PULSED OUT OF AWARENESS: EEG ALPHA OSCILLATIONS REPRESENT A PULSED
INHIBITION OF ONGOING CORTICAL PROCESSING

BY

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DISSERTATION

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**ABSTRACT**

Alpha oscillations are ubiquitous in the brain, but their role in cortical processing remains a matter of debate. Recently, evidence has begun to accumulate in support of a role for Alpha oscillations in attention selection and control. In this thesis, a series of studies is presented investigating the role of Alpha oscillations in visual processing, learning, and awareness. I propose that Alpha oscillations represent a general pulsed inhibition in the brain.

Chapter 1 contains a review of evidence that 8-12 Hz oscillations in the brain have a general inhibitory role in cognitive processing, with an emphasis on their role in visual processing. Chapter 2 presents additional evidence for this general inhibitory role, in a study where EEG Alpha is used to predict the rate of improvement in a complex video game training program. Chapter 3 summarizes research supporting the proposal that Alpha represents a pulsed inhibition of ongoing neural activity. The phase of the ongoing EEG can influence evoked activity and subsequent processing. It is proposed that Alpha exerts its inhibitory role through alternating microstates of inhibition and excitation. Chapter 4 and Chapter 5 discuss evidence that this pulsed inhibition can be entrained to rhythmic stimuli in the environment, such that preferential processing occurs for stimuli at predictable moments, leading to oscillations in visual awareness. The entrainment of a preferential phase of ongoing Alpha oscillations may provide a mechanism for temporal attention in the brain. Chapter 6 reports the results of an experiment combining fast optical imaging using the event-related optical signal (EROS) with EEG recording in a meta-contrast masking task. This multimodal combination is used to investigate the network of brain areas oscillating at Alpha frequencies and their influence on visual awareness, as well as the frontal and parietal areas modulating this oscillatory activity.

Chapter 7 concludes that together, this series of studies provides the foundation for an account of Alpha oscillations as a general pulsed inhibition mechanism which can be entrained by external stimulation and modulated by top down influences from the fronto-parietal attention network. Given the rhythmic nature of this proposed inhibitory mechanism, this pulsed inhibitory account of Alpha has important implications for many common cognitive phenomena, such as the attentional blink, and seems to indicate that our visual experience may at least some times be coming through in waves.

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# CHAPTER 1

# INTRODUCTION[1]

The bombardment of stimulation hitting our primary sensory areas necessitates selective enhancement of relevant information and suppression of whatever is irrelevant or interfering. Theories posit that salient properties inherent to the stimulus, top-down interventions, and fluctuations in attentional focus over time can modulate sensory processing, biasing it in favor of salient and task-relevant information at the expense of irrelevant or actively ignored stimuli (e.g., Luck, 2009; Corbetta and Shulman, 2002; Desimone and Duncan, 1995). Although a great deal of research has focused on understanding how top-down signals select task-relevant information, the specific mechanisms by which task irrelevant information is filtered out is less well understood. Recently, there has been growing evidence that Alpha oscillations (8–12 Hz) can play a significant role in modulating input information by inhibiting visual and other neural processing.

In this thesis, evidence is reviewed in support of three main theoretical points: (a) The role of the Alpha rhythm goes beyond that of a mechanism for sensory disengagement, as it is also involved in cognitive control and attention through modulatory influences; (b) Alpha oscillations act as a pulsed inhibition of neural processing, with synchronized oscillations in a brain area leading to periodic inhibition on every cycle, so that the phase of Alpha is critical in determining whether or not processing is suppressed; (c) The brain exploits the Alpha rhythm to

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[1] Mathewson, K.E., Lleras, A., Beck D.M., Fabiani, M., Ro, T., & Gratton, G. (2011). Pulsed Out of Awareness: EEG Alpha oscillations represent a pulsed inhibition of ongoing cortical processing. *Frontiers in Perception Science*, 2(99). doi: 10.3389/fpsyg.2011.00099.

For the review paper which is contained here and in Chapter 3, I contributed to the theoretical formulation and drafted the manuscript.

appropriately time microstates of excitation and/or inhibition so as to be optimally ready to process or inhibit incoming information.

When large ensembles of neurons fire in synchrony, an electric field is produced that is large enough to propagate through the brain and skull and can be measured with electrodes on the scalp. These ensembles of neurons fire at particular frequencies depending on their function and activity level. Thus, electroencephalographic (EEG) recordings provide data about the functional state of the neurons. Neural activity in the Alpha range (8-12 Hz) has been shown to reflect the state of awareness of an individual. In the original EEG recordings by Hans Berger (1929), and in subsequent work by Adrian and Mathews (1934), Alpha oscillations were shown to vary as a function of the level of attention paid by the subject to the visual environment. As subjects began to lose attentional focus, increased amplitude of Alpha oscillations was observed, with the largest Alpha amplitude occurring when the subjects' eyes were closed. For many years it was thus thought that Alpha represented an idling process in the visual system, such that the amplitude of Alpha oscillations in a given task could be used as an index of one's general level of arousal or focus. More recently, Alpha oscillations have begun to be viewed in a different light: that of an attention mechanism (e.g. Thut et al., 2006) or as a general inhibitory mechanism in the brain (e.g. Klimesch et al., 2007; Jensen & Mazeheri, 2010).

Oscillations in the Alpha band (8 – 12 Hz) are a ubiquitous characteristic of neural activity.  Alpha activity was the name given to synchronized 10 Hz activity measured in the EEG signal because it was the first, largest, and most easily identifiable signal in the single trace recorded by Berger's primitive equipment (Berger, 1929). Subcortical recordings have revealed that this synchronization of 8-12 Hz neural firing is subserved by both (1) a thalamo-cortical loop involving the LGN, the pulvinar and visual cortex (Steriade et al., 1990), and (2)

interconnections between visual cortical regions (Lopez de Silva et al., 1980; 1991). Intracranial recordings have further shown 8-12 Hz oscillations to be present throughout the cortex (Lopez de Silva et al.; 1991). At the scalp the largest Alpha amplitude is observed over parietal and occipital areas (e.g. Johnson et al., 2010), although its frequency is slower and its distribution tends to be more frontal in older subjects (Gratton et al., 1992). Alpha is also evident over motor cortices in the form of mu oscillations (Pfurtscheller & Neuper, 1994).

Since this initial interpretation of Alpha as a generic idling mechanism, increased focus has been placed on the *specific* influence of Alpha oscillations on cognitive and neural processes (e.g. Klimesch et al., 2007; Jensen and Mazaheri, 2010). Spontaneous (i.e., not stimulus driven) increases in Alpha oscillations have been shown to be associated with higher threshold detection rates across a wide range of stimulus types (e.g., Ergenoglu et al., 2004; Palva et al., 2005; Romei et al., 2007; 2008a; van Dijk et al., 2008; Wyart & Tallon-Baudry, 2009; Busch et al., 2009) and with poorer performance on a number of cognitive tasks (e.g., Linkenkaer-Hansen et al., 2004; Mo et al., 2004; Babiloni et al., 2006; Del Percio et al., 2007; Hanslmayr et al., 2007; Mazaheri et al., 2009). For example, in a recent study, we showed that the detection rate of a near-threshold target stimulus that preceded a metacontrast mask was dependent upon the level of Alpha power; detection rate increased monotonically as Alpha power decreased (Figure 3.1; Mathewson et al., 2009).

In other research, increases in Alpha have been linked to the successful inhibition of distracter items to aid working memory representations (e.g., Sauseng et al., 2009; Hamidi et al., 2009). During a visual working memory task, for example, a set of four items was monitored for change after a brief blank period, while the visual distracter information on the opposite side of the screen was ignored (Sauseng et al., 2009). During the retention interval, the occipital Alpha

power over the side contralateral to the ignored visual stimuli increased. This *asymmetric* increase in Alpha power was predictive of visual working memory performance across trials and subjects. The authors concluded that increased Alpha activity allowed for more efficient suppression of the distracting visual stimuli in the unattended field. This result is consistent with the more general observation that an inward shift of attentional focus towards mental operations (as in mental rotation tasks, visual imagery and other high-load working memory tasks) is typically accompanied by increases in posterior Alpha power, suggesting that, in such cases, Alpha might be working to inhibit sensory processing and decrease overall distractibility by sensory events (e.g., Jensen et al., 2002; Cooper et al., 2003).

More recently, studies have shown that the degree of Alpha lateralization or its involvement in sensory inhibition is modulated by attention. Shifting or maintaining attention to one side of visual space leads to predictable fluctuations in the power and topography of Alpha oscillations, which in general appear selectively increased ipsilaterally to the visual hemifield where the relevant information is presented (e.g. Worden et al., 2000). These controlled fluctuations in Alpha have in turn been shown to influence target detection and visual performance (Sauseng et al., 2005; Thut et al., 2006; Kelly et al., 2006; Rihs et al., 2007; 2009; Wyart & Tallon-Baudry, 2009; Capotosto et al., 2009; Rajagovindan & Ding, 2010). A similar relationship has also been shown during shifts of lateralized auditory attention (Kerlin et al., 2010). Increased Alpha oscillations also produce diminished transcranial magnetic stimulation (TMS) effects in both the visual (Romei et al., 2008b) and motor domains (Sauseng et al., 2009), indicating that Alpha influences the excitability of the cortex.

Shifts in Alpha power and/or scalp distribution have also been observed when participants are asked to attend to either the color or motion of visual stimuli (Min & Harman,

2007; Snyder & Foxe, 2010). Levels of Alpha power have been shown to be modulated by temporal expectancy of stimulus onsets (Min et al., 2008), rightward shifts of attention during fatigue (Perez et al., 2009) and following erroneous responses to visual stimuli (Carp & Compton, 2009), all indicating a role for Alpha in selective neural processing. In animal studies using intracranial recordings, this relationship between decreased attention, increased Alpha power, and selective processing has been shown to be present in areas V1, V2 and V4, whereas an opposite relationship has been measured in higher areas such as IT (Mo et al., 2004; Bollimunta et al., 2008, 2011).

In multimodal human studies combining EEG and fMRI, increased Alpha oscillations have generally been shown to be related to decreases in the BOLD signal and cortical metabolism in sensory areas, and increased activity in so called default-mode areas (e.g., Moosmann et al., 2003; Bin-Simon et al., 2008; Jann et al., 2010; Sadaghiani et al., 2010; Scheeringa et al., 2011). One must keep in mind when considering joint EEG-fMRI studies that the EEG power envelope measured on the scalp used to predict BOLD changes only represents a limited and spatially-smeared window into the oscillatory activity of the entire brain  - a window that is heavily weighted towards co-oriented sources close to the scalp.

Some past studies have shown that event-related brain potentials (ERPs) and subsequent BOLD signal measured concurrently are uninfluenced by the power of pre-stimulus Alpha oscillations (Becker et al., 2008; Reinacher et al., 2009; Scheeringa et al., 2011). These findings have been taken as evidence against a proposal that ERPs are the result of ongoing Alpha oscillations becoming phase reset to stimulus onset, since it would predict that trials with larger pre-stimulus power would have larger ERPs (Mazaheri & Jensen, 2006; Becker at al., 2009), although this debate continues (e.g. Risner et al., 2009; Klimesch et al., 2009). A recent finding

of a U-shaped function between Alpha power and ERP amplitude may explain these contradictory findings (Rajagovindan & Ding, 2010). It is likely that the relationship between Alpha power and evoked activity is a complicated interaction between the stimulus modality and the predominant source of the surface-measured Alpha activity. Recent advances in the use of multivariate variance decomposition techniques and source modeling are important for separating the various Alpha generators from each other and from other neural activity (Snyder & Foxe, 2010; Scheeringa et al., 2011).

Klimesch et al. (2007) has recently proposed a theoretical framework for Alpha oscillations. They propose that Alpha represents a general inhibition mechanism across cortical areas, and emphasize the important and complementary role played by Alpha oscillations in neural inhibition and timing. This framework not only explains the inhibitory modulations of Alpha activity with attention and fatigue but also explains the role of Alpha oscillations in other brain areas (e.g. Pfurtscheller & Neuper, 1994). The theory emphasizes the additional role played by Alpha beyond a general inhibition of neural activity in constraining the timing of neural firing. Importantly, this theory makes some predictions about tasks in which increased focus of attention should actually increase Alpha oscillations, when important inhibitory or timing processes are needed, which has indeed been observed (e.g. Sauseng et al., 2009; Ray & Cole, 1985). It is proposed that these timing mechanisms are subserved by the excitability cycle of Alpha oscillations. It is also often observed that the Alpha power differs between the two frontal hemispheres; a large amount of literature has investigated "frontal Alpha asymmetry" as a marker of depression. This asymmetry may reflect an unbalance in the level of control exerted by frontal regions on ongoing goals, tasks, and emotionality (for a review see Coan & Allen, 2004). A general role for Alpha as a control mechanism across cortical areas also explains large

decreases in Alpha power, referred to as either Alpha desynchronization, Alpha suppression, or Alpha blocking, during important mental and sensory processing (e.g., Klimesch et al., 1998). In support of the general role played by Alpha in many brain areas, in a recent EEG study of video game training, we have shown predominant changes in Alpha activity over the course of learning (Figure 3.2A). Subjects spent 20 hours learning the complex video game Space Fortress, in which a player controls a ship with the goal of destroying a combative central fortress (Donchin, Fabiani & Sanders, 1989). Subjects' EEG activity was recorded during and outside of game play, before and after training. The amount of evoked Alpha to relevant stimuli in the game increased as subjects learned to master the game (Figure 3.2B & 3.2C; Maclin et al., in press). Furthermore, the level of frontal Alpha power during the first session playing the game could predict almost 50% of the variance in the rate of learning (Chapter 2). Even the frontal Alpha power measured outside of the game, prior to training, could predict subsequent learning rate.

Furthermore, this effect could be dissociated from the mu-rhythm difference between left and right hemispheres associated with flying the ship, which was not predictive of subsequent performance. Finally, additional variance in game improvement was accounted for by event-related Alpha desynchronization in response to successful hits on the fortress. Together, these results reveal a number of distinct types of Alpha activity with different functional relevance for attention and performance. Importantly, these results suggest that frontal Alpha plays an important role in cognitive/attentional control, which is critical in learning to perform optimally in a complex video game. Recently, it has also been shown that eye movements can be influenced by frontal Alpha activity, and it has been proposed that frontal eye-field activity may be the source of these influences (Mazaheri et al., 2011; Drews & VanRullen, 2011). More research is needed to understand the difference between traditionally observed posterior Alpha

modulations and these recently observed frontal Alpha effects. Additional research could also shed light on the relationship between frontal Alpha modulations and the frontal theta differences reported in a number of studies (Cohen, Elger, & Ranganath, 2007; Cavanagh, Cohen, & Allen, 2009). Finally, it is also important to note that cognitive control involves inhibition as well as activation. Therefore, this theory is consistent with the general idea that Alpha is related to cortical inhibition.

**DIFFERENT SLOPES FOR DIFFERENCE FOLKS: ALPHA AND BETA EEG POWER PREDICT SUBSEQUENT IMPROVEMENT IN VIDEO GAME LEARNING RATE AND IN COGNITIVE CONTROL TASKS[2]**

**Introduction**

The state of the brain can have great influence on the processing of incoming information (Mathewson et al., 2009; Romei et al., 2008a,b; Thut et al., 2006; Boly et al., 2007). Although it is clear that the current brain state can predict the short-term processing of stimulus information (e.g., Mathewson et al., 2009), the extent to which it can predict behavior further in the future remains largely untested (but see Gruber & Otten, 2010; Xue et al., 2010). Here, we studied the relationship between electrophysiological measures of brain states (the electroencephalogram, or EEG and event-related spectral perturbations, or ERSPs) and the subsequent rate of learning in a complex video game, Space Fortress (Donchin, Fabiani, & Sanders, 1989). We tested whether the engagement of high-level cognitive control mechanisms at the onset of training could predict individuals' rate of subsequent learning in a Space Fortress training regime. This would provide evidence that the operation of such brain control system can have long-lasting consequences and thus influence learning and behavior on a much longer time scale than previously demonstrated.

We used EEG to analyze the on-line time-resolved brain activity as it unfolds in the game environment at the beginning of a training period, in order to better understand what particular dynamic brain functions are predictive of training success as well as of improvements in other

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2 Mathewson, K.E., Basak, C., Maclin, E.L., Low, K.A., Boot, W.R., Kramer, A.F., Fabiani, M., & Gratton, G. (Under Review). Different slopes for different folks: Alpha and Beta EEG power predict subsequent video game learning rate and secondary task improvement.

For this multiple author paper, I was involved in designing the analysis, and analyzing the data, partly by contributing analysis software and algorithms. I also drafted the manuscript and created the figures.

tasks outside of the game environment improvement, and how these dynamics unfold over time. Complex video games have long been recognized as useful investigative techniques for cognitive neuroscience as well as potential cognitive training tools (e.g., Donchin et al., 1989), largely because they afford investigators the possibility of testing subjects in situations closer to the complexity of real-life than standard laboratory tasks. Research using this approach has recently proliferated and broadened our understanding of the brain activity taking place during video game learning (Koepp et al., 1998; Green & Bavelier, 2008). Specifically, these include reports of changes in long-range connectivity (Voss et al., 2010; submitted) and of short term oscillatory brain activity with mastery of such complex tasks (Maclin et al., in press). Given this evidence, knowledge of the types of brain activity that can best predict performance and skill transfer is of great utility. The Space Fortress game (Figure 2.1) was developed as a cognitive tool for studying learning and training strategies (Donchin et al., 1989). The demanding nature of the multiple cognitive tasks embedded in this game simulates many real world tasks such as piloting a vehicle or air traffic control. It also provides analogies to well studied cognitive tasks from the psychology literature.

Recent research has found anatomical predictors of subsequent improvement in performance. Volumetric differences in the basal ganglia can predict individuals' change in score in the Space Fortress game with learning (Erickson et al., 2010). It has also been shown that pattern classification using a support vector machine of the tissue properties of basal ganglia structures can predict the level of improvement in the game (Vo et al., 2011). Together, these results indicate that the size and properties of anatomical structures important for learning can predict the effectiveness of training programs. The basal ganglia have been shown recently to play an important regulatory role on the activity of prefrontal attention control circuits (van

Schouwenburg, den Ouden, & Cools, 2010). We hypothesized that top-down control from such brain areas (frontal cortex, basal ganglia) exerted early in training would predict subsequent learning rate.

In order to assess the level of these top-down influences on behavior, we measured the levels of EEG power in the Alpha-frequency range (7-12 Hz). Alpha oscillations have been shown from the very first EEG recordings (Berger, 1924) to be related to the current level of attention and arousal. Recent research has shown an intimate link between Alpha oscillations and sensory processing, such that hemispheric-specific increases in Alpha power are associated with suppression of processing in the contralateral visual hemifield (Worden et al., 2000; Romei et al., 2008a,b). We have hypothesized this relationship to be due to pulses of inhibition associated with subsets of the Alpha cycle (Mathewson et al., 2009; Mathewson et al., 2010; Mazaheri & Jensen, 2010). A recent comprehensive review of Alpha oscillations posits that Alpha acts as a control and timing mechanism in all areas of the brain (Klimesch, Sauseng & Hansylmyr, 2007; see also Jensen & Mazaheri, 2010). Therefore, we used the amount of scalp-recorded frontal Alpha power (which we take here to reflect frontal lobe activation levels) as a measure of the engagement of control processes early in training. Further, following recent theorizing on the relationship between cognitive control, frontal lobe activity and learning (e.g., Miller & Cohen, 2001; Braver, Barch & Cohen, 1999) we hypothesized that the amount of frontal Alpha power early in training should predict subsequent learning in the Space Fortress task. We measured Alpha activity locked to a series of important in-game events, and correlated this activity with subjects' learning rates with performance improvements in cognitive-control tasks outside of the game environment.

We also tested if the evoked oscillatory activity elicited by these game events could further predict learning rate. Evoked and/or induced oscillatory activity represents a transient and short-term response to ongoing task demands (Makeig et al., 2004), but may also be indicative of particular brain states that are predictive of subsequent performance (e.g., Romei, Gross, & Thut, 2010; Gruber & Otten, 2010).

Recently, there has been a growing interest in the use of video games to train basic cognitive functions. This impinges on the possibly of transferring skills learned during a game to other cognitive tasks (Gopher, 1994; Frederickson & White 1989; Dye & Bavelier, 2004; Bavelier & Green, 2004; Dye, Green, & Bavelier, 2008; Green & Bavelier, 2008; Dahlin et al., 2008; Basak et al., 2008; Boot et al., 2006; Boot et al., 2010). As training may be expensive in terms of both time and costs, it would be very useful to be able to identify ahead of time those individuals for whom training would not only be most expedient and beneficial, but also for whom transfer outside of the training regimes scope will be optimal. We therefore also tested whether any of the electrophysiological predictors of subsequent game learning rate could also predict individuals' improvement on other non-game cognitive and memory tasks requiring skills similar to those important in Space Fortress.

To preview our results, we indeed found that frontal Alpha power before training predicts the rate of subsequent learning as well as improvement in cognitive-control task performance outside the game environment, tasks requiring processes that closely overlap with those important for Space Fortress (see Danlin et al., 2008). Further, a combination of EEG and ERSP predictors evoked by game events account for approximately 50% of the variance in learning rate when combined in a multiple regression model. Finally, some of the ERSP indices were also able to predict the amount of skill improvement outside of the game. Together these results

reveal that the state of the brain's cognitive control system early in training predicts the rate of subsequent learning after training, as well as the application of these skills outside of the game.

**Method**

*Participants*

Thirty-nine individuals (ages 18-28, 27 females) were recruited from the University of Illinois community, after indicating in an online survey that they played less than 3 hours of video games a week in the past two years. All subjects were right handed and had normal or corrected to normal vision, and were paid fifteen dollars an hour for their training and recording sessions. Data from one subject were excluded due to technical problems with EEG recording.

*Procedures*

To familiarize themselves with the game, subjects initially watched a 20-minute movie that explained all the details of the Space Fortress game, and then another 5-minute movie that summarized the most important rules. After viewing these movies, participants played twenty-four 3-minute-long games.

At this time the first EEG acquisition session was completed. Participants played ten 3-minute-long games while their EEG was recorded. Over the following months, this was followed by 20 hours of game training, with performance tracked throughout this period. At the end of training, a post-training session was completed. In the present paper, only the EEG activity from the pre-training session was considered as a predictor of subsequent learning during training. Data comparing the brain activity before and after training are presented elsewhere (Maclin et al., in press).

*Space Fortress Game.* Complete details of the Revised Space Fortress game used here can be found in Shebilske et al. (2005). Here we summarize the most important aspects of the game. The final score on each game of Space Fortress is a combined measure composed of four subscores. A major component of the game is flying the ship. Players are rewarded both for keeping their ship in the hexagonal game area (see Figure 2.1) and for keeping their ship below a threshold velocity. Players destroy the central fortress by first hitting the fortress ten times, and then hitting it with a fatal double shot. Players must avoid being hit by the fortress' missiles or on-screen mines, with four hits causing the ship to be destroyed. Finally, mines intermittently appear on the screen and must be neutralized and destroyed.

Participants were comfortably seated in front of a19-inch color LCD monitor, and made game inputs using the computer mouse and a Logitech Attack 3 Joystick.

*Additional Tasks.* Participants performed a secondary "auditory oddball" task while they were playing the game. Tone bursts of 340 ms duration were presented via speakers at ~70 dB every 1990 ms. Frequent tones (~80%) were 350Hz and rare tones (~20%) were 500Hz. Subjects were instructed to silently count the rare (high) tones, and report the total at the end of each block. An analogous oddball task was also completed by participants while EEG was recorded before they began the Space Fortress game.

Furthermore, a battery of cognitive tasks, testing attention, cognitive control and working memory, was completed by subjects before and after the training program. This battery was used to measure the improvement in performance in tasks requiring processes that overlap with those important for the Space Fortress game. These tasks are described in more detail in Boot et al. (2010). The subset of tasks relevant to this paper is presented in Table 1.

*EEG Recording and Analysis.* EEG data were collected in a sound-attenuated chamber from 64 electrodes embedded in a flexible electrode cap (ElectroCap International, Eaton, OH). Impedance was kept below 10 KOhm. Data were filtered online using a .01-30 Hz bandpass, and sampled at 100 Hz. The electrooculogram (EOG) was collected using two bipolar channels from electrodes placed above and below the left eye (vertical EOG) and on the left and right outer canthi (horizontal-EOG). Scalp channels were referenced to the left mastoid during data collection and then were re-referenced off-line to the average of the two mastoids.

EEG data were analyzed with custom scripts using Matlab and EEGlab (Delorme & Makeig, 2004). EEG data were first scanned for voltages at the A/D limits, and channels with excessive noise by this criterion were interpolated from nearby electrodes using EEGLAB's spherical interpolation function. The data were then epoched around the four events of interest; mine onsets, fortress hits, and rare tones within and outside the game. Epochs where any EEG channel had a range exceeding 1000 µV were discarded. Eye movements were corrected using the EMCP algorithm (Gratton et al. 1983). After eye movement correction the data were scanned again, and epochs with channels with a range exceeding 500 µV were discarded.

A wavelet analysis of the epoched data was performed using the *newtimef()* function of the EEGLAB toolbox. A complex group of tapered wavelets was computed with a width of 710 ms, with one cycle at the lowest frequency and increasing up to 19 cycles at the highest frequency. To increase frequency resolution, the data and wavelets were zero-padded with a ratio of 2. This allowed for the visualization of frequency information with a resolution of .75 Hz from 1.6 Hz up to 30 Hz, and from -645 ms to 1640 ms around the event of interest.

In order to measure the changes in brain activity evoked by and locked to events of interest, a baseline-corrected version of these time-frequency data was computed. The average pre-

stimulus power was subtracted from activity at each time point, for each frequency. The resulting

data, commonly referred to as ERSPs, reflect changes in oscillatory brain activity elicited by or

time-locked to the events of interest.

To measure the correlation between these electrophysiological indices and subsequent

learning, for each subject the resultant time frequency decompositions were averaged over trials.

Then, at each point in time and frequency, these values for each subject were correlated to

learning rate. These correlations were then plotted over time and frequency for each event of

interest. Windows were created for the Alpha oscillations from 7 to 12 Hz and from -500 to 1500

ms post-stimulus onset. Furthermore, ERSP activity that predicted learning rate was visually

identified, and windows in time and frequency were constructed around these clusters. The

ERSP activity in these windows was averaged and used to visualize the topographic extent of

this predictive activity, and was also submitted to a stepwise regression procedure. A direct

analysis of the change in oscillatory brain activity from pre- to post-training is reported

elsewhere (Maclin et al., in press).


**Results**

*Behavioral Results*

Subjects were trained for 10 two-hour sessions. Figure 2.2 shows the overall behavioral

improvement of individuals over the 20 hours of training (i.e., 10 training sessions).  For each

participant we modeled the learning curve based on the total game score ($\widehat{p'}$) over the 20 hours

of training using a logarithmic function:

$$\widehat{p'} = a + r * ln(session/hours)$$

where *a* represents the initial level of game play, and *r* is the slope estimated for each subject as a measure of the rate of learning. Median split of the initial 2 hours of composite total score indicated that participants with higher initial proficiency had a significantly lower learning rate (1086.91) than those with lower proficiency (1518.35), $t(37)=2.60$, $p<0.05$. Therefore, to avoid this potential confound, in our stepwise regression procedure described below, we first partialled out the variance accounted for by initial score.

