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Smith, Mary E.

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Investigating mechanisms of spatial and temporal selective visual attention

A dissertation submitted in partial satisfaction of the
requirements for the Degree Doctor of Philosophy

in

Psychology

by

Mary E. Smith

Committee in charge:

Professor John T. Serences, Chair
Professor Michael Gorman
Professor Donald MacLeod
Professor Ayse Saygin
Professor Bradley Voytek

2017

The dissertation of Mary E. Smith is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Chair

University of California, San Diego

2017

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VITA

Education

UC San Diego (2011 - 2017)
Ph.D. in Experimental Psychology
M.A. in Experimental Psychology (2013)

Carnegie Mellon University (2003-2008)
B.A. in Music Technology, with a minor in Psychology

Work Experience

Stanford University (2010)
Research Assistant

University of Pennsylvania (2008-2010)
Research Assistant

Carnegie Mellon University (2008)
Research Assistant

Publications

Witthoft, N., Poltoratski, S., Nguyen, M., Golarai, G., Liberman, A., LaRocque, K.F., **Smith, M.E.**, & Grill-Spector, K. (2016). Reduced spatial integration in the ventral visual cortex underlies face recognition deficits in developmental prosopagnosia. bioRxiv.

Witthoft, N., Nguyen, M., Golarai, G., LaRocque, K.F., Liberman, A., **Smith, M.E.**, & Grill-Spector, K. (2013). Where is human V4? Predicting the location of hV4 and VO1 from cortical folding. Cerebral Cortex.

LaRocque, K.F., **Smith, M.E.**, Carr, V.A., Witthoft, N., Grill-Spector, K., & Wagner, A.D. (2013). Global similarity and pattern separation in the human medial temporal lobe predict subsequent memory. Journal of Neuroscience. 33: 5466–5474.

Troiani, V., Stigliani, A., **Smith, M.E.**, & Epstein, R.A. (2012). Multiple object properties drive scene selective regions. Cerebral Cortex.

ABSTRACT OF THE DISSERTATION

Investigating mechanisms of spatial and temporal selective visual attention

by

Mary E. Smith

Doctor of Philosophy in Psychology

University of California, San Diego, 2017

Professor John T. Serences, Chair

Selective attention in vision undoubtedly uses many different types of mechanisms to achieve better processing of behaviorally relevant visual information. The present dissertation inspects two such possible mechanisms. The first proposed mechanism is through selective spatial attention. We proposed that "attentional control" regions of the brain send selective attention signals that relate to the differential attentional modulation measured in visual cortex, corresponding to the attended and ignored sides of visual space. We find, surprisingly, that the BOLD signal of attentional control regions do not appear to code for selective spatial attention in this manner. fMRI signals therefore appear to prioritize general arousal effects of attention more so than the types of attentional control signals that frontoparietal regions send to early visual cortex. The second proposed mechanism is through sampling visual information through time. It is hypothesized that intrinsic neural oscillations represent inhibitory waves of cortical processing ability, in which subjects are more or less able to detect visual stimuli depending on the phase of α oscillations in the brain. We used a paradigm involving visual entrainment; this paradigm has been used in the past to support the "pulsed inhibition of α" hypothesis. We find that the behavioral effects of this paradigm cannot strongly be supported by the pulsed inhibition of α because the neural effects of visual entrainment are transient and do not carry over into the target period.

CHAPTER 1

Introduction to the Dissertation

1.1 Mechanisms by which selective attention can modulate activity in early visual cortex

The visual scene is filled with information, both relevant and irrelevant to our behavioral goals. The brain is able to selectively process relevant stimuli in this mass of information through selective attention, and there are many ways in which this process might occur. In this dissertation, I will explore two general possibilities for the way in which selective attention affects the brain's processing of visual information.

One mechanism is through spatial selective attention in which "attentional control" regions of the brain provide feedback to visual cortex through different activity levels corresponding to different regions of (relevant) visual space. In Experiment 1 (Chapter 2) of the dissertation, humans performed a spatial attention task while in a functional magnetic resonance imaging (fMRI) scanner, and we compared the activity levels of attentional control regions with differential attention-related modulations in early visual regions.

The other selective attention mechanism is through rapid oscillations of selective temporal processing. This is hypothesized to work through intrinsic oscillations across brain regions, coordinating information processing according to the timing of inhibitory waves in the alpha band of frequencies. We examined this through a psychophysics (Experiment 2) and an electroencephalography (EEG) experiment (Experiment 3) in which human subjects perform a target detection task, covered in Chapter 3 of the dissertation, and the second part of this introduction.

1.2 Frontoparietal contribution to early visual modulations

Spatial attention, a widely studied branch of selective attention, can be examined between different regions of the brain. Discussed below are several experiments investigating the means of communication between selective attentional control regions and regions that process visual inputs.

Visually selective responses in the brain can be augmented by attention in different ways when attentional demands increase, compared to conditions of passive viewing and the absence of attentional demands. For example, neurons from visual cortex (VC) regions V1-V4 in the macaque monkey show a variety of response modulations for attended locations in visual space relative to ignored ones: attention increases the firing rate of cells, a process known as *gain modulation* (Motter, 1993; McAdams and Maunsell, 1998; Reynolds et al., 2000; Martinez-Trujillo and Treue, 2004; Reynolds and Chelazzi, 2004; Noudoost et al., 2010; Squire et al., 2013). This can be a multiplicative gain modulation, in which the preferred stimulus feature is selectively more increased than non-preferred features (e.g., see Motter, 1992). Gain can also be additive, meaning neuronal firing rate increases uniformly across both preferred and non-preferred stimuli (see **Figure 1-1a** and **Figure 1-1b** for illustration of additive and multiplicative shifts, respectively, in the orientation tuning functions of neurons). Furthermore, attention can decrease noise correlations and/or fano factor of spike rates (the ratio of variance to mean spike rate over a period of time) (Herrero et al 2013, Mitchell et al 2007, Niebergall 2011, Mitchell et al 2009), lead to faster response times in spikes and the local field potential (Lee et al., 2007; Sundberg et al., 2012), and also increase synchrony or coherence of spike timing between neurons (Cohen and Maunsell, 2009). In addition to changes in the shape of the orientation tuning functions due to additive and multiplicative gain, selective attention has also been shown to result in changes in the bandwidth of the tuning function (see **Figure 1-1c**; Saproo and Serences, 2010).

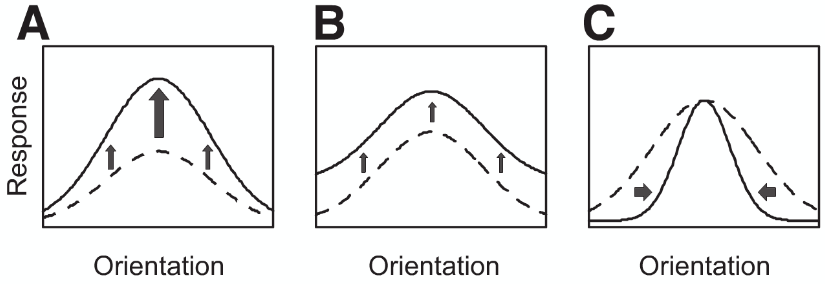

Figure 1-1: Taken from (Saproo & Serences, 2010), this figure demonstrates three types of feature (orientation) selective changes in the shape of the tuning function. a) multiplicative shift in amplitude reflects a selective gain of preferred orientations; b) additive shift in the baseline + amplitude reflects non-specific gain across all stimulus orientations; c) narrowing of the bandwidth of the tuning function reflects suppression of non-preferred orientations.

Similar to findings from single cell recordings in monkeys, homologous visual regions of the brain in humans, as measured by fMRI, have primarily shown increased BOLD response with selective attention (e.g., (Mangun et al., 1998; Chawla et al., 1999; Gandhi et al., 1999; Hopfinger et al., 2000; Kastner and Ungerleider, 2000; Saproo and Serences, 2010; Scolari et al., 2012). Others have shown increased functional connectivity in BOLD response between regions of cortex and subcortex (Saalmann and Kastner, 2011). Under attention conditions orientation tuning functions often show additive as well as multiplicative gain (Saproo and Serences, 2010; Scolari et al., 2012; Sprague and Serences, 2013).

1.3 A theory of attentional control: frontoparietal contributions

How do these different modulations come about? Many have proposed that visual attention-dependent modulations in VC seem to be driven by other regions of cortex, dubbed attentional control regions (Moore, 2006; Yantis, 2008). These regions, such as the frontal eye fields (FEF) and the intraparietal sulcus (IPS), collectively referred to as frontoparietal (FP) cortex, are thought to provide feedback to occipital VC with information about *where* or *what* to allocate attention within the visual scene. All of the different types of attentional modulations described above have been measured by behaviorally directing an animal's attention in one of several ways. To investigate the causal role of the attentional control regions during these modulations in VC, researchers have used electric microstimulation (EM) of neurons in monkeys. This involves injecting an electrical current into cells, resulting in increased firing of those cells, and other more distal cells that communicate with cells in the stimulated region.

Findings using EM show that when a particular FP region in the brain is electrically stimulated, this leads to modulations in VC that are similar to endogenous attention in occipital visual cortex. Thus, the stimulated region in FP cortex must be feeding information to VC under endogenous conditions as well. Many EM studies support the claim that selective attentional control originates from FP regions, which are able to modulate visual responses from afar. Regions for which this holds true have been found mostly in FP cortex, and often are retinotopically organized (such as the IPS) or related to eye movements (FEF). Tying together these ideas, (Premereur et al., 2013) showed increased occipital fMRI activity with FEF-microstimulation and showed that it was task-dependent. Importantly, EM of the FEF leads to better behavioral performance, which in turn mimics changes in behavioral responses observed when endogenous attention is voluntarily directed towards that receptive field (Armstrong & Moore, 2007).

Measures of functional connectivity in human neuroimaging include time series correlation and Granger causality (Gregoriou et al., 2009). Granger causality also aims to infer the direction of signals by calculating which brain region's time series appears to precede the other in time; thus the direction of a given signal can be inferred to start in one region and travel to the other. In monkey physiology, functional connectivity can be investigated by looking at the coherency between spike times and/or between local field potential signals (Ramalingham et al., 2013), and synchrony of signals, such as in the gamma frequency of the LFP (Bichot et al., 2005; Buffalo et al., 2011). While previous data in humans using large-scale neuroimaging techniques have shown correlations between FP regions and VC regions, with more activation in both during selective attention, it leaves the question of the mechanism of this activity open. Thus, Experiment 1 (Chapter 2) of the dissertation aims to answer whether we can use activity levels in FP regions to predict different types of selective spatial attentional modulations in occipital VC.

1.4 The importance of oscillations in visual perception & selective attention

Our exposure to the visual world is continuous, and our visual perception feels continuous, but our behavioral and cortical sensitivity to visual stimuli over time has been shown to wax and wane very quickly, at a rate of about 7-12 Hz (a band of frequencies called *alpha* oscillations). Researchers have claimed that sampling the visual world at around 10 Hz could explain the appearance of a visual illusion called the wagon wheel effect. The wagon wheel illusion – in which a wagon wheel rotates faster and faster until it appears to change directions and start rotating backwards – demonstrates how digital (or discrete) sampling through a camera lens can change our perception of the direction of rotation. At certain speeds, the wheel's axels will turn slightly more than a full rotation between the frames sampled by a video camera, which then makes the axels appear to move in the opposite direction. This illusion also surprisingly occurs with the naked eye, suggesting that our perception, like digital cameras, samples the world over time rather than continuously (VanRullen et al., 2006; Blais et al., 2013).

Oscillations in the brain, as can be measured through electrodes within the brain, or EEG or MEG outside the brain, have shown relevance for both visual perception and selective attention. For example, single stimuli are able to produce a wave of repeating oscillations in the brain: (Bartley and Bishop, 1932) sent an electrical impulse to the severed optic nerve of rabbits while measuring multi-unit neuron responses in the occipital visual cortex with an electrode. A single electrical impulse into the optic nerve (representing a single visual stimulus) resulted in 5 waveforms in visual cortex across one second of time: a 5 Hz rhythm. Similarly, (Chang and Kaada, 1950) found that single electrical stimulation of the optic nerve in cats leads to several oscillations in visual cortex. Although there is variability in the frequency of oscillations, these findings suggest the importance of oscillations in sensory perception even to single stimuli.

Going beyond relating alpha oscillations to general visual perception, this band of frequencies has shown specific importance during temporal selective attention. For example, the power of alpha oscillations has repeatedly shown a negative relationship with behavioral attention. Subjects are able to actively suppress the power of their alpha activity while they are selectively attending to a stimulus compared to when they are not engaging in selective attention (e.g., Berger 1929, Adrian and Matthews, 1934). Subjects also show a graded lateralization of alpha synchronization in line with spatial certainty about the location of a target (Gould et al., 2011). In addition, intrinsic alpha oscillations have shown to vary with detection rate in temporal attention tasks (Ergenoglu et al., 2004; van Dijk et al., 2008; Busch et al., 2009; Mathewson et al., 2009). Many have hypothesized that alpha waves act as an attention suppression mechanism in which brain regions processing irrelevant information utilize increased alpha power (Foxe and Snyder, 2011). Thus there appears to be an inverse relationship between alpha power and behavioral selective attention through time.

The alpha band of frequencies has also demonstrated its relevance to visual perception more so than other frequency bands in several manners. One example is through external stimulus perception at different flicker frequencies. (Bartley, 1939) conducted a study in which human subjects judged the brightness of a stimulus that flashed in several different frequency bands. When the flickering occurred around 10 Hz, subjects perceived the overall brightness to be twice as bright as a continuously presented stimulus with no flickering despite the fact that all stimuli were the same brightness and contrast level. At higher and lower than 10 Hz flashing, subjects' perceived brightness was lower than continuous stimulation, and at around 17 Hz, perceived brightness was the same. In other words, when stimuli flicker at around 10 Hz, they are perceptually enhanced compared to other frequencies, even including a continuous presentation without flickering. This increased perceived brightness in alpha frequencies supports the idea that alpha frequencies might be better perceived than others.

Another example is through cortical excitability cycles that occur in the alpha band. Chang (1951) recorded auditory cortex in cats after single electrical stimulation followed by a single auditory stimulus and recorded the response in auditory cortex via single unit recording. He tested the refractory period of the cortical response via first stimulating auditory cortex with an electrical impulse, then an auditory stimulus across many different temporal intervals. The conditioning shock stimulus elicited an event related potential (ERP) that was the same as the evoked response to the auditory stimulus when presented in isolation. So, varying the timing between these two stimuli enabled him to measure the refractory period after which the cortex was able to respond at the same amplitude for the auditory stimulus as for the conditioning shock stimulus. He found that the cortical excitability of auditory cortex, which was defined as the amplitude of the stimulus signal compared to the amplitude of the conditioning stimulus, waxed and waned at a rate of about 10 Hz (see **Figure 1-2** for different amplitudes of evoked responses and **Figure 1-3** for excitability cycles from Chang 1951). Given that cortex has a short refractory period after a conditioning stimulus, it appears that cortical excitability oscillates over time, depending on the timing between two (or more) external stimuli. Note however that this experiment only demonstrates excitability cycles in cortex, not in behavior; furthermore, these excitability cycles are not tied to intrinsic alpha oscillations in the brain.

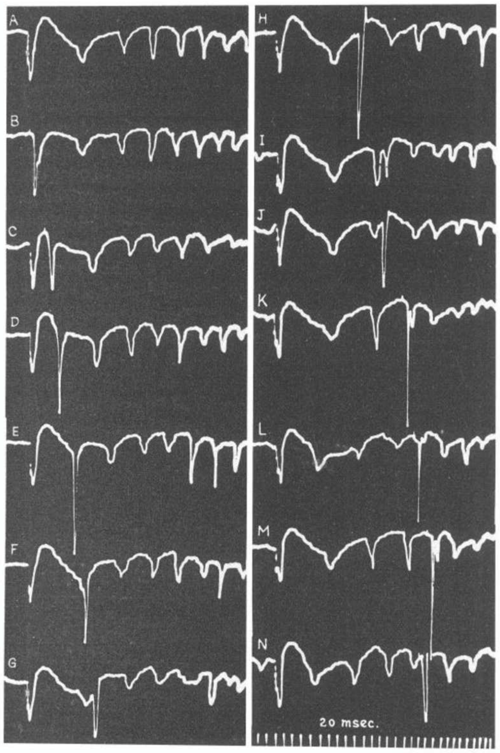

Figure 1-2: Chang (1951) shows different SOA times between a conditioning and auditory stimulus at different stimulus onset asynchronies. The magnitudes of the evoked potentials to the auditory stimulus are modulated according to the timing between the conditioning stimulus and the auditory stimulus.

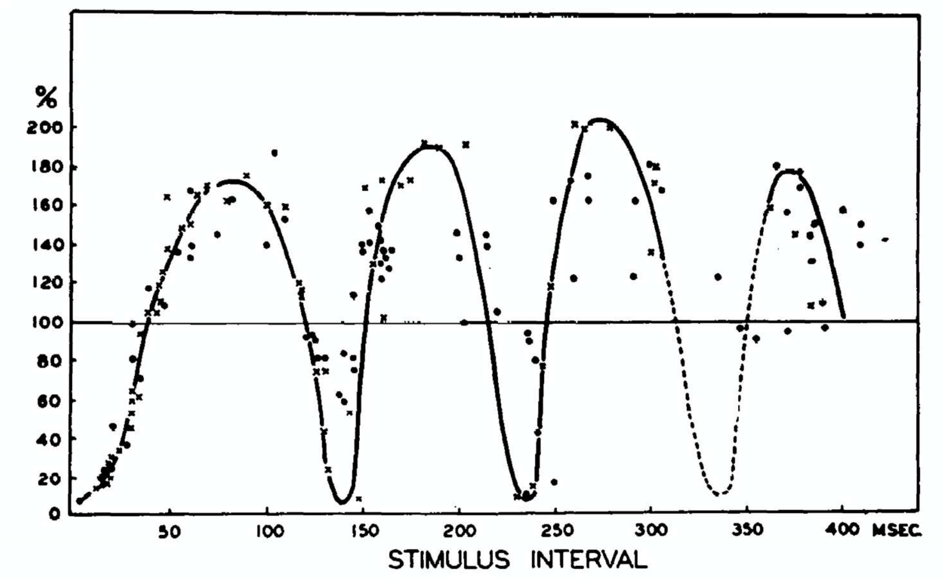

Figure 1-3: from Chang (1951). This plots out the magnitude of the evoked potential to the auditory stimulus (y-axis) after different onset asynchronies following a conditioning shock stimulus (x-axis). The magnitude of the evoked potential oscillates at about 10 Hz.

1.4.1 The cortical excitability hypothesis & pulsed inhibition with alpha hypothesis

Some researchers speculate that selective attention operates to selectively sample information from relevant stimuli in a rhythmic manner over time. Stemming from Chang (1951), Lindsley (1952) developed a “cortical excitability” hypothesis, which postulates that sensory cortex has a period of maximal responsiveness to external stimuli, followed by a period of minimal responsiveness. This oscillation in sensitivity to stimuli is strongest during periods of behavioral selective attention, suggesting that cortical excitability should be more apparent when alpha power is low. Mathewson et al. (2009, 2011) therefore expanded the cortical excitability hypothesis by adding the idea that the trough phase of alpha oscillations represent a periodic suspension of the inhibition of visual sensitivity, which is caused by strong alpha power. Mathewson (2009, 2011) dubbed this hypothesis the pulsed inhibition hypothesis. The idea proposed is that "… whereas the amplitude of an alpha oscillation reflects the degree of excitation or inhibition, the phase angle of the alpha oscillation indexes the excitatory or inhibitory state of the underlying neural generators within a cycle of the alpha oscillation" (van Diepen et al., 2015).

