables

Table 1. Locations of functional ROIs

Region	Peak Voxel Location (MNI) x	y	z	Cluster Size (voxels)
BOLD: Attend Cue – Interpret Cue				
Left Occipital	-42	-60	-8	493
Right Occipital	34	-66	-12	520
Left Parietal	-24	-58	46	282
Right Parietal	26	-54	52	108
Covariation: Ipsilateral Alpha				
Left Occipital	-26	-86	0	128
Right Occipital	38	-80	-4	290
Covariation: Early Contralateral Gamma				
Left Pulvinar	-14	-30	4	60
Right Pulvinar	14	-34	6	79

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