*Alpha Power Prediction of Learning Rate*

We predicted that the amount of top-down control, as indexed by EEG Alpha power early in training could predict the slope of the subsequent learning curves. Figure 2.3 shows the correlations between the learning rate for each subject and their average power at each frequency and time point, aligned to two important game events (Mine Onset, Fortress Hits) as well as the oddball tones both in and outside of the game, all from the left frontal electrode F5 where this correlation was maximal. The mean power over the time period from -500 to 1500 ms around the event was computed in the Alpha range (7-12 Hz). The amount of Alpha power was highly correlated across events (all $r > .98$, $p < .05$). In all cases there was a strong correlation between overall Alpha power and rate of learning (Mines $r = .44$, $p < .05$; Fortress $r = .44$, $p < .05$; Oddball in Game $r = .42$, $p < .05$). The higher an individual's Alpha power before they started their training regime, the steeper was his/her improvement in score during the training program. To assess whether this effect was specific to game play in the Space Fortress environment, we also measured EEG from a secondary oddball task outside of the game. Figure 2.3 (lower right panel) shows that this effect was specific to the Alpha band, but was somewhat weaker than for the in-game events ($r = .35$, $p < .05$). There was also a significant correlation between Alpha activity during oddball tones in and out of the Space Fortress game ($r = .83$, $p < .05$).

Figure 2.3 also shows topographic plots of the correlation between Alpha power and learning rate across subjects. For all events a consistent frontal distribution was found in the strength of the correlation of Alpha power with subsequent improvement.

*ERSP Predictors*

We also wanted to assess whether the oscillatory activity evoked or modulated by each of the important game events was predictive of the subsequent rate of learning as measured by the ERSP. We hypothesized that the greater the allocation of attention at the beginning of training, the greater the learning rate would be. Specifically we used two indices of attention allocation: Increased beta activity and reduction of Alpha activity in the periods following events of interest. Figure 2.4 shows the correlation over time and frequency of the ERSP with the learning rate. For all three events, the electrode with the maximal correlation in the chosen frequency band is shown. For each event, a window was placed around the cluster of maximal correlation, and the average in this window was used in a stepwise regression, and to create scalp maps of the correlation. In all cases, significant correlations were found between the change in oscillatory activity following the event, and subsequent behavioral improvements in the game. Following mines, the greater the occipital high beta activity (15-30 Hz) elicited by mines between 900 and 1300 ms, the more quickly the subject subsequently learned the game ($r = .52, p < .05$). The low beta activity (10-15 Hz) occurring1000-1500 ms after a fortress hit was also positively correlated with learning ($r = .42, p < .05$), whereas the theta/low-Alpha activity (5-10 Hz) elicited after 600-800 ms was negatively correlated with learning ($r = -.34, p < .05$). Finally, 7-15 Hz activity ("broad Alpha") elicited 600-800 ms after oddball tones in the game also negativity predicted learning ($r = -.52, p < .05$). In other words, Alpha suppression and beta increases (which

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according to extant literature both reflect allocation of attentional resources) were all predictive of subsequent learning.

*Stepwise Regression Analysis*

In order to determine the amount of variance in learning rate accounted for by the set of electrophysiological predictors identified by the previous analyses, we submitted them to a stepwise multiple regression. Due to the high correlation between the raw EEG measures of Alpha power, we used only the EEG Alpha activity from the mine onsets, providing us with one EEG and four ERSP predictors of subsequent learning rate. Table 2 shows the results of the stepwise regression procedure. First, in order to control for the influence of initial game score on the predictive value of the EEG, we added initial game score in the EEG session to the model. Next, to test the hypothesis that cognitive control engagement early in training (as measured by Alpha oscillations over frontal cortex) predicts subsequent learning, we added the EEG Alpha activity around mine onset to the model. This predictor remained significant after controlling for initial score. Finally, we submitted the three ERSP predictors to the model, with fortress-hit-locked low-beta increase, mine-appearance-locked beta increase, and fortress-hit-locked Alpha decrease being added in that order. Figure 2.5A shows the predicted scores from a linear combination of these five predictors ($R^2 = .47$, $p < .0001$), with the mine-appearance-locked beta increase accounting for the most variance (standardized $\beta = .36$, $p<.05$). It is important to note that the electrophysiological variables significantly augment the predictive value provided by the initial game score, accounting for more than 80% of the total predicted variance.

In order to test the robustness of our electrophysiological predictions, we performed a jackknife analysis in which the predicted value for each individual was computed using the

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regression coefficients based on the other subjects' data. Using this procedure, a significant

prediction of subsequent slope remained (Figure 2.5B; $R^2 = .43$, $p < .05$).


*Prediction of Improvement in Tasks Outside of the Game Environment*

The aim of these analyses was to assess whether any of the electrophysiological variables

from the initial game performance also predicted the level of skill improvement in tasks whose

processes overlapped with those important for Space Fortress. The means and standard

deviations of the cognitive tasks before and after training, as well as the number of participants

retained for each cognitive task are presented in table 3. There were missing data for one

participant for the task switching task and one participant for the Sternberg task from the before-

training session, and one participant for the 1-back task from the after-training session, resulting

in reduced number of participants for these tasks (see Table 3). For the subsequent analyses we

focused on the four ERSP measures described above. Mine-locked beta increases were

predictive of reductions in response times in the Sternberg memory search task [$r(37)=-.37$,

$p<.05$] and in the stop task [$r(38)=-.40$, $p<.05$]. Alpha suppression following fortress hits

predicted reductions in focus switch cost (i.e., in the capacity of efficiently switching between

items in working memory) [$r(37) = -.341$, $p<.05$]. This same Alpha suppression was also

correlated with increases in accuracy in the visual-spatial short-term memory task [$r(38) = .47$, $p$

$<.01$].

EEG Alpha power significantly predicted only changes in task switching. That is,

reductions in task-switching cost were positively correlated with all four EEG Alpha power

measures (i.e., with Mine Onset, Fortress Hits, and oddball tones inside and outside the game;

r's(37) > .33, all p's<.05). However, reductions in task-switching costs were not significantly related to any of the ERSP measures.

Note that in several cases the electrophysiological measures were correlated with individual difference in skill improvement, even when this improvement was not shown by all participants. This suggests that (a) improvement may only occur in some subjects but not others, and (b) that electrophysiological indices may be useful to identify which subjects will produce optimal improvement of similar skills outside of the game.

**Discussion**

We predicted that the engagement of brain cognitive control systems, as reflected by the Alpha power, could predict the subsequent rate of learning in a complex game. We indeed found that EEG Alpha power measured before training in the Space Fortress game environment predicts the rate of subsequent learning in the game. We have shown that with 20 hours of Space Fortress training, significant improvement in game performance is observed (see Boot et al., 2010). Here we estimated the learning rate of individuals across training sessions. We then tried to predict these rates of learning from the amount of Alpha power during game play before learning. We also found additional predictors of learning rate in the ERSPs following important game events. Using a linear combination of these predictors, we were able to account for almost 50% of the total variance in learning rate, over and above what was accounted for by the initial game score. The ERSP indices also predicted the amount of skill improvement in tasks measuring cognitive control outside of the game.

We first confirmed our hypothesis that brain activity associated with cognitive control, as indexed by the level of frontal EEG Alpha power, can predict learning rate. Subjects with greater

levels of Alpha power over frontal brain areas benefited most from the training program. This correlation with overall EEG Alpha power is intriguing. It was present almost identically in all epochs during the game and was also evident during the oddball task outside the game environment.   These data, and the high correlation between measures for each epoch, indicate that the relationship between frontal Alpha power and subsequent learning is consistent across a number of different conditions, and perhaps represents a general mode of responding of individuals to the experimental situation.  Those subjects who most engaged in this mode of responding ended up being the better learners.  Previous work (Klimesch, Sauseng, & Hanslmayr,  2006; Jensen & Mazaheri, 2010) has linked frontal Alpha to control processes and attentional engagement, perhaps related to the suppression of irrelevant information (such as it might occur while switching between different sub-components of the task) or to the control of motor activities (such as ship flying).  In any case, engagement of these control mechanisms appear closely related to task learning. The additional finding that frontal EEG Alpha oscillations are also predictive of learning in other cognitive-control  tasks (such as task-switching) provides further support for the interpretation that this form of brain activity is related to individual differences in cognitive control.  Interestingly, they raise the possibility that transfer of learning between the Space Fortress video game and other tasks (such as task switching) may vary between subjects and depend on the extent to which the videogame engages cognitive control operations, and that  EEG measures, such as frontal Alpha, may be used to monitor this engagement.

Importantly, our stepwise regression analysis revealed that this Alpha power predicted learning over and above the variance accounted for by the initial score in the game. This indicates that brain states manifested by frontal Alpha have explanatory power that goes beyond

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merely reflecting the current skill level. These activities may represent a state of the brain favoring the learning system. In previous work, we have found a link between the size of the basal ganglia and subsequent learning of the Space Fortress task (Erickson et al., 2010; Vo et al., 2011). These deep brain structures have close connections to the frontal cortex and the attention control system (van Schouwenburg et al., 2010). It is possible that the basal ganglia may also play a role in the brain circuit that is responsible for the frontal Alpha. More research is needed to confirm this relationship. A caveat that we need to consider here is that our measures of Alpha (and other EEG activity) are taken at the scalp, and their relationship with underlying brain structures is not well determined, but can only be hypothesized.

In addition to the base level of Alpha power, we were also interested in the oscillatory activity evoked (or invoked) by particular brain events measured with the ERSPs. This activity also reflects mobilization of attentional and processing resources. Here we found different evoked oscillatory activities for different in-game events. Several of them were predictive of subsequent learning. The amount of evoked high frequency beta activity in the couple of seconds following mine onset predicts who will most improve in the game. This predictive activity is maximal occipitally, indicating that the more attentional resources are dedicated to mine processing early in training, the more subjects will subsequently improve (see Wrobel, 2000 for this interpretation of beta activity). Also predictive of subsequent learning was the amount of low beta activity evoked 500-1000 ms after a fortress hit. This predictive Alpha activity is largest over parietal brain areas. Beta activity in a fronto-parietal network of brain regions has been tied to the engagement of attention systems (e.g. Klimesh et al., 1998; Romei et al., 2008a,b; Romei et al., 2010). Within the context of this study, beta activity may indicate the exertion of top-down control following successful fortress hits, which in turn may lead to faster

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learning. The amount of Alpha suppression elicited by fortress hits and the rare oddball tones was also predictive of the rate of subsequent learning. Since the phasic reduction of Alpha after stimulation likely reflects a shift of attentional resources, this finding further corroborates the idea that the extent to which cognitive control operations are engaged during the Space Fortress task is a good predictor of subsequent learning.

In order to test the relationship between these various predictors, we submitted them to a stepwise multiple regression. The resultant model, including mine-locked Alpha, ERSP beta, and fortress-locked Alpha increases accounted for almost 50% percent of the variance in score improvement, once the effect of initial game score was partialled out. Thus, our model based on the EEG activity recorded from an individual playing their first game of Space Fortress predicts relatively accurately the rate of their subsequent improvement. This provides an inexpensive and easy method of determining which subjects or trainees will most benefit from our training program. This predictive information is especially useful given the high test-retest reliability of EEG and ERSP measures (e.g. Neuper et al., 2005; Towers & Allen, 2009). Note also that each of these electrophysiological indices related to different game events provides an *independent* contribution to the learning variance. This may reflect the complex nature of the Space Fortress task. However, in general all these contribution to learning variance appear to be mediated by attention control mechanisms.

The ERSP measures also predicted improvements in tasks requiring processes similar to or overlapping with those used in Space Fortress, such as task switching and working memory (see Dahlin et al., 2008). Mine-locked beta increase was negatively correlated with changes in reaction time in the Sternberg memory task and with changes in stop time in the stop-signal task from measurements taken before and after training. Furthermore, fortress-locked decreases in

theta power were negatively correlated with improvements in focus switch cost, but positively correlated with the improvements in visual short-term memory. One possible explanation for these correlations is that, at least for some subjects, control processes were enhanced by the training regime to such an extent as to create advantages outside of the game environment. This would imply that game specific learning can transfer to other tasks and that subjects for whom a greater transfer is observed are those who, according to our EEG measures, were engaging control processes the most during initial learning. An alternative explanation is that our predictors represent some propensity for subsequent, generalized skill acquisition or learning in tasks requiring cognitive control, within *and* outside the game environment. Future research involving additional control conditions will be able to discriminate between these two accounts. Irrespective of the specific interpretation, however, these data provide support for the role of attention control mechanisms in learning and indicate that it may be possible to harness individual differences to optimize training and skill improvement.

In conclusion, we here showed that the state of the brain's cognitive control networks early in training can predict the rate of subsequent learning in the Space Fortress game, as well as the degree of skill improvement to untrained cognitive tasks, particularly task switching, cognitive control and working memory. When the initial game score was controlled for, those individuals exhibiting the largest EEG Alpha power over frontal regions had the fastest subsequent rate of learning, and improved the most at task switching outside of the game. We also found additional ERSP predictors of learning, likely related to control and attention systems in the brain; this is further evidenced by the observation that ERSP measures also predict improvements in attention control and working memory tasks outside the game environment. Together these electrophysiological predictors provide a low cost, non-invasive, and fast method

to preselect individuals for whom training on a complex task and skill improvements outside the

training task environment are more likely to be successful.

**Tables**

Table 2.1. Additional Tasks Outside the Game Environment

| Task | Response | Dependent Measure |
|---|---|---|
| **Cognitive-Control Tasks** | | |
| Task Switching (Pashler, 2000) | Odd/Even vs. High/Low Digit | Switch Cost (Switch RT – Stay RT) |
| Stop Task (Logan et al., 1998) | X or O/ Stop if rare tone, Staircased SOA | Stop RT (Averaged SOA/ Go RT) |
| **Working Memory Tasks** | | |
| Visual Short Term Memory | Delayed match to 4 object sample | Overall Accuracy |
| Sternberg | Delayed match to 3-5 letter sample | Response Time |
| N-Back | 1-back, 2-back letter match in stream | Focus Switch Cost (2-back RT--1-back RT) |

Table 2.2. Hierarchical Regression

| | $\beta$ | $R^2$ | $R^2_{adj}$ | F to Enter(df) | p |
|---|---|---|---|---|---|
| *Step 1* | | | | | |
| Initial Score | -0.34 | .11 | .09 | 4.57 (1,36) | < .05 |
| *Step 2* | | | | | |
| Initial Score | -0.24 | | | | |
| Mine EEG α | 0.38 | .25 | .20 | 6.38 (1.35) | < .05 |
| *Step 3* | | | | | |
| Initial Score | -0.20 | | | | |
| Mine EEG α | 0.37 | | | | |
| Fortress ERSP β⁻ | 0.39 | .40 | .35 | 8.85 (1,34) | < .01 |
| *Step 4* | | | | | |
| Initial Score | -0.11 | | | | |
| Mine EEG α | 0.28 | | | | |
| Fortress ERSP β⁻ | 0.36 | | | | |
| Mine ERSP β | 0.32 | .48 | .42 | 5.15 (1,33) | < .05 |
| *Step 5* | | | | | |
| Initial Score | -0.12 | | | | |
| Mine EEG α | 0.16 | | | | |
| Fortress ERSP β⁻ | 0.41 | | | | |
| Mine ERSP β | 0.33 | | | | |
| Fortress ERSP α | -0.32 | .57 | .50 | 6.09 (1,32) | < .05 |

Table 2.3. Mean (and standard deviation) of the cognitive tasks for the pre- and post-testing sessions.  Stop Prob. = Stop Probability. FS cost = Focus switch cost.

| **Task** | **Pre-test mean (*SD)*** | **Post-test mean (*SD)*** |
|---|---|---|
| *Task Switching (n=38)* | | |
| Non-switch RT | 920.98(135.16) | 851.8(116.29) |
| Switch RT | 1142.2(187.26) | 1023.37(160.3) |
| Switch Cost | 221.21(114.64) | 171.57(112.52) |
| *Stopping Task (n=39)* | | |
| Stop RT | 211.03(64.45) | 192.17(62.28) |
| Go RT | 614.88(186.94) | 616.75(179.62) |
| Stop Prob. | .52(.06) | .51(.04) |
| *Visuo-spatial Short-term memory (n=39)* | | |
| Accuracy | .68(.09) | .69(.09) |
| *Sternberg Memory Test (n=38)* | | |
| RT | 816.27(228.9) | 768.92(234.01) |
| *N-Back Task (n=38)* | | |
| 1-back RT | 609.91 (110.97) | 600.21(129.07) |
| 2-back RT | 830.98(225.07) | 731.1(165.13) |
| FS cost | 221.07(191.33) | 130.89(126.33) |

**Figures**
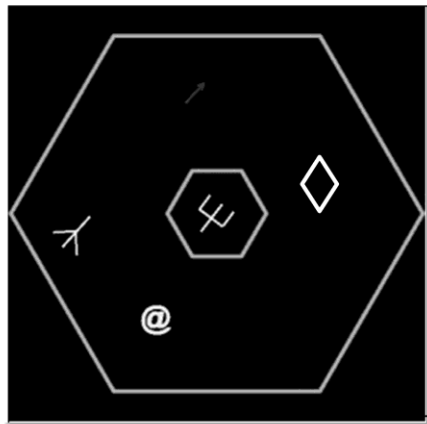


Figure 2.1. Typical display in the Space Fortress game. Subjects controlled the thrust and angle of a flying ship in a low friction environment. The goal was to fire missiles at the central Space Fortress, inflicting enough damage to destroy it. The fortress fired back at the ship, and mines appeared intermittently, having to be classified and disengaged before they hit the ship. Subjects were rewarded for flying slowly, and within the hexagonal playing field, for destroying the fortress, and for handling the mines, and were penalized for getting hit by the fortress or the mines.
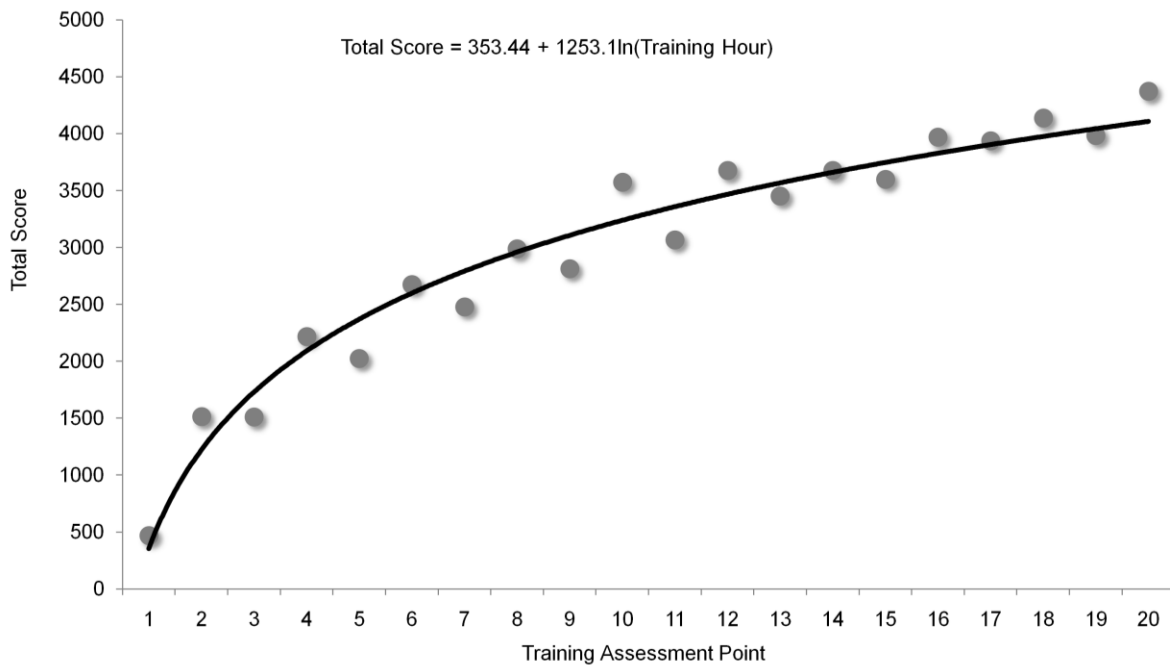
Figure 2.2. Average score for each of twenty assessment points over 10 training sessions. A logarithmic function best fit the subjects improvement in total game score over the 20 assessment points (a + r*ln(session)) where r is the learning rate.
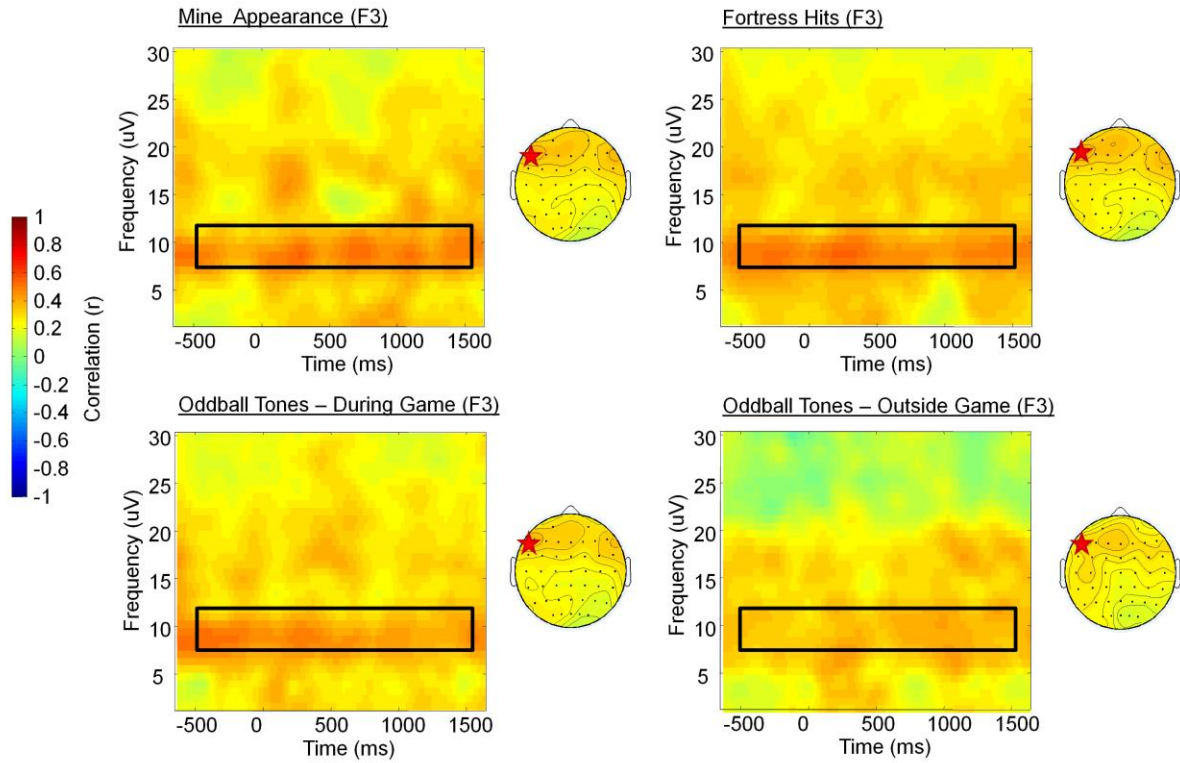
Figure 2.3. Color maps representing the correlations (r), computed separately at each point in time and frequency, between the average EEG activity for each subject and their rate of learning. Separate plots are shown for three events during the game: Mine Appearance, Fortress Hits, and rare Oddball Tones, as well as rare tones during an oddball task outside the game environment. All maps refer to activity recorded at the left frontal electrode F3 (stars on scalp maps). Shown alongside each event's correlation map is a scalp plot of the average correlation in the Alpha (7 − 12 Hz) range, in the time period from -500 to 1500 ms indicated by the black rectangles. These indices were highly correlated (all r > .80, p < .05).
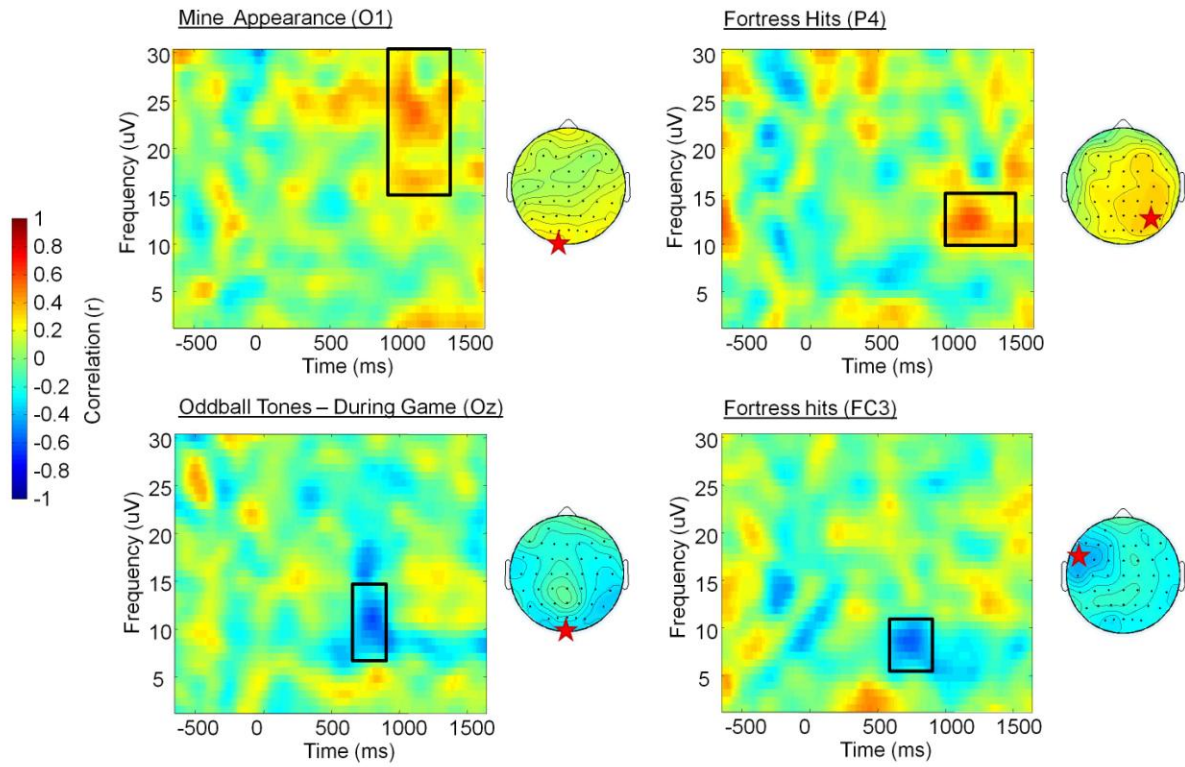
Figure 2.4. Color maps representing the correlations (*r*), computed separately at each point in time and frequency, between the ERSP activity, computed by subtracting the baseline before each event's occurrence, and the subject's learning rate. Separate plots are shown for three events during the game: Mine Appearance, Fortress Hits, and rare Oddball Tones. Shown alongside each event's correlation map is a scalp plot of the average correlation in each of the black rectangles, with a star indicating the electrode from which the correlation maps were computed.
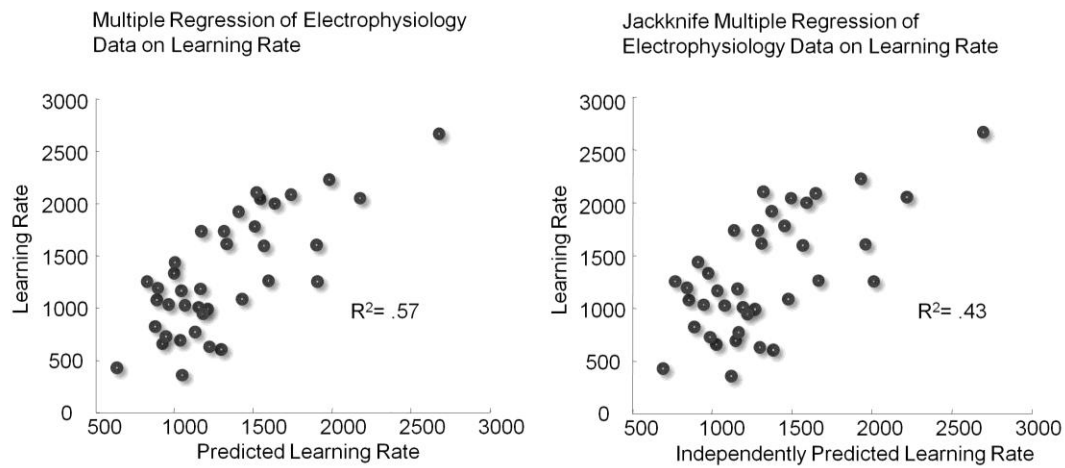
Figure 2.5. (Left) Scatter plot of the actual learning rate (ordinate) as a function of the learning rate predicted on the basis of the initial score and four electrophysiological predictors (abscissa). (Right) Same plot based on the results of the jackknife procedure.