Importantly, the field of work supporting the pulsed inhibition hypothesis utilizes a method of flickering stimuli in the alpha band with the hopes of entraining (phase-locking) *evoked* (not intrinsic) alpha rhythms to an external stimulus. This is known as visual entrainment and will be covered in detail in a section later in this introduction. In contrast to this notion of pulsed inhibition, which depends on phase-locking intrinsic alpha oscillations in order to control temporal attention, I will argue that using visual entrainment is more likely to entrain a person's temporal expectation of stimuli rather than phase-locking intrinsic neural oscillations and thus affecting behavior.

In brief, selective attention prioritizes stimulus processing based on the behavioral relevance of the stimulus, whereas temporal expectations constrain visual interpretation based on the likelihood of the stimulus occurring (Summerfield and Egner, 2009). In addition, expected stimuli lead to lower amplitude cortical responses to stimuli, whereas stimuli that are selectively attended produce larger evoked responses in cortex (Summerfield and Egner, 2009; Arnal and Giraud, 2012).

1.5 How intrinsic alpha oscillations relate to the brain & behavior

1.5.1 Cortical effects of intrinsic alpha oscillations

The cortical excitability hypothesis postulates that regions of cortex are more or less able to maximally respond (for example, through an event-related potential, ERP) to a stimulus depending on the timing of the stimulus. The effects of alpha oscillations (both in power and phase) show different patterns of responses on the single neuron level as well as global signals such as the fMRI BOLD signal. Haegens et al. (2011) found that troughs in intrinsic alpha oscillations (measured via LFP) correlate with more spikes in somatosensory, premotor, and motor cortex than times in which alpha peaks occur (see **Figure 1-4**). This supports the idea that the troughs of an alpha cycle could represent a release from inhibition, allowing cells to fire more than during the peaks of the alpha cycle. However, these findings do not directly support the pulsed inhibition hypothesis, because they are not linked to a behavioral measure.

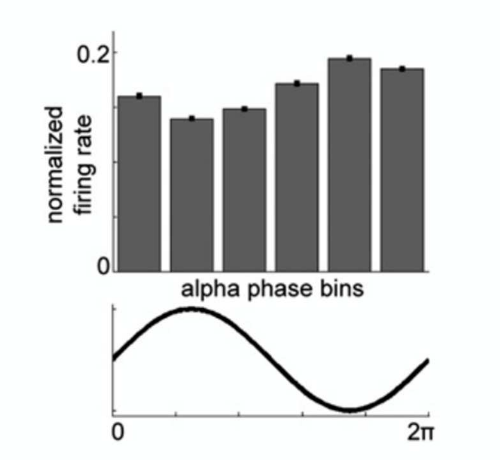

Figure 1-4: from Haegens et al, 2011. Firing rate in relation to (binned) alpha oscillation phase.

There is also evidence for the cortical excitability hypothesis during different amplitudes and phases of alpha in more global neuroimaging measures such as the BOLD signal in fMRI. Scheeringa et al. (2009) found that increased alpha power is associated with decreased BOLD signal in occipital (visual) cortex: a negative relationship between alpha power and BOLD activity. In addition, the same group (Scheeringa et al., 2011) found that stimuli presented in the peaks of the alpha cycle resulted in lower BOLD signals in V1 & V2, whereas stimuli presented in the troughs of the alpha cycle resulted in higher BOLD signal in V1 & V2.

Several experiments have also found a link between the amplitude of an evoked response (in EEG) to identical stimuli vary with the phase of oscillatory signals in alpha (Trimble and Potts, 1975; Brandt et al., 1991; Mathewson et al., 2009; Busch and VanRullen, 2010) and in other frequency bands as well (Lakatos et al., 2008) at the onset of the visual stimulus. Busch & Van Rullen (2010) found that a relationship between alpha phase and global field power of the EEG signal. Furthermore, this correlation between signals was stronger for attended than for unattended stimuli. Thus, waves in cortical excitability are apparent in both spike rates of cells, BOLD signal and evoked potentials, according to the timing of stimuli at different phases of an alpha oscillation. Likewise, higher alpha power results in lower overall cortical excitability in the BOLD signal. These results are able to link cortical excitability cycles to intrinsic alpha power and phase, whereas the original findings already discussed (Chang, 1951) did not link the idea of cortical excitability with intrinsic alpha oscillations.

1.5.2 Behavioral effects of alpha power and phase

The power of alpha oscillations before the presentation of a target stimulus leads to differing effects on behavior: lower prestimulus alpha power predicts better behavioral detection rates, whereas higher prestimulus alpha power predicts lower detection rates (Ergenoglu et al., 2004; Thut et al., 2006; van Dijk et al., 2008; Busch and VanRullen, 2010; Haegens et al., 2011; Hanslmayr et al., 2011; Bauer et al., 2014). Selective attention also results in a decrease in alpha power (Bollimunta et al., 2011; van Diepen et al., 2015), meaning that subjects are able to actively modulate the power of their intrinsic alpha oscillations before the expected onset of a behaviorally relevant stimulus. Supporting the idea that alpha power can be modulated in time according to a person's attentional demands, (Romei et al., 2010) used TMS at alpha (10Hz) as well as two control frequencies (5Hz and 20Hz), and found that TMS stimulation at alpha – to simulate an increase in alpha power – significantly decreased perceptual abilities in visual target detection. Thus, prestimulus alpha power can affect the likelihood of behavioral detection of a stimulus. In addition to prestimulus alpha power, the phase of intrinsic alpha oscillations at the time of the target stimulus has also shown differences in behavioral measures such as detection rate and reaction time.

Dustman and Beck (1965) presented subjects with full-field flashes while measuring brain waves through EEG. They found that the reaction time of subjects' flash detection varied as a function of the phase of the alpha band in the EEG signal. Specifically, the fastest reaction times occurred during the trough and slowest reaction times were on the up-rise going into the peak of the alpha cycle. This finding suggests that certain phases of the intrinsic (non-evoked) alpha band could reflect the readiness of subjects to detect a visual stimulus during a specific point in time. Also see Callaway and Yeager (1960) for similar findings.

Mathewson et al. (2009) measured accuracy in a target detection task while measuring the EEG signal in human subjects. They found that subjects were less likely to detect a faint and brief visual target when target stimuli were presented during the trough of an intrinsic alpha oscillation. Peaks and troughs were calculated 100ms before the onset of the target stimulus. This was only true for trials in which the power of alpha was relatively high; trials with low alpha power did not differ in phase between detected and undetected trials. A caveat of this study is that they did not distinguish the particular frequency that they investigated, but rather chose a band of frequencies within alpha and averaged across them. This makes interpretation of prestimulus alpha phase difficult since the phases of different frequencies within the alpha band could be very different from each other over a short period of time.

Similarly, Busch et al. (2009) and Busch and VanRullen (2010) had subjects press a button when they detected a point of light at a cued location, which had variable onset time after the start of a trial. They found that trials in which subjects detected the target resulted in a significantly different phase distribution of the prestimulus 7 Hz EEG signal (not within the alpha range) than trials in which subjects did not detect the targets. In contrast to Mathewson et al (2009), Busch et al found that the prestimulus alpha phase could not predict behavioral detection performance (see Hanslmayr et al., 2011 for review).

Van Diepen et al. (2015) asked whether prestimulus alpha phase could be actively modulated by selective temporal attention conditions. They used a predictable

SOA time between cues and target stimuli and investigated whether the neural signal's response, in both power and phase of alpha, could be modulated in order to optimize behavioral attention for the predictable target time. In other words, were subjects able to either decrease alpha power and/or change the phase of alpha to align with the expected timing of the target stimulus? They found that expectation (via a predictable time after a cue) does not modulate alpha phase, but does decrease alpha power before the onset of the target stimulus.

In sum, experiments generally agree that the lower the prestimulus alpha power, the better the behavioral performance. There is evidence that the amplitude of alpha is actively, selectively modulated with behavioral attention (e.g., van Diepen et al, 2015), meaning that subjects are able to modulate the power of alpha in response to an expected target stimulus. As for the prestimulus phase of alpha, some results support the idea that behavior is linked to prestimulus alpha phase whereas others could not replicate this finding. Regardless, the phase of alpha oscillations does not appear to be actively modulated for expected times of a target stimulus: a predictable time between a cue and a target (e.g., Busch et al 2009, 2010; van Diepen et al 2015) does not alter the phase of alpha oscillations to enable subjects to better detect a target stimulus.

1.6 Behavioral detection rate oscillations are not in the alpha band

Studies that have found oscillations in behavioral detection rate without the use of entrainment stimuli (to be covered in the next section) have largely found oscillations in frequency bands other than alpha (such as delta, around 1.5Hz, or beta, between 4-8Hz). These effects are ones in which detection rate to a target stimulus waxes and wanes according to the timing between only two stimuli (a cue followed by a target). For example, Landau and Fries (2012) analyzed target detection performance across different SOAs between the target (a dimming of one of 2 stimuli) and a task-irrelevant flash event that occurred at the left or right side of visual space. They found that for flash events occurring at the right visual field, a 4Hz rhythm appeared in detection performance at both stimulus locations and the two rhythms were in antiphase from each other. Visual flashes on the left side of space resulted in 6-10Hz oscillations in detection rate, depending on the target side of space. In addition, Fiebelkorn et al. (2013) used a paradigm in which subjects are cued to the location of a target within two white parallel bars. The subjects had to detect a brief, faint target that occurs in the cued location, or in an uncued same-object location, or uncued different-object location. They found that the detection rate fluctuated with the cue to target time differently in the three conditions across subjects. The target detection rate tended to oscillate at around 8 Hz between the cue time and target time. Another example is Drewes et al. (2015) who found detection rate oscillations at 5 Hz.

Thus, studies using only a cue followed by a target have shown oscillations in detection rates in frequency bands other than alpha. Is there a relationship between the behavioral oscillation frequency and the frequency of cortical oscillations with respect to selective temporal attention? If so, are we able to manipulate behavioral oscillations to occur in the alpha band to compare these oscillations with temporal attention signals (alpha oscillations) in the brain? Some studies aimed to manipulate behavioral oscillations to occur in the alpha band by using “entrainment” stimuli: flickering stimuli within a certain frequency band in order to stimulate and augment the behavioral and cortical effects of intrinsic alpha oscillations. The goal of visual entrainment in the alpha band is to link cortical alpha oscillations with behavioral oscillations in detection rate. Stimulus entrainment in the alpha band has led to behavioral as well as cortical effects, covered in the next section.

1.7 The effects of entrainment stimuli on behavior and the brain

1.7.1 Entrainment effects on behavior

Tying together the effects of prestimulus alpha power and phase with behavioral oscillations in detection rates and reaction times, experimenters have turned to visual entrainment. Visual entrainment utilizes flickering of visual stimuli at a specific frequency (for example, in the alpha band), with the goal of phase-locking *intrinsic* alpha oscillations so that their phase timing is under experimental control (Spaak et al., 2014). The hope of experiments using this method is that oscillations in behavior will be directly tied to the flicker sequence occurring before the onset of a target stimulus in a detection task. Several experiments, outlined below, have indeed found oscillations in behavior in the alpha band following visual entrainment stimuli. However, the specific entrainment frequencies used, as well as the phase effects on behavior, are not consistent across these studies. Additionally, the neural effects of visual entrainment in the alpha band also show discrepancies across studies, which will be covered in the following section.

Several studies have used visual entrainment in the alpha band and found resulting behavioral oscillations in detection rate, at the same frequency (or a harmonic) as the stimulated frequency. Specifically, Mathewson et al. (2012) used entrainment at

12.1Hz, followed by a target stimulus at different SOA times after the entrainment sequence. They found that in-phase target stimuli have higher detection rates than antiphase stimuli. The same group (Mathewson et al., 2010) also used 2, 4, or 8 entrainer stimuli and found evidence that behavioral oscillation effects were larger when preceded by more entrainers. De Graaf et al. (2013) also used entrainment at alpha (10.6Hz) and beta (5.3Hz; a sub-harmonic of the alpha frequency). They found behavioral oscillations at 10Hz following entrainment in both of these frequencies (see **Figure 1-5**), and that target stimuli presented in-phase led to higher detection rates than antiphase-timed target stimuli. It is interesting to note that the behavioral oscillations found in this study were best fit for 10Hz, even though entrainment was either 10 or 5 Hz. Would behavioral oscillations be prone to other entrainment frequencies such as 8 Hz (the behavioral oscillation frequency found by Fiebelkorn et al, 2013, for example)?

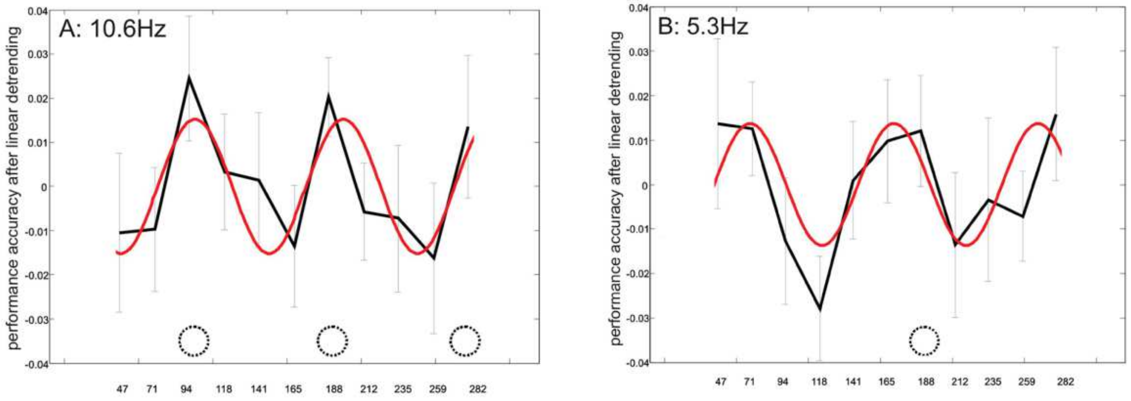

Figure 1-5: from de Graaf et al (2013): behavioral detection rate oscillations were found at 10Hz following both 10.6Hz and 5.3Hz entrainment stimuli. Note that these oscillations are not related to each other in phase.

Spaak et al. (2014) used entrainment in the alpha band and found resulting behavioral oscillations at the stimulation frequency. Specifically, they used rhythmic entrainment on one side of visual space and jittered entrainment on the other side. Targets could appear on the attended side of space at any of several different SOA times after the entrainment period. Interestingly, they found the opposite results for the phase of the target stimulus with respect to the entrainment sequence: antiphase stimuli resulted in higher detection rates than in-phase stimuli. Additionally, the fluctuations in behavior appear to mostly occur in the non-rhythmically entrained side of space whereas the rhythmic side does not appear to fluctuate in behavior at all.

A few experiments have also used the method of visual entrainment at other frequencies, specifically in the delta band. Both Lakatos et al. (2008) and Stefanics et al. (2010) used delta entrainment stimuli, and found faster reaction times during delta troughs and slower RTs during delta peaks of the measured neural oscillation signal. These findings are similar to alpha entrainment effects on behavior, except it holds true for much slower (1.5Hz) frequency than alpha, which calls into question the importance of the alpha band with reference to visual entrainment. One possible outcome of visual entrainment is that it could afford subjects the ability to predict the timing of a target stimulus following an entrainment sequence, regardless of the frequency that is being presented. This idea is supported by the temporal expectation hypothesis, as opposed to the pulsed inhibition hypothesis of alpha oscillations (e.g., Rohenkohl & Nobre, 2011; Rohenkohl et al, 2012; Cravo et al, 2013; Morillion et al, 2016; Arnal & Giraud, 2012; Calderone et al, 2014). This prediction, unlike visual entrainment, does not necessarily depend on a relationship between alpha power/phase and behavioral fluctuations over time, however the neural mechanism for this phenomenon is still under question.

1.7.2 Entrainment effects on cortical oscillations

What does stimulus entrainment do to the neural response during and following the entrainment sequence? This question is especially important in the scope of the pulsed inhibition hypothesis because it should link the phase of alpha oscillations with the phase of behavioral detection rates over time. The definitive answer remains unclear as some studies (de Graaf et al., 2013; Keitel et al., 2013; Spaak et al., 2014) found increases in alpha *power* following alpha entrainment, whereas others (Mathewson et al, 2012) did not find such an increase in alpha power. Furthermore, the effect of alpha entrainment on the *phase* of alpha is only demonstrated in a single experiment (Mathewson et al 2012), whereas many others did not find that visual entrainment caused neural phase-locking in the alpha band (Rohenkohl and Nobre, 2011). After entrainment at 12.1Hz, Mathewson et al see a difference in phase-locking index (PLI) between the rhythmic and variable entrainment conditions; however, they did not see a significant difference in PLI between the rhythmic and control conditions. They explain this lack of significance by saying that the control condition’s evoked ERP interferes with the phase locking in the late time period (after entrainment, during the target period). Because Mathewson et al did not see a difference in alpha power during or following alpha entrainment, they conclude that the visual entrainment is acting on phase synchrony rather than on increasing power of alpha. However, the lack of this effect in both power and phase in other visual entrainment studies calls this conclusion into question.

Other studies have used entrainment at lower frequencies and found phase locking effects in the EEG signal. Lakatos et al (2008) used flickering stimuli in the delta band (1.5 Hz) with the goal of phase-locking monkeys' delta oscillations (as well as their behavior) to the onsets of the flickering visual stimuli. Lakatos et al hypothesized in their study that presenting relevant flickering stimuli in a predictable manner should entrain (phase-lock) the EEG signal and serve as "instruments of sensory selection." The task used was visual flashes and auditory beeps, with oddball target stimuli that the monkeys responded to. The timing of the visual oddball stimuli varied across different SOAs within the stimulus trains. Stefanics et al (2010) also used delta entrainment and also found phase entrainment of EEG signal in humans in delta band.

In addition to experiments that use visual entrainment stimuli in order to entrain intrinsic rhythms of the brain to phase-lock to a certain presented frequency, the field of steady state visually evoked potentials (SSVEP) uses visual entrainment with a different goal. These experiments assume that any phase locking of the neural signal to a physical stimulus is an evoked response to the stimulus, and can be used as a method to frequency-tag the neural response to a particular stimulus (Keitel et al, 2014). In addition, some (e.g., Hanslmayr et al., 2011) interpret the use of visual entrainment as the same as an SSVEP signal whereas others (Spaak et al., 2014) interpret visual entrainment to be linked to manipulating intrinsic oscillations. Given the varying findings on the neural effects of visual entrainment in the alpha band, it is hard to interpret whether the effects of visual entrainment on behavior are actually related to alpha oscillations, and if so, how.

1.8 Neural excitability and behavioral evidence for pulsed inhibition of alpha

A missing link in the relevant literature focusing on the pulsed inhibition of alpha and its effects on behavior is whether the size of the neural evoked response to a (target) stimulus is actually related to better or worse behavioral performance. It seems clear that cortical signals do tend to oscillate around the alpha band of frequencies (Chang, 1951; Haegens et al, 2011). There is also evidence that behavior seems to oscillate around the alpha band following entrainment in the alpha band (Mathewson et al 2009; 2012; De Graaf et al 2013; but see behavioral oscillations found at other frequencies e.g.: Lakatos et al 2008; Stefanics et al 2010; Fiebelkorn et al 2013; and opposite temporal phase effects in Spaak et al 2014).

Ergenoglu et al. (2004) found that the amplitude of the ERP response was related to behavioral detection rates, and that the prestimulus alpha power negatively correlates with the amplitude of the ERP response as well as with behavior. In contrast, Zanto et al. (2014) found that faster reaction times were associated with smaller amplitudes in the early ERP response to a visual stimulus. The field of temporal expectation proposes the opposite relationship that selective attention does: expected temporal stimuli will evoke smaller responses than unexpected stimuli (Rohenkohl & Nobre, 2011). Perhaps this difference in prediction of evoked amplitude could be used in future studies to make sure that selective temporal attention is being used as opposed to temporal expectation in studies using visual entrainment.