# CHAPTER 3

## ALPHA AS A PULSED INHIBITION[3]

### Introduction

Thus far, we have reviewed studies indicating the inhibitory role played by Alpha activity in ongoing processing. Importantly these studies all make the assumption that modulation in Alpha power represents an all-or-none brake applied to neural processing. By its very nature, however, Alpha is an oscillatory phenomenon. Thus, is the inhibition indexed by Alpha continuous or does it vary according to the peaks and troughs in the Alpha cycle? An important corollary to this question is whether the presence of Alpha is a correlate of inhibition or in fact a direct index of some of the mechanisms supporting inhibitory processes in the brain. Over the last century, interest has been directed towards understanding the cyclic nature of Alpha oscillations. Speculations about the significance of different phases of the Alpha cycle were already presented by Bishop (1933). These original speculations were echoed in 1955 by Donald Lindsley, who proposed that the Alpha rhythm "represented for the cell, or for the aggregates of cells with which it is associated, an oscillation in cortical excitability". Lindsley's prediction leads to the proposal that inhibitory effects should vary with the phase of Alpha. Cheng (1951) showed that the output of a frog neuron, given a constant level of stimulation oscillates at a frequency of roughly 10 Hz, indicating that the cell went through 10 Hz oscillations in its excitability. In subsequent decades, studies revealed an effect of the phase of the ongoing Alpha

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activity on simple reaction time measures, with the slowest RTs for stimuli whose presentation was yoked to the scalp positive peak (Callaway & Yeager, 1960). Recently, Hamm et al. (2010) reported a higher likelihood of saccades to a lateralized target in association with particular Alpha phases. Nunn and Osselton (1974) showed that masked visual presentation of the word "DANGER" led to skin conductance response changes that were modulated by the phase of ongoing Alpha oscillations at the word onset, suggesting that this word was better processed at preferred phases of Alpha oscillations.

The idea that Alpha oscillations represent oscillations in cognitive processing has led some to speculate that the very nature of conscious visual perception occurs in perceptual moments or frames, and that perhaps a portion of the Alpha cycle indexes the duration of these perceptual moments. Evidence for this has been provided in a study by Vallera (1981) in which subjects were presented with either simultaneous or sequential visual stimuli at either the peak of the trough of the scalp measured EEG Alpha oscillations. Visual events presented asynchronously together during the positive phase of an Alpha oscillations were much more likely to be labeled incorrectly as simultaneous than those presented together during the troughs. However, this effect has since been hard to replicate (Gho & Varela, 1988; Koch & VanRullen, 2003).

More recent studies have further investigated the extent to which the processing of information varies as a function of the phase of ongoing local excitability cycles. Animal studies have shown that a subset of neurons preferentially fire during specific phases of the ongoing local field potential (LFP; Jacobs et al., 2007; Lakatos et al., 2008; Lőrincz et al., 2009). A great deal of research has also shown that evoked responses (N1 and P1 components) to identical visual stimulation vary as a function of the phase of ongoing oscillations at the time of

stimulation (Trimbel & Potts, 1975; Brandt et al., 1991; Jansen & Brandt, 1991; Barry et al., 2003; 2004; Kruglikov & Schiff, 2003; Sachdev et al., 2004; Lakatos et al., 2008; Mathewson et al., 2009; or Haig & Gordon, 1997 who found later P3 differences). It is important to note, however, that evidence that these evoked potentials are not independent of the ongoing EEG phase cannot be considered as evidence that ERPs are merely artifacts of phase resetting, since additional ERP variance is unexplained by ongoing oscillatory activity (Kruglikov & Schiff, 2003; Mazaheri & Jensen, 2006; Becker at al., 2009). This debate is beyond the scope of the current review, but is germane to its thesis since Klimsech et al. (2007) have proposed that this phase resetting would serve to re-align the preferential processing phase of the Alpha cycle to maximize stimulus processing. Recently, evoked BOLD responses to brief fixation events have been shown to vary as a function of the phase but not the power of independent Alpha components of the simultaneously recorded EEG (Scheeringa et al., 2011), indicating that these phase effects can even have metabolic consequences. Together, these findings provide support for the view that Alpha oscillations represent fluctuations in the ongoing excitability of the underlying cortical areas (Lindsley, 1952).

The interpretation of Alpha phase as representing different levels of cortical excitability leads to the prediction that identical visual stimuli may engender different perceptual representations depending on their synchronicity with the Alpha phase (Lindsley, 1952). Indeed, an early study found that identification of an auditory stimulus amongst noise differed as a function of the ongoing Alpha phase (Rice & Hagstrom, 1989).

In order to directly test this hypothesis, in a recent study we presented participants with brief targets that were followed closely in time by a metacontrast mask (Figure 3.3; Mathewson et al. 2009). We adjusted the timing and stimulus conditions such that, on average, our subjects

detected about half of the targets that were presented, while maintaining low levels of false alarms on catch trials. This balance allowed us to directly compare targets that were and were not detected. We were specifically interested in the time period before the onset of the target, and the relationship between the Alpha oscillations during this time period and subsequent awareness. Crucially, we showed for the first time that on trials with high levels of Alpha power over posterior areas, the *phase* of the Alpha activity preceding the stimulus could predict the subsequent detection of the masked target. Targets presented in one half of the phase cycle were much less likely to be detected than targets presented at the opposite phase or on trials with low Alpha power (Figure 3.3A). This seems to indicate that the modulation is specific to a particular phase of the Alpha cycle when Alpha is high. Thus, there are two routes to detection: the first is to decrease Alpha power, which increases cortical excitability and permits a consistent level of processing of the target; the second, when attention wanes and Alpha power is high (or if a part of visual space is being inhibited and Alpha power is high in the area of cortex processing that target), then certain phases of this increased Alpha activity inhibit processing. Therefore, on average, targets will be less likely to be detected with larger levels of Alpha power and/or when their timing is out of when their timing is in-phase with the inhibitory portion of the Alpha cycle.

A possible methodological issue with the finding of an interaction between Alpha power and phase effects on visual awareness is that on low-Alpha trials the signal-to-noise ratio of the phase measurement will be inevitably lower. Thus any differences in the Alpha-phase/detection relationship observed between high- and low-power trials may be due to increased error in phase estimation for low-power trials. From a statistical standpoint it is very difficult to tease apart the influences of phase and power, as the reliability of the phase measurement inevitably varies as a function of the power level. Note, however, that our theory stems not only from the interaction of

power and phase but also from the main effect of power. A crucial finding of the Mathewson et al. (2010) paper (see Figure 3.3A) is that detection rate is *higher* overall for low- than for high-Alpha power trials. The most parsimonious account of these two effects (the interaction of power and phase, and a the main effect of power) is to propose that the observed effects of phase and power on detection are linked by a single common mechanism; cortical excitability. In particular, awareness occurs when a threshold of cortical excitability is reached, be that during a certain phase when Alpha is high or when Alpha is low overall. When Alpha is low, and thus cortical excitability is high, detection will be high *regardless* of the phase of Alpha. An alternative account may propose that the influences of phase on neural activity are independent and dissociable from the influence of Alpha power on the same activity. However, such an account is less satisfying as it is difficult to imagine independent effects of phase and power on neural activity and performance, given what we know about how synchronized fluctuations of neural activity give rise to the oscillatory activity we measure.

The finding that visual awareness fluctuates as a function of the phase of ongoing oscillations in the EEG was corroborated by a subsequent study that analyzed the temporal and frequency breadth of this effect for threshold-level targets (Busch, DuBois, & VanRullen, 2009). In their study, the targets, instead of being masked, were rendered difficult to detect by reducing their presentation time with a staircase procedure, such that each subject detected about half of them. Again, differences in the EEG preceding detected and undetected targets were examined. The authors considered a broad range of times and frequencies, and summarized the difference in phase between the two conditions using a succinct statistic, the phase bifurcation index (PBI), which measured simultaneously the phase consistency and phase separation between two conditions. They predicted that if the phase of EEG oscillations differed between detected and

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undetected targets, then PBI should be high in that frequency, as each condition should have a preferential and opposite phase. Indeed, it was found that around 100 ms before the onset of the stimulus, 7-10 Hz oscillations in EEG had opposite phases for detected and undetected targets, thus replicating the core finding of the earlier Mathewson et al (2009) study in the same journal, Interestingly, the authors found that the site of the maximal phase difference was frontal (Busch & VanRullen, 2010; Drews & VanRullen, 2011). The discrepancy in peak location of the phase effect between our study and those of the VanRullen group may be due to the different visual stimuli used in the tasks. Metacontrast masks are believed to limit visibility of the target by interrupting feedback information from higher visual areas, blocking any prospect of widespread reverberation of target information (Ro et al., 2003). In our paradigm, this would have limited the representation of the target to early visual areas. Not having masked the target, and thus not limiting its neural representation, Busch et al. (2009) may have maximized the influence of oscillatory activity occurring within higher-level visual areas on target detection. Furthermore, it is important to keep in mind that scalp topography can misrepresent the distribution of underlying sources. It is especially important to consider the reference to which each channels voltage is compared, which is unfortunately not reported in either the Busch and VanRullen's or Drews and VanRullen's papers (for reviews of the influence of EEG phase on visual detection, see Wyart & Sergent, 2009; Hoogenboom & Romei, 2010).

In a review recently published in this journal, VanRullen, Busch, DeBois, and Drews (2011) provide a brief overview of their own research on the influence of EEG phase on visual perception and reaction time, as well as the relationship between these processes and attention. Unfortunately, the author's characterization of the results of Mathewson et al., (2009) contains a number of factual errors. First, VanRullen et al. (2011) claim that the data presented in

Mathewson et al. (2009; reproduced in Figure 3.3B of the current paper) show the band-passed time-average EEG activity when in fact the data depict the broadband ERP signal, indicating a large and obvious difference in phase between detected and undetected targets. Second, the authors claim that our fixed inter-target interval may have introduced overall phase locking to stimulus onset; however, the grand-average ERP across all trials (i.e., detected and undetected) also presented in the same figure, clearly shows no phase-locking to the onset of the target, indicating that phase locking was not a generalized phenomenon (see gray line in figure 3.3B). Lastly, the authors claim that we restricted our analyses to a time-averaged inspection of the waveforms. However, Mathewson et al., (2009) presented the results of five other analyses on the single trial phase and amplitude of Alpha, all corroborating the finding of a difference in Alpha phase between detected and undetected items (here see Figures 3.3A and 3.3C for examples). In sum, our careful and extensive analyses clearly show the influence Alpha phase on visual awareness, and rules out a number of alternative explanations for the effects.

In summary, a number of studies have shown that the phase of ongoing Alpha oscillations can influence the fine-grained timing of perception. These findings have received further support by Lorincz et al. (2009) who correlated the scalp-measured EEG in behaving cats with the local field oscillations (LFO) in the LGN, the first relay node on the main visual pathway. They showed that the output of thalamo-cortical relay neurons from the LGN is phase-locked to ongoing Alpha oscillations in the LGN itself. The authors argue that the strong correlation between these two oscillations justifies the use of in vitro LGN preparations, which spontaneously sustain their Alpha rhythm. In their cellular and network analyses the authors reported that the phasic output of the relay-mode thalamo-cortical neurons was locked to the

phase of the ongoing LFO, with two groups of cells preferring to fire at the positive and negative Alpha peaks, respectively.

**Pulsed Inhibition**

Based on this converging evidence we propose that Alpha oscillations represent a *pulsed inhibition* of ongoing visual processing. As we have shown, when Alpha oscillations are high in power, their phase has an influence on subsequent visual awareness. Brief visual events occurring in a particular phase of ongoing oscillations do not reach awareness, while those in the opposite phase do (Figure 3.3; Mathewson et al., 2009). This view is presented in Figure 3.4.

When inhibition of some part of visual space, some part of time, or some visual feature is needed, top-down signals from fronto-parietal areas control the level of Alpha oscillations (e.g., Sauseng et al., 2005; Capotosto et al., 2009). These ongoing oscillations can also fluctuate as a function of the current level of task engagement and vigilance (e.g., Mathewson et al., 2009). When Alpha power is low in cortical areas, or during evoked Alpha desynchronization, the excitability of that area is relatively high and above a threshold of awareness, leading to uniformly high performance. When Alpha power is increased, the excitability becomes, on average, lower, leading to decreased performance. Inhibition is not constant, however, but is in fact pulsed as a function of the phase of the Alpha oscillations, with periods of punctuate inhibition alternating with others of relatively intact processing (this is indicated in figure 3.4A by the Alpha wave oscillating around the threshold). In other words, phase and power are interdependent, with two possible states determined by power and with phase becoming important only when the power is high.

The proposal that Alpha represents a pulsed inhibition of ongoing brain activity is consistent with both Klimesch and colleagues' (2007) theory that Alpha reflects an inhibitory

timing mechanism based on excitability cycles, as well as Jensen and Mazaheri's (2010) recent

proposal that Alpha represents pulses of inhibitory gating of neural processing. The pulsed

inhibition mechanism we propose is similar to the asymmetric modulations in Alpha that have

been suggested by Mazaheri and Jensen (2010). The authors propose that Alpha oscillations

represent bouts of inhibition induced by GABAergic interneurons on the co-aligned pyramidal

dendrites. Increases in this inhibitory activity would only modulate the peaks and not the troughs

of Alpha activity, since these dendritic currents are predominantly unidirectional. It has further

been shown that these asymmetric modulations in Alpha can account for some commonly

observed slow ERP potentials (Mazaheri & Jensen, 2008; van Dijk et al., 2010).  Asymmetric

modulations in Alpha amplitude can also account for the fact that increases in Alpha power lead

to decreases in overall target detection, averaged across different phases.

Despite this common ground, there are also some differences across these accounts of the

role of Alpha oscillations. In our theory we stress an additional mechanism by which oscillatory

Alpha activity inhibits sensory processing. We have already considered the large amount of

evidence for oscillations representing fluctuations in the excitability of the underlying cells.

Increases in EEG Alpha are associated with larger populations of neurons firing in synchrony

with one another (e.g., Bollimunta et al., 2011). During periods of large-scale Alpha synchrony,

any given cell has less of a chance of firing during particular phases of the cycles. It is during

these brief periods of widespread inhibition that Alpha comes to exert its inhibitory effect on

processing.

Thus, we propose that scalp-recoded Alpha occurs when the excitability or inhibitory

periods become synchronized over large populations of neurons. When there is less

synchronization, these inhibitory periods are random and signals processed in the area can stand

out against the noise. However, when oscillations become highly synchronized, periods of inhibition occur simultaneously across the population of cells, drowning out any signal representation. Interestingly, this theory has much in common with recent theories of attention from single cell recordings, where it has been shown that attention acts by decorrelating low-frequency noise in sensory areas (Mitchell et al., 2009).

To portray the theory in a metaphor, we imagine the oscillatory activity in a processing area as a large crowd at a football stadium. When the individual fans cheer at random times, any loud person can be heard over the hum of the crowd (e.g. "COLD BEER!"). However, when the same applause becomes synchronized in a unified cheer, brief periods of widespread sound drown out any other important sounds. Similarly, we propose that inhibition acts on sensory areas by synchronizing the oscillatory excitability cycles of neurons in those areas, drowning out incoming signals.

As mentioned, Jensen and Mazeheri (2010) propose that inhibitory GABA activity in sensory areas manifests itself as an asymmetric increase in Alpha power due to its unidirectional current flow. In other words, they emphasize cellular-level mechanisms that may explain the same phenomena addressed by our model at a more global level of analysis. As such, the two theories are complimentary. However, these theories do lead to different predictions that can be tested experimentally. For instance, our theory would predict that *any* source of synchronized neuronal oscillations in sensory areas would inhibit processing, not just inhibitory GABAergic coupling. For instance, entrainment of cortical oscillations with TMS, or transcranial current stimulation would synchronize oscillatory activity presumably through electrical induction to a greater extent than by interneuron connections. Such data (see Thut & Miniussi, 2009) provide support for our theory, demonstrating that phase effects on cortical processing are observed for

entrained brain oscillations (see below for a review that entrainment of oscillatory brain activity obtained with rhythmic visual stimulation can also have similar effects as spontaneous Alpha in sensory processing).

Importantly, our pulsed-inhibition account of Alpha can consolidate disparate theories of Alpha activity. Palva and Palva (2007) have proposed that increases in Alpha can also represent important active control processes, and emphasize the phase synchrony between frontal and parietal brain networks in the Alpha band. In our model increases in Alpha synchrony would not only be associated with widespread inhibitory pulses, but also with brief synchronized excitable periods in counter phase. Thus, active cognitive and inhibitory roles of Alpha oscillations may be two sides of the same pulsating coin. Importantly the Palva and Palva (2007) proposal also emphasizes the phase-amplitude coupling of Alpha oscillations with higher frequency (e.g., gamma) neural activity. In other words, increased amplitude of high-frequency activity is seen during certain phases of lower-frequency Alpha activity (Palva et al., 2005, 2010; Osipova, Hermes & Jensen, 2008; Cohen, 2008; Voytek et al., 2010). Given the enhanced and coordinated processing known to be associated with gamma activity (e.g. Tallon-Baudry & Bertrand, 1999), phase-amplitude coupling would provide an important strengthening of any low-frequency phase interactions.

An important feature of this conceptualization of Alpha as a pulsed inhibition of visual processing is its relation to top-down attention. Busch and VanRullen (2010) have investigated the relationship between the phase effects on visual awareness and attention. They first cued subjects to monitor a continuous stream of possible targets on one side of the visual field. However, subjects were also told to respond to targets presented in the uncued visual field. The authors found that the phase of EEG oscillations could predict target detection, but only when

targets were presented on the cued side of the visual field. They interpret this finding as calling into question our proposal that increased Alpha power and Alpha phase effects go hand in hand. Their reasoning is that, since increased attention should decrease Alpha power, the pulsed inhibition theory of Alpha should predict that effects would be highest when Alpha is high and targets are presented at an unattended location in the visual field (e.g., Thut et al., 2006, Mathewson et al., 2009). Importantly, the latter inference is predicated on the assumption that targets presented at the uncued location should be processed in a cortical region where Alpha is particularly large. However, Busch and VanRullen did not measure the lateralization of Alpha oscillations induced by the cue, and how the phase effects interacted with Alpha power on a trial by trial basis. Furthermore, the data do indeed show a trend towards an effect of Alpha phase for targets presented at the unattended location, almost as large as that for those presented at the attended one, though not reaching significance. A further problem with their interpretation comes from the nature of the task itself, which in fact requires participants to respond to targets appearing at the "unattended" location. Thus, one may question to what extent that location was truly unattended, which, in turn, may have limited the extent to which Alpha power was increased at that location; a strong inhibition of processing for stimuli presented at the unattended location should have produced large decreases in subjects' performance, which did not occur.

Recently Capotosto et al. (2009) have begun to elucidate the brain networks responsible for top-down control of Alpha variations. When repetitive TMS (rTMS) was applied to the FEFs and the IPS, the modulation of Alpha activity as a function of attention leading up to the target onset diminished. Further, the Alpha asymmetry elicited by spatial attention was also affected by rTMS and subjects no longer showed the benefits of spatial attention typically observed in a

Posner cueing task. This provided the first causal evidence that attentional orienting by the FEF and IPS, in preparation of upcoming visual processing, is modulated by Alpha oscillations. Indeed, Hamidi et al. (2009) also found that 10-Hz rTMS to IPS and FEF biased Alpha oscillations and influenced target detection. Furthermore, simultaneous EEG and fMRI recordings reveal that activity in the dorsal attention network is negatively correlated with Alpha power (Sadaghiani et al., 2010). We have recently combined the use of fast optical imaging of neuronal activity using the event-related optical signal (EROS; Gratton & Fabiani, 2010) and EEG to investigate the regions associated with changes in Alpha activity. We found areas in both frontal and parietal regions whose activity correlated with changes in Alpha power (Mathewson et al., in preparation).

In summary, we propose that Alpha oscillations represent a pulsed inhibition on ongoing processing. The power of these Alpha oscillations can be controlled by top-down attention from fronto-parietal structures with the goal of biasing ongoing processing in favor of the task-relevant or attended stimulus. Indeed, the FEF and IPS are thought to bias visual processing largely through the pulvinar thalamic nucleus (Corbetta, Patel, & Shulman, 2008), which in turn has been shown to account for a significant proportion of the variance in posterior cortical Alpha power (Steriade et al., 1990). These controlled modulations of Alpha power then influence cortical excitability, inhibiting the processing of unattended or actively ignored items. When Alpha power is high, the phase of the ongoing Alpha oscillation can predict amount of processing, target detection, and response time.

**Entrainment of Temporal Attention**

Our proposal that Alpha oscillations represent a pulsed inhibition of ongoing processing would predict that if one were able to control the phase of these oscillations, one could

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manipulate these fluctuating periods of enhanced and inhibited firing. Indeed, research has

shown that the phase of ongoing oscillations in the EEG can become automatically entrained to

rhythmic stimuli in the environment (Adrian & Matthews, 1934; Walter & Walter, 1946). This

so called steady-state visual evoked potential (SS-VEP) has been shown for a range of

frequencies from 1 - 100 Hz (Herrmann et al., 2001; Pastor et al., 2002; 2003) and attention

enhances this effect (Morgan, Hansen, & Hillyard, 1996; Rosenfeld et al., 1997; Muller et al.,

1998; Lakatos et al., 2008), suggesting that entrained oscillations in cortical excitability may

represent a mechanism for temporal attention to rhythmic environmental events (Large & Jones,

1999; Coull, 2004; Buhusi & Meck, 2005; Schroeder & Lakatos, 2009). It is unclear, however, if

entrained oscillations in the cortex have the same functional impact as do endogenously

controlled changes in cortical oscillations.

Manipulations and theories of visuo-spatial attention are ubiquitous in the cognitive

psychology literature (e.g , Posner & Peterson, 1990; Corbetta & Shulman, 2002; Reynolds &

Heeger, 2009). However, only a small amount of research has extended these constructs into the

temporal domain, investigating how attention to sensory objects fluctuates with time (Coull &

Jones, 1976; Large & Jones, 1999; Coull & Nobre, 1998; Coull et al., 2004; Schroeder &

Lakatos, 2009). Many parallels can be drawn between what can be characterized as visual

attention and temporal attention, respectively. Both consist of mechanisms by which processing

of a stimulus is enhanced at the expense of that of other stimuli (i.e., James, 1890; Posner, 1990;

Levinthal & Lleras, 2008b; Yashar & Lamy, 2010). Theorizing about attention in the temporal

domain has been limited, (but see Jones, 1976; Coull & Nobre, 1998; Coull et al., 2004;

Schroeder et al., 2008). In our day-to-day conversations, we are bombarded with rhythmic

auditory information, which we can parse into individual sound units or phonemes, whose serial

order can be distinguished with delays as short as 30 ms (Schmidt-Kassow & Kotz, 2008). Our ability to successfully attend to the relevant features of sound or speech developing over time thus relies on some sort of internal clock mechanism, which is able to predict from the ongoing information the timing of important upcoming events.

Jones (1976) proposed that, "…organisms are basically rhythmical and possess their own temporal structures which are manifested psychologically in a series of tunable perceptual rhythms…" In a more recent quantitative explication of the theory, Large and Jones (1999) posit the presence of internal oscillators representing pulses of "attention energy" that can be entrained to the timing of external rhythms. In their theoretical framework, attention allows for these internal oscillators to adjust their parameters in order to time their pulses of "attention energy" with relevant environmental stimuli, in a sense coupling the internal rhythms with those in the environment. Both the phase and the period of the internal oscillations become coupled to the phase and period of oscillations in the environment. Thus the future onsets of environmental stimuli will occur at times predicted by the entrained internal oscillations. This will allow the pulse of attention energy to enhance processing. To test this proposal, Jones et al. (2002) presented subjects with a standard auditory tone followed after a set of rhythmic distracters by a comparison tone. Subjects were best at comparing the two tones when the comparison tone was presented in phase with an embedded rhythmicity in the irrelevant distracter tones. This was taken as evidence that waves of attentional energy can be built up to preferentially process temporally predictable stimuli.

To extend these series of studies to the visual modality we asked whether we could see evidence of entrainment for visual stimuli presented in the Alpha range. We conducted the first behavioral test of this hypothesis as depicted in Figure 3.5 (Mathewson et al., 2010). We

presented 8, 4, or 2 annuli prior to the onset of the target. These annuli, identical to the

subsequent mask, were present at regularly spaced intervals, every 83 ms, leading to a

presentation rate of 12 Hz, within the normal range of Alpha oscillations. After the onset of the

final entrainer, we presented the target at various lags with respect to the timing of the previous

entraining stimuli. Targets were either presented in phase with the preceding entrainment, out of

phase with the entrainment, or in between. We predicted a quadratic effect as a function of lag

after entrainment, with a peak in detection for targets in phase with the entrainment, when the

optimal phase of their excitability cycle would occur due to the processing of the previous

stimuli.

As can be seen in Figure 3.5b, we indeed found an effect of the entrainment, such that

targets presented in phase were better detected than targets presented out of phase. Furthermore,

this effect scaled as a function of the number of entrainers, indicating that the entrainment

process takes time to build up. When only 2 annuli were presented, but with a long gap in

between to control for the length of the 8-entrainer-foreperiod condition (book-end condition),

only a linear increase in detection was observed, with no peak in detection at 83 ms. In other

words, in the absence of rhythmic entrainment, a single annulus preceding the target actually

decreases target visibility (so called *forward* masking). Yet, when this last annulus is one of

several in a rhythmic sequence, targets are released from forward masking and visibility changes

in a phase-dependent manner. Importantly only the peak detection at 83 ms in the 8-entrainer

condition was greater than the baseline detection rate with no preceding stimuli (Figure 3.5b),

indicating that this rhythmic stimulation predominantly resulted in poorer detection for out-of-

phase targets, but little or no enhanced processing for in-phase targets. This is consistent with the

view that Alpha is a pulsed inhibition on visual processing, in that the majority of the change from the control condition was inhibitory and resulted in poorer detection.