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CHAPTER 2

Frontoparietal BOLD is not sensitive to differential attentional modulations in visual cortex

2.1 Abstract

Selective spatial attention in vision is proposed to originate in regions of frontoparietal cortex dubbed ‘attentional control’ regions. Stimulating regions within FP cortex causes improvements in both behavioral and neural measures of vision, whereas lesions to these regions cause drastic deficits in selective visual attention. In addition, neuroimaging studies in the past have shown various correlative measures of activity between frontoparietal and visual cortex activity. However, there has not been an examination of whether the differential activity in visual cortex can be tracked by the activity in frontoparietal cortex. Differential activity here refers to the relative activity level across both hemispheres during a single trial, indicating the level of selective attention during that trial. In the present study, human subjects performed a spatial attention task in which they attended to the left or right side of visual space while in the fMRI scanner. We used various BOLD activation measures in frontoparietal cortex to map the differential activity in visual cortex. Surprisingly, we found that many measures of frontoparietal activity could not be related to the differential activity levels in visual cortex, though we still see correlations in the overall activity between these regions. We conclude that the BOLD signal might be dominated by more large-scale fluctuations making it insensitive to these types of modulations in the brain.

2.2 Introduction

Humans and other animals rely on their ability to guide attention towards behaviorally relevant information, and to filter out visual information that is not directly relevant to behavioral goals. The ability to select relevant sensory inputs is referred to as selective attention, and it operates in part by modulating neural activity within regions of sensory cortex that represent low-level stimulus information – in vision this includes simple features such as orientation, location, color, or contrast. Here we investigated how attention to a particular region in space would modulate early visual responses and the information represented in these regions. Moreover, we asked whether activity in higher-level attentional control regions could be linked to changes in early sensory cortex.

Behavioral (endogenous) attention can lead to a variety of attentional modulations in visual cortex. Attention has been shown to result in multiplicative gain in orientation tuning (i.e., selective increase in firing rate for preferred over non-preferred stimuli) (Moran and Desimone, 1985; Spitzer et al., 1988; Luck et al., 1997; McAdams, 1998; McAdams and Maunsell, 1999; Reynolds et al., 2000; Mitchell et al., 2007; Ruff et al., 2006), additive shift (i.e., boost of firing rate across all stimulus types, both preferred and non-preferred), a decrease in fano factor (the ratio of variance to mean spike rate) (Mitchell et al., 2009; Middleton et al., 2012; Herrero et al., 2013), decrease in noise correlations (co-occurrence of random spike timing between cells) (Cohen and Maunsell, 2009; Mitchell et al., 2009), increased synchrony in neural spike timing (Serences and Yantis, 2006; Gregoriou et al., 2009a, 2009b, 2015; Voytek et al., 2010; Musall et al., 2012; Sundberg et al., 2012; Anderson et al., 2013), and increased functional connectivity between BOLD responses in regions of cortex and subcortex (Bressler et al., 2008; McAlonan et al., 2008; Lauritzen et al., 2009; Greenberg et al., 2012; Saalmann et al., 2012; Gregoriou et al., 2015).

It has been proposed that attentional modulations in visual cortex are driven by higher-level regions of cortex, dubbed attentional control regions (Kastner et al., 1999; Kastner and Ungerleider, 2000; O'Connor et al., 2002; Moore et al., 2003; Yantis and Serences, 2003; Bisley and Goldberg, 2003, 2010; Behrmann et al., 2004; Moore, 2006; Shomstein and Yantis, 2006; Yantis, 2008; Bressler et al., 2008; Capotosto et al., 2009; Lauritzen et al., 2009; Greenberg et al., 2010; Bisley, 2011; Ptak, 2011; Squire et al., 2013; Scolari et al., 2015). These regions, such as the frontal eye fields (FEF, or sPCS in humans) and the intraparietal sulcus (IPS), collectively referred to as frontoparietal (FP) cortex, are thought to provide feedback to occipital visual cortex (VC) with information about where or what to allocate attention within the visual scene. Supporting this hypothesis, FP regions such as the IPS show retinotopically-selective responses, but only under conditions of endogenous selective attention: the IPS does not selectively respond to passive viewing of stimuli as early occipital VC regions do, but adding an attentional task results in clearer retinotopic organization in the BOLD signal of IPS (Silver et al., 2005). Therefore, it has been proposed that these (albeit retinotopic) FP regions serve a different – attention control related – purpose than responses that can be measured from occipital VC (Lauritzen et al., 2009).

Besides these regions showing attention-related retinotopy ("attendotopy"), FP cortex also plays an important role in selective attention, as demonstrated by behavioral deficits with its absence through lesions, and behavioral improvements with injected neural stimulation. When regions within parietal cortex are damaged, this results in severe unilateral neglect in humans: the inability to direct attention to one side of visual space (Mesulam, 1981; Posner et al., 1984). Similarly, when FP regions in the macaque monkey are lesioned, monkeys show behavioral deficits in selective visual attention (Robertson et al., 1988; Lynch and McLaren, 1989). Within the posterior parietal cortex lies the FEF, important for saccadic eye movements as well as selective covert attention. One method used to induce increased activity of cells is electric microstimulation (EM), injecting an electrical current into neurons with an electrode. EM of FEF in the macaque leads to a gain modulation in VC neurons whose receptive fields overlap with those of the stimulated FEF neurons (specifically neurons in VC subregion V4) (Moore and Armstrong, 2003; Moore and Fallah, 2004; Armstrong and Moore, 2007). Interestingly, this gain change in V4 responses mimics similar gain response changes observed when attention is voluntarily directed towards that receptive field (Armstrong and Moore, 2007). Thus, FEF is implicated in attentional control because EM of the FEF leads to V4 modulations similar to those seen with shifts in endogenous attention.

Given this evidence, the FEF and IPS are good candidate attentional control regions, proposed to send top-down attention feedback signals that change the way visual sensory information is processed in occipital VC. This hypothesis implies that during selective attention, different activation levels in attentional control regions should be related in some way to the magnitude of representations in occipital visual regions of the brain. In other words, increased FEF/IPS activity should lead to increased attentional modulations in occipital visual cortex (i.e., better representations) because increased FEF/ increased activity corresponds to stronger top-down biasing signals and thus larger attentional modulations in VC within this framework. The way in which VC shows its attentional modulations could be in a number of ways, for example additive or multiplicative gain of orientation tuning functions, or an increase in the overall BOLD amplitude of the retinotopically relevant regions of VC (corresponding to an attended region of space).

Electrophysiological and human neuroimaging data indeed support the idea that greater activity in FP regions leads to enhanced behavioral and neural attention effects. Several human neuroimaging studies show correlations between VC and FP BOLD activation over time, using various measures of functional connectivity including correlation, granger causality and coherency (Büchel and Friston, 1997; Bressler et al., 2008; Vincent et al., 2008; Lauritzen et al., 2009; Ramalingam et al., 2013). Such correlations over time are often referred to as ‘functional connectivity,’ indicating which regions of the brain are likely communicating with each other given that their functional responses over time are similar. However, while these analyses show a correlation between overall response amplitude between regions, they do not demonstrate that higher FP activation actually relates to *differential* activity levels in the regions of retinotopically organized regions in VC that respond to attended stimuli as attention is shifted to a particular region of visual space. The difference between cortical representations of attended and ignored parts of space at a specific time should indicate the amount of selective attention being allocated.

To measure the differential attention effect in VC during spatial selective attention, we used neuroimaging techniques that are capable of measuring multiple brain regions simultaneously. Since single-unit recording studies are only able to measure one or a small number of neurons at any given time, a neuron's response is generally recorded under several experimental conditions to assess the degree of attentional modulation. For example, studies of this kind will commonly compare a neuron's firing when a stimulus in its receptive field is attended ('attend toward') vs. when the animal is attending a stimulus outside of the neuron's receptive field ('attend away'). This requires comparing a single neuron's response to itself at different points in time under different attention conditions. However, measuring multiple brain regions at the same time would allow comparison across conditions at the same point in time. Thus, we took advantage of fMRI to take these simultaneous measurements in the present experiment.

In the current experiment, we used a task in which subjects selectively attend to either the left or right side of visual space while in an fMRI scanner. Given that each trial contains an attended and ignored part of retinotopic space, we were able to calculate the inter-hemispheric difference (IHD) in VC, which represents the amount of differential attentional modulation on each trial in VC. We also examined whether the activity level of FP regions was able to track the IHD enhancement of behaviorally relevant signals in VC. We predicted that trials with larger IHD indicate higher levels of selective attention and should therefore correlate with higher overall activity levels in FP cortex.

In addition to measuring the IHD of VC, we assessed the quality of orientation information by examining changes in the amplitude of *channel response functions* (CRFs) – a method that uses the pattern of activation across all voxels in a visual area to estimate the degree of orientation selective information as a function of selective attention. When top-down biasing signals are strong, we predict more FP activity as well as an increase in the gain and the precision of CRFs representing attended and ignored sides of space, as compared to trials in which attentional biasing signals are less pronounced (and thus lower overall FP activity).

To preface our results, we found that neither the IHD nor the CRFs in occipital VC varied systematically with the magnitude of responses in FP regions – at least not in a way we could detect through the present experiment. We did, however, replicate basic attentional modulation effects in occipital visual cortex: regions corresponding to the attended side of space showed overall higher amplitude BOLD signal than regions corresponding to ignored sides of visual space, in both VC and FP cortical regions. Thus, these data suggest that FP regions and VC regions both participate in mediating selective spatial attention. However, despite our sensitivity to detect attentional modulations across visual space, we do not find evidence supporting a clear functional role for FP regions in providing a top-down biasing signal to regions of early VC.

2.3 Methods

2.3.1 Subjects and general procedure

Nine volunteers (ages 24-30; 5 females) with normal vision were used as subjects. Two of these subjects were not included in any analyses because of excessive movement in the scanner, and because of early removal from the scanner due to discomfort. Therefore, seven subjects (4 females) are included in all analyses below. All subjects signed informed consent forms as regulated by the IRB of UC San Diego, and were paid for their time. All subjects were pre-trained for 1-2 hours on each of the paradigms in order to learn the paradigms. In order to train participants to hold their fixation steady their gaze was tracked with an SMI infrared remote eye tracker during these practice sessions. Subjects were given feedback on whether eye movements were made after each training trial, and they were trained until they were able to maintain fixation.

After training, subjects participated in three days of fMRI data acquisition for two hours each day, two days of which contained 8 runs each of experimental trials (36 trials per run, totaling 576 total trials per subject). On the final day IPS sub-region mapping was acquired and used for both occipital visual and intraparietal sulcus (IPS) retinotopic mapping.

2.3.2 Imaging

We scanned all participants on a 3T GE MR750 research-dedicated scanner at equipped with a 32-channel head coil at the Keck Center for Function MRI, University of California, San Diego. Anatomical images were acquired using a T1-weighted sequence that yielded images with a 1mm resolution (TR/TE=11/3.3ms, TI = 1100ms, 172 slices, flip angle = 18°). Functional images in the IPS mapping task were collected using a gradient EPI pulse sequence and a Nova 32-channel head coil at the Keck Center for Functional MRI, University of California, San Diego (19.2 x 19.2 cm FOV, 96 x 96 matrix size, 31 3-mm thick slices with 0 mm gap, TR = 2250 ms, TE = 30 ms, flip angle = 90°), yielding a voxel size of 2 x 2 x 3 mm. We acquired oblique slices with coverage extending from the superior portion of parietal cortex to ventral occipital cortex. Functional images in the main task were acquired using a gradient echo EPI pulse sequence that covered the entire brain with 35 axial slices. Slices were acquired in ascending interleaved order with 3mm thickness (TR=2000 ms, TE = 30 ms, flip angle = 90°, image matrix = 64 (AP) x 64 (RL), with FOV = 192mm (AP) x 192 (RL), voxel size = 3x3x3 mm). Scans on the three days for each subject were Talairach normalized, and then all scans were coregistered to the first day's anatomical scans so that data for each subject was in the same space. Data were preprocessed through custom scripts in both Matlab and Brain Voyager 2.4 and underwent inhomogeneity correction, sinc-interpolated slice timing correction, and rigid body motion correction.

2.3.3 IPS mapping

All stimuli were generated in Matlab (version 2010b, Mathworks) using Psychophysics toolbox (Brainard, 1997) and back-projected onto a screen at the base of the magnet bore and viewed through a mirror mounted to the head coil. All subjects participated in an IPS mapping task used to define borders between IPS subregions (Sereno et al., 2001; Schluppeck et al., 2005; Swisher et al., 2007; Sheremata et al., 2010; Jerde et al., 2012). On all runs, we used a wedge stimulus spanning 72° polar angle and presented the checkerboard stimulus inside eccentricities of 1.75° and 8.75°; the wedge rotated with a period of 24.75 s. On alternating runs, the wedge was either a 4 Hz flickering checkerboard stimulus (black/white, red/green, or blue/yellow) or a field of moving black dots (0.3°, 13 dots/°, moving at 5°/s, changing direction every 8 s). During checkerboard runs, participants responded after detecting a brief (250 ms) contrast dimming of a portion of the checkerboard. During moving dots runs, participants quickly responded after detecting a brief (417 ms) increase in dot speed. Targets appeared with 20% probability every 1.5 s. Difficulty was adjusted to achieve approximately 75% correct performance by changing the magnitude of the contrast dimming (checkerboard) or dot speed increment (moving dots) between runs. Subjects completed between 10 and 16 total IPS mapping runs, usually totaling about 2 hours of scan time.

IPS mapping data were analyzed by first computing the best visual field angle for each voxel in IPS; we shifted signals from counter-clockwise runs earlier in time by 13.5 s (in order to account for the hemodynamic lag after reversing the time series), then removed the first and last full cycle of data (22 TRs total), then reversed the time series so that all runs are "clockwise." These steps were taken so that we could present stimuli going in both directions of rotation while still being able to use all data instead of half the data, similar to procedures in other labs (e.g., see (Jerde et al., 2012)). We then averaged these time-inverted counter-clockwise-rotation runs with the clockwise-rotation runs. We computed power and phase at the stimulus rotation period frequency (1/24.75 Hz) and subtracted the HRF delay (6.75 s) to align signal phase in each voxel with visual stimulus position. Finally, we projected maps onto reconstructed cortical surfaces for each subject and defined IPS 0-3 by identifying upper and lower vertical meridian responses (as in Swisher et al., 2007; Sprague and Serences, 2013). Low statistical thresholds were used, computed using normalized squared power at the stimulus frequency, to identify borders of IPS subregions. We were also able to define occipital visual cortical (VC) regions V1, V2, V3, V3a, and V4 through this method, also by distinguishing between the meridian-sensitive areas.

2.3.4 Main experiment

Subjects fixated on a 0.5° dot in the center of the screen, and were told to restrict eye movements throughout all trials. On each trial, the left and right of fixation contained a wedge (extending horizontally from ~3.2° to 9.1° of visual angle on each side of fixation; see **Figure 2-1**). Each wedge was a 120° polar angle wedge that contained a square-wave oriented grating at a spatial frequency of 1 cycle/degree of visual angle. The orientation of the grating was one of 9 possible orientations (evenly spread across 180° of orientation space), and the two sides' orientations were independent of one another. The wedges appeared for 200ms followed by blank for 200ms, in 10 cycles (thus flickering at 2.5 Hz) lasting for 4 seconds each trial. The inter-trial interval was 3 seconds. Subjects' accuracy was staircased on a run-by-run basis so as to obtain a ~75% accuracy rate (mean accuracy across subjects was about 80.3%). Each block contained a single fMRI collection period consisting of 36 trials at 7 seconds each plus 12 null trials and a 6 s end fixation (171, 2-second TRs; totaling 5m 52s per run). There were 576 trials in total for each subject across 2 days of runs. Each day contained 288 trials, split across 8 runs (16 runs across 2 days).

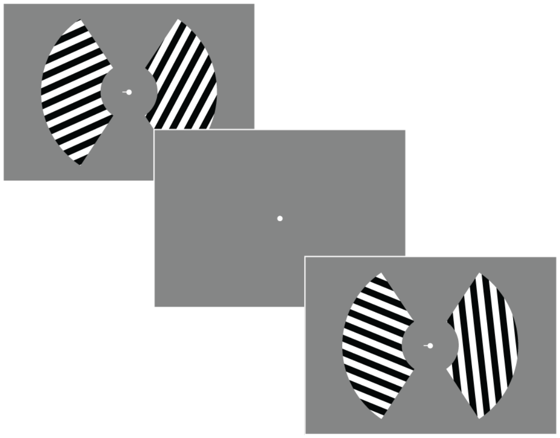

Figure 2-1: Experimental task. Wedges flickered on and off for 4 seconds at 2.5 Hz. Stimulus presentation was followed by a 3-second inter-trial interval. Subjects made a spatial frequency change detection judgment (lines get bigger or smaller in one of ten flickers per trial) on the attended side (pointed to by the white cue off the fixation point on each trial). All subjects' performances were titrated for difficulty so that they achieved ~75% accuracy overall.

2.3.5 Main experiment: Univariate ROI BOLD time course correlations analysis

For each region of interest (ROI), we extracted the BOLD signal for every trial (by taking the beta weight for each hemisphere within a region in the second TR after the onset of the trial), and either subtracted the right from the left hemisphere (inter-hemispheric difference; *IHD*), or averaged both hemispheres together (mean bilateral signal). We used the IHD as a measure of the magnitude of the attention effect for each trial, because the task required subjects to either attend the left or right part of visual space. Importantly, in order to ignore any potentially inherent laterality effects, we specifically did not use the attended hemisphere minus ignored hemisphere; rather, we used left minus right regardless of the attended side on each trial. This measure provides an unbiased way of looking at the difference in activity between hemispheres, without having to take into account experimental conditions. In addition to the IHD, we calculated the averaged bilateral BOLD signal of each of our 10 bilateral ROIs (V1, V2, V3, V3a, V4, IPS0-3, and sPCS [the human homologue of the monkey Frontal Eye Fields]) for each trial in the experiment. Then, we correlated each ROI's IHD signal with the IHD and with the mean bilateral signal in every other ROI (**Figure 2-2a-b**). Each ROI pair is then plotted in a correlation matrix (for example, the IHD against IHD is plotted in **Figure 2-2c**), where each matrix contains the correlations between two of the signals, across all ROIs.

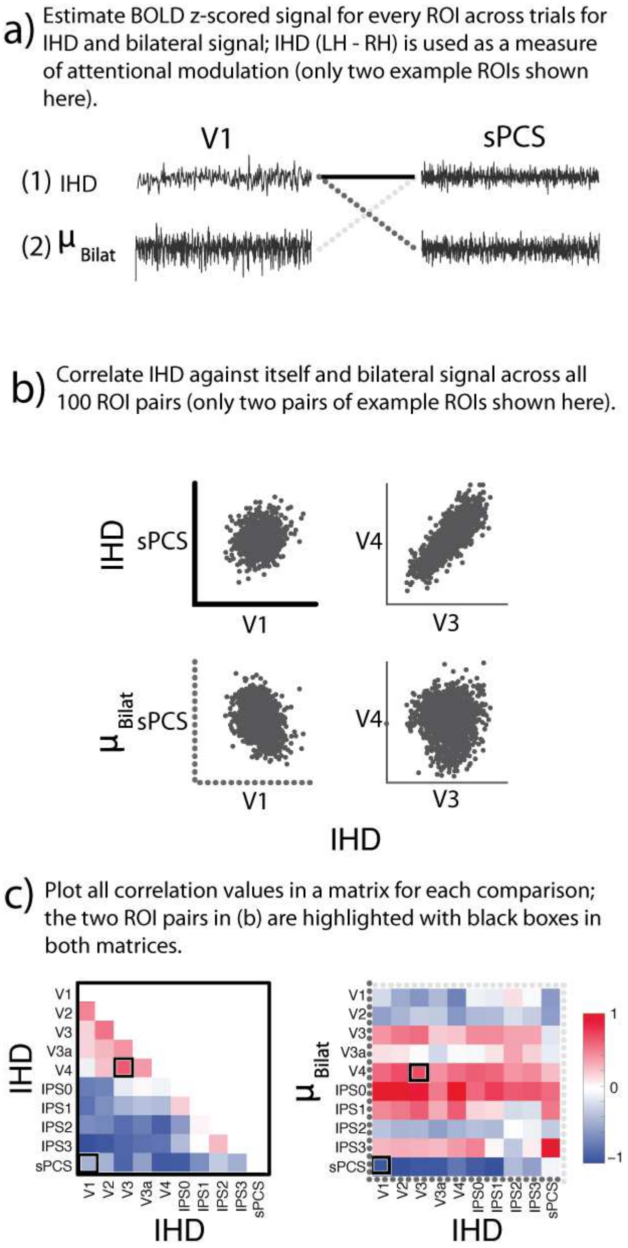

Figure 2-2: Univariate correlation data analysis procedure. This is an example subject s01 from a single day's data across all 288 trials from that day. For each subject, we estimated the beta values of the z-scored BOLD signal. We used each ROI's IHD (left hemisphere minus right hemisphere) for each of our 10 ROIs. We also extracted the time course in each ROI's averaged bilateral signal. We then compared the IHD to the IHD and to the bilateral signal (a). IHD vs. IHD is symmetrical in both directions (depicted in black), but the other is not. Within each ROI comparison, we calculated the correlation between each pair of ROI signals across trials (b), for a total of (100/2 - 10) unique correlation comparisons (for IHD vs. IHD), or 100 unique correlations for IHD vs. bilateral signal. We then plot all correlation values in a matrix (c; example correlations in [b] are outlined with black boxes).

2.3.6 Main experiment: Channel Response Functions

Besides standard pattern classification of the IHD, we analyzed the fidelity of orientation representations by looking at channel response functions (CRFs). To this end, we used an inverted encoding model to measure orientation-selective channel responses in occipital visual regions of cortex (V1, V2, V3, V3a and V4) as described previously (Serences et al., 2009; Brouwer and Heeger, 2011; Freeman et al., 2011; Serences and Saproo, 2012).

Specifically, each voxel measured using fMRI within occipital visual cortex contains an uneven distribution of subpopulations of neurons tuned to different orientations. We use this anatomical feature to assume the response in any given voxel is proportional to the summed responses of all neurons in that voxel. Because of this heterogeneous distribution, we can infer the concentration of each subpopulation within a single voxel by measuring its BOLD response to several different orientations (totaling nine in this experiment). We then characterize the orientation selectivity of a given voxel as a weighted sum of nine orientation channels, each with an idealized tuning curve or basis function. In this case, we use a basis set of nine sine waves raised to the sixth power.

Once we have nine weights for each voxel in a given occipital visual region, we can convert from voxel space into channel space, where each channel is a linear combination of responses in each voxel across a region of interest. We can then measure the response of all nine channels to each presented orientation, yielding nine channel response functions (CRFs). After shifting these nine CRFs to a common center, we can average the responses across all presented orientations to achieve a population CRF (resulting CRFs depicted in **Figure 2-6**).

Because the inverted encoding model needs to be trained on an equal number of trials per condition, we had to subsample the number of trials per condition each subject was presented with. The number of times each orientation was presented on the left vs. the right side of space was not controlled for on the ignored side of space, so we subsampled the number of trials in the training set so that each of the 9 orientations had an equal number of times presented on the left and right. All extra trials (e.g., all trials that did not have a partner trial on the opposite side for that orientation) were not included in the training set. However, all trials were tested in the inverted encoding model. We randomized which trials we left out using permutation and got an average CRF for each subject, after randomly choosing 1000 combinations of training trials.

Error bars on the average CRF (as in **Figure 2-6** & **Figure 2-7**) are 95% confidence intervals for each of our 9 orientation channels. Confidence intervals were calculated by resampling trials for each subject with replacement 2500 times for each condition combination. We then averaged across all subjects for each of the 2500 iterations to obtain our distribution of CRFs. We did this same procedure for calculating error bars for the difference between attended and ignored hemifield stimuli.

2.4 Results and Discussion

2.4.1 Univariate BOLD responses

When subjects are attending a certain hemifield, we should see higher activity in the contralateral side in visual cortex (e.g., (Mangun et al., 1998; Chawla et al., 1999;

Gandhi et al., 1999; Hopfinger et al., 2000). As a sanity check, we plotted attend left ("attL"), attend right ("attR") for each hemisphere (LH and RH) for each of our 10 ROIs (**Figure 2-3**). In visual areas V1-V4 we see the expected pattern of results for each subject, where the hemisphere contralateral to the attended side of space shows greater BOLD activity than the ipsilateral hemisphere. In IPS regions, the average BOLD response across subjects for left hemisphere goes in the expected direction (attended > ignored; i.e., contralateral > ipsilateral to the attended side of space), but the right hemisphere shows the opposite pattern in IPS2 and IPS3, on average.

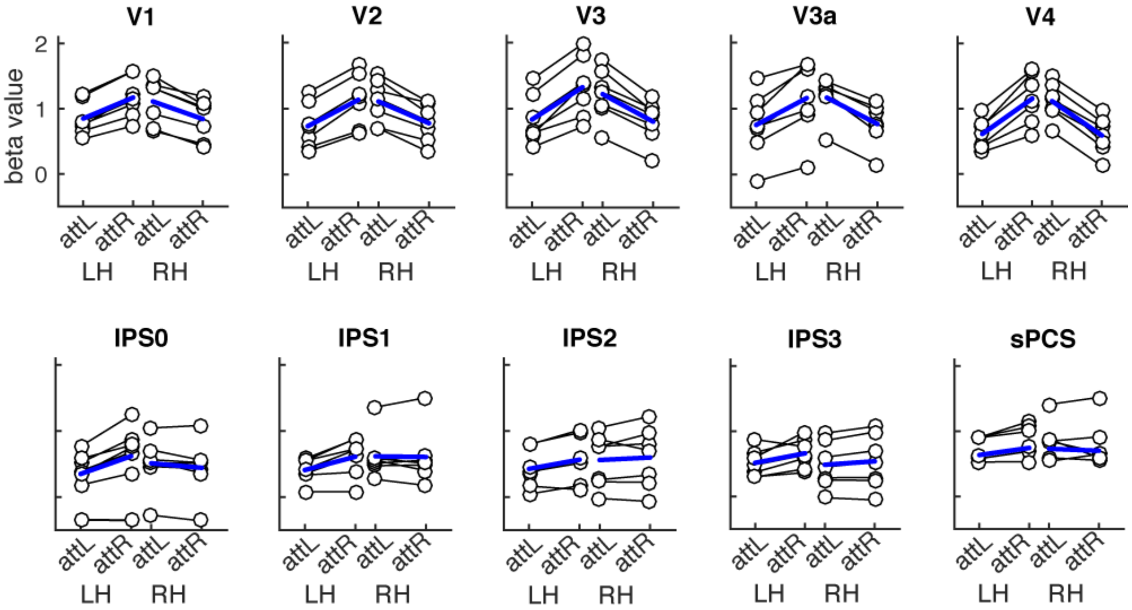

Figure 2-3: Univariate BOLD response in each of 10 bilateral ROIs to attend left vs. attend right side of fixation. Each blue line represents the mean across subjects, and each barbell is a single subject (n=7; note that one subject did not have a definable ROI for the sPCS, so n=6 for the sPCS region). The expected direction for these results is to have higher activity in the hemispheres contralateral to the attended side of space (e.g., attend right [attR] should be higher than attend left [attL] in left hemisphere [LH] regions, and attL should be higher than attR in the RH). This is the direction we see for visual regions V1-V4, and IPS0-1. In IPS2-3 and sPCS, both hemispheres tend to have higher activity for attend right (attR) than for attend left (attL).

To test our univariate BOLD results for significance, we performed a 3-way repeated measures ANOVA (hemisphere, ROI, and attention side) and found a main effect of ROI ($F(9,54) = 10.5$, $p < 0.0005$) but not of attention side or hemisphere. We also found significant interactions between attention and hemisphere ($F(1,6) = 173$, $p < 0.0001$), and a 3-way interaction for attention side, hemisphere, and ROI ($F(9,54) = 46.2$, $p < 0.0001$).

We then performed ten, 2-way repeated measures ANOVAs, one for each region of interest (V1, V2, V3 ,V3a, V4, IPS0, IPS1, IPS2, IPS3, and sPCS), to test for the interaction between hemisphere and attention side and for a main effect of attention side. The results from these ANOVAs can be found in (**Table 2-1**). All regions had a significant interaction between attention side and hemisphere except for IPS3 and sPCS, indicating that contralateral and ipsilateral hemispheres react differently to the attended side of space across most ROIs. There is more of a difference between hemispheres for preferred side of space for earlier visual regions (i.e., each hemisphere prefers the contralateral side of space), and less of this contralateral bias moving into IPS regions. These results are similar to findings from (Sheremata et al., 2010), who found that left hemisphere in IPS regions tend to show a rightward bias, whereas the right hemispheres in these regions do not tend to show a bias towards either side of visual space.

Table 2-1: Results from 2-way repeated measures ANOVAs of univariate BOLD data. All regions except IPS3 and sPCS show a significant interaction between attention condition and hemisphere. Corrected for multiple comparisons using FDR (corrected p = 0.006).

ROI	**F (interaction)**	**p**
V1	139.5	0
V2	138	0
V3	102	0
V3a	102	0
V4	146	0
IPS0	29.7	0.002
IPS1	17.3	0.006
IPS2	27.9	0.002
IPS3	4.9	0.067
sPCS	6.8	0.047

2.4.2 Univariate ROI BOLD time course correlations

We calculated two types of BOLD signal for each ROI: the IHD (left hemisphere minus right hemisphere within a given ROI) and the averaged bilateral signal. We correlated each of those two signals with the IHD, plotted in (**Figure 2-4**). Here, we see that the IHD in most regions is highly correlated with the IHD in each other region. Specifically, IPS0 and IPS2 have correlated IHD across almost all VC regions. However, when comparing the IHD with the mean bilateral signal across regions, no comparisons are significantly correlated (or anti-correlated) with each other.

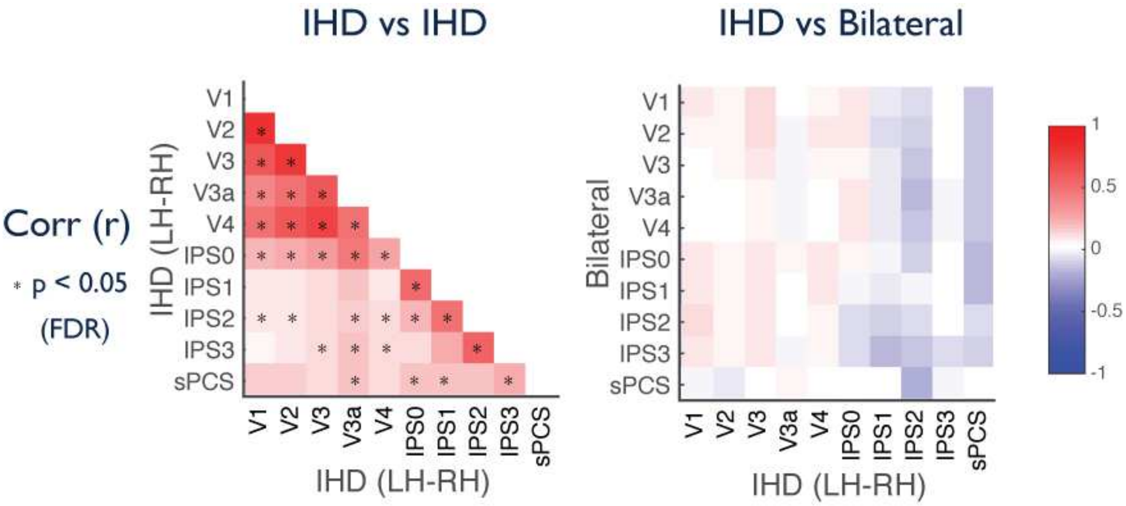

Figure 2-4: Univariate correlation results. Averaged correlation values across all 7 subjects. On the left is each ROI's IHD against each other's IHD; on the right is IHD against the mean bilateral signal in each region. We performed t-tests for correlation difference z-score against a zero difference score for each cell. Cells with significant correlation values, corrected for multiple comparisons using FDR per matrix individually, have black asterisks in them.

2.4.3 Channel response functions

The channel response functions (CRFs) for each occipital visual region were reconstructed using half of the trials with the highest vs. half of the trials with the lowest activity in each bilateral frontoparietal ROI, for the attended and ignored sides of visual space. Each FP region has two columns in (**Figure 2-6**) and (**Figure 2-7**): one for low bilateral IPS activity and one for high activity. Data were separated in half according to low or high mean bilateral FP BOLD signal. The CRF for each VC, using only half of the trials, is plotted in the rows. See figure caption for more information.

As expected, all CRFs were centered on the preferred orientation regardless of attention condition or frontoparietal activity condition. Trials that had higher FP activity also showed higher overall activity in VC regions. This is reflected in the higher normalized BOLD responses in the CRFs for high FP trials compared to low FP trials. See (**Figure 2-6**): all CRFs on the right columns (higher FP activity) have higher BOLD responses than all CRFs in the left columns (lower FP activity).

Visual inspection of the difference in CRFs between attended and ignored stimuli (**Figure 2-6**) in regions V1-V3a appears to show a mostly additive shift. This can also be seen in (**Figure 2-7**), which directly plots the difference between the attended and ignored side of space. Here, an additive shift in the CRF would be reflected in a uniformly upward shift of the grey difference line along the y-axis (i.e., a horizontal line above zero would represent a perfectly additive shift). Again, there is no clear relationship between the activity level of frontoparietal regions and the attention-related changes in visual cortex representing orientation information.

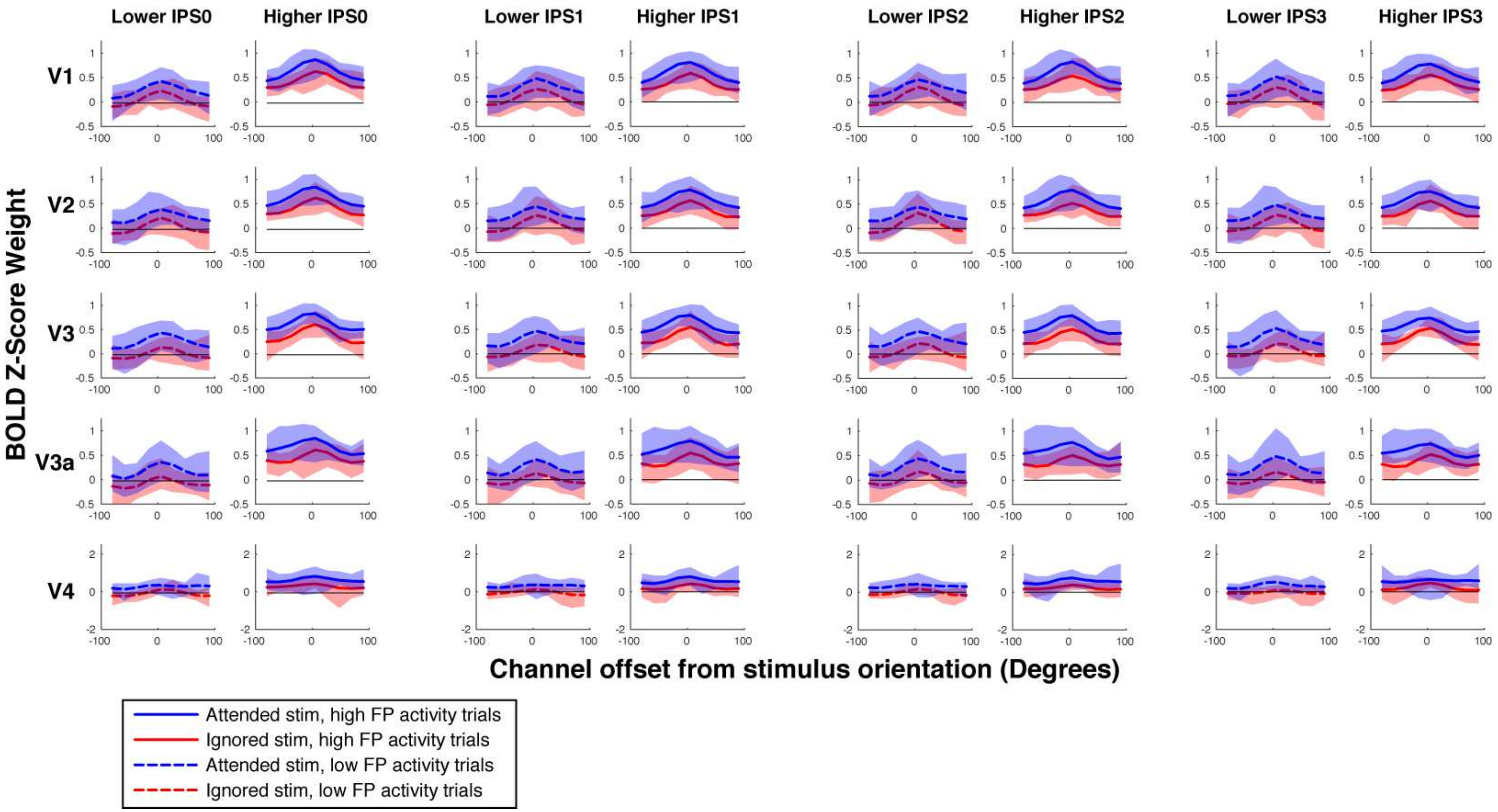

Figure 2-6: Channel response functions (CRFs) for attended (blue) and ignored (red) stimuli, as sorted by high and low IPS activity, for each early visual ROI. The first row plotted, across all columns, represents CRFs from V1, using trials that were either above or below the mean activity level of each of the IPS regions (each pair of columns). Furthermore, CRFs for attended (contralateral) and ignored (ipsilateral) are color coded blue and red, respectively. We see an overall additive shift from low to high IPS activity levels across all five VC ROIs.