The results of Mathewson et al. (2010) provide strong support for Jones et al.'s (2002) proposal, and reveal that detection of visual stimuli is influenced by their temporal predictability with respect to preceding visual events. Relatedly, Schmidt-Kassow et al., (2009) found that the P3b ERP response was earlier in response to stimuli in a regular sequence compared to a random sequence, indicating faster processing. In keeping with this hypothesis, in non-human primates, low frequency (1.5 Hz) local field potential oscillations can become entrained to external stimulus periodicity in an attended modality. The phase of these entrained oscillations then influences both the evoked response and RTs (Lakatos et al., 2008). This same effect has recently been replicated in humans (Stefanics et al., 2010) and has been shown in intercranial recordings in human patients to be enhanced by both attention and the predictability of stimuli (Besle et al., 2011). Further effects of temporal expectancies and entrainment of oscillations have been shown in the gamma range (over 30 Hz). Gamma flickering that is undetectable by subjects has nonetheless been shown to influence attentional orienting performance, thus indirectly influencing visual detection (Bauer et al., 2009). Finally, gamma has been driven by optogenetic stimulation, affecting sensory responses (Cardin et al., 2009). Rhythmic stimulation of the whiskers of a rat has also been shown to entrain related sensory areas (e.g., Tamereanca et al., 2008), as does sound stimulation (Gao et al., 2009). Somewhat frightening, Williams et al., (2004) have shown that the refresh rate of video displays such as computer monitors can entrain neural oscillations.

In order to make the crucial link between the EEG Alpha phase effects we observed in Mathewson et al. (2009), and the behavioral influence of entrainment at these same Alpha

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frequencies on subsequent timing of visual awareness (Mathewson et al., 2010), we next recorded EEG activity in a modified version of the entrainment paradigm (Mathewson et al., submitted). We predicted that a rhythmic visual sequence in the Alpha range would not only entrain Alpha but at the same time entrain visual awareness. In the Mathewson et al. (submitted) study, we asked if the hypothesized pulsed inhibition represented by the phase of Alpha oscillations could be controlled. Specifically, we predicted that stimuli presented at 12 Hz would entrain brain oscillations. We presented 8 entraining stimuli directly before the onset of a metacontrast-masked visual stimulus identical to that used in Mathewson et al. (2009). We compared the 8-entrainer condition from the previous study to both the same book-end condition and an additional condition in which we added variability to the rhythmicity of our entrainment sequence. On variable entrainment trials, the same overall sequence length as the 8 entrainer condition was used, but the timing of the entrainers was jittered such that they were not presented at regular intervals. On each trial, one of these three prestimulus conditions was presented, followed by the target. The target was presented at one of seven lags after the onset of the final entrainer. This way, we had two target presentations that were in phase with the preceding entrainment (first and second peak of the presumed oscillation), two that were out of phase, and three intermediaries.

To what extent are these induced fluctuations in awareness dependent on induced oscillations in the brain? First, entrainment led to increased phase locking to the rhythmic stimuli compared to the variable condition, the degree of which predicted detection rate across subjects. Second, entrainment led to differences in the phase of 12-Hz oscillations over parietal areas between in-phase and out-of-phase targets, the size of which predicted the difference in detection between in- and out-of-phase targets. Finally, we found an analogous difference in Alpha phase

between detected and undetected targets, replicating our previous findings (Mathewson et al., 2009). Interestingly, these effects were partially dependent on both pre-trial and pre-experiment oscillations in the Alpha range, providing further evidence of a link between Alpha and the entrainment of awareness.

These entrainment data can be accounted for by an expansion of the thalamo-cortical interaction model proposed by Lorincz et al. (2009). In their model, the output of the feed-forward neurons transmitting information from the retina to the cortex is modulated by a set of inhibitory inter-neurons in the LGN whose activity occurs in 10-Hz bursts, which act as pace-makers for the cortical Alpha rhythm. Recently it has even been shown that the oscillating electrical fields created by neural populations can entrain the firing of local neurons through ephaptic coupling of gap junctions (Anastassiou et al., 2011). In the entrainment condition, we may assume that the interneuron activity is itself modulated by the feed-forward sensory input. This would cause the interneuron activity to be phase-locked with the entrainers. As a consequence, cortical Alpha activity would also be entrained. Thus, modulated signals arrive in V1 already under the influence of modulatory oscillations, and these modulatory oscillations also are represented at later visual stages where they can continue to influence perception (Figure 3.4B). This synchronization suggests a mechanism for how specific phases with respect to stimulus onset lead to better performance on a wide range of cognitive tasks (e.g., Jensen and Brandt 1991; Haig & Gordon, 2003; Mathewson et al., 2009).

These studies of the entrainment of ongoing oscillations have been supported by recent work using various transcranial stimulation protocols, and together with previous results attest to the causal role played by the power and phase of Alpha oscillations on visual processing. Entrainment of beta oscillations over motor areas by transcranial alternating current stimulation

(tACS) increased beta oscillations and in turn slowed movements (Pogosyan et al., 2009).

Repetitive TMS at Alpha frequencies has been shown to bias Alpha oscillations in working

memory tasks, leading to effects very much like those observed for spontaneous Alpha (Hamidi

et al., 2009; Sauseng et al., 2009). Both tACS and rTMS at 10 Hz have been shown to increase

Alpha oscillations (Johnson et al., 2010; Zaehle et al., 2010; Romei et al., 2010) and lead to

analogous effects on visual detection as endogenous Alpha oscillations (e.g., Romei et al., 2010).

TMS has also been shown to entrain oscillations in animals (Ozen et al., 2010). However, given

the highly unnatural nature of TMS, it is likely that entrainment by TMS or tACS will have

different and possibly more unpredictable consequences on underlying EEG oscillations and

behavior.

Entrainment of the phase of ongoing oscillations may explain some important and

pervasive effects in common psychological tasks. For instance, when distracters are presented at

fixation in a rapid serial visual presentation (RSVP, most often at 10 Hz; Raymond, Shapiro, &

Arnell, 1992) task, targets embedded in the regular sequence are usually easily detected, with

some important exceptions. Participants' ability to identify the target in the rapid sequence

increases monotonically as a function of position in the series, from about 70% for position 2 to

above 90% for position eight, after which performance asymptotes (Ariga & Yokosawa, 2008;

Ambinder & Lleras, 2009). This increase in performance as a function of position in the stream

has been labeled "attentional awakening" to indicate that temporal attention to the sequence is

becoming entrained to the rhythm of the RSVP, as the stream unfolds. This effect is very much

consistent with the data reported by Mathewson et al. (2010), where increasing the number of

pre-target entrainers increased detection monotonically from 0 to 2 to 4 to 8 entrainers. Thus,

even though the targets in the RSVP sequences were all in-phase with the distracters, this

preferential phase locking requires time to build up (Large & Jones, 1999; Mathewson et al., 2010). Indeed, when the timing of the distracters in the RSVP sequence is jittered such that their sequence is not perfectly rhythmic, initial target detection decreases (Martin, Enns & Shapiro, in press).

A common manipulation in RSVP paradigms is to insert a second target (T2) into the sequence and investigate how its visibility is influenced by its temporal position with respect to the first target (T1). It is typically found that T2 accuracy is diminished when it follows T1 by 2-7 items, an effect referred to as the *attentional blink*. One possibility for this effect is that the entrainment of Alpha phase by the distracters is interrupted by the processing of the target. A phase interruption would seem to be necessary in order to stop the enhanced processing of the subsequent distracters from drowning out the target information. This preferential phase would then need to be reestablished by another gradual entrainment, explaining the similar time course of the attentional awakening and attentional blink (but see Ambinder & Lleras, 2009). Martin, Enns, and Shapiro (in press) found that the attentional blink was also decreased if jitter was added to the distracters prior to its presentation, indicating that the regular distracter intervals are an important precursor to the blink.
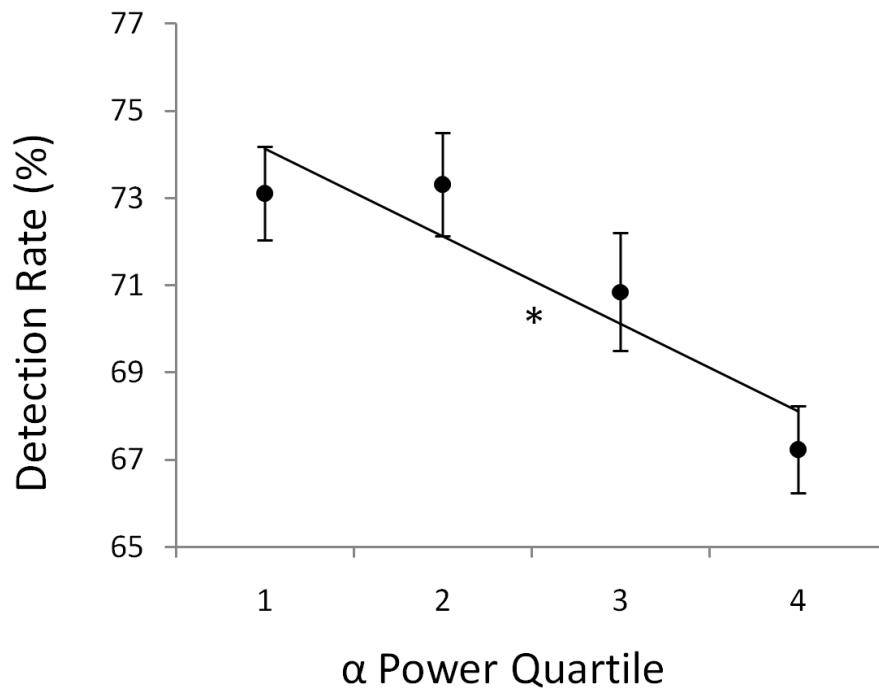
**Figures**



Figure 3.1. Detection rate of a metacontrast-masked target decreased with increasing levels of pre-stimulus Alpha power quartiles (1=lowest, 4=highest) measured on single-trials at electrode Pz. Error bars represent within-subject SE, *p < .05. (Figure adapted from Mathewson et al., 2009, *Journal of Neuroscience*, reprinted with permission).
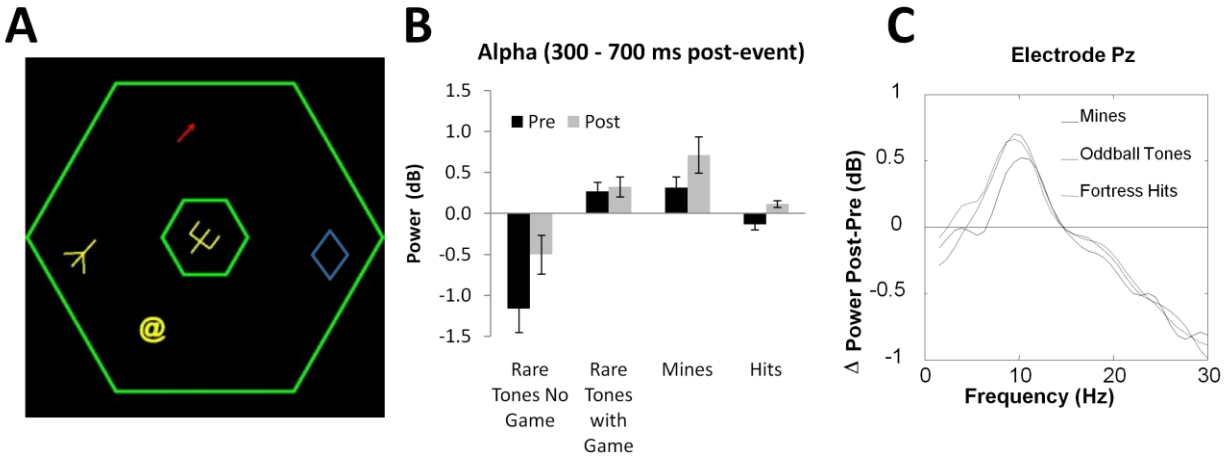
Figure 3.2. (A) Display for the game Space Fortress, on which subjects were trained for 20 hours. (B & C) Changes in frontal and parietal mean evoked Alpha oscillations between pre- and post-training EEG recording during the Space Fortress game, from 300-700 ms after stimulus onset. Error bars represent within-subject SE. (Figure adapted from Maclin et al., in press, *Psychophysiology*, reprinted with permission).
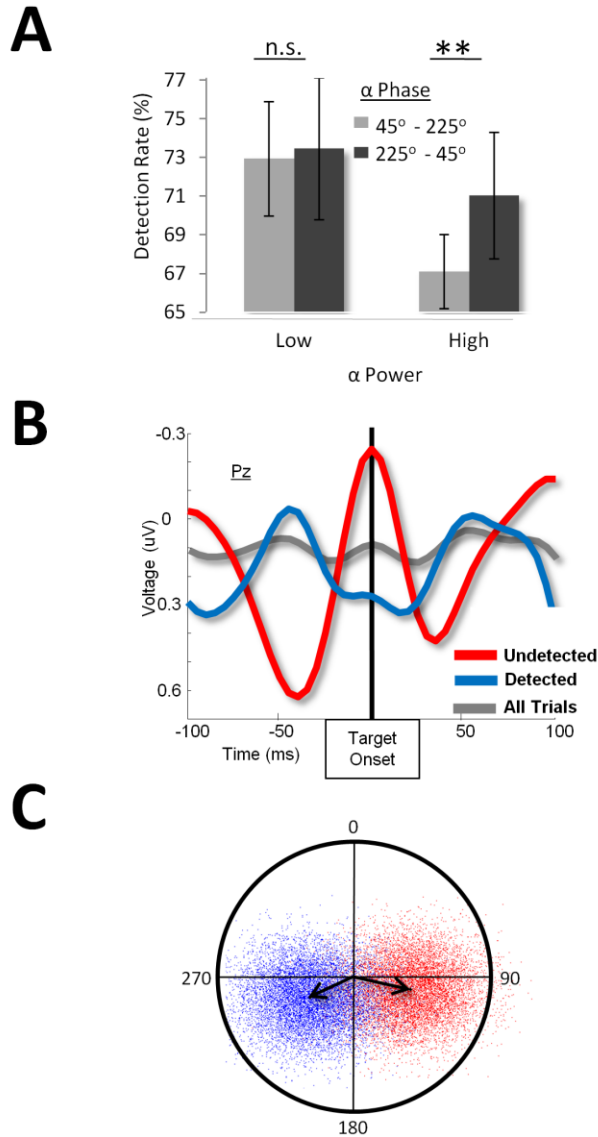
Figure 3.3. (A) Detection rate as a function of Alpha power and phase before stimulus onset. When Alpha power is low (left bar graph), there is no difference in masked-target detection as a function of pre-target Alpha phase. When Alpha power is high (right bar graph), however, not only is detection lower overall, but it differs between opposite Alpha phases. (B). Grand average ERP at the Pz electrode for detected (blue), undetected (red) and all (gray) targets. Results show the presence of counter-phase Alpha oscillations between detected and undetected targets, whereas the overall average is flat, indicating that subjects did not phase lock to the stimulus before its onset. (C) Polar plot of a bootstrap-derived distribution of the average phase (angle) and amplitude (distance from origin) of pre-target 10-Hz oscillations for detected (red) and undetected (blue) targets. Each dot is the grand average phase over the 12 subjects for one of 10,000 equally-sized random samples from the two conditions. The arrows represent the centroids of the distribution of mean phases. (Figure adapted from Mathewson et al., 2009, *Journal of Neuroscience*, reprinted with permission).
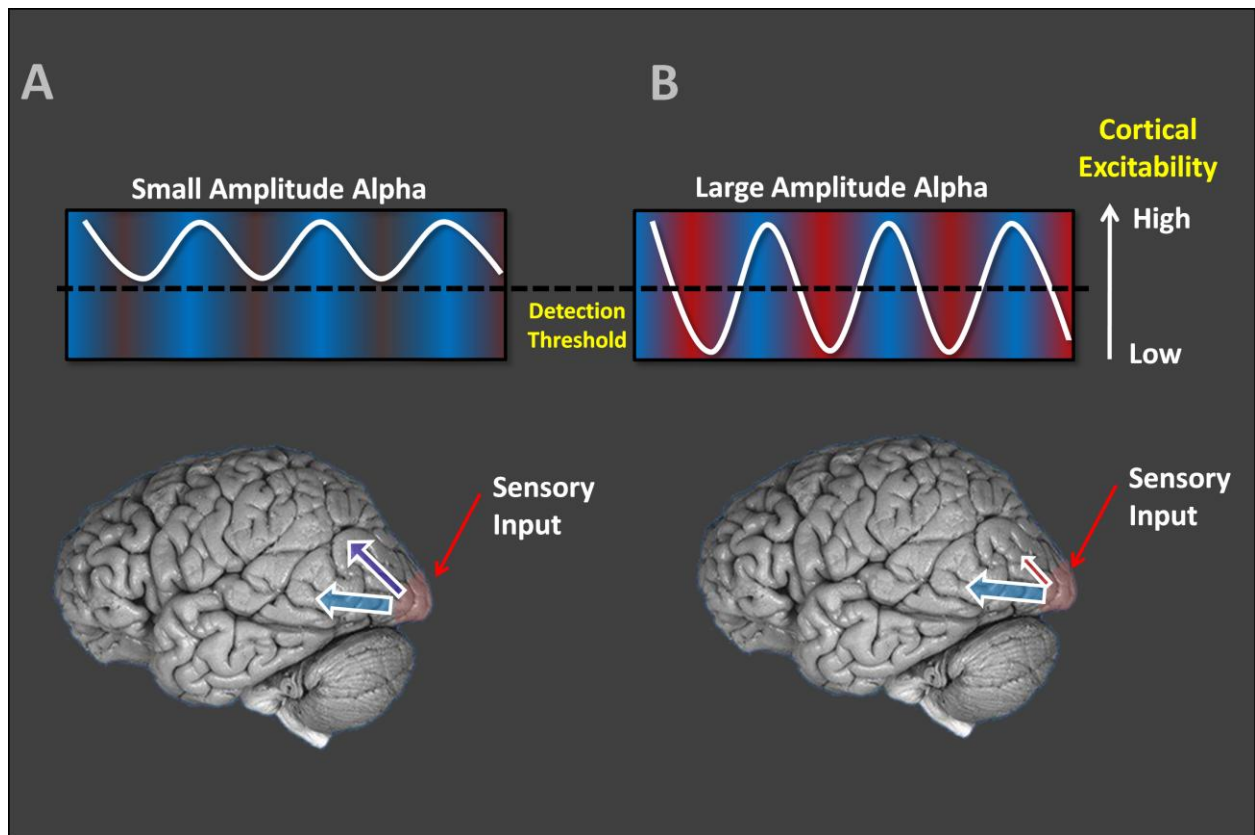
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Figure 3.4. A schematic of the pulsed-inhibition account of Alpha oscillations. (A, left column) When Alpha amplitude is low, cortical excitability is sufficiently high to produce consistently high levels of processing, and constant detection regardless of phase. (B, right column) When Alpha power is high, certain periods of its phase are inhibitory for visual processing and target detection differs as a function of the phase at which the target was presented.
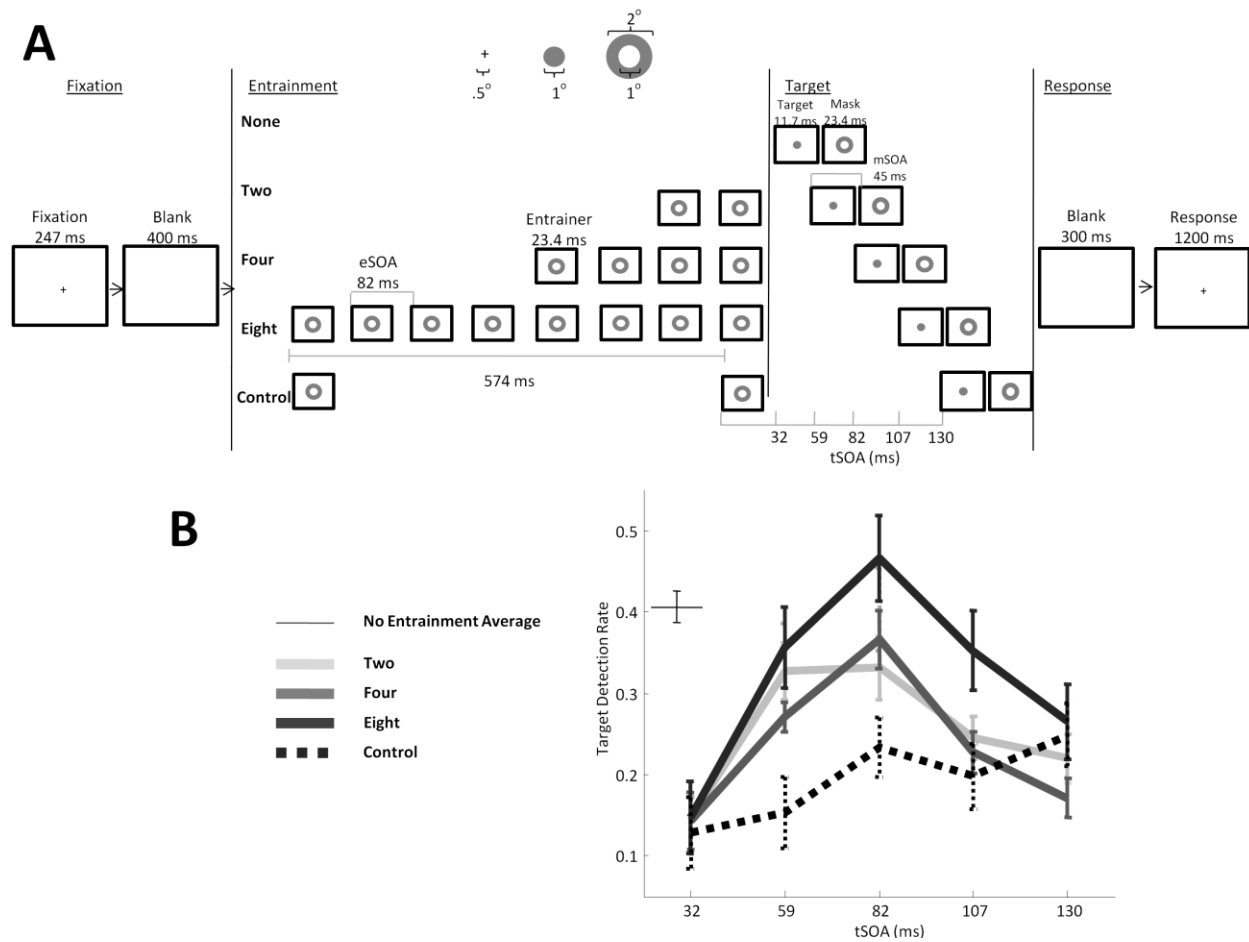
Figure 3.5. (A) Schematic of the trial timeline and stimulus dimensions from Mathewson et al. (2010). Subjects were presented with a masked visual target at various lags after a series of periodic preceding annuli. (B) Targets were better detected if they occurred in synchrony with the preceding rhythmic flashes, and this effect scaled as a function of the number of pre-target periodic stimuli. (Figure adapted with permission from Mathewson et al., 2010, *Cognition*).

## RESCUING STIMULI FROM INVISIBILITY: INDUCING A MOMENTARY RELEASE FROM VISUAL MASKING WITH PRE-TARGET ENTRAINMENT[4]

**Introduction**

When stimuli are masked to be at the threshold of consciousness, identical stimulus presentations can result in very different states of awareness. Psychophysical laws interpret these variations as stochastic phenomena and do not address why any given stimulus reaches awareness. However, given that the stimulus parameters are identical, the source of this variability in awareness must reflect variability in the state of the visual system, which is typically not under experimental control. Here we ask whether these differing states can in fact be manipulated, inducing predictable variations in awareness via rhythmic visual signals in the environment.

*Entraining to Rhythmic Events*

Prior work has shown modulation of auditory processing by a rhythmic series of tones, resulting in enhanced sample matching at times in phase with the preceding tones (Jones et al., 2002). Jones et al. presented participants with a target tone at the beginning of a trial, followed by a series of irrelevant tones with an embedded rhythmicity. A probe tone was presented at variable intervals following the end of the rhythmic sequence. Highest matching-task performance was found on trials when the probe tones were presented in phase with the rhythmic

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[4] Mathewson, K. E., Fabiani, M., Gratton, G., Beck, D. M., & Lleras, A. (2010). Rescuing stimuli from invisibility: Inducing a momentary release from visual masking with pre-target entrainment. Cognition, 115(1), 186-191.

For this multiple author paper I designed the study, collected the data, analyzed the data, and drafted and edited the manuscript, and created the figures.

sequence, compared to those presented out of phase. The authors interpreted this finding in terms

of "tuning" of temporal attention by predictable events; periodic tones (even if irrelevant) had the

effect of narrowing the temporal selection window of attention (more precise time-based

selection), and increasing the attentional gain (better signal-to-noise ratio). Similarly, it has been

shown that oddball targets in a series of attended standard tones elicit larger mismatch negativity

(MMN) in a constant rate train than those in a variable rate train of tones (Erickson & Hetrick,

2009), again indicating enhanced auditory processing for environmental stimuli occurring at

predictable times.

Following Jones et al.'s work in the auditory modality, a related effect has been

documented in temporal attention in the visual modality (the "attentional awakening" effect, see

Ariga & Yokosawa, 2008; Ambinder & Lleras, 2009). In those experiments, participants were

asked to identify a white letter embedded in a rapid stream of visually presented (RSVP) blue

letters. Ariga and Yokosawa observed that performance in this task was poor for targets

appearing early on in the RSVP stream, but improved to asymptote as the RSVP unfolded. Much

like Jones et al.'s auditory temporal tuning account, this effect was interpreted as evidence of

temporal attention tuning-in to the timing of the series of visual events with the goal of better

processing each individual item.

Moreover, it has recently been shown that sensory processing and awareness vary with

respect to the phase of the ongoing EEG Alpha rhythm (Mathewson et al., 2009; Busch et al.,

2009; Lakatos et al., 2008). Given that rhythmic visual stimuli have been shown to induce

comparable oscillations in neural firing (Herrmann, 2001; Pastor et al., 2002; Williams et al.,

2004; Lakatos et al., 2008), the present study also sought to corroborate the findings of

concomitant oscillations in neural firing and awareness, investigating for the first time the effect

of the phase of these induced oscillations on visual awareness.

*Current Study*

Our goal in the current study was to ask whether the visual system could be entrained to produce temporally well defined peaks in sensitivity at predictable times in a sequence. Moreover, we asked whether such entrainment could be used to modulate awareness of near-threshold masked stimuli. That is, given attention to a single location in space, can predictable events in the environment improve visual sensitivity to better process brief periods in time, such that we can manipulate which stimuli will reach consciousness? We hypothesized that the threshold of visual awareness could be entrained or synchronized to the expected occurrence of rapid, rhythmic events; with maximal sensitivity occurring for targets presented in phase with the preceding entraining stimulation, and reduced sensitivity for out-of-phase targets. The experimental task was to detect the presence of a luminance disk at fixation. We used a metacontrast mask (at optimal stimulus-onset-asynchrony; SOA) to reduce target visibility to near-threshold levels and minimize contributions from trace processing of post-target visible persistence activation by diminishing re-entrant activity (Di Lollo, Enns, and Rensink, 2000; Ro et al., 2003; Enns, 2004).

**Method**

*Participants*

Sixteen students from the University of Illinois at Urbana-Champaign received course credit in a Psychology class for participation and signed informed consent.