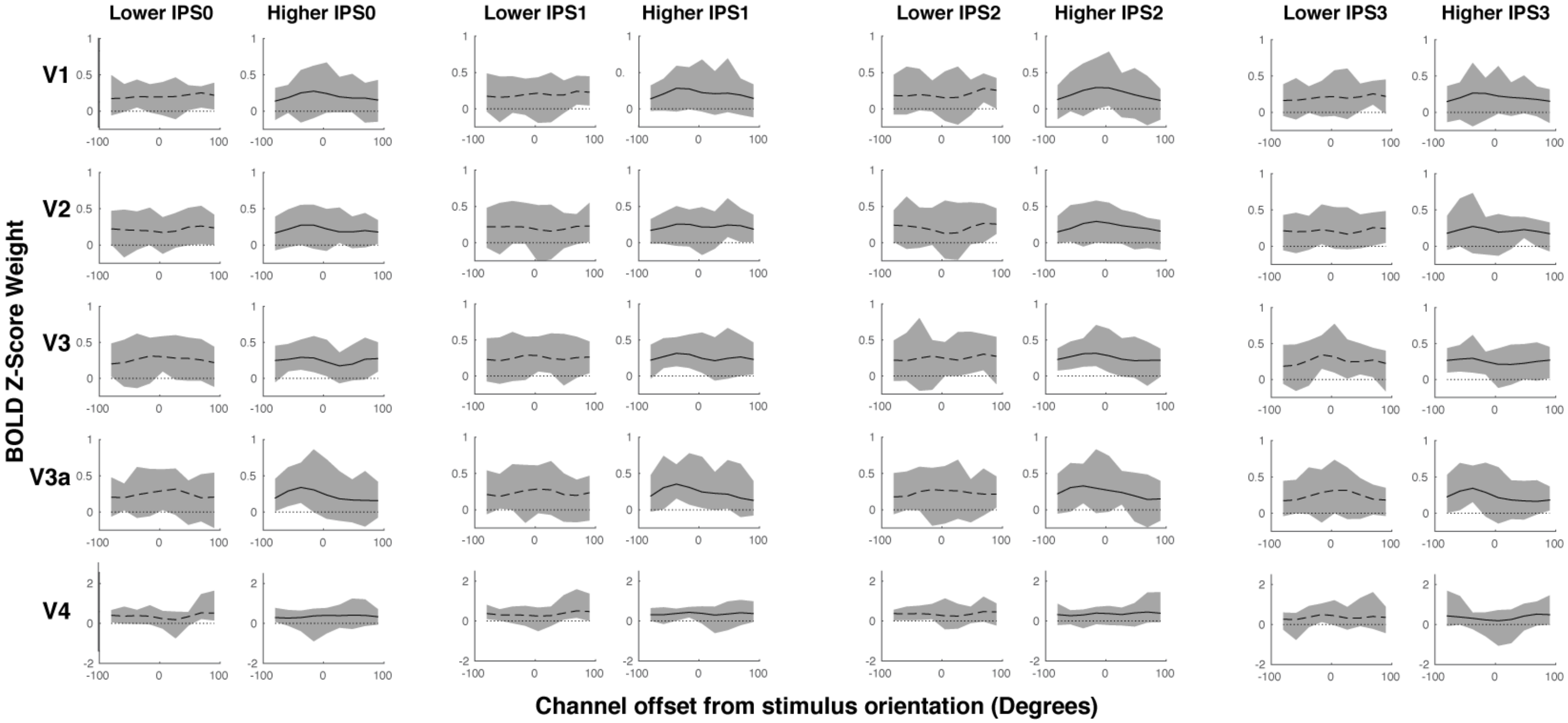

Figure 2-7: Differences in CRFs (attended minus ignored stimulus). To assess whether orientation representations differed between attended and ignored stimuli, here the difference between attended (blue in Figure 6) and ignored (red in Figure 6) stimuli is plotted. When the grey areas are above the dotted zero line, this means that the representation was enhanced on attended trials. Note the different scale for V4 CRFs compared to V1-V3a. Dashed black lines represent trials where bilateral IPS activity was lower, and solid lines are trials that bilateral IPS activity was higher.

2.5 Conclusions

Here we used fMRI to investigate the relationship between the BOLD responses of frontoparietal (FP) regions and differential activity in occipital visual cortical (VC) regions during a spatial attention task. We predicted that if FP regions send attentional control signals to VC during selective spatial attention related to the differential activity between attended and ignored parts of space, then FP signals should be related to the differential BOLD signal in VC. We used a paradigm in which subjects directed their spatial attention to either the left or right side of visual space on each trial. This allowed us to estimate a differential attentional modulation corresponding to retinotopic space in VC; a larger difference in BOLD signal between hemispheres (a larger IHD) should indicate greater spatial attention than a smaller difference between hemispheres (a smaller IHD). Similarly, greater FP activity should indicate more selective attention on a given trial than lesser FP activity. We therefore compared the IHD in VC with the overall FP activity on each trial and predicted that these two measures should be correlated. Surprisingly, we were unable to recover a significant relationship between FP BOLD activity and differential VC activity across trials.

First, we mapped univariate BOLD activity in contralateral regions of the brain. Then, we analyzed data by simply correlating VC and FP time series BOLD data together. Finally, we calculated the channel response functions (CRFs) in VC regions and found that there was a hint of an additive shift from ignored to attended stimuli, with trials sorted by higher or lower FP activity.

There are several possible explanations for these results, which seem to be at odds with previous work. In single- or multi-unit electrophysiology studies, evidence supports the idea that there is some relationship between FP and VC IHD responses. It could be that fMRI is not sensitive enough to detect the relevant attentional signals in each of our regions, or that we were looking for the wrong types of signals within each region. It also could be that more data is needed – however, even though our number of subjects is relatively low (seven subjects), we did collect a large amount of data per subject. The simplest interpretation of results supporting the idea that attentional control regions actually do send signals to VC in order to modulate their responses, at least at the level that fMRI BOLD is able to measure, is called into question given the findings from this experiment.

If we assume there really is no measurable relationship between FP and differential VC activity during selective attention using BOLD fMRI activity, what could this mean in reference to the existing body of research on this topic? It is possible that our measure of differential attention (the IHD within a single VC region on a given trial) does not, in fact, reflect the amount of visual attention that a subject is allocating during that trial. For example, attention to one hemifield might be spread to the other hemifield at a given point in time, rather than taking away information from the ignored side of space.

Another possibility is that the BOLD signal is not sensitive enough to track this kind of signal. The BOLD signal might be dominated by more global-scale fluctuations across the entire brain, which would then mask our ability to see what single-unit studies would predict. Although FP and VC regions do correlate their BOLD activity levels over time, so do most (or all) other regions of the brain. This could still be in line with single unit and EM studies if the BOLD signal is dominated by these larger-scale modulations during attention or otherwise.

Additionally, EM of FP regions could induce phase synchrony across multiple regions of the brain – such as in the alpha or gamma bands of frequencies. Global phase synchronization has shown to be affected by behavioral attentional control (Buzsáki and Wang, 2012). If so, this would support the role of cortical phase synchrony as well as the effects of EM to FP regions during selective attention. To target this question, one could utilize EM and EEG to measure the effects of EM on global phase synchrony in different frequency bands. Microstimulation could be done in FP regions as well as VC or other regions of the brain; perhaps EM of FP regions specifically induces global alpha phase synchrony whereas EM of other (non attentional control) regions might target other bands, or not induce phase synchrony at all. There is an inverse relationship between alpha band power and BOLD signal in some regions, such as in VC and the dorsal attention network (Spreng et al., 2010; Bressler et al., 2013), so exploring this could link the role of alpha oscillations with both attentional control and the BOLD signal during selective visual attention.

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CHAPTER 3

Behavioral oscillations following visual entrainment stimuli are not due to neural α oscillations

3.1 Abstract

Evoked neural responses to stimuli wax and wane over time, and many have hypothesized that the size of the evoked response is due to inhibitory waves that oscillate in the α band (~7-12Hz). In a different set of studies, behavior has also been shown to oscillate over time, either with respect to the timing of the stimulus relative to other stimuli, or with respect to intrinsic oscillations in the brain. In the current experiment, we investigate the link between behavior and neural oscillations by using rhythmic visual stimulation to moderate oscillations in the α band while assessing different psychophysical measures of visual perception. We find that visual entrainment stimuli cause oscillations in behavior due to rhythmic visual stimulation along with an increase in α power. However, there are no differences in α phase locking, nor is there a difference in prestimulus phase of the entrained α oscillations. We conclude that the behavioral effects of visual entrainment stimuli are not likely to be caused by the entrainment of α oscillations in the brain.

3.2 Introduction

Rhythmic oscillations in the brain are hypothesized to play an important role in mediating visual awareness (Jansen and Brandt, 1991; Lakatos et al., 2008; Busch et al., 2009; Mathewson et al., 2009, 2010, 2011; Busch and VanRullen, 2010; Haegens et al., 2011; Scheeringa et al., 2011). An oscillation is a rhythmic pattern of brain activity found in the firing rate of single neurons, local field potentials, electroencephalography (EEG), and magneto encephalography (MEG). Oscillations can be characterized by the speed of their period (frequency), magnitude of response (amplitude), and phase (the timing of the peaks vs. troughs of the oscillation). In visual perception, the α band of frequencies (around 7-12 Hz) has been a major point of research. For example, single external stimuli are able to produce multiple waves of activity in the cortex of animals around the α band of frequencies (Bartley, 1939) . Similarly, the magnitude of neural responses to multiple stimuli at different onset times varies at about 10 Hz (Chang, 1951), and behavior also oscillates with different amounts of time between stimuli (Landau and Fries, 2012; Fiebelkorn et al., 2013) .

The prestimulus amplitude of α rhythms has been shown to vary with measures of visual awareness such as behavioral detection rate (Ergenoglu et al., 2004; Thut et al., 2006; van Dijk et al., 2008; Romei et al., 2010; Bollimunta et al., 2011; Haegens et al., 2011) , or size of the neural response to a stimulus (Scheeringa et al., 2009, 2011; Haegens et al., 2011). Recent evidence also suggests that during certain phases of an α oscillation, people are better at detecting a stimulus than that same stimulus presented at other phases of the oscillation (Busch et al., 2009; Mathewson et al., 2009; Busch and VanRullen, 2010; Keitel et al., 2013; van Diepen et al., 2015). In addition, experimenters have proposed that α oscillations in the brain can be “entrained,” or phase-locked, to external flickering stimuli at different frequencies, similar to the method of steady state visually evoked potentials (SSVEPs) (Bartley, 1939; Lakatos et al., 2008; Mathewson et al., 2010, 2012; Spaak et al., 2014). By using visual entrainment, experimenters hope to be able to predict and manipulate the phase of ongoing α oscillations in the brain, allowing them to then link α phase in the brain with behavioral oscillations (Bartley, 1939; Lakatos et al., 2008)

Mathewson et al (2011, 2012) presented subjects with a rhythmic stimulus (a visual “entrainer”) in the α range (12 Hz) at the fovea, after which a target stimulus was presented at several onset asynchronies. Some “in phase” targets appeared in sequence with the flickering entrainment stimuli, whereas others showed up out of phase or antiphase to the entrainment stimuli. Subjects’ behavioral detection rates of the target stimuli oscillated in time: detection was improved at times during which the target was expected and worse at times when the target was unexpected. This behavioral oscillation occurred at the same frequency as the entrainment frequency. In addition, Mathewson et al. (2012) found that although there was not a significant increase in the power of the 12.1Hz oscillation in the EEG signal, there was significant phase-locking in the rhythmic vs jittered (but not the rhythmic vs. control) entrainment conditions.

While some evidence for rhythmic fluctuations in the α band exists – e.g., de Graaf et al., (2013) also found behavioral α oscillations following 10 Hz entrainment – several other findings are not consistent with this pattern of results. For example, an entrainment study by Spaak et al. (2014) found the opposite behavioral results when using entrainment stimuli at a lower entrainment frequency of 10 Hz in which the left or right side of fixation could be rhythmically or non-rhythmically entrained: targets occurring during expected (in-phase) times produced *lower* detection rates than those during unexpected times. Still others have found oscillations in behavioral detection rate without the use of entrainment stimuli, and those results show oscillations outside of the α band (e.g., Fiebelkorn et al., 2013) . Finally, visual entrainment has also been utilized in other frequency bands, and behavior tends to oscillate at whatever frequency the visual entrainment is presented (delta 1.5 Hz, Lakatos et al., 2008). This suggests that behavioral oscillations following visual entrainment might more related to temporal expectation as opposed to any neural entrainment in a specific frequency band. For example, work on selective temporal attention has shown that temporal expectations can have a profound impact on behavior (Summerfield and Egner, 2009; Rohenkohl and Nobre, 2011; Gazzaley and Nobre, 2012; Rohenkohl et al., 2012; Cravo et al., 2013; Morillon et al., 2016) .

For the purposes of the current study, we sought to clarify the effects of visual entrainment stimuli on the brain and on behavior. We aimed to replicate and extend the initial behavioral and EEG findings from Mathewson et al. (2009; 2012) to critically test the hypothesis that the magnitude and phase of EEG α oscillations (1) can be "entrained" to a visual entrainment sequence in the context of their experimental paradigm, and (2) that any such neural entrainment can be linked to behavioral oscillations in the α band resulting from visual entrainment. We also investigate individual subjects' behavioral oscillations, which allow us further explore the richness of individual subject data and the extent to which an entrainment stimulus can drive behavioral fluctuations of detection performance.

Here we find that behavior fluctuates over time, roughly in time with the frequency of a physical entrainer stimulus. We then examine neural entrainment to this frequency over posterior EEG electrode Pz, and find that power of entrained activity does in fact increase in the rhythmic entrainment condition compared to the control condition. However, the EEG signal at the entrained frequency does not show significant phase locking to the external flickering stimuli throughout or after the entrainment period in posterior electrodes. In sum, our results confirm previous reports that physical entraining stimuli can affect behavior. However, entrainment stimuli in this paradigm do not appear to significantly affect the phase or power of the α signal in the brain. Based on this evidence, we argue that modulations in behavior in this type of paradigm likely reflects some other mechanism of attention, such as temporal expectations, as opposed to the entrainment of neural activity in the α band.

3.3 Methods

3.3.1 Participants

Twenty-four subjects in Experiment 2 (psychophysics) were recruited from the UC San Diego undergraduate psychology program and provided written informed consent. Subjects were run over 2 days, and were given credit for coursework or were paid $10/hour for their time. Three subjects were excluded from the analyses because they performed with an average d’ lower than -1, meaning their false alarm rate was greater than their hit rate, so they were not properly performing the task. Thus, in total 21 subjects were included in the analyses from Experiment 2. The first demonstration of the behavioral effects of visual entrainment in α collected data from 13 participants (Mathewson et al., 2012) .

In Experiment 3 (EEG) we ran 24 subjects in one experimental session. Six subjects were excluded because of technical issues or excessive movement (see **Table 3-1**) leaving 18 subjects for analyses. Subjects were paid $15/hour for their time and provided written informed consent. Both studies received ethical approval from the local institutional review board (IRB). All subjects reported normal or corrected to normal vision.

Table 3-1: Reasons for excluding subjects in Experiment 3 (EEG). n=18 after excluding these subjects from Experiment 3 (EEG). “Bad trials” refers to trials with large artifacts in the data.

Subject name	Reason for taking out
s404	acquired at 512 Hz instead of 1024 Hz
s406	Technical issues with EEG data collection equipment
s407	100% bad chans; 40% bad trials
s409	100% bad chans; 25% bad trials
s413	28% bad chans; 25% bad trials
s418	21% bad chans; 26% bad trials

3.3.2 Stimuli & Procedure

The paradigms for both experiments were based closely on the paradigms used in Mathewson et al (2009; 2012). A schematic of the stimuli is depicted in **(Figure 3-1).** Entrainment stimuli consisted of centrally presented dark grey rings (1º inner diameter; 2º outer diameter) shown against a medium grey background. The target stimulus was a centrally presented circle (1° diameter). Stimuli were generated using Matlab and the Psychophysics Toolbox (Brainard, 1997) , presented on a CRT monitor with an 85 Hz refresh rate, and a viewing distance of 51cm. EEG data (Experiment 3) were collected at 1024 Hz sampling rate using BioSemi software, using a 64-electrode cap.

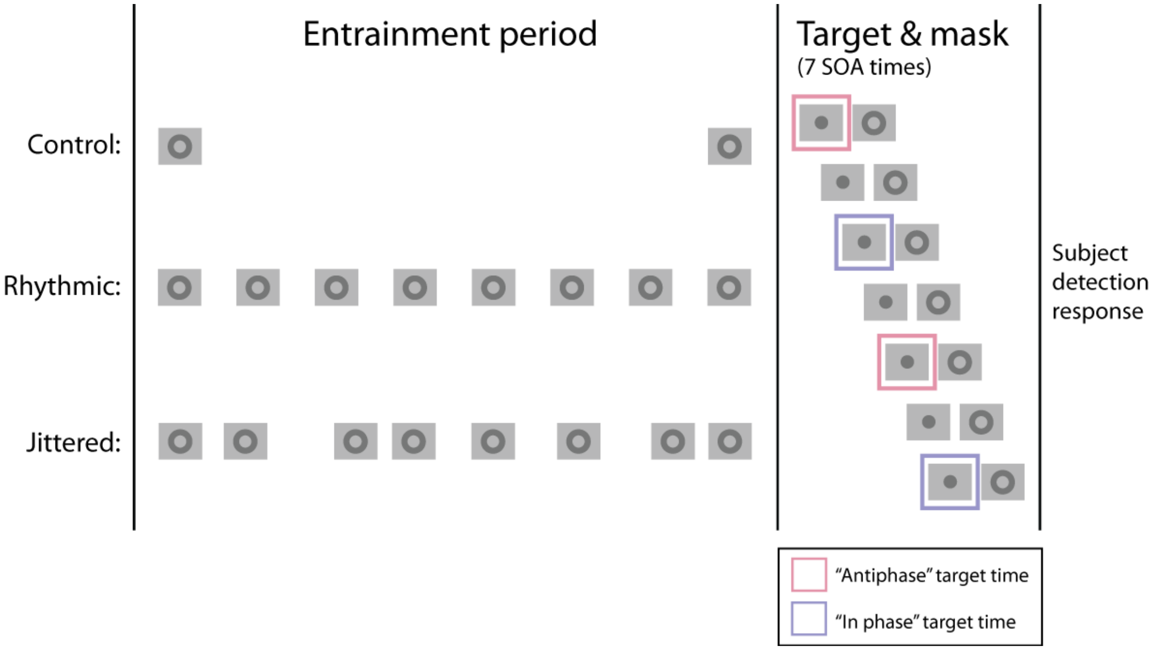


Figure 3-1: Experiment 2 psychophysics paradigm. Figure based off Mathewson et al. (2012). Each trial consisted of an entrainment period, target & mask period, response period, and an 459ms inter-trial interval during which just a fixation cross (0.5°) was on the screen. Subjects responded whether or not they saw the target stimulus after each trial with a button press. There were 7 different target times relative to the offset of the last entrainment stimulus, and 80% of all trials contained targets while on the remaining 20% of trials no target was presented. No-target trials still contained a mask stimulus.

In Experiment 2, the entrainment period (lasting a total of 600 ms) could consist of one of three possible sequences: control (one stimulus at the beginning and one at the end of the entrainment period), rhythmic (8 stimuli equally spaced across the entrainment period), and jittered (8 stimuli unevenly spaced throughout the entrainment period, with the restraint of having at least 1 blank frame between any two stimuli). Note that for the rhythmic condition stimuli were presented at 12.1Hz. After the entrainment period, the target disc could appear at any of 7 possible stimulus onset asynchronies (SOA) after the onset/offset of the last flash of the entrainment sequence. Possible SOA's were 36, 60, 83 106, 130, 154 and 177 ms after the onset of the last entrainer stimulus. Subjects responded with a button press if they detected the target, and with a different button if they did not detect the target on each trial. All trials ended with a mask stimulus (identical in appearance to the entrainment stimuli) regardless of whether the target had been presented or not. On trials where a target stimulus had been presented, the mask appeared 4 frames (~47 ms) after the target. If there was no target stimulus, the mask still appeared 4 frames after what would have been the target stimulus.

Each of 21 possible conditions (3 entrainment conditions by 7 SOA conditions) was presented 62 times for each subject (the same number of presentations as in Mathewson et al., 2012). The target was present on about 80% of the trials, leaving 49-50 trials per condition for trials containing a target stimulus, and 12-13 no-target trials per condition (variability was due to an accidental bug in the code). In total, the experiment took about 2 hours to complete (data collected over 2 days).

In Experiment 3, the paradigm was exactly the same except (1) there was no jittered entrainment sequence, and (2) null trials were added (40 total) during which there was a fixation cross for the duration of the trial (600 ms). These trials were randomly interleaved with normal trials. Subjects were instructed to blink between trials while the fixation cross was on the screen. Across all subjects, an average of 3.4% of the trials were excluded from analyses because of blink or motion artifacts, and 2 (out of 64) electrodes were taken out because of large voltage variations (bad electrodes). Perceptual contrast thresholds were not adjusted per participant (staircased), but rather all were the same across participants as in the Mathewson et al studies.

Before starting the EEG phase of the experiment, subjects were trained on one or more blocks of practice trials (51 trials per block) during which they were given accuracy feedback after each trial. Their task, again, was to detect the presence or absence of the target stimulus via different keyboard buttons. Subjects completed a total of 20 blocks of 51 trials each. Most subjects completed the EEG portion within about 2 hours, but some needed extra behavioral training runs in which case the EEG experiment was split across 2 days (2 subjects).

3.3.3 Analyses

For the behavioral data from both Experiments 2 and 3, we calculated the d', hit rate, criterion and false alarm rates across the different entrainment conditions and SOA target times. First we performed an ANOVA to find main effects and interactions between the conditions. We then tested whether these measures oscillated at the flicker frequency (12.1Hz) across the 7 SOA target times by using multiple linear regression. In this, we used four regressors: a constant, a linear function going from 0 to 1 across the 7 SOA times, a sine wave and cosine wave. We then calculated the phase angle for each behavioral measure by taking the four-quadrant arctangent of the sine and cosine beta weights from the regression. The result is a polar plot of the average phase angle (and vector length) for each subject for each psychophysical measure. Subjects were then circularly averaged together to produce an average vector for phase angle for each psychophysical measure.

We computed the Bayesian Information Criteria (BIC) for all possible models combining subsets of the 4 regressors and a model including all 4 (constant, line, sine & cosine) was the best model. We performed a Rayleigh test for nonuniformity (Berens, 2009) of the phase angles across trials in each of our entrainment conditions: we have a distribution of subjects' phase angles and test whether these phases significantly point in a certain direction, or whether they are distributed uniformly across all phase angles thus indicating no significant direction of phase.

In Experiment 3, we were also interested in the EEG signal "entraining" (phase-locking the evoked response) to the physical flickering stimulus at 12.1Hz. We transformed our data into the frequency domain using a 12.1 Hz gaussian-filtered wavelet with a bandwidth of 0.15 (103ms). We calculated the power of the wavelet transform by taking the absolute value of the complex coefficients and squaring them. Then we removed the baseline power for each electrode by subtracting the power 100 ms before the onset of the first entrainment stimulus from every proceeding time point in the averaged trials. This produced an estimate of the SSVEP power at 12.1 Hz for each subject and for each time point. In addition, we calculated the difference in SSVEP power in each electrode for the entrained condition minus the control and then performed a t-test for the difference in entrained α power, and used FDR correction for multiple comparisons.

In addition, we calculated a phase-locking index (PLI) as previous experiments have done (Ding et al., 2006) in which we the wavelet transform was calculated for each trial separately, then was averaged data across trials for each entrainment condition. Then we took the average vector length by taking the absolute value of the transformed data to get the PLI. We performed t-tests the difference between conditions, and corrected for multiple comparisons using FDR.

Finally, in order to tie our results to findings about the specific phase of α oscillations during a prestimulus period, we calculated the phase angle of the entrained EEG α oscillation before the onset of in-phase and antiphase target stimuli. We plotted the phase in occipital electrodes for all subjects and calculated the average phase angle across subjects 100ms before the onset of the target stimulus.

3.4 Results and Discussion

3.4.1 Psychophysics results (Experiments 2 and 3)

To directly compare our behavioral results with those in previous studies, and to test whether there is an oscillation in our subjects' psychophysical thresholds across time, we plotted four psychophysical measures – d', hit rate, criterion, and false alarm rate – across our 7 stimulus onset asynchrony (SOA) target times for each entrainment condition (rhythmic, jittered, & control; **Figure 3-2** for Experiment 2, and **Figure 3-3** for Experiment 3). Following previous studies, we expected to see an oscillation in some or all of the psychophysics parameters, with, for example, higher hit rates during the SOA times that were in phase with entrainment stimuli, and lower hit rates for the anti-phase (unexpected) SOA target times. Our hit rates are similar to those found in Mathewson

(2012), showing evidence of an oscillation in the rhythmic and jittered conditions but not in the control condition. Note that the pink highlighted SOA times across the x-axis are anti-phase: occurring at the time *between* the last entrainment stimulus and the next expected entrainment stimulus; the blue-highlighted SOA times are in-phase with the entrainment stimuli. Also note that higher criterion levels mean that the subject is more cautious about reporting a “target seen” response.

We performed a repeated-measures two-way ANOVA on the psychophysics results for Experiment 2 (**Figure 3-2**) and found a main effect of entrainment condition for the following: hit rate: F(2,42)=18.44, p<0.0005; criterion: F(2,42)= 16.57, p<0.0005; false alarm rate: F(2,42)=9.69, p<0.0005, but d’ did not show a main effect of entrainment type. We also found a significant main effect of SOA for all behavioral measures: d’: F(6,126)=2.79 , p<0.05; hit rate: F(6,126)=10, p<0.0005; criterion: F(6,126)= 4.07, p<0.001; false alarm rate: F(6,126)=2.25, p<0.05. Finally, there was a significant interaction between entrainment and SOA conditions in hit rate: F(12,252)=4.47, p<0.001; criterion: F(12,252)=2.08 , p<0.05; and false alarm rate: F(12,252)=2.95, p<0.05, and d’ did not have a significant interaction.

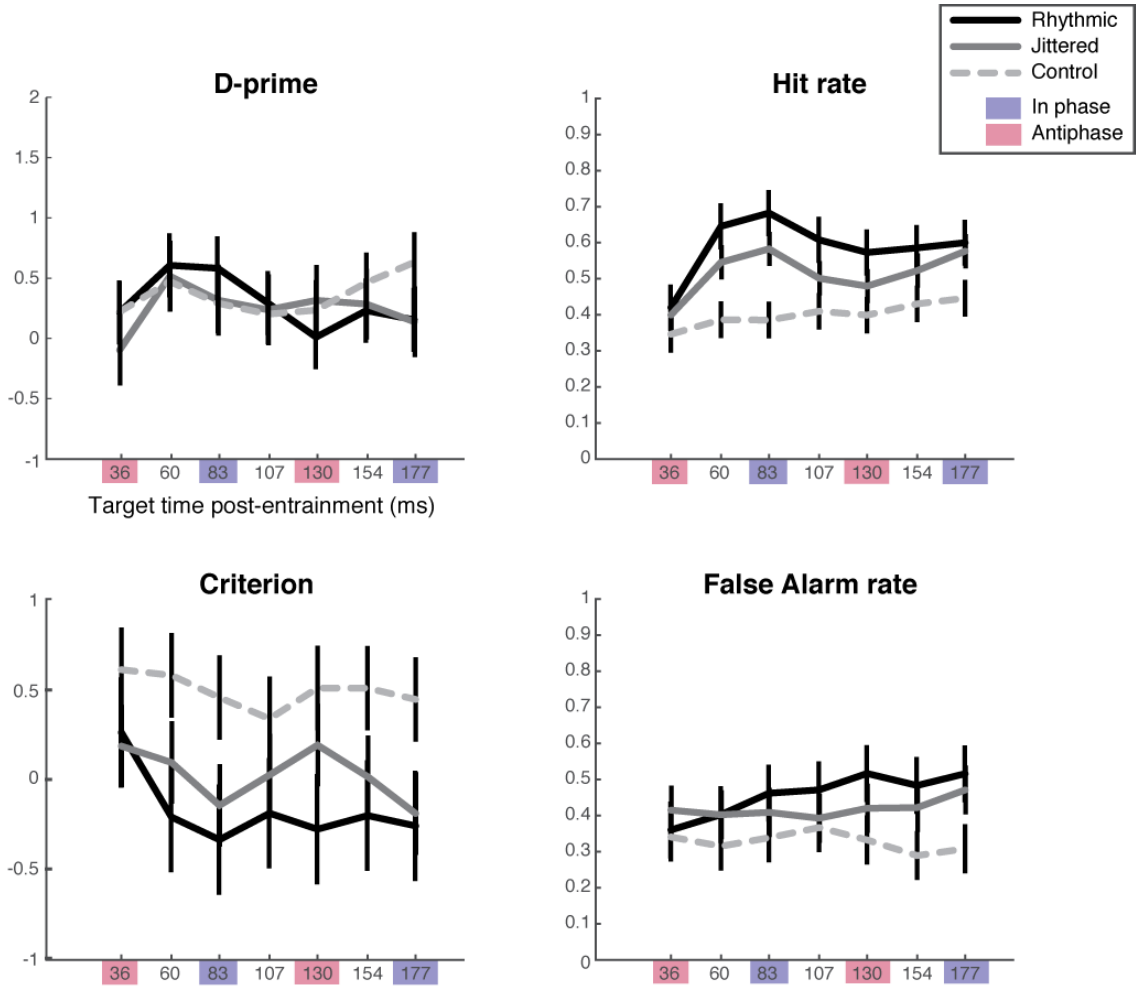


Figure 3-2: Experiment 2 psychophysics results. (n=24) The average of each behavioral measure across all subjects. Error bars are SEM. The blue highlights on the x-axis represent the “in-phase” target times whereas the pink highlights represent the “antiphase” SOA target times. ANOVAs showed a significant main effect of entrainment condition in hit rate, criterion and false alarm rate, and a main effect of SOA time in all four measures, and a significant interaction in all except d’.

Similarly, for Experiment 3 we ran a two-way repeated-measures ANOVA on each of our psychophysics measures (plotted in **Figure 3-3**). We found a main effect of entrainment condition in d’: F(1,17) = 17.14, $p < 0.05$ and hit rate: F(1,17)=19.05, $p<0.0005$; the criterion and false alarm rate did not have a significant main effect of entrainment condition. The SOA target time condition also showed a main effect in d’:

$F(6,102) = 2.85$, $p<0.05$; hit rate: $F(6,102)=7.907$, $p<0.0005$; and criterion: $F(6,102)=3.55$, $p<0.005$; false alarm rate did not show a main effect of SOA time. The interactions between entrainment condition and SOA time were significant for d': $F(6,102)=5.47$, $p<0.0005$; hit rate: $F(6,102)=4.51$, $p<0.0005$; false alarm rate: $F(6,102)=2.77$, $p<0.05$; the criterion interaction was not significant.

The behavioral results from Experiment 3 show overall higher performance than Experiment 2, as can be seen with higher d' levels across subjects and very low false alarm rates. For main effects of entrainment condition, our two experiments showed slightly varying results. With respect to entrainment condition main effects, Experiments 2 and 3 both show significant effects in hit rate, but show varying results for d' (Experiment 3 only), Criterion (Experiment 2 only), and False Alarm Rate (Experiment 2 only). For main effect of SOA target time, hit rate and criterion show main effects in both experiments, but d' and False Alarm Rate are only significant in one of the 2 experiments. Finally, interactions between the two conditions are consistent in hit rate and false alarm rate, but not for d' (Experiment 2 only) or criterion (Experiment 3 only).

In terms of main effects of SOA target time, the hit rate, d', and criterion all showed main effects across both experiments, but false alarm rate only significantly varied with SOA time in Experiment 2 but not Experiment 3. We speculate that the overall higher performance rates for subjects in Experiment 3 can be explained by several factors that ensured these subjects were more motivated to perform well over subjects in Experiment 2. Subjects in Experiment 3 were monitored verbally between each block of trials and they knew their performance was being monitored. Experiment 2 subjects, on the other hand, were not being watched, and self-paced their own blocks of trials.

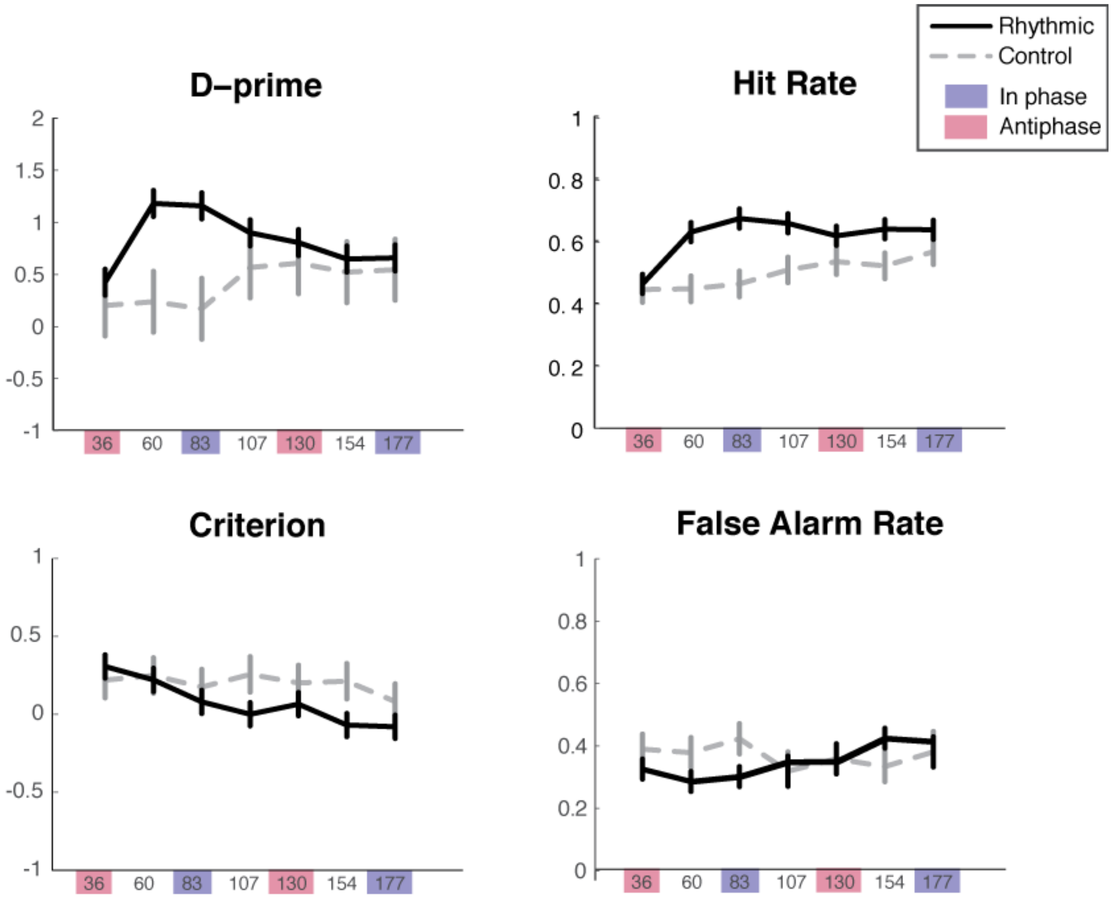


Figure 3-3: Experiment 3 (EEG) psychophysics results. (n=18). Error bars are SEM. Note that the false alarm rate is on a different scale here than in Figure 1. We saw a significant main effect of entrainment condition in d’ and hit rate; significant main effect of SOA time in d’, hit rate, and criterion. ANOVA showed significant interactions in d’, hit rate and false alarm rate.

A look at individual differences between subjects for hit rates across SOA times for Experiment 2 can be seen in (**Figure 3-4**). This underlines the variability across subjects’ performance levels as well as apparent oscillations in the hit rates across SOA target times. Several subjects performed at ceiling, several at floor, and many do not vary in performance across entrainment conditions, whereas others vary in different ways.

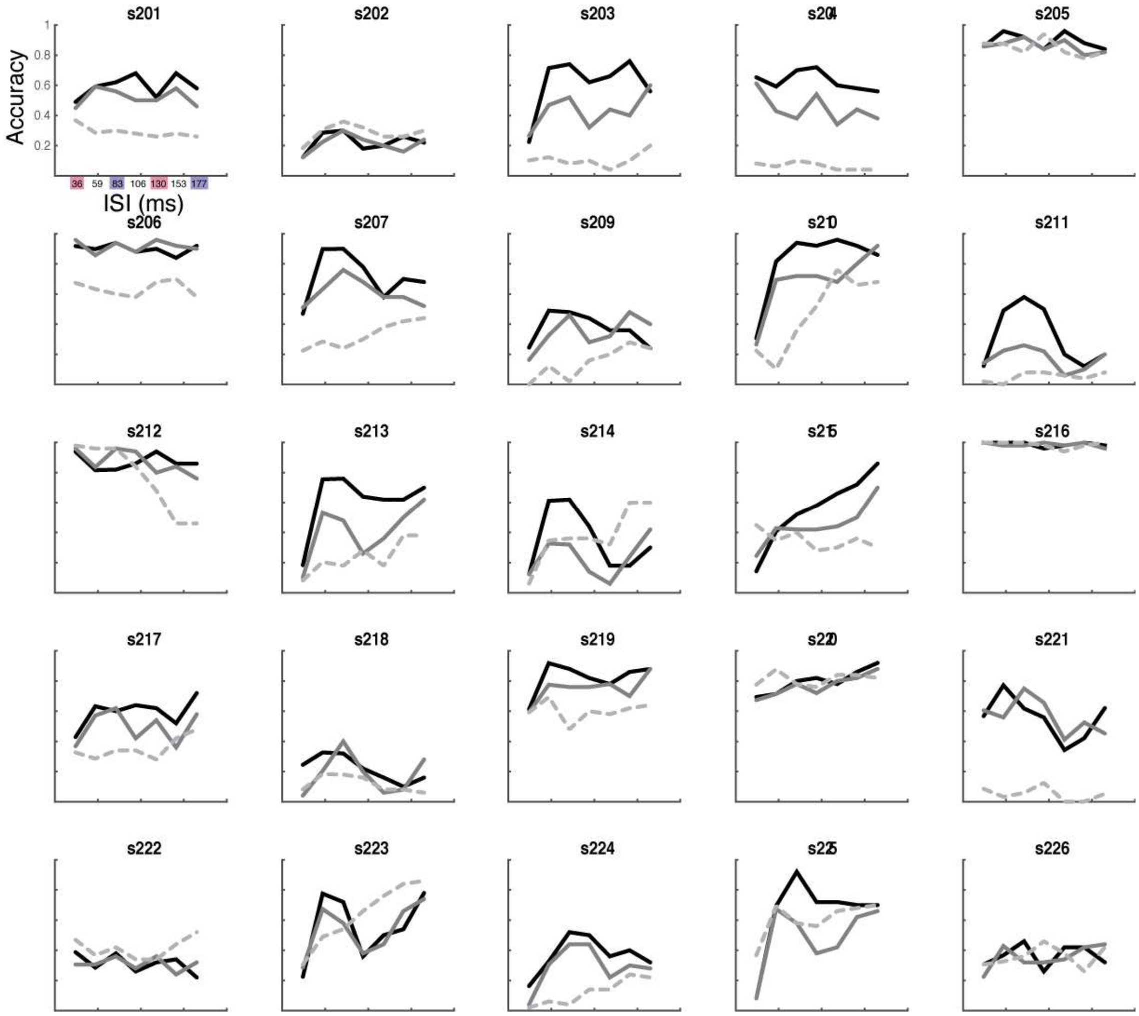


Figure 3-4: Experiment 2 individual subject hit rates across the 3 entrainment conditions. Subject s208 did not complete the study, so these are the remaining 25 subjects. This figure demonstrates the large variability in performance as well as the apparent oscillations seen in the rhythmic/jittered entrainment conditions compared **to** the control entrainment condition. We decided to take out 3 subjects because their d' levels were lower than -1, indicating higher false alarm rates than hit rates. These were subjects s205, s221, and s225.

Similarly, individual subject differences in Experiment 3 are shown in (**Figure 3-5**). Note that even for subjects who appear to have differences between hit rates in entrainment conditions, the "oscillation" across SOA times is only apparent in some of the subjects.