*Materials and Design*

Subjects were seated 57 cm away from a 21 inch CRT monitor set to 85 Hz in a dimly lit

room. Figure 4.1 shows the stimulus dimensions and task sequence. All stimuli were presented at fixation. The target consisted of a $1^o$ disk. The mask annulus was $2^o$, with a $1^o$ center cut out, and was also used as the entraining stimulus. All stimulus presentations were multiples of the 11.7 CRT monitor refresh cycle, thus representing single or double pulsed presentations.

After a 247 ms fixation cross and a 400 ms blank screen, a variable number of masks were presented as entrainers (0, 2, 4, or 8). Entrainers were presented at 12.1 Hz for 23.6 ms each (two monitor refreshes), yielding an entrainer-stimulus onset asynchrony of 82 ms (eSOA). We varied five different SOAs between the final entrainer and the target onset (tSOA): a tSOA of 82 ms (when the target appeared in phase with the entraining sequence); as well as out-of-phase tSOAs ahead of (32 ms and 59 m), and after (107 and 130 ms) the expected time. After the tSOA, the target (presented for 11.7-ms; one monitor refresh) was followed by a metacontrast mask annulus (presented for 23.6-ms; two monitor refreshes) with a constant 45-ms target-mask SOA (mSOA). The subject then had 1500 ms to respond before the next trial began, with a fixation cross reappearing 300 ms after the appearance of the final mask. On 20% of trials, the target was omitted in order to assess false alarms.

A control condition was included with only two pre-target annulus stimuli separated by a 574 ms interval in order to simultaneously control for the forward masking effects of the entrainers (Breitmeyer, 1984), the foreperiod length of the 8-entrainer condition (Drazin, 1961; Bausenhart, Rolke & Ulrich, 2008), and the overall number of stimuli in the 2-entrainer condition.

*Procedure*

Subjects were instructed to indicate on each trial whether or not they detected the presence of the target, which they were told was absent on some trials. They did not receive

feedback on their detection performance. After completing a practice block, subjects completed

12 blocks of trials with self-paced rest periods in between each block. Each block consisted of 75

trials, randomly intermixing 15 of each entrainment condition (0, 2, 4, 8, or control). The tSOA

(32, 59, 82, 107, or 130 ms) was also randomly varied throughout each block.

**Results**

The average detection rate in the no-entrainers condition ($M = 0.41$) indicated

considerable metacontrast masking. It should be noted, however, that this condition is not

directly comparable to the remaining conditions because it lacks a forward masking stimulus:

that is to say, in all entraining conditions (as well as in the control condition), the last entraining

annulus in the sequence served as a forward masking stimulus to the target, further reducing

target visibility.

Figure 4.2 plots the average detection rate for each entrainment condition and the control

condition as a function of tSOA between the final entrainer (or control stimulus) and the target.

Target detection in the control condition was lower ($M = 0.22$) than in the no-entrainer condition,

confirming the forward masking effects of the last "entrainer".

Both linear and quadratic trends as a function of tSOA were computed with orthogonal

linear contrasts weights, separately for each entrainment condition. There was a small and

positive linear trend in the control condition, with detection performance increasing slightly with

increasing tSOA ($t(15) = 3.0, p < .01$). This result suggests the possibility of decreased forward

masking at longer tSOA intervals, or warning effects arising at the longer tSOAs. That said, there

were no significant linear trends observed in the 2-, 4- and 8-entrainers conditions (all $t < 2$).

Moreover, the difference in linear trends between the control condition and the entrainment

conditions was confirmed by a fixed-effects ANOVA ($F(4,60) = 3.75$, $p <.01$).

Crucially, the presentation of entraining stimuli prior to the onset of the target, elicited a peak in detection at the moment the next entrainer would have occurred (82 ms tSOA), as well as poorer detection for targets before or after this point in time. The quadratic trend across tSOAs varied with entrainment condition ($F(4,60) = 16.02$, $p <.0001$). Further, the slope of these quadratic effects across entrainment conditions was greater than zero (0-Control-2-4-8; $M_b = .22$, $t(15) = 6.53$, $p < .0001$) indicating a scaling of the effect with the number of entrainers. Planned comparisons showed that the quadratic effects for *Two* ($t(15) = 3.5$, $p <.01$), *Four* ($t(15) = 4.9$, $p <.001$), and *Eight* ($t(15) = 5.5$, $p < .0001$) entrainers were reliable, whereas the quadratic components for no and control entrainment were not different from zero ($t < 1$). The quadratic nature of this release from masking confirms our prediction of a temporally precise effect of sensory entrainment.

Because detection rates are known to be susceptible to differences in decision biases, we also computed d-prime (d') for each subject, as a measure of sensitivity (Figure 4.3). However, because of the low occurrence of false alarms, we collapsed observations across the 2-, 4-, and 8-entrainer conditions to obtain valid estimates of d'. As expected, d' in the entrainment conditions showed a significant quadratic trend in visual sensitivity as a function of tSOA ($t(15) = 4.3$, $p <.001$), with the best sensitivity arising in phase with the preceding entrainers. In contrast, the quadratic component in the control condition was not significant ($t(15) = .64$, *n.s.*).

Finally, planned comparisons revealed that visual sensitivity at the tSOA in phase condition (82 ms) was significantly greater following entrainment ($M = 1.34$) than following the control condition ($M = .86$; $t(15) = 3.5$, $p <.01$). In contrast, visual sensitivity at counter-phase time points did not differ between the entrainment and control conditions (for tSOA=35 ms: $M =$

.50 vs. $M$ = .18; $t(15)$ = 1.9, *n.s.*; for tSOA=130 ms: $M$ = .52 vs. $M$ = .87; $t(15)$ = 1.7, *n.s.*),

indicating that the entrainment manipulation specifically caused an increase in sensitivity at the

predicted point in time (when target appeared in phase with the entrainment sequence) rather

than a decrease for targets appearing out-of-phase with the preceding entrainment. It should be

further emphasized that the 8-entrainer condition resulted in a substantial (55%) increase in

visual sensitivity and a 100% increase in the average detection rate compared to the control

condition.


**Discussion**

Here we showed for the first time that a momentary release from the effects of visual

masking can be elicited by rapid presentation of visual stimuli, causing a temporally-precise peak

in visual sensitivity. When targets were presented in phase with preceding entrainers, target

detection and sensitivity were substantially improved. In contrast, targets presented out-of-phase

with the previous entrainment were less likely to reach awareness, although they were no less

detectable than targets in the control condition (with no entrainment).

The current findings indicate that rhythmic stimuli in the environment can influence the

visual system, increasing the sensitivity to events occurring in phase with other ongoing sensory

events. One possibility is that the time at which future events are likely to occur is being

*predicted* from preceding rhythmic environmental events, so as to enhance neural processing at

that precise moment. In this respect the current results fit well with emerging evidence regarding

the inherently predictive nature of brain processing (Enns & Lleras, 2008).

One might argue that the observed momentary release from masking merely represented

a phasic shift in sensitivity occurring after any pre-target stimulus, which scaled monotonically

with the number of stimuli presented. Our control condition calls into question this alternative explanation; both it and the 2-entrainer condition had an identical number of pre-target stimuli, yet the momentary spike in sensitivity at 82 ms only occurred after the rapid entrainment, when the next entrainer would have occurred. Such an account could be rescued, however, if the phasic shift in sensitivity induced by a preceding stimulus decays with time and can be summed across stimuli. Under such conditions the 2-entrainer condition would produce a higher peak in sensitivity than the control condition because the two entrainers follow each other more closely in time than the two control stimuli. Work is currently underway to distinguish between these two possible explanations for this effect.

The use of the mask as the entraining stimulus raises the possibility that the momentary increase in visual sensitivity was an effect of changes in mask processing due to the prior presentation of identical stimuli, rather than changes in target processing. The quadratic nature of the induced oscillation calls into question any coarse adaptation account (i.e., more masks make later masks weaker). Further, such accounts would predict a different relation between masking strength and tSOA: if entrainment caused increased inhibition of mask processing at in-phase intervals after the last entrainment, then one ought to have observed the weakest masking at the tSOAs of 32 ms and 130 ms, when the mask appeared in-phase with the entrainers (entrainer-to-mask SOAs of 77 ms and 175 ms, respectively). In fact, sensitivity was worst at these tSOAs, strongly suggesting that our results do not arise from suppressed mask processing, but rather enhanced target processing.

It has recently been shown that the variability in conscious awareness may be a function of the phase of natural rhythmic Alpha oscillations in the brain (Mathewson et al., 2009; Busch et al., 2009), supporting the theory that neural oscillations represent cycles of excitability in

particular cortical areas (Lindsley, 1952). When presented in the trough of the oscillation, targets were less likely to be detected compared to targets presented at the peak. Both sets of results suggest that awareness of the target is strongly dependent on how ready the visual system is at any given point in time to process the incoming target. One possibility is that the induced activity elicited by the entraining stimuli measured with EEG (Lakatos et al., 2008; Williams et al., 2004; Pastor et al., 2002; 2003; Herrmann, 2001) and the endogenous oscillatory activity (Mathewson et al., 2009; Busch et al., 2009) reflect similar oscillations in cortical excitability, representing analogous mechanisms. Further supporting this claim is a recent study showing that inducing gamma activity by 50 Hz flicker has the same attentional enhancement effect as increases in naturally occurring gamma activity (Bauer et al., 2009).

Other recent work suggests that entrainment of neural oscillations may play a part in speech perception (Schroeder et al., 2008; Schmidt-Kassow & Kotz, 2008), and attentional selection (Lakatos et al., 2008; Large & Jones, 1999). Entrained excitability cycles can begin to explain many seemingly unrelated phenomena, complementing research on the effect of ongoing oscillations on cognition (Ward, 2003). For instance, in a number of RSVP paradigms, distracters and targets are presented serially at 10 Hz (see for instance the large literature on the Attentional Blink; Raymond, Shapiro & Arnell, 1992; Olivers, 2007), and as documented by Ariga & Yokosawa (2008), target identification rates increase as a function of the number of preceding distracters (see also Ambinder & Lleras, 2009). It may very well be that the degree of synchronization to the RSVP stream is related to the magnitude of the Attentional Blink (AB), or to the likelihood of observing a release from the AB (e.g., Arend, Johnston & Shapiro, 2006; Olivers & Van der Burg, 2008). This conjecture is consistent with results from an MEG study showing evidence of cortical synchronization to RSVP stimulation (Gross et al., 2004).

*Conclusion*

Our results show that in the presence of rapid, periodic visual events, visual processing appears exogenously synchronized to the frequency of visual stimulation to produce phase-locked peaks of sensitivity. This entrainment may represent a mechanism by which temporal attention is tuned to produce temporally-precise peaks in visual sensitivity, to both anticipate and optimize visual processing of brief visual events. The phase effects here mirror those related to endogenously generated brain rhythms, raising the possibility that the two phenomena rely on similar underlying mechanisms. Rhythmic visual entrainment has a dramatic effect on visual sensitivity, providing us with a powerful technique to experimentally control with fine temporal precision whether or not near-threshold stimuli reach conscious awareness.
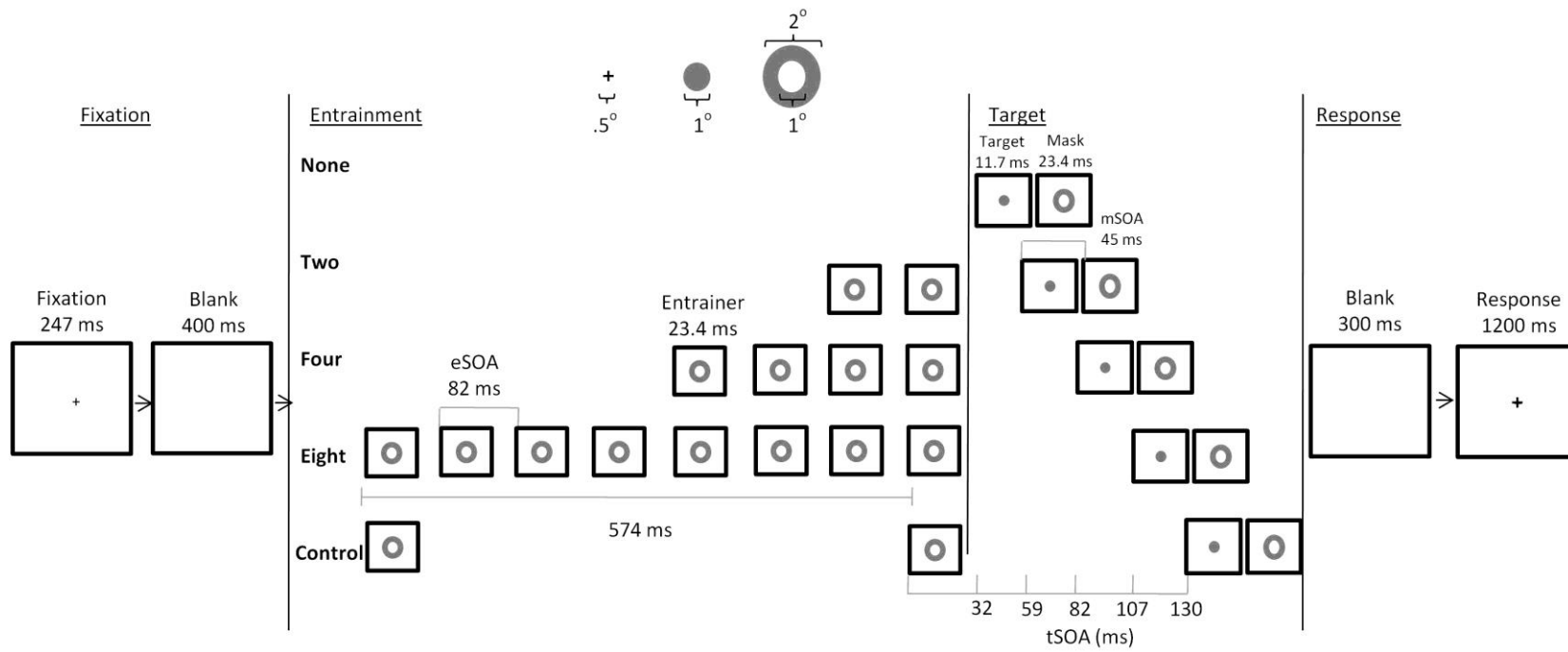
**Figures**



Figure 4.1. Stimulus dimensions and trial timeline.
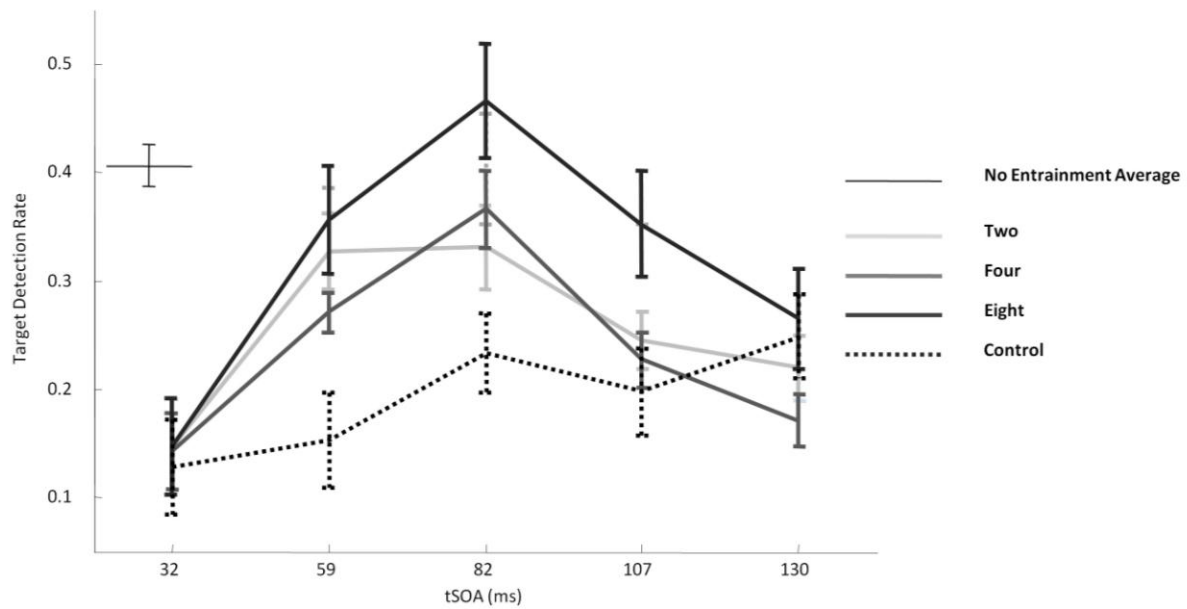
Figure 4.2. Mean target detection rate as a function of the time after final entrainer onset (tSOA) for each entrainment condition across subjects. Apparent is a peak in detection in phase with the preceding entrainment. Error bars represent within-subject SE (Loftus & Mason, 1994).
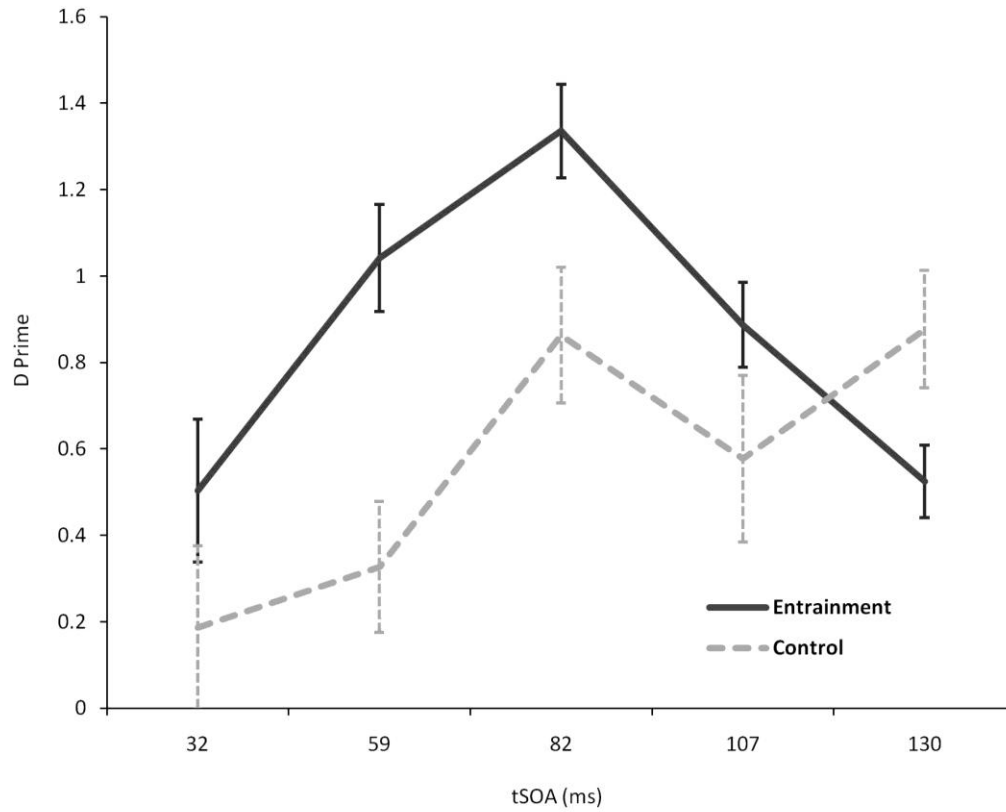
Figure 4.3. Mean d' collapsed across entrainment condition compared to the control condition. Error bars represent within-subject SE (Loftus and Mason, 1994).

## CHAPTER 5

## MAKING WAVES IN THE STREAM OF CONSCIOUSNESS: ENTRAINING OSCILLATIONS IN EEG ALPHA AND FLUCTUATIONS IN VISUAL AWARENESS WITH RHYTHMIC VISUAL STIMULATION[5]

**Introduction**

Rhythmic stimulation is present throughout the natural and modern world. Similarly, our brain's networks are dominated by rhythmic activity (Adrian and Matthews, 1934), measured as local field potential (LFP) or the electroencephalogram (EEG). It has long been theorized that these periodicities represent oscillations in neuronal excitability (e.g., Lindsley, 1952). In keeping with this theory, recent evidence has shown optimal processing at preferential *phases* of ongoing oscillations, with suppression at opposite phases.

Neurons preferentially fire during specific phases of the LFP (Jacobs et al., 2007; Lőrincz et al., 2009). Evoked responses and fMRI activation to identical visual stimulation vary as a function of the phase of ongoing oscillations (Jansen & Brandt, 1991; Barry et al., 2004; Lakatos et al., 2008; Mathewson et al., 2009; Scheeringa et al., 2011). Furthermore, reaction times (RTs; Callaway & Yeager, 1960; Stefanics et al., 2010), saccadic latency (Hamm et al., 2010; Drews & VanRullen, 2011), simultaneity judgments (Varela et al., 1981), somatosensory detection (Monto et al., 2008), and visual awareness (Mathewson et al., 2009; Busch et al., 2009) have all been shown to vary as a function of the phase of ongoing oscillations in neural activity.

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[5] Mathewson, K.E., Prudhomme, C., Fabiani, M., Beck, D., Lleras, A., & Gratton, G. (In preparation). Making waves in the stream of consciousness: Entraining oscillations in visual awareness and ongoing EEG Alpha with rhythmic visual stimulation.

For this multiple author paper I was involved in the original design of the study, in the collection of data, the analysis of data, and in drafting and editing the manuscript, and creating the figures.

Moreover, the phase of spontaneous oscillations can become entrained to rhythmic environmental stimuli (Adrian & Matthews, 1934; Walter & Walter, 1946). Flicker or steady-state studies show that rhythmic visual stimuli can induce cortical oscillations (Herrmann, 2001; Pastor et al., 2002; 2003). Given that attention enhances this effect (Morgan, Hansen, & Hillyard, 1996; Lakatos et al., 2008), it has been suggested that entrained oscillations in cortical excitability represent a mechanism for temporal attention (Lakatos et al., 2008; Large & Jones, 1999; Coull, 2004; Buhusi & Meck, 2005). In humans and non-human primates, low frequency (1.5-Hz) LFP oscillations can become entrained to external stimulus periodicity in an attended modality. The phase of these entrained oscillations then influences both the evoked response and RTs (Lakatos et al., 2008; Besle et al., 2011). Furthermore, temporal expectancies created by auditory trains shorten RTs to predicted auditory targets and lock the phase of ongoing delta oscillations (Stefanics et al., 2010).

To test the hypothesis that the phase of entrained EEG oscillations could influence visual perception, we presented observers with rhythmic visual stimuli at fixation, followed by masked visual targets appearing at various lags with respect to the stimulation phase. We tested for periodic changes in visual awareness as a function of this phase (Mathewson et al., 2010). We recorded EEG to examine the relationship between induced oscillations in awareness and the oscillations in neural activity that become locked to this rhythmicity.

To preview the results, EEG phase locking to the visual stimulation and separation in 12-Hz phase predicted the magnitude of the differences in detection rate as a function of target timing. Furthermore, these effects depended on (a) the amount of resting Alpha power before the experiment and (b) the power at 12 Hz at the start of each trial, suggesting that ongoing oscillations in cortical activity are being entrained.

**Method and Materials**

*Participants*

Seventeen paid subjects (Age 18-26; 5 males) gave informed consent before participating. Data from four subjects whose detection rate in the Rhythmic condition was < 9% were removed from the dataset, leaving 13 subjects. Electrophysiological data from one of these subjects were contaminated by extensive artifacts, and so all EEG analysis was restricted to data from the remaining 12 subjects.

*Materials*

A metacontrast paradigm was used. Figure 5.1 shows the stimulus dimensions (A) and trial timeline (B). Subjects sat 57 cm from a 17 inch monitor that refreshed every 11.7 ms. The subject's task was to detect the presence of a 11.7 ms circular target (1° diameter) at fixation. The target was always backward-masked by a 23.4 ms annulus (2° diameter; 1° center cutout), with 45.6 ms mask stimulus onset asynchrony (mSOA). Subjects had 1500 ms from the onset of the target to indicate whether or not they had detected the target.

Each trial began with a 247 ms fixation cross followed by a 456 ms blank screen. Then, one of three pre-target sequences was presented at fixation. In the *Rhythmic* condition, eight annuli identical to the mask were presented for 23.4 ms each, one every 82.3 ms (~12 Hz). In the *Variable* condition, the gap between each annulus was varied between 11.7 and 257.4 ms such that the overall duration from first- to last-annulus onset was identical to that in the Rhythmic condition. Ten different randomly chosen Variable sequences were used in this condition. In the *Control* condition, only two annuli were presented with a SOA of 517.4 ms, such that the pre-

target periods of all three conditions had the same overall length. This controlled for the possible forward-masking effects of the final entrainer (Mathewson et al., 2010).

Following the final pre-target annulus entrainer, the target was presented after one of seven lags, sampling various phases with respect to the preceding entrainment. On each trial, this lag (i.e., SOA between the final entrainer and target; tSOA) was randomly chosen from 36, 60, 83, 106, 130, 154, or 177 ms. These S0As were fully counterbalanced with respect to the 3 pre-target conditions, providing 21 stimulus variations. Subject completed 24 blocks consisting of 54 trials each, providing an average of 62 trials for each of the entrainment by lag combinations. On 20% of the trials the target was omitted.

*EEG Recording*

The EEG was recorded at 200 Hz from 20 scalp locations referenced online to the left mastoid, re-referenced offline to the left and right mastoid average. The electrooculogram was recorded from two bipolar electrode pairs, above and below the left eye, and on the outer canthus of each eye. Data were filtered online with a half-amplitude bandpass from .01 to 30 Hz, rejecting common mode noise.


*Preprocessing*

The EEG data were divided into 3500-ms segments locked to the onset of the initial fixation cross, including a 1000-ms baseline period. Trials with voltage fluctuations larger than 750 μV, response times less than 200 ms, or trials with no responses were discarded. Eye-movement artifacts were then corrected with a regression procedure, removing all variance in the EEG channels that could be accounted for by either horizontal or vertical eye movements

(Gratton, Coles, & Donchin, 1983). Trials with voltage deflections greater than 125 μV after eye-movement correction were also removed.

### *EEG Power and Phase*

A wavelet analysis of the segmented data was computed using the *newtimef()* function of the EEGLAB toolbox (Delorme & Makeig, 2004). A complex group of Morlet tapered wavelets were computed with parameters set to obtain an optimal balance of temporal and frequency resolution at all frequencies ($m$ = 3.15; $\sigma_t$ = .20; $\sigma_f$ = 3.13). Tapered wavelets had 3 cycles at the lowest frequency (4.7 Hz) and increasing by a factor of .01 up to 19 cycles at the highest frequency (30 Hz; cutoff of online filter). These parameters provide estimates of power and phase every 0.8 Hz from 4.7 Hz up to 30 Hz, and from -642 ms to 2137 ms around the event of interest.

### *Phase-Locking Index*

We measured the phase-locking index (PLI), or the consistency of the phase at any given frequency and time across trials (i.e., *newtimef()*'s inter-trial coherence), with respect to the onset of the entrainment sequence. In part to minimize multiple comparisons, all analyses were computed at electrode Pz, the site of maximal phase-awareness interactions in Mathewson et al. (2009), as well as the site of maximal phase-locking in the current study (see Figure 5.3B & Figure 5.4B). This is also the site of maximal steady state response in the Alpha range (Johnson, Hamidi, & Postle, 2010).

### *Single Trial 12-Hz Phase*

Additional segments were taken from -1000 to 2500 ms around the onset of each target. These were pre-processed and analyzed using the same wavelet analysis described above. The phase of the 12-Hz activity at 100 ms prior to the onset of the target was recorded for each trial,

given that Mathewson et al. (2009) and Busch et al. (2009) found maximal effects of phase on awareness at -100 ms. For each subject, the average phase was then computed separately for targets presented in- and out-of-phase with the preceding rhythmic stimulation. The difference between these average phases was then computed, and tested against a zero-phase difference using a Hotelling's Bivariate $F$-test on the sine and cosine components.