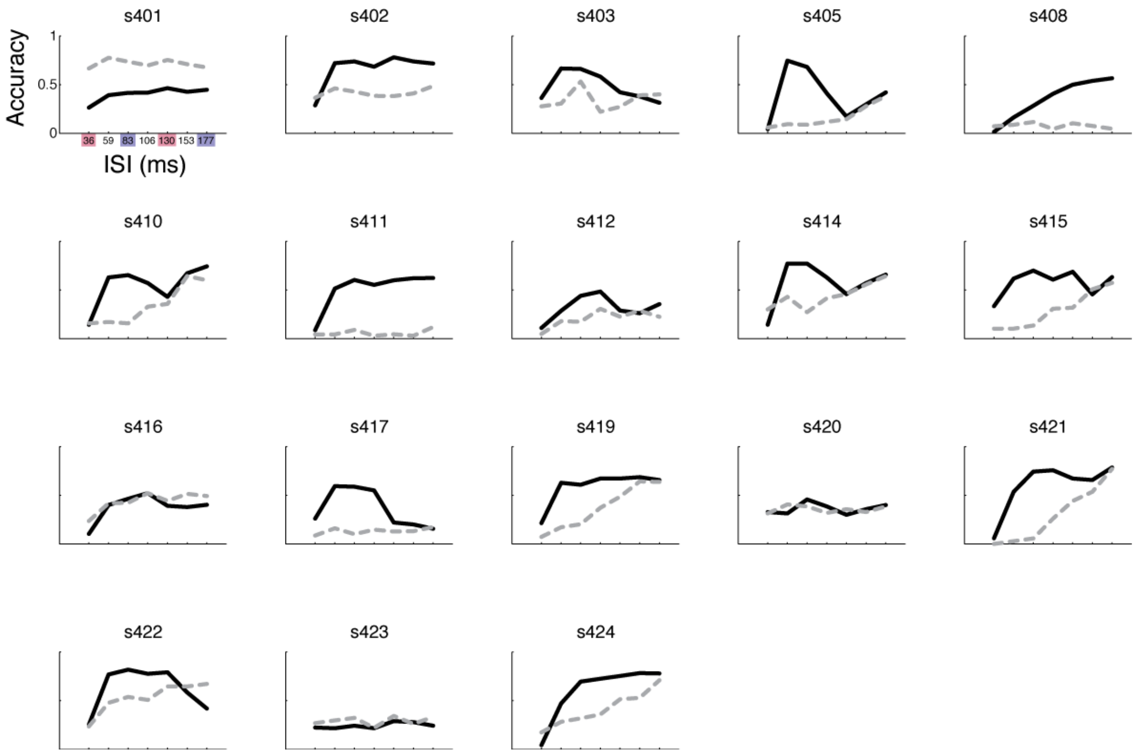


Figure 3-5: Experiment 3 hit rates per subject. Some subjects appear to have a periodicity in their hit rates for the rhythmic entrainment condition, however others do not show this pattern, or do not show any difference between rhythmic and control entrainment conditions.

3.4.2 Periodicity of psychophysics results (Experiments 2 and 3)

Figure 3-6 shows the best-fit phase angles for each condition in each psychophysical parameter for Experiment 2. The Rayleigh tests for phase distribution uniformity showed the following (see **Table 3-2)**: The rhythmic entrainment condition was significantly different from a uniform distribution of phases for hit rate (rhythmic entrainment Z: 11.45, $p < 0.00005$; jittered entrainment Z: 7.699, $p = 0.0003$) but not for d’, criterion, or false alarm rate for either rhythmic or jittered conditions. The control condition was not different from a uniform phase distribution in any behavioral measure. These tests confirm that the hit rate data during the rhythmic condition does have an oscillating periodicity, as it appears to in the behavioral figures in **(Figure 3-2** & **Figure 3-3)**. However, the d’ does not. To test for specific predicted phase angles of the data, we also performed a one-sample t-test using circular statistics for the mean direction pointing at 0 degrees (the in-phase target time). We found that the rhythmic and jittered conditions for hit rate did have a mean direction of 0 degrees (rhythmic Z: -0.25; jittered Z: -0.0397). In addition, we tested whether any of the entrainment conditions were different from each other in the hit rate distributions and found that neither the rhythmic nor jittered conditions had significantly different phase angles than the control condition (rhythmic vs. control F: 0.593, p = 0.446; jittered vs. control F: 0.543, p = 0.466).

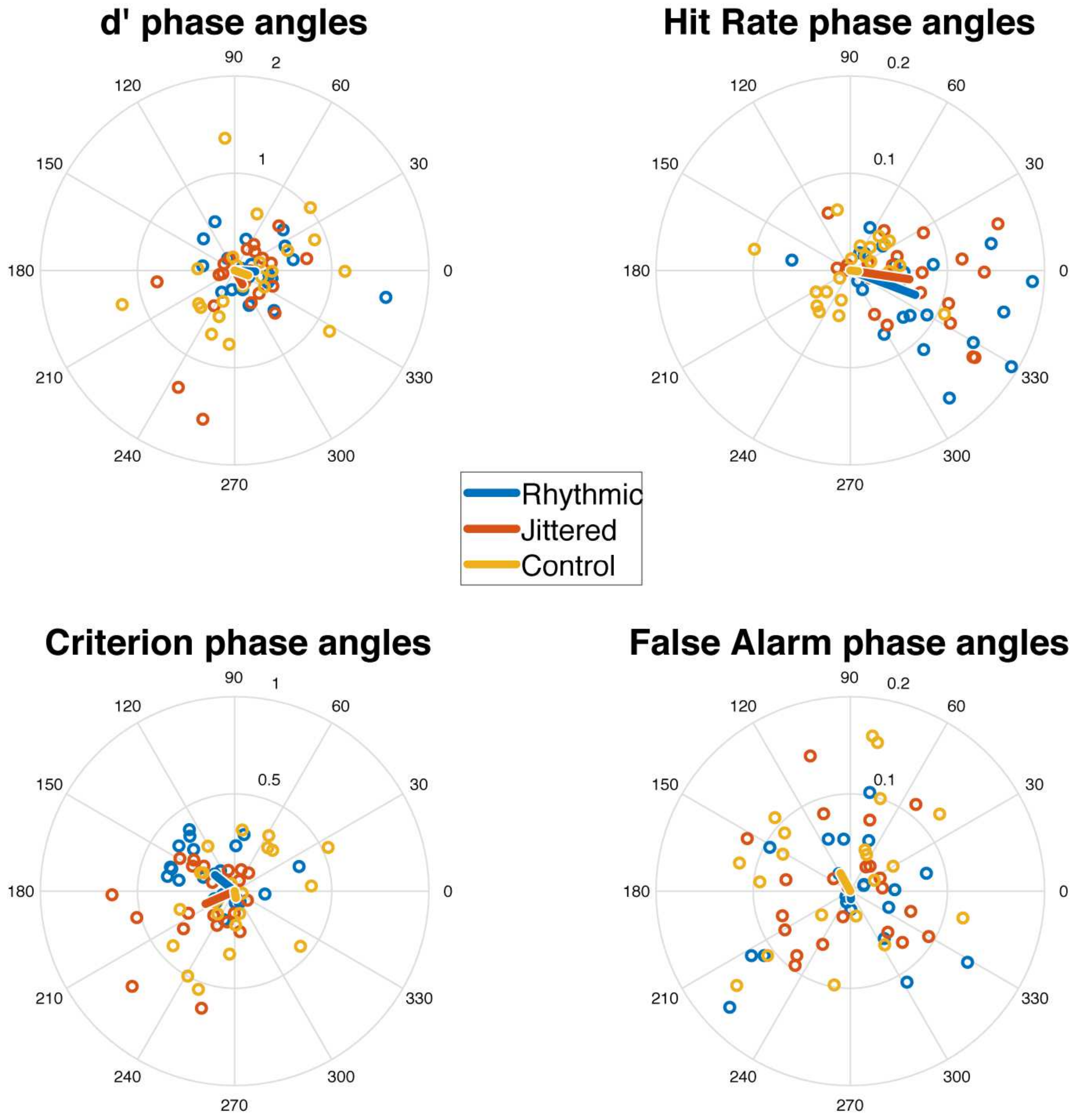


Figure 3-6: Experiment 2 phase angles of behavioral measures. We ran the behavioral data through sine and cosine regressors to find the best phase angle of each entrainment condition. The regressors were predicted to start at the end of the entrainment period and had an oscillation at 12.1Hz (the stimulation frequency that we predict behavior should follow). Each dot is a subject for each entrainment condition, and each line coming from the center is the average vector of each entrainment condition across subjects. Significant phase angles across subjects are found in (Table 3-2).

Table 3-2: Rayleigh tests for phase angle distributions of psychophysics data from Experiment 2. The rhythmic and jittered entrainment conditions had significant phase angles across subjects (nonuniform distribution of phase angles) for d', hit rate, and criterion. Corrected for multiple comparisons using FDR correction (threshold p = 0.000025). Both the rhythmic and jittered conditions were found to have an average phase angle of 0 degrees from a circular t-test.

Expt 2	**Rayleigh test**	**Z**	**P-val**
D'	Rhythmic	4.095	0.015
	Jittered	1.728	0.178
	Control	1.554	0.213
Hit rate	Rhythmic	11.446	<0.00005
	Jittered	7.699	0.0003
	Control	1.103	0.336
Criterion	Rhythmic	3.879	0.0189
	Jittered	3.238	0.037
	Control	0.304	0.742
False Alarm rate	Rhythmic	0.906	0.409
	Jittered	0.041	0.961
	Control	0.151	0.863

For Experiment 3, we have the same analysis in which we calculated the phase angle of the group-averaged behavioral measures using linear regression, and the resulting polar plots (**Figure 3-7**), followed by statistics testing for significant phase angles of the behavioral data (**Table 3-3**). We found a significant main effect of the phase of the rhythmic condition for d' (Z: 5.05, p = .005), and hit rate (Z: 5.79, p = .002), but not for criterion or false alarm rate, and the control condition was not significant in any of the psychophysical measures. Results from this analysis indicate that the mean direction of the rhythmic condition does not significantly point to 0 degrees (the in-phase direction; d' Z = -0.749; hit rate Z = -0.576). In addition, we tested whether any of the entrainment conditions were different from each other in any psychophysical measure and found the rhythmic condition does in fact have a significantly different phase angle for d’ (F: 21.969, $p < 0.000005$) and also for hit rate (F: 31.02, $p < 0.0000005$).

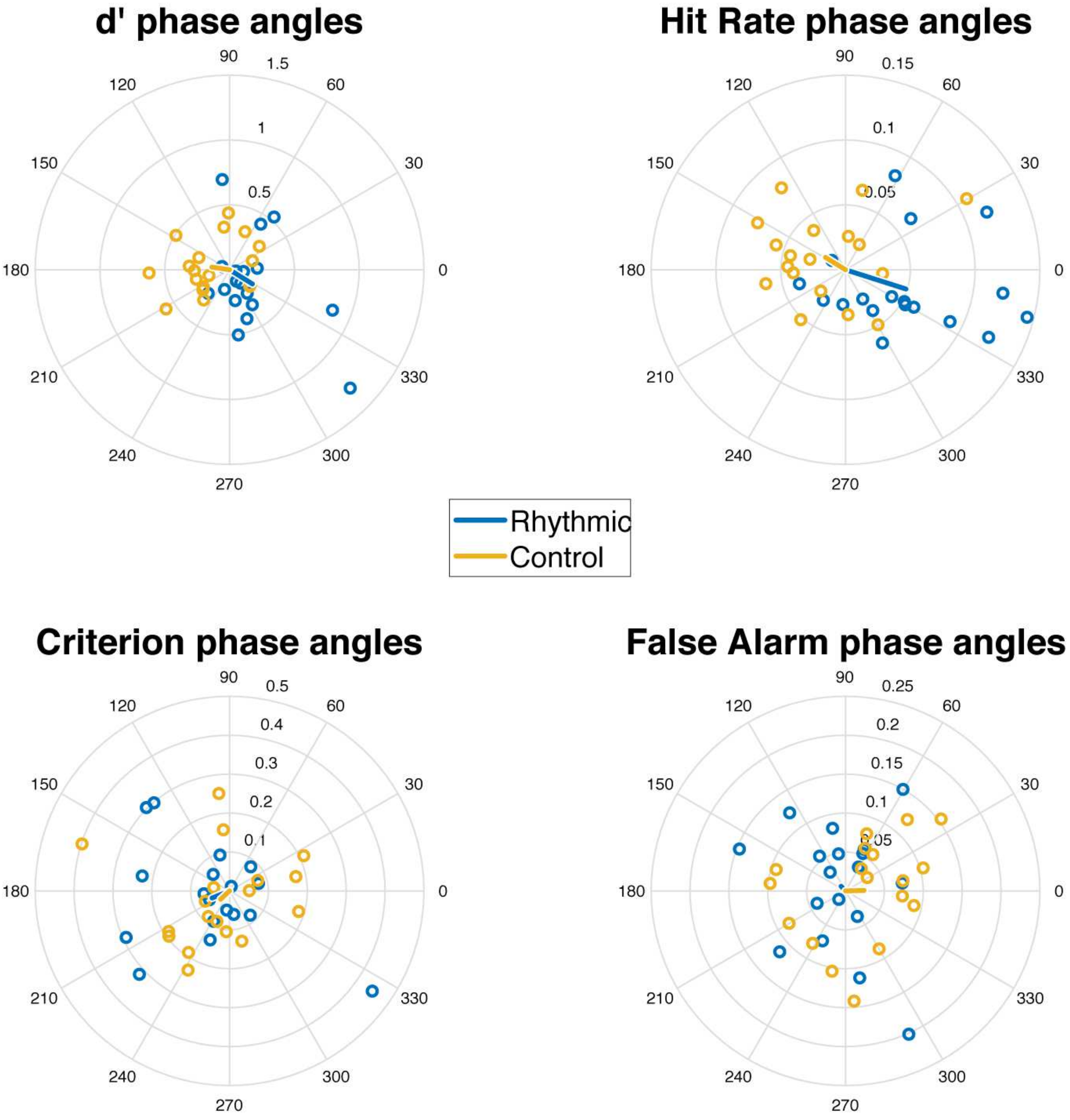


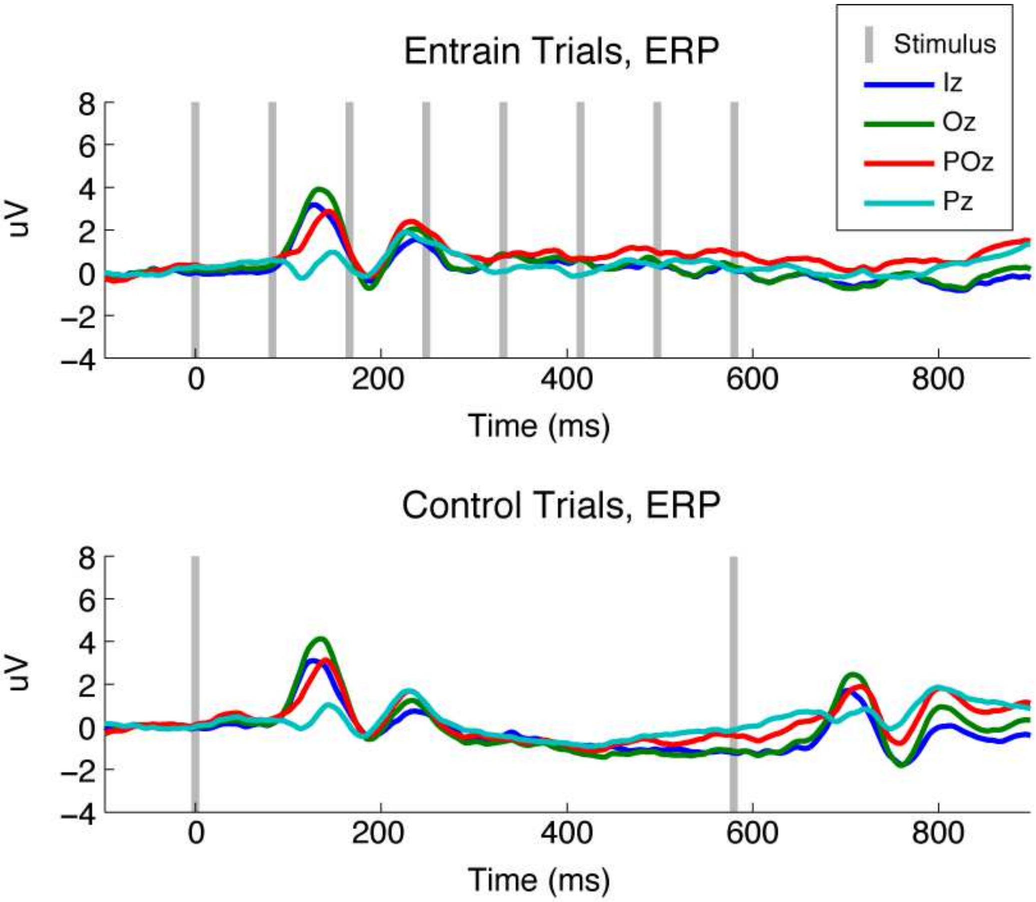
Figure 3-7: Experiment 3 behavioral phase angle fits. See Figure 3-6 for description. Note that Experiment 3 did not contain a jittered entrainment condition.

Table 3-3: Rayleigh test results for nonuniformity on behavioral data in Experiment 3 (EEG). Significant phase angles were found for the rhythmic entrainment condition for both D’ and hit rate. P-values are significant with an FDR correction for multiple comparisons (threshold p = 0.005). However, neither the d’ nor hit rate rhythmic conditions were found to have a significant phase angle pointing at 0 degrees (circular statistics t-test).

Expt 3	**Rayleigh test**	**Z**	**P-val**
D'	Rhythmic	5.05	0.005
	Control	2.11	0.12
Hit rate	Rhythmic	5.79	0.0021
	Control	2.42	0.088
Criterion	Rhythmic	0.98	0.38
	Control	1.02	0.367
False Alarm rate	Rhythmic	0.58	0.57
	Control	1.75	0.17

3.4.3 EEG results (Experiment 3)

We also examined the event related potentials (ERPs) in four occipital electrodes Iz, Oz, POz, and Pz across subjects (**Figure 3-8**). Similar to results from Mathewson (2012), we see an initial evoked potential after the first entrainment stimulus in both the rhythmic and control conditions, and an additional evoked potential after the last entrainment stimulus in the control condition. These transient responses are likely due to phase resetting of the α oscillation when stimulus onsets or offsets occur (Makeig et al., 2002; Mathewson et al., 2012) .


Entrain Trials, ERP

Control Trials, ERP

Figure 3-8: Experiment 3, ERPs in control and entrain trials in occipital electrodes. Averaged across 18 subjects. The control condition shows two distinct α resetting signals at the beginning and end of the entrainment cycle – similar to those found in Mathewson et al. (2012).

To investigate whether evoked α power increased at the stimulus-entrained frequency (12.1Hz), we performed a wavelet analysis at 12.1Hz and plotted the power at electrode Pz across all subjects, split into the rhythmic and control conditions, and the difference between them (**Figure 3-9**). Although there is an overall increase in 12.1Hz power in the rhythmic and difference, these were not significant increases (FDR corrected for multiple comparisons). Importantly, these increases in power did not last into the important part of the trial related to behavior, the target period.

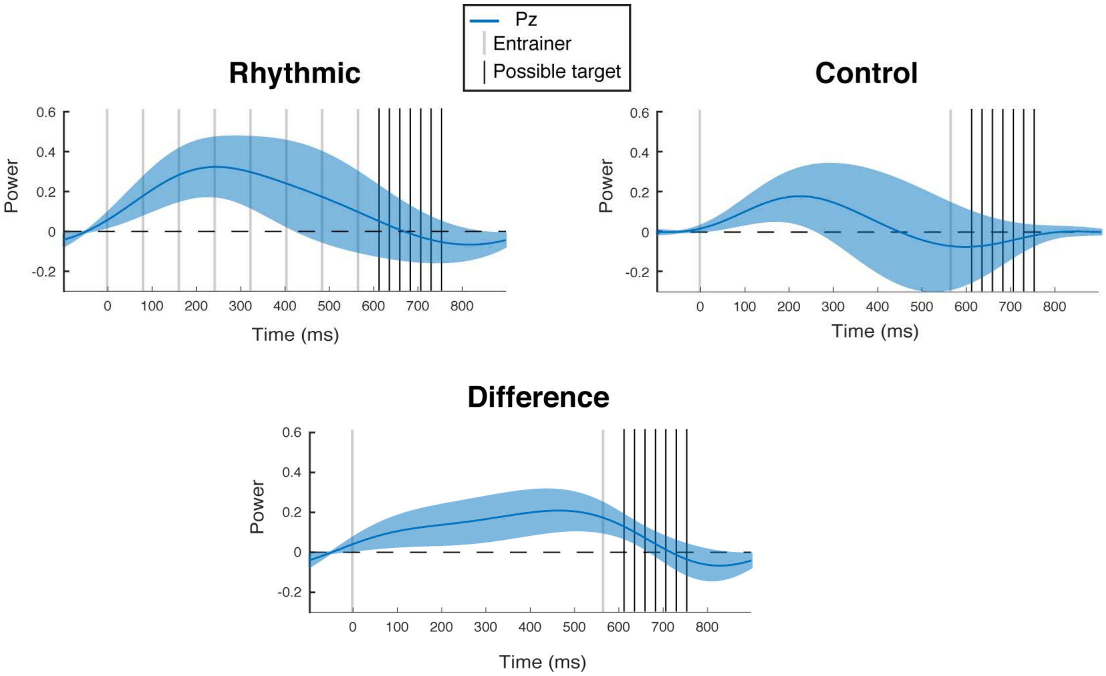


Figure 3-9: SSVEP power at entrainment frequency and significant phase angles across time in occipital electrode Pz. Plotted on the y-axis is wavelet power (at the stimulation frequency 12.1Hz); vertical lines are the stimulus times. There were no significant increases in wavelet power in any of the plots (FDR-corrected for multiple comparisons). Error bars are standard error of the mean.

We also tested the change in PLI for the rhythmic and control conditions, and took the difference between these (**Figure 3-10**). We found a significant increase in PLI for the rhythmic condition during the entrainment period (outlined in black in **Figure 3-10**), but found no significant difference in PLI between rhythmic and control conditions in any time point (FDR corrected). This indicates that the entrainment stimuli did not significantly affect either the power or the PLI of evoked α oscillations, in contrast to some previous findings (e.g., Mathewson et al., 2012; de Graaf et al., 2013; Keitel et al., 2013; Spaak et al., 2014), but in agreement with others (e.g., Mathewson et al., 2012). This finding further calls into question the purpose of using entrainment stimuli as a means to affect neural oscillations in the α band. Visual entrainment in the α band seems to affect behavior and α power at the entrained frequency, but does not significantly affect the phase locking of alpha rhythms in the brain.

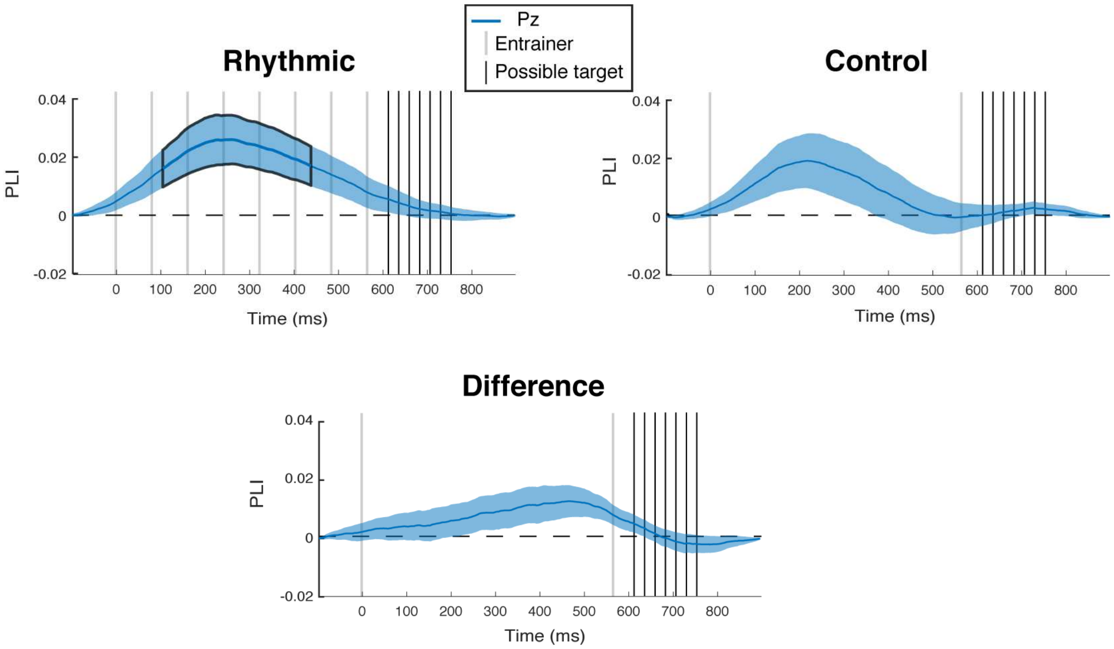


Figure 3-10: Phase locking index (PLI) values for rhythmic, control, and difference between conditions in the early and late window. The average PLI values for each electrode within early and late windows (outlined in black) are the same as defined in Mathewson et al (2012). Unlike their results, we did not see a significant difference in PLI between the rhythmic and control entrainment conditions. Error bars are standard error of the mean.

The pulsed inhibition hypothesis puts particular importance to the direction of the phase angle of α oscillations just before the onset of a stimulus. Specifically, peaks of α oscillations are proposed to represent periods of time where both cortex and the subject's behavioral abilities are dampened to visual stimuli; troughs of α oscillations are proposed to represent a release from this inhibition, enabling the subject to have higher detection rates. If visual entrainment is able to modulate the timing of the phase of α in order to optimize visual awareness during certain periods of time, then we should see a difference in the phase angle of α activity (at the entrained frequency) just before the expected target time. To test this, we calculated the phase angle of the α activity at 12.1Hz, 100ms before the onset of the in-phase and antiphase targets (similar to a calculation from Mathewson et al., 2012). The results are plotted in (**Figure 3-11**). We indeed see a significant difference in prestimulus alpha phase between in-phase and antiphase target stimuli, for the rhythmic condition, but this is also significant in the control condition. These differences in phase angles were not significantly different across entrainment conditions (circular Watson-Williams t-test F(1,32) = 0.105, p = 0.748).

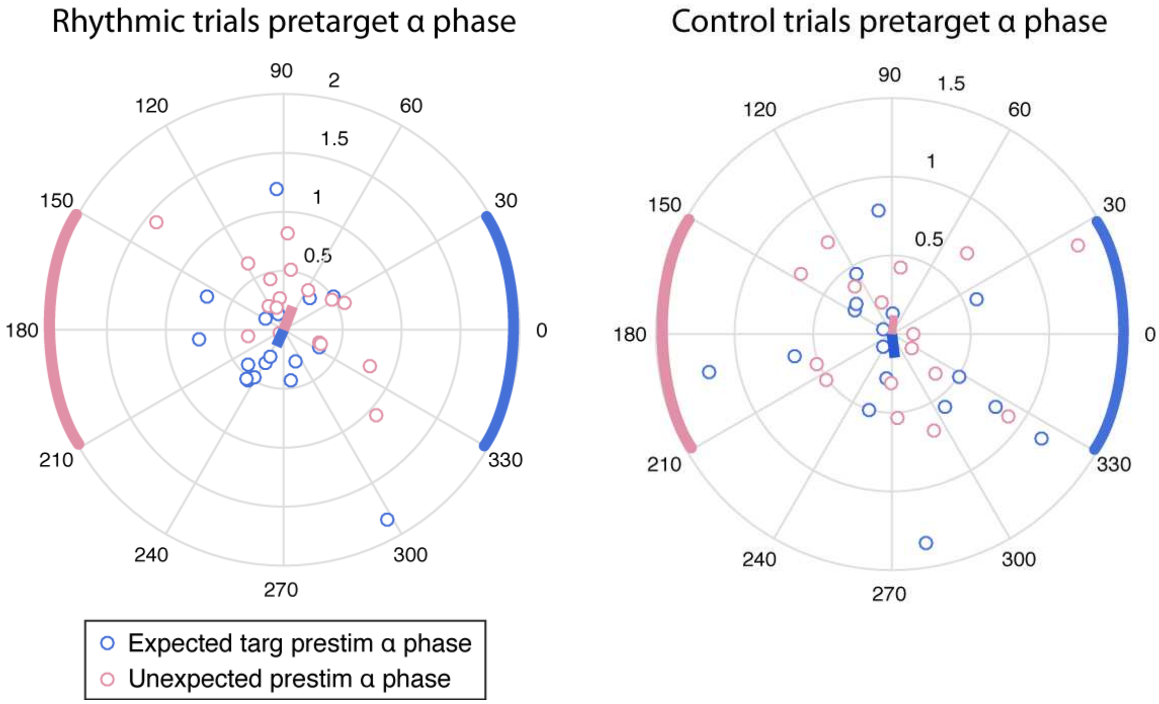


Figure 3-11: Phase angles of wavelet-transformed (12.1Hz) signal in rhythmic (left) and control (right) conditions in electrode Pz, 100ms prior to onset of target stimulus (target-present trials only). Each dot represents a single subject, and the vectors from the center represent the average EEG phase angle at 12.1Hz across subjects. We expect that the prestimulus phase angle of in-phase targets should be around the trough of the α oscillation, whereas the prestimulus phase prior to antiphase targets should be at the peak. The expected and unexpected target times are significantly different from each other across both the rhythmic and control conditions. These differences are not different from each other, indicating that the rhythmic condition does not cause a change in entrained phase angle any more so than the control condition does.

3.5 Conclusions

Repeated-measures ANOVAs in Experiment 2 showed interactions between entrainment condition and SOA target time for hit rate, criterion, and false alarm rate (but not for d’). Experiment 3 showed a significant interactions for d’, hit rate, and false alarm rate (criterion was not significant). The two experiments showed common interactions in the hit rate and the false alarm rate. The fact that the false alarm rate (and criterion in

Experiment 2) systematically changed between SOA target time and entrainment condition indicates that some change in subject response bias was changed according to the condition and target time. A change in response bias is different than a change in perceptual ability (which would be supported by an interaction in d’, which was not significant in Experiment 2 but was in Experiment 3). The variability in these psychophysical measures across the two experiments also demonstrates the delicate nature of inducing behavioral oscillations following visual entrainment stimuli in the α band.

In addition, pilot data from multiple iterations of similar experiments (three iterations of experiments using n=12; n=16; n=31) utilizing visual entrainment at 12 Hz (not reported here) were unable to produce any oscillations in detection rate following rhythmic entrainment periods. Several differences in the paradigms made it hard to disentangle the important parameters necessary for behavioral oscillations. However, most differences lied in the stimuli (entrainment stimuli were white noise with a spatial gaussian filter, and targets were oriented grating stimuli). This suggests that inducing behavioral oscillations in the α band is hard to replicate using this particular paradigm given different stimuli.

The individual differences in hit rates in both experiments showed many varying response patterns across SOA target time and entrainment conditions. Some subjects showed an oscillating response in the rhythmic condition and no change in control condition, but others do not show any peaks in oscillations, and still others do not show any differences between entrainment conditions at all. Perhaps this difference in behavioral oscillations has to do with subjects’ peak α (as demonstrated through a correlation between peak α in the MEG signal and best-fit frequency in behavioral detection rate oscillation following visual entrainment; de Graaf et al., 2013).

We also performed multiple linear regression on the psychophysical data in both experiments to find the best-fit phase angle in the behavioral psychophysical data at the stimulation frequency. We tested whether the distribution of phase angles across subjects was significantly nonuniform and found that the rhythmic and jittered conditions had significantly nonuniform phase distributions for d’ (Experiment 3 only) and hit rate (both experiments). The rhythmic and jittered conditions in hit rate pointed in the in-phase direction across subjects in Experiment 2 only; however, the d’ (both experiments) and hit rates (Experiment 3) did not have a best-fit phase angle at the time of in-phase targets. Finally, we found significant differences in behavioral phase angles between entrainment conditions for d’ and hit rate (Experiment 3 only), indicating that visual entrainment caused behavioral oscillations in detection rate, but these oscillations were variably matched to the timing of the entrainment sequence.

Moving on to the EEG data in Experiment 3, we calculated the SSVEP power at the stimulated frequency (12.1Hz) in four occipital electrodes (Iz, POz, Pz, and Oz). We tested for a significant difference in 12.1 Hz power between the rhythmic and control conditions and found that 12.1 Hz power did indeed increase for the rhythmic condition compared to the control condition. However, the phase-locking index (PLI) showed that there was not significant phase-locking to the flickering stimuli. These findings indicate that although we see a behavioral oscillation for the rhythmic but not control conditions for the hit rate (and d’ in Experiment 3) across time, this oscillation in behavior cannot be explained by entraining oscillations in occipital cortex via the PLI. The explanation to why this behavioral result occurs after visual entrainment is still up for debate, but there are several possibilities that can be further researched.

Besides the variability in the frequency and phase of behavioral oscillations across studies, several factors could affect these results. When subjects have higher prestimulus α power, the phase of the EEG signal has been linked in previous studies to behavioral detection rates, whereas the EEG α phase is indistinguishable between detected and undetected trials when α power is low (Mathewson et al., 2009). In addition, the specific flicker frequency within the α band has been shown to differentially affect neural phase-locking and power increases at the flicker frequency (Ding et al., 2006). Lower α band (8-10 Hz) entrainment leads to a more global network in which increases in SSVEP power are not associated with phase-locking to the stimulus, whereas higher frequency entrainment (10-11 Hz) tends to lead to increases in SSVEP power as well as phase-locking within an occipital/frontal network. Many other factors could also play important roles contributing to the variability of results in both neural and behavioral oscillations following visual entrainment stimuli. For example, the distribution of the α oscillation in cortex, the frequency and retinal location of the flickering stimulus, the amount of selective attention being employed, whether there is a competing stimulus in the visual field (Keitel et al., 2013), the contrast/visibility of the entrainment and target stimuli (Bartley and Bishop, 1932), the subjects' peak α frequency which has been shown to vary with behavioral oscillations (de Graaf et al., 2013), and the prestimulus endogenous α power – just to name a few.

The goal of visual entrainment is to entrain evoked α rhythms to phase-lock to flickering stimuli at the same frequency in the brain. In this way, experimenters hope to manipulate the phase timing of α oscillations in the brain so that they can predict both neural and behavioral oscillations over time. Experimenters interested in investigating the effects of α oscillations on selective attention should utilize new technologies such as measuring endogenous α phase on the fly, and using this to present stimuli during certain phases of endogenous rhythms. This would allow for experimenter-manipulated presentation times of stimuli given the phase of endogenous α. In addition, future experiments could look into the interactions between peak α of individual subjects and how this interacts with perceptual modulations.

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CHAPTER 4

Conclusion to the dissertation

4.1 Major Findings

Changes in visual perception due to selective attention can be shown both through responses in the visual system and changes in behavior. The brain undoubtedly utilizes many different mechanisms in concert to achieve the beneficial results of selective visual attention. Two candidate mechanisms were investigated in the present dissertation: 1) idea that alpha oscillations in the brain represent a pulsed inhibition of cortical activity, and this mechanism can be investigated through the use of visual entrainment stimuli; 2) frontoparietal regions of the brain send signals related to the differential activity levels of visual cortex (representing the attended and ignored regions of visual space).

In Experiment 1, we used functional MRI to trace the differences in allocated attention within visual cortex and tried to predict these changes given frontoparietal activity in the brain. Replicating previous data, we found that overall activity levels between FP and VC regions were highly correlated. Regions representing the attended side of space tended to show higher amplitude BOLD responses than regions representing the ignored part of visual space. When calculating the relative difference between these two representations in the brain within visual cortex, we could not clearly uncover a signal in FP cortex that tracked this change. However, we did find a high prediction rate between IPS0 activity and the differential modulation in VC region V3a. This likely indicates that the BOLD signal is not sensitive to such changes. In addition, the orientation representations in visual cortex also did not show a clear difference between high and low activity levels of frontoparietal regions.

The findings from Experiment 1 indicate that although it seems quite clear from previous experiments that frontoparietal regions are communicating with visual cortex during selective attention, the BOLD signal within FP cortex does not appear to be sensitive enough to detect differential activity corresponding to attended and ignored regions of space, as measured by the BOLD signal in occipital visual cortex.

In Experiments 2 and 3, we used psychophysics and EEG to study the effects of temporal attention using visual entrainment stimuli. Given that oscillations in behavioral detection rate over time tend to occur in frequency bands outside of alpha oscillations, experimenters have turned to the use of visual entrainment (flickering) stimuli in alpha frequencies to target brain oscillations in the alpha band – a frequency band in the brain related to selective attention. Experimenters have proposed that alpha oscillations in the brain represent a pulsing of inhibitory activity, enabling the subject to sample stimuli over time in line with the phase of the alpha signal. Furthermore, the specific phase of alpha activity prior to the onset of the trial is predicted to correlate with the expected timing of the target stimulus, and with behavioral detection rate of the target stimulus.

The idea is to use flickering stimuli in the alpha band in order to entrain evoked oscillations in the brain, so that the phase of the alpha band can be experimentally manipulated and thus be linked to behavioral oscillations. The use of entrainment stimuli must do three things to support the pulsed inhibition of alpha hypothesis set forth by Mathewson et al (2009, 2011): 1) detection rate over time must be related to the rhythmicity of entrainment stimuli preceding the target stimulus; 2) phase-locking in the alpha band of the EEG signal must co-occur with the flickering stimuli; 3) the phase of the resulting alpha activity must relate to stimuli that are in-time or not in-time with the preceding entrainment stimuli.

In Experiments 2 and 3, we found evidence for behavioral oscillations in time with the previous entrainment stimuli in the alpha band. This indicates that the flickering stimuli are indeed having an effect on behavioral oscillations. However, we were unable to uncover evidence that the brief period of flickering stimuli was able to phase-lock alpha rhythms in the brain. Furthermore, the prestimulus phase of alpha oscillations did not change according to the in-phase or antiphase timing of target stimuli. This suggests that subjects are not using the phase of their (evoked) alpha activity to selectively process information in time with flickering stimuli. Thus, although we can confirm that visual entrainment stimuli did indeed impact behavioral oscillations, these changes in behavior are not readily explained by the pulsed inhibition theory of attention. Instead, we postulate the entrainment stimuli establish temporal expectation, and that this temporal expectation influences behavior.

Selective visual attention is clearly a multifaceted process that the brain undergoes, given such varying types of attention-related modulations in visual cortical regions. In Experiment 1, we gave evidence that the BOLD signal does not seem sensitive enough to detect differential modulation signals during selective attention. In Experiments 2 and 3, we demonstrated that although the pulsed inhibition of alpha hypothesis is a likely candidate for a mechanism of selective temporal attention, using visual entrainment stimuli does not help to address this hypothesis. Instead, a different mechanism – one of temporal expectancy – is more likely to explain the behavioral oscillations present in previous experiments.

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