### Pre-trial Alpha Power

To understand the relationship between induced oscillations in neural activity and subjects' spontaneous Alpha oscillations, we re-sorted the trials based on the amount of 12-Hz power at the start of each trial. For each subject, the average power between 10 and 14 Hz in the 200 ms before each trial was computed. The detection performance across conditions was then calculated separately for trials in the top and bottom quartiles of Alpha power.

### Resting Alpha Power

Before and after the set of 24 blocks, one minute of spontaneous EEG was recorded from subjects while their eyes were closed. We predicted that if we are entraining ongoing Alpha oscillations, the entrainment effects on EEG and awareness should be dependent on the level of spontaneous Alpha power. To understand the relationship between induced oscillations in neural activity and subjects' spontaneous Alpha oscillations, we took 30 consecutive 2000 ms segments of data from the eyes-closed EEG recordings of 10 subjects for whom we had available data from the period immediately preceding the experimental task[6]. We submitted these 2000 ms segments to a stationary fast Fourier transform, averaged the log-transformed spectra across each subject's segments, and measured the peak power within a broad Alpha range (7-15 Hz).

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[6] Although one-minute of eyes-closed EEG recording is not ideal to measure spontaneous Alpha power due to long term fluctuations in power (e.g. Linkenkaer-Hansen et al., 2001), we found strong reliability between our estimates of Alpha power when comparing the EEG recorded before and after the experimental blocks for the 9 subjects for which we had post-session estimates ($r = .90$; $p < .001$).

**Results**

*Entrainment of Visual Awareness*

Figure 5.2A plots the detection rates for all three pre-target conditions as a function of the lag between the last entrainer and target presentation (tSOA). A repeated-measure ANOVA with a Greenhouse-Geisser correction for lack-of-sphericity revealed significant main effects of pre-target entrainment type ($F(1.12,13.40) = 7.87, p < .05, \varepsilon = .56$) and of target lag after final entrainer ($F(2.56,30.76) = 15.94; p < .00001, \varepsilon = .43$), as well as an interaction such that the effect of lag differed as a function of the type of entrainment ($F(2.93, 35.16) = 7.88, p < .001, \varepsilon = .24$).

Figure 5.2A shows increased detection for targets in-phase (83 and 177 ms) compared to out-of-phase targets (36 and 130 ms) with the preceding entrainment for both the Rhythmic and Variable conditions. Overall, there was a significant difference in detection rate for in-phase ($M = .45$) compared to out-of-phase targets ($M = .17; t(12) = 5.71, p < .0001$ ). This measure will be used as an indicator of the magnitude of the behavioral effect for each subject. At 83 ms (in-phase with the rhythmic entrainment), detection was higher in the Rhythmic ($M = .50$) than in the Variable ($M = .40; t(12) = 4.11, p < .01$) and Control conditions ($M = .16; t(12) = 5.50, p < .001$). Detection was also higher in the Variable than in the Control condition ($M = .40$ vs. $M = .16; t(12) = 5.01, p < .001$). Detection rate at 177 ms (in-phase with the rhythmic entrainment) was again higher for both the Rhythmic ($M = .39$; one tailed $t(12) = 2.20, p < .05$) and the Variable conditions ($M = .40$; one tailed $t(12) = 2.58, p < .05$) than the Control condition ($M = .27$), but there was no difference between the Rhythmic and Variable conditions ($t(12) = .15$, *n.s.*). The presence of a second detection peak at 177 ms suggests that the effects of the

Rhythmic and Variable conditions are not just isolated peaks at 83 ms, but the result of a periodic increase in detection in phase with the entrainment.

To determine whether the effect of entrainment condition on target detection was a change in sensitivity and not just a change in threshold, we computed d' for each tSOA and pre-target condition. Six of the subjects had few or no false alarms, making it impossible to determine d' on an individual subject basis. The d' computed from the grand average hit and false alarm rate for each pre-target and tSOA combination is plotted in Figure 5.2B. The overall shapes of the curves for d' and detection rate are similar, indicating that the detection effect is an oscillation in sensitivity, not in response bias.

It is evident from Figure 5.2A and 5.2B that we have induced fluctuations in visual awareness as a function of the phase with respect to the entrainers. To evaluate the significance of these oscillations, we fit linear and cubic functions across the target lags for each subject. Specifically, for each pre-target condition, there were 7 different lags following the final annulus entrainer. Linear trends across the 7 lags were modeled with the weights: -3, -2, -1, 0, 1, 2, and 3. The cubic trends were modeled with the weights: -2, 0, 2, 0, -2, 0 and 2. We normalized the detection rate across all lags and pre-target conditions for each subject, and then multiplied these normalized scores by their respective linear or cubic weights. This way, the more these normalized scores tended towards the trends represented by the weights, the greater the resultant product would be. In both the Rhythmic ($t(12) = 5.86$, $p < .0001$) and Variable conditions ($t(12) = 3.53$, $p < .01$) a better fit was found when subjects' detection was fit to a cubic rather than a linear function, but not for the Control condition ($t(12) = 1.60$; n.s.), indicating that detection oscillates as a function of the timing of the target onset for the Rhythmic and Variable conditions.

*Phase Locking*

In order to test if we were consistently entraining the phase of 12 Hz oscillations, we examined the PLI with respect to the onset of the entrainment sequence. Entrained oscillation would be evident as consistent phase across trials specifically at the presentation frequency. Figure 5.3A shows the PLI over frequency and time for each of the three pre-target conditions. Evident is a broadband increase in PLI following the onset of the fixation as well as the onset of the entrainment sequence. This reflects the visual evoked potentials elicited by these stimuli, which have consistent latencies over trials. Notably, this large evoked activity to the first annulus quickly diminishes for the subsequent repetitive annuli. Also evident in the Control condition is a third broadband increase in PLI following the onset of the second and final annulus (~1400 ms). This increased evoked activity is due to the more distinct stimulus onset in this pre-target condition, given the long inter-annulus gap in this condition (e.g., see scalp maps in Figure 5.3C & 5.3D, far right for the posterior scalp distribution of this broad frequency evoked activity). Unfortunately, this broadband effect overlaps with the period of interest around target onset, so the Control condition does not serve as a good comparison in this respect.

Importantly, in the Rhythmic condition only, an additional narrow frequency increase in PLI centered at 12 Hz (the entrainment frequency) develops during and extends after the entrainment period. This phase-locking extends 200-300 ms after the entrainment stimuli end, indicating that this does not merely reflecting the visual-evoked potential elicited by the annuli. Thus, all further analyses of the PLI were performed on a time-frequency region of interest (ROI) window comprising the 200 ms *following* the entrainment sequence between 10-14 Hz. The amount of 12-Hz phase locking after the pre-target period was correlated with the average detection rate for the Rhythmic condition ($r = .55$; directional $p < .05$). In the Variable condition

this correlation was slightly reduced ($r = .44$; directional $p = .07$). However, in the Control condition, the correlation between Alpha PLI and detection was negligible ($r = -.10$, *n.s.*), even though there was a high level of phase locking due to the visual evoked activity from the final pre-target annulus. The differences in timing, topography, frequency extent, and behavioral correlation between the evoked activity and the sustained entrained 12-Hz activity indicate PLI increases in the Rhythmic and Control conditions are separable phenomena.

Figure 5.3B shows the *difference* in PLI between the Rhythmic and Variable conditions, indicating that the increase in PLI occurs only at the 12-Hz entrainment frequency and only following the rhythmic entrainment stimuli. The average PLI for each subject between 10 and 14 Hz in the 200 ms interval following the final entrainer onset (late ROI; black) was greater in the Rhythmic condition ($M = .11$) than the Variable condition ($M = .07$; $t(10) = 2.94$, $p < .05$). The average PLI activity in an additional window during the last 300 ms of the entrainment sequence (Early ROI) also showed significant differences between the Rhythmic and Variable conditions($t(11) = 4.30$, p <.005). Figure 5.3B (bottom) also includes maps of the scalp distribution of the average difference in PLI in the two measurement windows (last 300 ms of entrainment sequence and first 200 ms following the end of entrainment). The difference was maximal over parietal and occipital visual areas both before and after the final entrainer. Interestingly, the correlation between the difference in PLI and the difference in detection between the two conditions did not reach significance ($r = .25$, *n.s.*). A test of the difference in evoked Alpha power within this same window between the two conditions found no difference ($t(11) = .41$, *n.s*), suggesting that ongoing oscillations in 12-Hz activity are being entrained not induced in the brain.

Figure 5.3C shows the difference in PLI between the Rhythmic and Control conditions, indicating the same increase in phase locking during the early ROI ($t(11) = 4.45$, $p <.005$). In the late ROI this effect is overshadowed by the evoked activity in the Control condition, as can be seen from the scalp topography. The topographic extent of this evoked activity is clearly distinct from that of the entrained 12-Hz activity suggesting they are separable phenomena. Finally, Figure 5.3D shows the difference in PLI between the Variable and Control conditions. Here no difference was found in PLI in the last 300 ms of the entrainment sequence (Early ROI: $t(11) = 1.25$, *n.s.*), and again any later difference was obscured by the broadband PLI in the Control condition, due to the evoked ERP components. Given this overlapping phase-locking effect that appears as high phase consistency in a broad frequency band including 12 Hz, all further analysis of single trial phase were constrained to the Rhythmic and Variable conditions.

These data suggest that the 12-Hz phase locking can be differentiated from the overlapping evoked activity elicited by the repetitive stimulus onset, on the basis of a number of criteria, including scalp distribution, time course, and frequency band. Specifically, the evoked activity is only large in response to the first entrainer, and is not sustained throughout the whole entrainment interval. Furthermore, this broad-frequency evoked activity has a different spatial distribution than the 12-Hz specific sustained activity. Lastly, the temporal extent of this 12-Hz phase locking outlasts the entrainment sequence considerably as well.

To corroborate this distinction between sustained entrained activity and rhythmic evoked activity, the Rhythmic condition PLI data for which the subject average at electrode Pz is depicted in Figure 5.3A were decomposed using Parallel Factor Analysis (PARAFAC; Harshman, 1970)[7]. We used the four-mode PARAFAC model to analyze the 12 subjects × 65

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[7] PARAFAC is a straightforward extension of Principal Component Analysis (PCA): PCA maximally explains variation in a two-mode data matrix via a summation of rank-1 second-order tensors, whereas PARAFAC

frequencies × 200 time points × 20 electrodes data array comprising the PLI. The model was fit using the alternating-least-squares algorithm with ten random starts. The frequency loadings were constrained to be nonnegative to facilitate the interpretation of the factors. Also, to ensure that factors were non-redundant over time and across electrodes, the temporal and spatial loadings were constrained to be orthogonal. Different numbers of factors were extracted to find the most interpretable solution.

A four-factor solution explains the majority of the data's variation ($R^2$=.773) and clearly distinguishes the sustained entrained activity from the rhythmic evoked activity. Nearly all of the explained variation relates to the first factor ($R^2$=.760), which captures the overall (i.e., across all frequencies and electrodes) evoked activity due to the fixation and the entrainment (Figure 5.4A,B). Although this factor explains the majority of the data's variation, it is of little substantive interest and can be considered noise in the signal due to the evoked activity. Likewise, the second ($R^2$=.010) and third ($R^2$=.002) factors are also of little substantive interest, given that they capture finer aspects of the onset of the entrainment and fixation evoked potentials, respectively (Figure 5.4A,B). However, the fourth factor ($R^2$=.001) clearly captures the 12-Hz activity that was sustained after the entrainment sequence offset. Unlike the first three factors, this fourth factor loads exclusively around 12 Hz, is active mainly towards and after the end of the entrainment sequence, and is influential mostly over parietal areas (Figure 5.4A,B). In addition, the subject loadings on this fourth factor correlate with the ROI phase-locking measure ($r$=.81; Figure 5.4C) and with differences in detection rates for in-phase versus out-of-phase targets ($r$=.53; Figure 5.4D). Thus, this PARAFAC solution offers evidence that (a) 12-Hz

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maximally explains variation in an $n$-mode data array via a summation of rank-1 $n$th-order tensors. However, unlike PCA, PARAFAC benefits from the *intrinsic axis property*, which means that PARAFAC solutions do not suffer from rotational indeterminacy (see Harshman & Lundy, 1994, for a comprehensive introduction to PARAFAC, and Miwakeichi et al., 2004 and Mørup et al., 2006, for applications of PARAFAC to EEG data).

sustained phase-locked activity is distinct from both the broadband and the discrete evoked activity elicited by the stimuli, and (b) this distinct 12-Hz phase locking relates to differences in detection performance.

*Sequence Variability*

The Variable pre-target condition induced a similar yet diminished oscillation in visual awareness compared to the Rhythmic condition. The temporal attention model of Large and Jones (1999) predicts that the entrainment phenomenon should be robust to noise in the temporal sequence. Given that the overall length of the Variable sequences was equal to that of the Rhythmic condition, with the same number of annuli, the average entrainer SOA (eSOA) was equivalent in the two conditions. Thus, some vestige of entrainment likely occurred in the Variable condition. If this is the case, we should expect that this vestigial entrainment should scale with the degree of irregularity. To assess the degree to which the Variable sequences deviated from the Rhythmic sequence, we measured the variability of the annulus eSOAs at the start of each sequence. We predicted that the greater the absolute difference between the first two eSOAs in the sequence (i.e., the more irregular the start of the sequence), the smaller the average detection rate should be in the 83 ms lag condition.

Figure 5.5A shows target detection rate as a function of lag after the final entrainer (tSOA) for the Variable sequences with high- and low-variability (respectively, less and more similar to the Rhythmic sequence, where the difference in eSOA is zero). Detection rates for the Rhythmic condition are also included for comparison. For low-variability sequences (i.e., more similar to the Rhythmic sequences), the data show a peak in detection equal to that on Rhythmic trials ($t(12) = .13$, *n.s.*). Importantly, the high-variability sequences had lower detection than both the low-variability, ($t(12) = 3.11$, $p < .01$) and Rhythmic sequences ($t(12) = 2.92$, $p < .05$). Thus,

the more similar the early part of the sequence was to the Rhythmic entrainment, the greater the peak in detection in-phase with the timing of entrainment.

Figure 5.3D revealed no apparent phase locking difference between the Variable and Control conditions. Could the high-variability sequences introduce sufficient noise in the PLI index to mask some level of EEG entrainment that may occur for the low-variability condition, leading to no apparent phase locking in Figure 5.3 Figure 5.5B shows the difference in PLI with respect to the start of the sequence between the low- and the high-variability sequences. As predicted, there was greater phase-locking in the 200 ms following the Variable sequence for the low-variability than high-variability sequences. In the 10-14 Hz frequency band the difference was significant ($t(11) = 2.31$; $p < .05$) and strongly predicted, across subjects, the increase in detection at 83 ms for low- as compared to high-variability sequences ($r = .72$; $t(11) = 3.28$; $p < .01$). The maximal extent of this difference was also over occipito-parietal brain areas. However, the peak PLI in this subtraction was 17 Hz, indicating phase locking at a higher frequency than Alpha. An additional analysis using an ROI between 15 and 20 Hz found that this increase was also significant ($t(11) = 3.01$; $p < .05$). This may correspond to the indication in Figure 5.5A that the peak detection rate in the Variable conditions occurred at lags shorter than 83 ms. Indeed, there was a lower average eSOA for the last three annuli of low-variability sequences (73 ms) compared to the high-variability ones (79 ms). Curiously, the correlation between the difference in PLI in this ROI and the increase in detection rate at 83 ms was negligible ($r = .02$; $n.s.$). Together these results reveal that the effects of entrainment on detection and phase locking scale with the regularity of the rhythmic sequence, and are relatively robust to sequence noise.

### Single-trial 12-Hz Phase

If the induced oscillations in awareness are due to entrainment of the phase of ongoing EEG oscillations, there should be different EEG phases for targets in- and out-of-phase with entrainment, which had very different perceptual fates. Figure 5.6A shows circular histograms of the single trial phase of 12-Hz EEG oscillations at electrode Pz with respect to target onset, pooled over all trials and subjects. We compared the average 12-Hz phase between in-phase (tSOA of 83 and 177 ms; Circular Grand Mean (CGM) = 76.2°) and out-of-phase targets (tSOA of 36 and 130 ms; CGM = 246.9°). These phases differed significantly (Mean Difference = 135°; Hotelling's $F(2,11) = 20.3$, $p < .005$ ), indicating a difference in Alpha phase as a function of target timing (Figure 5.6B).

Figure 5.6B shows histograms over all subjects and trials for targets appearing at the four lags after the last entrainer onset, two in-phase, and two out-of-phase with entrainment. Both the distributions of the phase and the grand average phase across all subjects (arrows) mirror the overall difference between in- and out-of-phase targets shown in Figure 5.6A. In order to minimize the influence of the early potentials evoked by the entrainers, we focused on the 130 and 177 ms tSOAs only. Importantly, the difference in average phase between the 130 and 177 tSOA (out- and in-phase, respectively) was predictive of the difference in detection for these same targets (Circular-Linear Correlation; $r = .72$; $\chi^2(2) = 6.18$ , $p < .05$; see Figure 5.6C)[8]. This correlation was restricted to the targets most distant from the entrainers (130 and 177 ms) to minimize the influence of the early components of their evoked potential on the results, and to maximize the influence of the sustained entrained activity.

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[8] The circular linear correlation was performed on the sine and cosine components of the difference in phase based on techniques described by Zar (1999). Since two subjects had negative differences in detection, we used their absolute detection difference to visualize the correlation.

Figure 5.6D shows these same effects in the Variable condition. Here we still consider

the same in- and out-of-phase targets, given that the average eSOA between the entrainers is still

83 ms. Targets in-phase with the stimulation (CGM = 121.3°) again had a significantly different

average 12-Hz phase than those out-of-phase with the entrainment (CGM = 241.2°; Mean

Difference = 140°; Hotelling's $F(2,11) = 17.1$, $p < .005$ ). Also shown are histograms of the 12-

Hz phase for targets at four different lags, again indicating differences in phase as a function of

the target timing with respect to the preceding stimulation. In this case, the correlation between

the difference in 12-Hz phase and the difference in detection between 130 and 177ms did not

reach significance (Circular-Linear Correlation $r = .25$; $\chi^2(2) = 1.5$ , $n.s.$), in agreement with the

weaker effects of phase seen here than in the Rhythmic condition. In order to test for a difference

in correlation between the two conditions, we utilized a jackknife procedure, holding out one

subject at a time and computing the two correlations on the remaining subjects. In all cases the

correlation was larger in the Rhythmic than the Variable condition, and there was a marginal

difference in the Fisher-transformed correlations between the two conditions ($t(11) = 1.37$; $p =$

.09). While this is evidence that the correlation was indeed stronger in the Rhythmic conditions,

we should note that we expect some correlation between phase separation and detection

difference in the Variable condition, since the influence of stimulus timing on detection is still

present albeit to a lesser extent.

### *12-Hz Phase Predicts Detection*

We have observed differences in both detection and 12-Hz phase as a function of the

target onset with respect to preceding visual stimulation. We are proposing that this visual

stimulation entrains the 12-Hz phase, leading to the fluctuations in awareness. To make this link,

we next tested if the phase of 12-hz EEG activity on each trial could predict detection

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(Mathewson et al., 2009). For homogeneity of stimulus conditions and to achieve adequate numbers of trials per condition, we considered only targets appearing at the 130, 154, or 177 ms lags. We computed the average phase separately for detected and undetected targets averaged over all lags. Figure 5.7A shows histograms of the 12-Hz phase pooled over all subjects and trials, separately for detected and undetected targets, along with the grand average phase (arrows). Both Rhythmic and Variable conditions are shown. Figure 5.7B shows the difference in average 12-Hz phase for each subject (black arrows). A test of these differences in the Rhythmic condition against zero indicated a significant difference in the phase of 12-Hz activity between trials in which the targets were detected (CGM = 55°) and undetected (CGM = 283°; mean difference = 243°; Hotelling's F(2,11) = 13.74, p < .05). In the Variable condition, the 12-Hz phase also differed between detected (CGM = 200°) and undetected targets (CGM = 93°; mean difference 218°; Hotelling's $F(2,11) = 17.42$, $p < .005$) Thus, as in Mathewson et al. (2009) the phase of 12-Hz EEG oscillations predicts variations in detection performance on a trial by trial basis.

### *Alpha Power Predicts Entrainment*

We next tested if subjects' amount of spontaneous Alpha at the start of each trial and prior to the experiment could predict the degree to which their awareness and neural oscillations were entrained. We first sorted our trials based on the average 10 to 14-Hz power in the 200 ms before fixation. We then computed the detection performance separately for trials in the top and bottom quartiles of 10 to 14-Hz power (Figure 5.8). Evident in the Rhythmic condition is a larger peak at 83 ms lag for trials beginning during high Alpha power ($M = .605$) than those with low Alpha power ($M = .529$; directional $t(11) = 1.99$, $p = .07$). Furthermore, there was a larger difference between the Rhythmic and Variable conditions (directional t(11) = 1.87, p = .08) and

between the Rhythmic and Control conditions (directional t(11) = 3.70, p < .005) at the 83ms lag

for high Alpha power. This indicates that the amount of Alpha power prior to the start of the trial

could predict the effectiveness of the visual entrainment at biasing detection performance.

We also sought to understand the relationship between resting levels of Alpha oscillations

and the observed effects. To quantify Alpha activity in the spontaneous EEG spectra collected

prior to the experimental task, we measured the peak log power in a range from 7 to 15 Hz.

Subjects with more resting Alpha power had larger differences in detection between in- and out-

of-phase targets in the Rhythmic ($r = .55$, $p < .05$) and Variable conditions ($r = .53$, directional; $p$

$= .05$). Furthermore, the amount of resting Alpha power predicted the entrainment of neural

oscillations, as measured by either the average PLI after entrainment in the Variable condition ($r$

$= .54$, directional, $p = .05$), the difference in 12-Hz PLI between the high- and low-variability

entrainers ($r = .56$, directional, $p < .05$), or by the difference in 12-Hz phase at the onset of in-

and out-of-phase targets (Circular-linear correlation $r = .62$, $p =.05$). This indicates that the

amount of spontaneous Alpha power can predict the degree to which both subjects' awareness

and their Alpha oscillations are entrained by rhythmic 12-Hz stimulation.


**Discussion**

We identified a clear increase in visual awareness for targets presented in-phase with

preceding 12-Hz visual stimulation. This effect was found to scale with the regularity of the

entrainment sequence, and was not present at all when the pre-target period and forward masking

effects of the preceding stimuli were controlled for but no rhythmicity was present. Furthermore,

an overall increase in phase-locking was observed following the Rhythmic sequence, which was

maximal over parietal and occipital visual areas. The amplitude of this phase-locking predicted

the increase in visual awareness due to entrainment across subjects, and could be separated from the evoked activity due to the entrainers.

The increase in target detection for in-phase targets was also predicted by the separation in the phase of ongoing 12-Hz EEG oscillations at the onset of in- and out-of-phase targets. Detection was particularly likely when targets are presented during one phase of the Alpha EEG oscillations, and conversely low when the stimuli are presented during the opposite phase. Further, background levels of EEG oscillations could predict the size of the effects. Trials with higher 12-Hz power were associated with increased detection for targets in phase with the entrainment. In addition, subjects with more Alpha power before the experiment showed more effectively entrained oscillations in awareness and brain activity, revealing a correspondence between the experimental effects and spontaneous, as opposed to induced, neural oscillations. We show for the first time that the phase of ongoing Alpha oscillations and their effect on visual processing and awareness can be harnessed and controlled.

It may be argued that, due to the use of the annulus as both the entrainer and the mask, the impact of entrainment on target detection may be due to either changes in target processing, or changes in the efficacy of the mask, or both. Indeed, when the targets in our study were best detected, in-phase with the entrainment, their masks consistently followed at 45 ms such that they were always out-of-phase. The observed effects may thus be due at least in part to influences on mask processing in addition to target processing. Further research manipulating the style of entrainer is needed to tease apart these possibly complementary effects.

### *Alpha Oscillations as a Pulsed Inhibition*

Our data extend previous findings of phase-dependent effects of 12-Hz oscillations on visual awareness. When considered in light of the dependency of these effects on the pre-

experiment and pre-trial 12-Hz power, these results provide further evidence for an account of Alpha oscillations as a *pulsed inhibition* of visual processing (Mathewson et al., 2009; Mathewson et al., *under review*). When Alpha is high, its phase can be entrained to influence visual processing and awareness (Mathewson et al., 2009). This may represent a mechanism analogous to the pulsing brake of an automobile, such that pulses of inhibition alternate with periods of relatively intact processing in which information from the environment can be readily detected. Recently, Busch and Van Rullen (2010) have shown evidence that the attentional spotlight in a continuous attention task is oscillatory. In particular, periodic fluctuations in the enhancing effects of attention appear to depend on the phase of ~7 Hz fronto-central neural activity. Importantly, they show that this effect is strongest at previously cued locations. They argue that this dissociation calls into question a central assertion of our pulsed inhibition model, namely that the phase effects should only be observed when there are high levels of Alpha power, since with focused attention Alpha should be low. Here we show that this periodicity in perceptual sampling, and its susceptibility to entrainment are dependent on the amplitude of an individual's spontaneous brain activity at the same frequency, supporting our proposal that the influence of entrained Alpha phase on EEG processing indeed has a relation to Alpha power.

***Entrained Excitability Cycles***

Here we show for the first time that Alpha oscillations can be entrained to analogous rhythmicities in the environment, such that their preferential processing phase can be aligned to relevant and predicted visual events. These data are in accordance with previous behavioral investigations that found increased visual awareness and sensitivity for targets presented in-phase with preceding entrainment (Mathewson et al., 2010) and suggest that Alpha entrainment may underlie those effects. Similar effects on evoked neural responses and RTs have been found

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from intracranial electrodes in monkeys and humans, but at much lower frequencies (1.5 Hz) and dependent on visual attention (Lakatos et al., 2008; Besle et al., 2011). Humans have recently been shown to develop temporal expectancies about auditory sequences that influence the RTs to embedded targets as a function of the phase of the target onset with respect to that of the larger sequence (Stefanics et al., 2010). In the current paper we demonstrated that these entrained excitability cycles can induce oscillations in visual awareness, and are dependent on individual's spontaneous Alpha power, suggesting that ongoing brain oscillations are being entrained. Other recent work has shown that much higher frequency oscillations (40Hz) can be controlled by visual entrainment, leading to phase independent attention increases at the stimulated location, even when observers were unaware of the entrainment (Elliott & Muller, 1998; Bauer et al., 2009). Furthermore, repetitive transcranial magnetic stimulation (rTMS) at Alpha frequencies (10 Hz), has been shown to induce retinotopic decrements in visual awareness, irrespective of phase, by modulating Alpha activity (Romei et al., 2010).

Is anything special about the particular frequency (12 Hz) used in the current study? Whereas some previous work (Elliott and Muller, 1998; Lakatos et al., 2008; Cardin et al., 2009; Bauer et al., 2009) indicate that other frequencies may be entrained, other studies (Mathewson et al., 2009; Mathewson et al., 2010; Busch et al., 2009) as well as the current paper indicate that "spontaneous" EEG oscillations within the Alpha band appear particularly relevant to visual perception and awareness. It is noteworthy that our study does not explicitly manipulate attention conditions, whereas this manipulation was important for those showing effects at other oscillatory frequencies (e.g. Lakatos et al., 2008; Busch & VanRullen, 2010; Stefanics et al., 2010). It is possible that, although cortical oscillatory activity may be generally critical for sustaining or controlling information processing, different brain regions and different

experimental conditions may utilize oscillations occurring at different frequencies. Within this framework, it is conceivable that Alpha band oscillations may be particularly important for modulating early visual processing, and therefore be critical for simple detection tasks, whereas other frequency bands may be important in other areas and for other tasks.

*Temporal Attention*

Could the purpose of these entrainable excitability cycles be to provide a mechanism of temporal attention? A cognitive theory has posited the existence of internal oscillators whose pulses of attentional energy can become entrained to rhythmicities in the environment in order to best process stimuli occurring at predictable times (Large & Jones, 1999; Jones et al., 2002; Mathewson et al., 2010). This proposal is strongly supported by recent neural recordings in monkeys and humans (Lakatos et al., 2008; Stefanics et al., 2010; Besle et al., 2011). Here we find that temporal expectancies create phase-locking in ongoing brain oscillations, allowing for maximal processing of targets occurring at predictable moments in time. The entrainment of internal attention oscillators by rhythmic stimuli may be a mechanism supporting temporal attention in the brain (e.g., Shroeder and Lakatos, 2009), and may explain many common perceptual effects, such as those observed during rapid serial visual presentation (RSVP) sequences in which target detection has been shown to increase as a function of the number of intervening distracters presented around 10-Hz (Ariga & Yokosawa, 2008; Ambinder & Lleras, 2009). A further distinction has been put forward between rhythmic and continuous mode of attention (Shroeder & Lakatos, 2009). Here, attention was likely operating in the rhythmic mode given the regularity of the stimuli. This rhythmic attention system seems to be robust to variability in the temporal sequence (Figure 5.2 & 5.4; Stefanics et al., 2010). The ability to

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harness these internal oscillations in attention has the promise of providing important practical applications, for example in the design of attention-capturing displays (Skelly et al., 2003).

### *Waves in the Stream of Consciousness*

The fluctuations in awareness that we have observed locked to the timing of rhythmic visual stimuli provide support for a proposal that our perceptual awareness of the visual world is not the continuous unfolding stream that it has long been thought of (James, 1890) but instead consists of discrete snapshots (Dehaene, 1993; Van Rullen & Koch, 2003; Busch & Van Rullen, 2010). The data presented here suggest that these snapshots may be due to oscillations in neural excitability in the Alpha band frequency. The pulsed inhibition of ongoing cortical activity represented by Alpha oscillations may create these fluctuations in awareness, making waves in the ongoing conscious stream. Here we provide a powerful technique to control these waves of consciousness, indicating that the brain is able to harness these perceptual snapshots of high excitability and optimal processing and align them with external events, a highly adaptive feature given the rhythmicity of our sensory world.
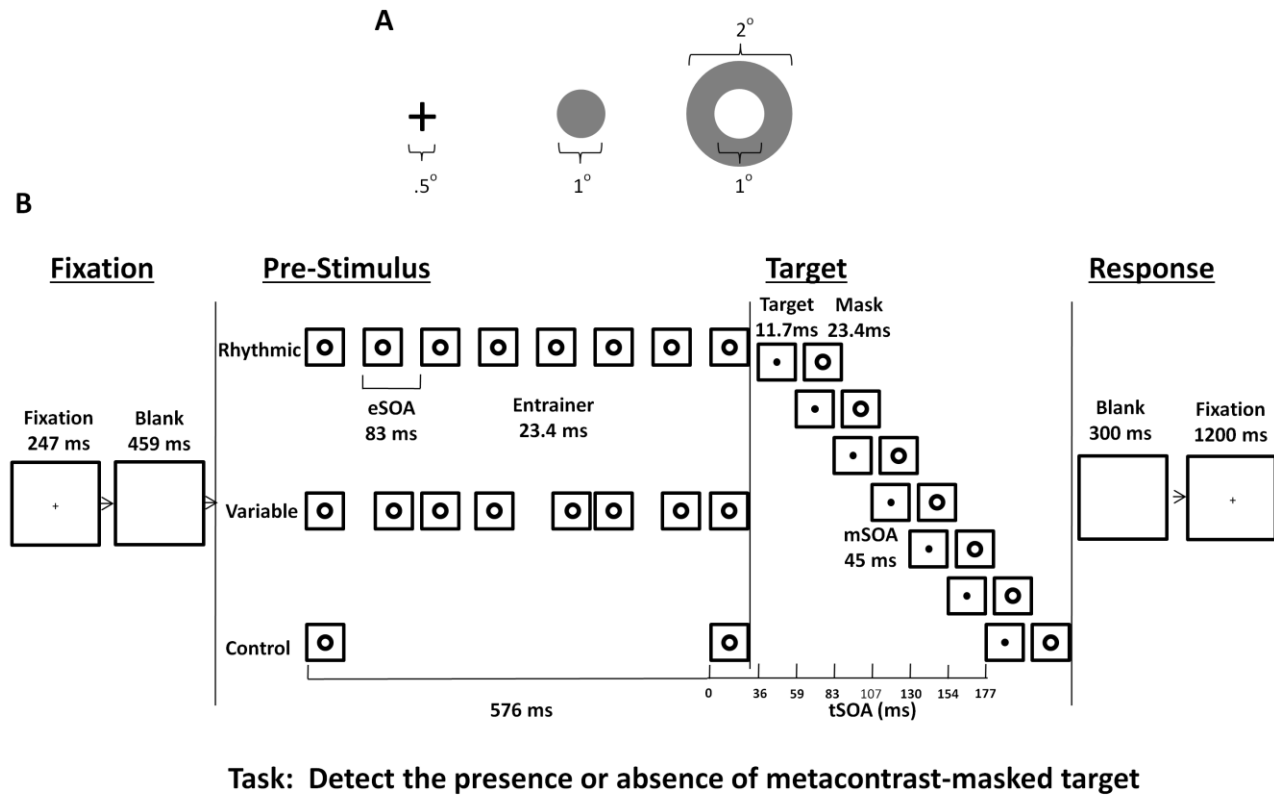
**Figures**



Figure 5.1. (A) Stimulus dimensions and (B) Trial timeline. (SOA - Stimulus onset asynchrony; e - entrainer; t - target; m - mask).
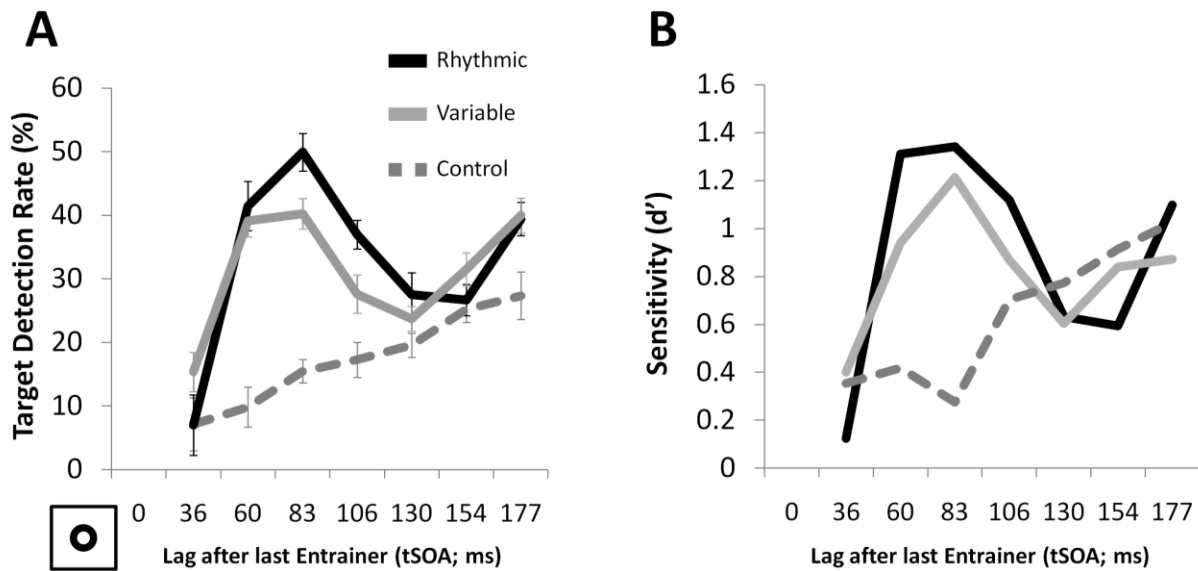
Figure 5.2. (A) Target detection percentage as a function of presentation lag. Error bars represent within-subject standard errors of the mean (SEM; Masson and Loftus, 2003). (B) d' as a function of the target presentation lag after the final annulus entrainer (tSOA), for all three pre-target conditions, computed on the grand average hits and false alarms.
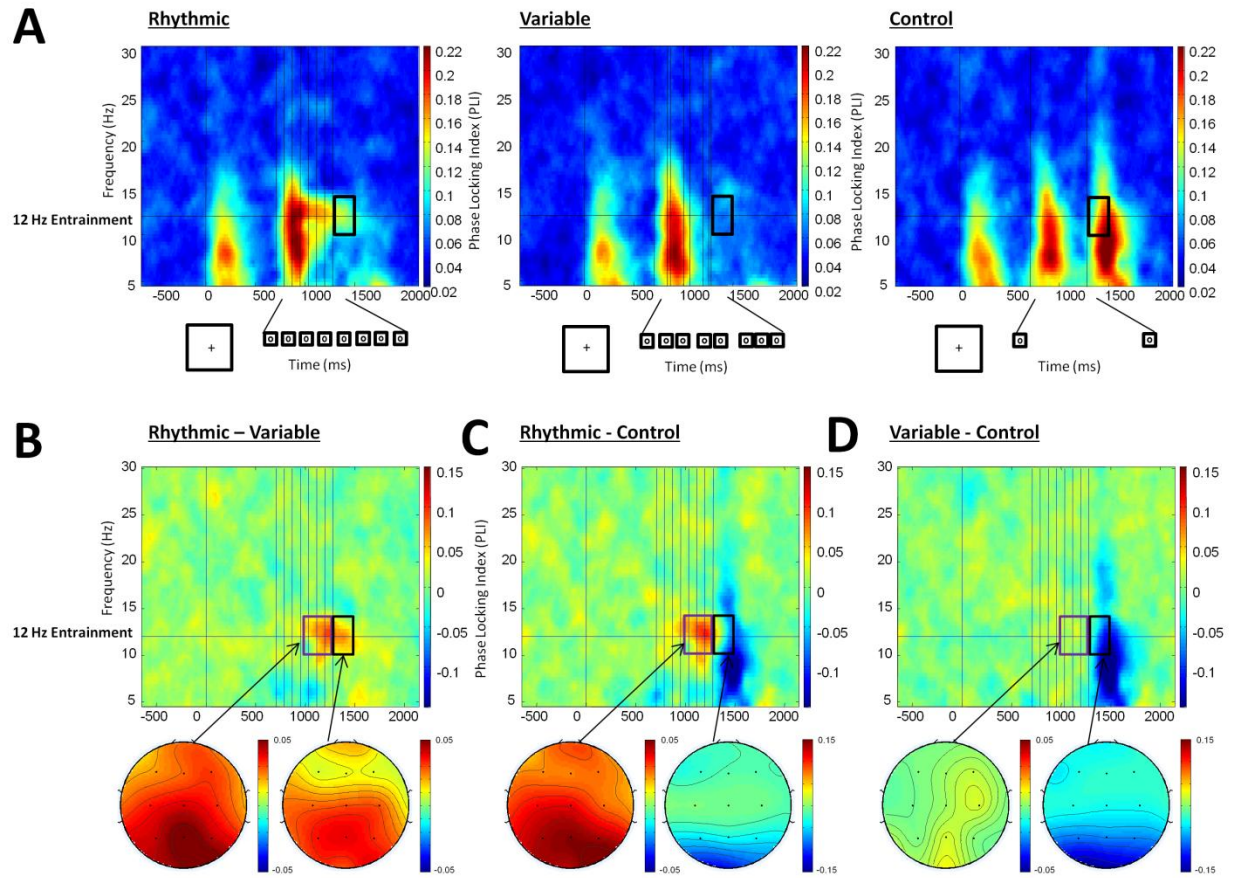
Figure 5.3. (A) Average Phase-Locking Index (PLI), locked to the onset of the entrainment sequence, displayed over time and frequency for the entire trial period for each sequence type, including a baseline period before the fixation onset. Fixation onset and the onset of each pre-target annulus are indicated by vertical lines. A horizontal line indicates the rate of 12-Hz entrainment in the Rhythmic condition. The square boxes indicate the period after annulus offset during which estimates of the entrained PLI were taken for further analysis. All time-frequency plots refer to electrode Pz. (**B:** Rhythmic and Variable conditions; **C:** Rhythmic and Control conditions; **D:** Variable and Control conditions) Time-frequency display of the difference in PLI between conditions. Two regions of interest (ROI) windows ranging from 10 to14 Hz are marked: the 300 ms before the end of the sequence (purple box) and the 200 ms after the end of the entrainment sequence (black box). . The scalp maps presented below each plot indicate the topographic distribution of the differences in each ROI.
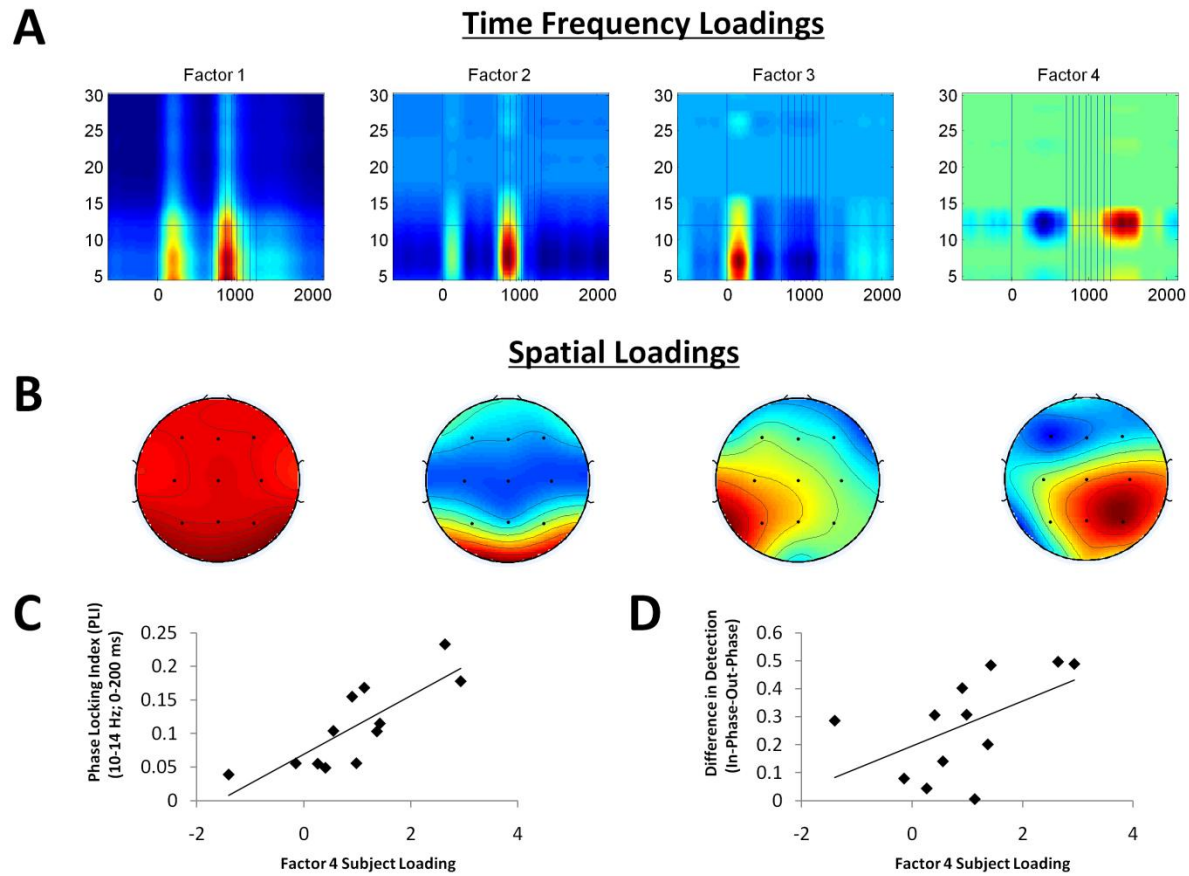
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Figure 5.4. Results of the four-mode PARAFAC of the PLI data in the Rhythmic condition. (A) Time-frequency loadings for each of the four factors. (B) Spatial loadings for each of the four factors. (C) Scatter plot showing the relationship between PLI in the late ROI and subject loadings of Factor 4. Since the scale of the data was kept in the subject mode, loadings for all other modes are scale invariant (D) Scatter plot showing the relationship between the difference in detection between in- and out-of-phase targets and subject loadings of Factor 4.
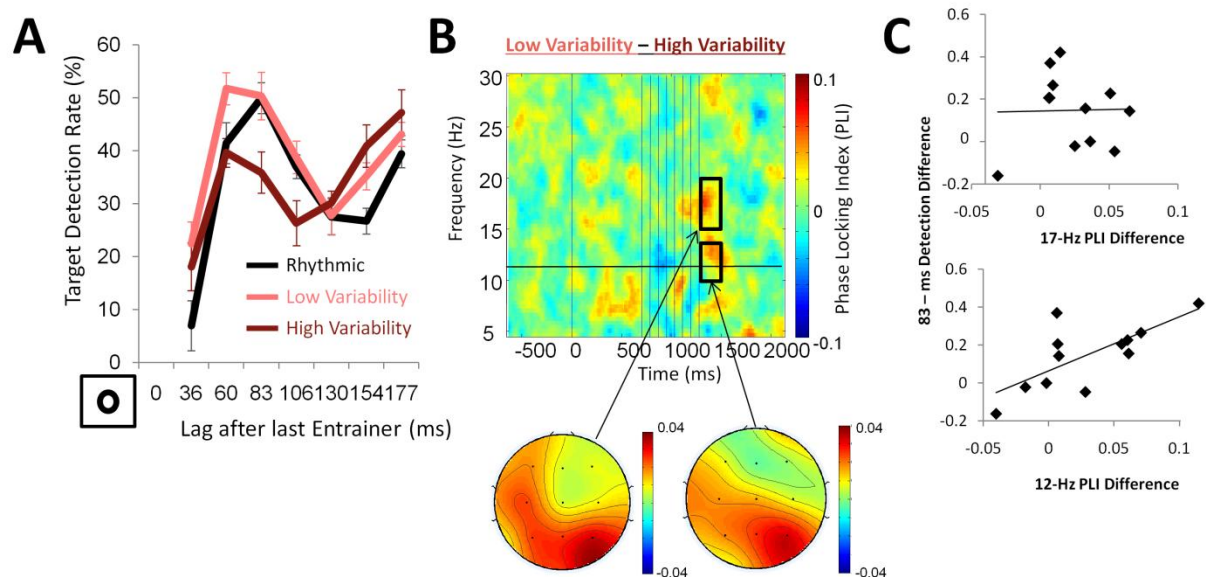
Figure 5.5. Variability of entrainment analysis. (A) Shows the same detection profile as in Figure 2, but now with the Variable condition divided into random sequences that had lower or higher variability of stimulus onset asynchronies (eSOAs) in the beginning of the sequence. Error bars represent within-subject SEMs (B). Time-frequency plot of the difference in PLI between low- and high-variability irregular pre-target sequences. The scalp maps indicate the distribution of the average PLI difference for each ROI. (C) Scatter plots of the difference in detection between low- and high-variability conditions at 83 ms tSOA and the average PLI difference in each of the two ROIs shown in (B).
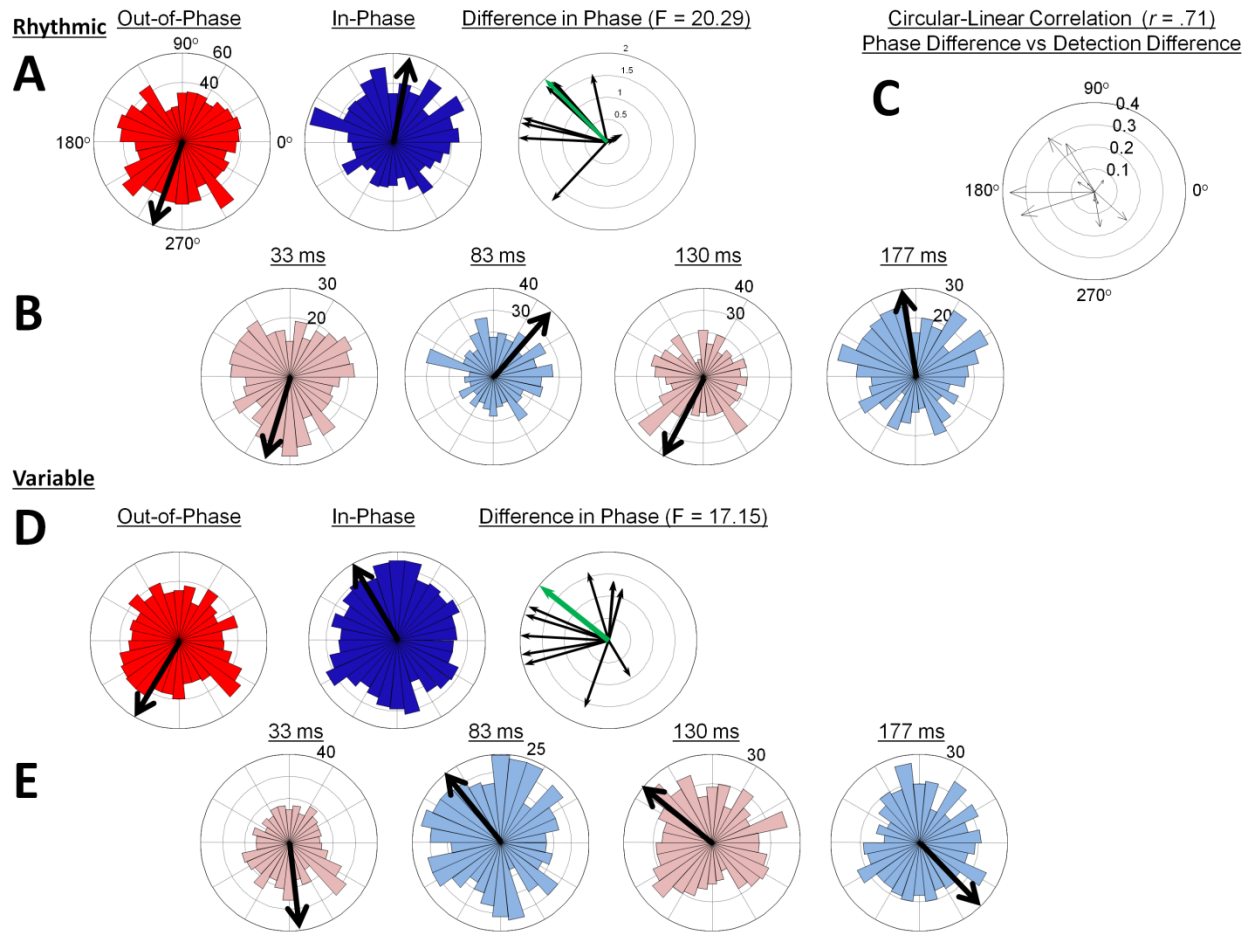
Figure 5.6. Single trial 12-Hz phase analysis. (A) Circular histograms of the single trial 12-Hz phase 100 ms prior to the onset of the target, for both out-of-phase (red) and in-phase (blue) targets, pooled for all trials and all subjects. The dark black arrows represent the circular grand mean phase, computed as the grand average of each subjects average phase. Also shown are the differences in 12-Hz phase between in- and out-of-phase targets (black arrows) for each subject. The green arrow represents the average of these phase differences. (B) Circular histograms of 12-Hz phase, separately for four different target lags, two in-phase (83 and 177 ms) and two out-of-phase (33 and 130 ms) with the entrainment, as well as the grand average 12-Hz phase in each condition (dark black arrow). (C) Circular plot showing the relationship between the separation in 12-Hz phase and differences in target detection for in- and out-of-phase targets presented at 177 ms and 130 ms respectively. The angle on the circle represents the difference in mean 12-Hz phase between in- and out-of -phase targets, whereas the length represents the difference in detection between the conditions. The larger the separation in EEG phase, the larger their difference in detection between in- and out-of-phase. (D, E) Shows the same plots as in A and B for the variable condition.
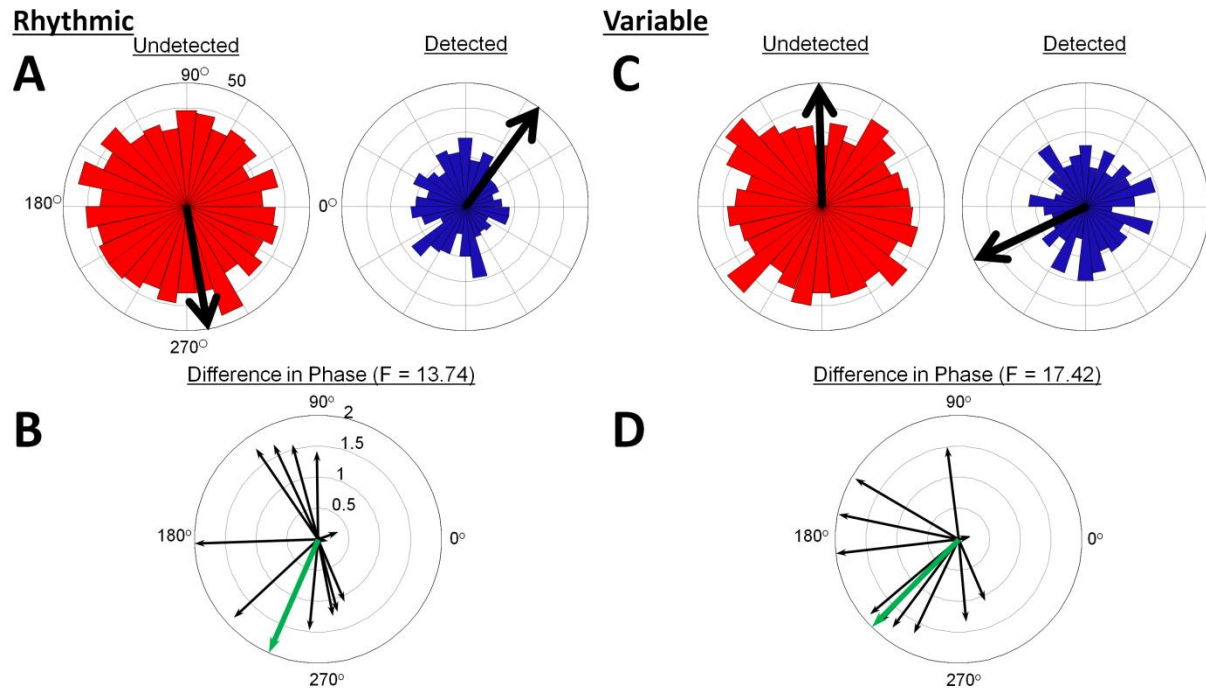
Figure 5.7. Relationship between 12-Hz phase and target detection. (A) Two circular histograms of the phase of 12-Hz oscillations 100 ms prior to target onset, for detected and undetected targets presented at 130, 155, or 177 ms after entrainment. Arrows indicate the circular grand mean (CGM). (B) Shows the difference in average phase between detected and undetected targets for each subject (black arrows), as well as the mean of these differences (green arrow) (C, D) Shows the same types of plots for trials preceded by Variable entrainment.

Figure 5.8. Plots of target detection rate as a function of tSOA, separately for trials with low (left) and high (right) 12-Hz EEG power prior to fixation onset. Error bars represent within-subject SEMs.

# CHAPTER 6

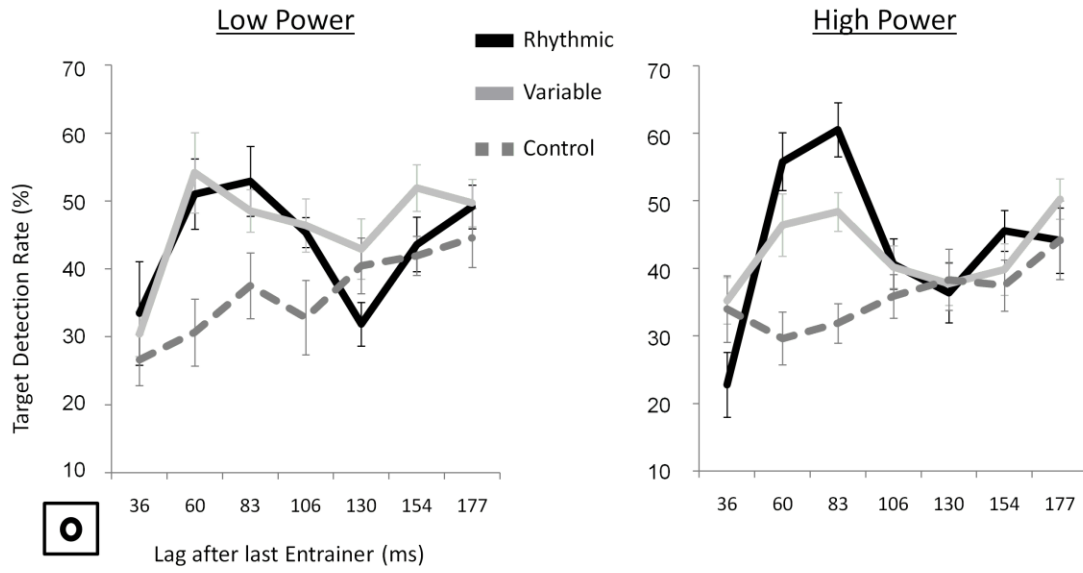## WHO'S CONTROLLING THE BRAKES? PULSED INHIBITORY ALPHA EEG IS LINKED TO PREPARATORY ACTIVITY IN THE FRONTO-PARIETAL NETWORK MEASURED CONCURRENTLY WITH THE EVENT-RELATED OPTICAL SIGNAL (EROS).[9]

**Introduction**

In the first recordings of the human electroencephalogram from the head of his son, Hans Berger (1929) found that increases in the boy's level of attention were associated with changes in the amplitude of 8-12 Hz *Alpha* oscillations in his brain activity. This was the start of a long tradition of human and animal electrophysiology, considering Alpha oscillations as a measure of the general level of inactivity in a cortical area (e.g., Lopes da Silva, 1973; 1980). However, a recent surge of experimental focus, based on single trial analysis of oscillatory activity, has begun to consider Alpha in a new light, that of a general control mechanism having more specific and dynamic interactions with neural processing than a mere indication of inactivity.

Evidence began to accumulate indicating a more dynamic nature of alpha oscillations. Klimesch and colleagues (1998) observed the blocking or suppression of Alpha following the onset of task-relevant stimuli and proposed that this so called event-related desynchronization (ERD) indicated decreases in inhibitory activity in areas needed for tasks processing. This framework has developed into proposals that Alpha oscillations represent an inhibitory and timing mechanism in the brain (e.g., Klimesch et al., 2007; Jensen & Mazaheri, 2010).

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[9] Mathewson, K. E., Ro, T., Lleras, A., Beck, D. M., Maclin, E. L., Low, K. A., Fabiani, M., & Gratton, G. (In Preparation). Who's controlling the brakes? Pulsed inhibitory Alpha EEG correlates with preparatory activity in the fronto-parietal network measured concurrently with the event-related optical signal (EROS).

For this multiple author paper I was involved in the original design of the study, in the collection of data, the analysis of data, and in drafting and editing the manuscript, and creating the figures.

We have recently proposed an encompassing model of Alpha oscillations, as a pulsed inhibition of ongoing sensory activity (Mathewson et al., 2009; 2011). This model is based on the long-standing observation that Alpha oscillations, "represent for the individual cell or the aggregates of cells with which they are associated, an alternating excitability cycle," (Lindsley, 1952). Some neurons are more excitable and fire more often during a particular phase of the ongoing field potentials in the area (e.g., Jacobs et al., 2007; Lorincz et al., 2009; Mo et al., 2011; Lakatos et al., 2008). Increases in Alpha in a sensory area are associated with an increased impact of the excitability cycles, leading to alternating periods of heightened activity, and punctuate inhibition. We have proposed that it is through this pulsating inhibition that Alpha oscillations come to inhibit neural processing.

An important feature of our model is the mechanism by which top-down control and vigilance influence visual perception and performance. We propose that top-down control processes in the fronto-parietal attention network can bias the power of Alpha oscillations in sensory areas, thereby influencing sensory processing. This model finds parallels in the mechanisms of an automobile's anti-lock brakes system (ABS; Mathewson et al., 2011). When one presses the brake on an icy patch of road and begins to slip, the ABS activates and pulses the brake (coincidentally also at ~10 Hz!). The power of these oscillations is under control of the "brake", and when Alpha power is high these 10-Hz pulses of inhibition attenuate processing. For the car, this pulsating decreases its speed, but importantly continues to keep it in touch with the road, just as the pulses of inhibition represented by Alpha oscillations inhibit neural processing, while providing brief periods of relatively intact processing to keep one in touch with the environment.

The idea that Alpha oscillations are related to top-down modulation in the fronto-parietal network is based on evidence from studies using functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS). Alpha oscillations have generally been shown to correlate with decreases in BOLD signal and cortical metabolism in sensory areas, and increases in activity in so-called default-mode areas (e.g., Moosmann et al., 2003; Laufs et al., 2003; Ben-Simon et al., 2008; Jann et al., 2010; Sadaghiani et al., 2010; Scheeringa et al., 2011). In their study combining EEG and fMRI recording in passive resting subjects, Laufs and colleagues (2003) found that activity in the middle and inferior frontal gyri and in the superior and inferior parietal lobules negatively correlated with the simultaneous Alpha power envelope.

Furthermore, Capotosto and colleagues (2009) found that repetitive transcranial magnetic stimulation (rTMS) of either the right inferior parietal sulcus (IPS) or the right frontal eye fields (FEF) inhibited the normal modulations in Alpha oscillations seen with shifts of spatial attention, attenuating the typical behavioral advantage accrued by attended stimuli. The authors concluded that activity in these areas was thus associated with control of the posterior Alpha modulations needed to bias visual processing in favour of the attended items. Further, Hamidi and colleagues (2009) showed that 10-Hz rTMS to the IPS and FEF biased Alpha oscillations and altered target detection. These data provide causal evidence of an involvement of the fronto-parietal network in modulating sensory-relevant Alpha oscillations. Here we sought to test this hypothesis of a relationship between this top-down network and Alpha oscillations, and better understand the spatio-temporal dynamics of this control network.

In order to identify the network of regions associated with trial-to-trial changes in Alpha activity, we measured EEG simultaneously with the event-related optical signal (EROS; Gratton et al., 1995a; Gratton & Fabiani, 2010) in a meta-contrast masking task. We have previously

found changes in Alpha power and phase to be predictive of target detection in this masking paradigm (Mathewson et al., 2009; Mathewson et al., 2010). By shining near-infrared light into the brain, and measuring the time the light takes to diffuse through a patch of cortex and arrive back at a nearby detector, a window is provided onto the neural activity in the diffusive area. The delay in light is due to changes in the scattering properties of active/depolarized neural tissue compared to tissue that is at rest (Rector et al., 1997; 2005). Along with the ionic transfer associated with neuronal depolarization and firing, osmosis leads to an influx of extracellular water into the cell.  This influx of liquid stretches the flexible membrane of the cell, allowing a more unimpeded path for the light to take through the area (Sato et al., 1997; Sykova, 2003). This additional distance travelled in the more transparent tissue leads to a picosecond-range delay in the time of flight of photons transversing active brain tissue, providing a non-invasive, temporally and spatially precise window into neural activity.

EROS has been used in the past two decades in a number of areas of cognitive neuroscience, including auditory and language processing (Rinne et al., 1999; Fabiani et al., 2006; Sable et al., 2007; Tse, Tien, & Penney, 2006; Tse & Penney, 2008; Tse et al., 2007), motor execution and preparation (Gratton et al., 1995; DeSoto et al., 2001; Wolf et al., 2002; Morren et al., 2004; Franceschini & Boas, 2004), high level executive control tasks (Low et al., 2006; Gratton et al., 2009), and a large number of visual and attention tasks (Gratton et al., 1995a; 1997; 1998; 2000; 2006; Gratton, 1997; Gratton, Goodman-Wood, & Fabiani, 2001; Gratton & Fabiani, 2003; Toronov et al., 2005; and Tse et al., 2010). Importantly, Tse and colleagues (2010) showed the possibility of measuring oscillatory activity using EROS, by comparing the frequency-domain EROS steady-state response to visual stimulation at three

different frequencies. This result opens the possibility of measuring oscillatory activity in the brain non-invasively with high spatial precision.

Here, for the first time we set up a system for recording EROS and EEG from the entire cortical surface within each single session, in order to identify the network of brain regions that was associated with task-relevant modulations in Alpha activity. We measured Alpha activity both in the EEG signal, and in the EROS data using time-frequency transformations. Importantly, we simultaneously recorded EROS and EEG, allowing for an investigation of the areas of the brain that correlate with and predict the EEG Alpha changes observed in this task.

We expect to replicate our findings from Mathewson and colleagues (2009) of decreases in Alpha activity in the period preceding subsequently detected targets, when compared to that preceding undetected targets. We predict that when carrying out the same comparison with EROS-recorded Alpha activity we should also see decreases in Alpha prior to detected compared to undetected targets, with the EROS data providing spatial localization of the modulations in Alpha activity. Importantly, these data represent actual measurements of the oscillatory activity in the Alpha range, not merely correlations with the envelope of Alpha power as in previous fMRI/EEG studies, and as such provide direct localization information.

In order to better compare our results with those of past multimodal imaging studies, we also re-sorted the EROS data based on single-trial EEG Alpha power. This computation identifies, independently of the previous analysis, regions of the brain whose activity scales with the level of scalp measured EEG Alpha oscillations. We predict that the two analyses will converge on a common group of areas in the fronto-parietal attention network that predict both subsequent Alpha differences, as well as subsequent detection. Lagged cross-correlation analysis will be used to identify the co-variations in this network, and asses the temporal order of activity

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in different areas. Together, these analyses will establish the spatio-temporal dynamics of the top-down modulation of Alpha oscillations in sensory areas during task preparation, and illuminate the influence of this preparatory activity on subsequent awareness.

**Method**

*Participants*

A total of 16 paid subjects (9 female; age range 19-29) were recruited from the University of Illinois community, and gave informed consent as approved by the Institutional Review Board of the University of Illinois at Urbana-Champaign. Each subject completed the experimental protocol over a number of sessions. Two experimental sessions in which both EROS and EEG were recorded from the entire head were completed by each subject, as well as one devoted to 3D digitization. In addition, if one was not already available, a T1-weighted volumetric structural magnetic resonance image (MRI) was obtained in a separate session.

*Meta-Contrast Masking Task*

Subjects performed two sessions of a meta-contrast masking task on different days. Each session consisted of 24 task blocks. Each block consisted of 48 trials. Each session thus consisted of 1152 trials, for a total of 2304 trials per subject over both sessions. The task timeline is shown in Figure 6.1. The task was identical to that used in an electrophysiological investigation by Mathewson and colleagues (2009). Each trial began with a 247 ms fixation cross, followed by a 400 ms blank screen. A 1-degree circular target was then presented at fixation for 11.7 ms, one refresh cycle of the 85 Hz Sony Trinitron® cathode ray tube monitor. The target was followed after a 46.8 ms blank inter-stimulus interval (ISI) by a 22.3 ms meta-contrast annulus mask, with

an outer diameter of 2 degrees and a 1-degree aperture. Finally, for the next 1520 ms, subjects were required to respond with an E-prime® button box to indicate whether they had (button 1) or had not (5) detected the target. All stimuli were dark grey on a light grey background. The stimulus contrast, luminance, and durations were adjusted in pilot studies such that the target was detectable on roughly half of the trials. On 20 percent of the trials the target was omitted in order to measure false alarms. All participants performed at least one block of practice trials prior to the experimental manipulation to familiarize them with the stimuli and responses.

*EEG Recording and Preprocessing*

We measured the EEG from 8 customized Ag/AgCl electrodes. The electrodes were placed at the end of 6 cm plastic tubes that were filled with conductive gel, and were fashioned such that the conductive area of the electrode was perpendicular to the length of the tube and flush with the bottom. These tubes were inserted into specific holes in the same helmet that secured the optical sources and detectors. The electrode locations were close to electrodes F3, F4, P3, P4, T5, T6, O1, and O2 placements in the 10/20 system, and were in the same positions across recording sessions and subjects. These electrodes were referenced to the left mastoid online, and to an arithmetically-derived linked average mastoid offline. Bipolar electrode pairs above and below the right eye and on the outer canthus of each eye recorded the vertical and horizontal electro-oculogram, respectively. Data were recorded at 100 Hz, with an online bandpass filter with half-amplitude cutoffs between .01 and 30 Hz. Electrode impedance was kept below 20 kΩ. Offline, data were epoched into 2200 ms segments (-847 to 1353 ms of the trial timeline, with 0 being the time of target onset). First, trials with an absolute voltage exceeding 1000 µV were discarded to remove trials with digitizer saturation or physical electrode

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displacements. Next, the influence of eye movements on the EEG channels was removed using a regression technique described in Gratton, Coles, and Donchin (1983). Finally, trials with voltage fluctuations greater than 500 μV were removed to minimize the influence of any remaining artifactual activity.

*EEG Time-Frequency Analysis*

A moving window FFT was applied on the 2200 ms long trial epochs. The hamming window was 640 ms long and was zero-padded with a ratio of 4. The FFT provided estimates of spectral power between 1 and 30 Hz, every 0.78 Hz. On each trial, the average spectra over the 1000 ms pre-fixation period was subtracted, in order to visualize the differences in oscillatory activity developing throughout the trial. This measure is commonly referred to as the Event-Related Spectral Perturbation (ERSP; Makeig, 1993) or event-related desynchronization (ERD; Pfertscheller & Lopes da Silva, 1999). We were specifically interested in the power of Alpha activity prior to the onset of the target, which we have previously found to be larger prior to subsequently undetected targets (Mathewson et al., 2009). We measured the average activity between 8 and 12 Hz, during the 647 ms blank screen and fixation directly preceding the onset of the target.

*EROS Recording*

We recorded the EROS using four synchronized frequency-domain oximeters (Imagent; ISS, Inc., Champaign, IL), with eight additional detectors, for a total of 24 detectors. Near-infrared light from a total of 64 laser diode sources (830 nm) was carried to the scalp by 400 micron silica optic fibers in plastic sheathing. The 24 photomultiplier tube detectors collected the

resultant light passed through 3 mm optic fiber bundles held flush against the scalp, with the hair

moved aside. The laser diodes were modulated at a rate of 110 MHz (Maclin et al., 2007), while

the gain of the detectors was modulated at 110.003125 MHz, creating a heterodyne beat

frequency in the output of the detectors at 3.125 kHz. The electrical output of the photomultiplier

detectors was digitized at a rate of 50 kHz, and Fast-Fourier Transforms (FFTs) of 1.6 ms

segments of the resultant data were computed, providing relative phase delay measurements of

the modulated light's beat frequency in degrees. The resultant signal was then converted into

picoseconds.  We refer to this measure as phase delay, or delay.

In order to rule out any cross-talk between a pair of co-illuminated laser sources whose

light reach the same detector, only four light sources were illuminated at any given time, and of

the four light sources illuminated during any multiplex cycle, no more than one was within 6 cm

of any given detector. Given the large number of sources and detectors, solving these constraints

without computer assistance was unfeasible. We therefore developed an algorithm inspired by

graph theory (Jensen & Toft, 1996) to assign specific sources to particular intervals within the

multiplexing cycle.  This approach recognizes that this task is analogous to that of attributing

colours to the lines connecting a lattice of points (vertices), with the restriction that two lines

connected to the same vertex cannot have the same color.  This is a well-known problem in

graph theory and cartography.  Our program is based on an iterative, random start, graph

colouring algorithm, considering each source location as a vertex and any pair of sources jointly

within the 6 cm range of any one detector as being connected by a link. An attempt is then made,

shuffling randomly through source vertices, to colour the resulting graph in 16 multiplex colours,

with no two linked vertices having the same colour, or in this case no two sources turn on at the

same time within the range of a single detector. If no solution is found, a new random start is

made with a new random order of assigning the multiplex orders to the sources. This procedure is iterated until a solution is found in which no pair of laser sources (within the four banks of 16 multiplexed laser sources) are co-illuminated within the range of any single detector. Thus, each of the 24 detectors is illuminated by 16 multiplexed light sources providing 384 channels per session. The resulting sampling rate for whole-brain imaging is 39.1 Hz, providing a whole brain image every 25.6 ms.

Source and detector fibers were held in position against the scalp by a modified, fitted, motorcycle helmet with securing adapters. Care was taken to eliminate any environmental or stimulus light from entering the enclosed helmet. To increase spatial sampling resolution, we shifted the montage of source and detector locations to the left or right across the two experimental sessions, with the order counterbalanced across subjects. The locations of the 128 source and 48 detector fibers over the MRI of one subject is shown in Figure 6.2A. Locations were spread out maximally over the two recording sessions in order to strike a balance between coverage of as much of the cortex as possible, achieving an optimal density of recording in each brain area, and maximizing the number channels with of source-detector distances between 1.5 and 6.0 cm apart.

*EROS preprocessing and 3D Reconstruction*

Data from the 768 recording channels were preprocessed using P-POD (Pre-processing of Optical Data, MATLAB code). First, any channels with a distance greater than 6.0 cm or less than 1.5 cm were removed from further processing as they are too noisy or provide no information about activity of the brain (Gratton et al., 2000; 2006). Further, any channel with a standard deviation of the phase measurement greater than160 picoseconds was removed to limit

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the influence of noise. The phase delay data were then corrected for phase-wrapping, normalized and de-trended to remove low-frequency drifts. Next, the pulse signal was removed from the data according to a time-warping regression procedure (Gratton & Corballis, 1995). The data were then band-pass filtered with half-amplitude cutoffs between .1 and 15 Hz to remove signal due to non-biological processes and biological noise (Maclin, Gratton, & Fabiani, 2003). Next, 2200 ms segments of these continuous data, locked to the onset of each target (-847 to 1353 ms) were selected and averaged over trials, separately for a given stimulus or electrophysiological condition, providing trial averages of the brain activity for each source-detector pair.

The 3D location of each source and detector was obtained with a Polhemus "3Space" Fasttrak 3D digitizer ® (Colchester, VT) with an extended stylus, and Locator 4.1 software (Source Signal Imaging, Inc., San Diego, CA). These locations (Figure 6.2A), as well as an oversampled collection of scalp and face locations (Figure 6.2B) were co-registered onto the T1 weighted volumetric structural MRI of each subject, by first co-registering common fiducial landmarks of the nasion and preauricular points, and then using least-squares fitting procedures to adjust the fit to minimize errors below 5 mm as described in Whalen and colleagues (2008). The co-registered brain locations were then transformed into common Talairach coordinates for group-level analysis (Talairach & Tournoux, 1988).

Next, in-house software Opt-3D (Gratton, 2000) was used to make a reconstruction in voxel space of the resultant light diffusion path (modeled as a curved ellipsoid). The average phase delay signal from each channel was thus attributed uniformly to the 3D-reconstructed volume of the light's path. Voxels of the brain with two or more estimated overlapping light paths were assigned an average of those channels (Wolf et al., 2000). Idealized representations of the 3D volumes sampled by the recording channels between 1.5 and 6.0 cm apart are presented

for a single representative subject over the co-registered MRI data in Figure 6.2C, indicating the broad and consistent coverage provided by the full-head optical montage. Further indication of the broad coverage can be seen in the EROS data images, where dark grey areas represent those sampled by the optical channels.

The resultant voxel data were then orthogonally projected onto templates of the superior axial and posterior coronal surface of the brain, as well as onto slices through sagittal sections. Only data superior and posterior to the anterior commissure were projected onto the axial and coronal surfaces, respectively, while the sagittal slices represent only the activity from that slice. Data were spatially smoothed with an 8-mm spatial filter. In order to make statistical inferences about the EROS activity we computed at each pixel of the projection a $t$-statistic at the group level with an error term pooled over time for each relevant contrast described below, which were then converted to $z$-scores. A statistical parametric map (SPM) of this $z$-score was computed. A region of interest (ROI) analysis was employed, controlling for multiple comparisons using random field-theory SPM techniques (Friston et al., 1994; Kiebel et al., 1999; Gratton, 2000). The label, coordinates of, and justification for each ROI, are reported in Table 6.1. The points of peak EROS activation, the $z$-scores, and the adjusted critical $Z$ value necessary for $p < .05$ in a one-tailed test are reported below in the text. Each ROI was analyzed independently.

*EROS Time-Frequency Analysis*

To measure the areas of the brain with coherent Alpha power prior to the onset of the target, and to compare Alpha activity in these areas between detected and undetected targets, we next took the average EROS phase delays for each channel over time and submitted them to a FFT with a 205 ms moving window with a pad ratio of 2, providing estimates of oscillatory

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information every 2.4 Hz. We considered the activity over time in the bin centered at 9.8 Hz, closest to the center of the Alpha frequency range. These Alpha-power envelopes were computed for each optode channel, for each subject, and were then submitted to 3D reconstruction of the light paths. Regions of interest were constructed around the frontal and parietal areas associated with task preparation and the dorsal attention network (Corbetta & Shulman, 2002; He et al., 2007; Low et al., 2006; 2009) as well as other areas that have been shown from previous research to be associated with modulations of Alpha oscillations in the superior and middle frontal gyri, the inferior parietal lobes and temporal-parietal junction, the cuneus and the medial prefrontal cortex, (Laufs et al., 2002; Moosmann et al., 2003; Sadaghiani et al., 2010). See Table 1 for a list of the coordinates of each ROI, and see Figure 6.4B & 6.6C for a visual representation of their extent. The peak activities in these ROIs were compared over subjects. We hypothesized that Alpha oscillations should be smaller before detected targets in these regions.

*Sorting EROS by EEG Alpha Power*

As another method of examining the brain sources associated with increases in Alpha power to complement the EROS and EEG findings, we measured the EEG Alpha power on each trial and re-sorted the EROS data to test for brain areas whose activity positively or negatively correlated with single trial EEG Alpha power. For 4 subjects recording errors prohibited matching of EROS and EEG trials, precluding the data from these subjects from being considered in the EEG Alpha sorted EROS analysis, leaving only 12 subjects in this analysis.

We measured the evoked Alpha (7-12 Hz) power on each trial in the 200 ms prior to the onset of the target from parietal electrodes. We divided each subject's trials into four quartiles of Alpha power based on these window averages. We then re-averaged the EROS data into four

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separate averages, one for each quartile of Alpha power measured simultaneously on the same

trials. A linear contrast was then created to identify any brain areas whose phase delay

significantly increased or decreased as Alpha power on that trial increased. Positive loadings

indicate brain areas positively correlated with Alpha activity on that trial, while negative

loadings indicate areas whose activity is smaller on trials with high Alpha activity. The resultant

images were then averaged over the entire pre-target period (650 ms), providing a single brain

volume of Alpha-correlated EROS activity.


*Lagged Cross Correlation*

In order to identify the network of brain areas associated with pre-target modulations in

Alpha oscillations, we measured the backwards lagged cross-correlation between the areas of

maximal EROS Alpha difference in the cuneus ROI (where alpha activity related to subsequent

detection was maximal in the pre-target period) and every other voxel. This was done in two

complementary ways. First, the 10-Hz EROS Alpha activity was correlated with the time series

from the seed Alpha cuneus activity. Second, the broadband time-domain EROS signal was

correlated with this Alpha seed activity. In both cases, each subject's average time series at the

seed location was correlated over time with the activity from any other voxels in the brain. The

resultant correlations were then Fisher $r$-to-$z$ transformed to allow the removal of the

correlation's restricted range. $T$-statistics, based on the Fisher-transformed individual subject's

correlations, were then obtained across subjects and transformed into $Z$-scores for plotting and

correction for multiple comparisons. This analysis was repeated using simultaneous time-series

in the seed and target locations, or by shifting the target location time series by different negative

lags compared to the seed's. This tests not only for the instantaneous correlations activity in two

regions, but also for whether activity in one region predicts the difference in 10-Hz Alpha activity in the cuneus at some time in the future. In both the Alpha and broadband EROS analyses, we tested for significant correlations between the EROS cuneus activity and activity in each of the ROIs independently.

**Results**

*Target Detection Performance*

When the target was presented unmasked, it was easily detected ($M_\% = 98.4\%$; SD = 2.0%; Range = 93.2 - 100 %). With the mask, subjects reported detecting the target only 63.8% of the time (SD = 19.1%; Range = 29.2 - 90.7%), indicating the effectiveness of the metacontrast mask ($M_D = 34.6\%$; $t(15) = 7.76$; $p < .05$). In comparison, false alarms, in which subjects indicated that a target was present when only a mask was shown, were rare ($M_{FA} = 9.5\%$; SD = 8.1%; Range = 0.3 - 25.1%). In order to combine these measures to estimate the ability of subjects to differentiate the masked target from noise, we compute a $d'$ measure for each subject ($M_{d'} = 1.91$; SD = 0.60; Range = 0.75 - 2.98). Values of $d'$ greater than 1 indicate subjects' ability to detect the target. Importantly, the balance between hits and misses, combined with the large number of trials, allowed us to separately measure brain activity for detected and undetected targets for each subject.

*EEG Alpha Power*

Figure 6.3A shows the difference in ERSP between detected and undetected targets. Plotted is the difference in power for the average of electrodes O1 and O2, over visual areas. The average activity in the 8-12 Hz interval between the onset of the fixation and the onset of the

target was significantly lower prior to subsequently detected targets (M = -.98) than undetected targets (M = -.69; $t(15) = 3.31$, $p < .05$). Figure 6.3B shows the topography of the difference in Alpha power in the interval box shown in 6.3A, indicating frontal and occipital maxima. As can be seen from Figure 6.3A, this Alpha difference was maximal from 200 to 400 ms prior to the onset of the target.

*EROS Alpha Power*

In order to find the areas of the brain oscillating in the Alpha range in the pre-target period concomitant with the observed EEG Alpha difference, we next considered the coherent oscillatory Alpha activity present in the EROS data. Shown in Figure 6.4A are two orthogonal projections of the difference in 10-Hz EROS activity in the 400 ms prior to the onset of detected as opposed to undetected targets. Coloured circles indicate the peak of significant differences in Alpha activity in the corresponding ROI from Figure 6.4B. Evident is decreased EROS Alpha activity prior to detected targets in left superior frontal regions at 332 ms pre-target (peak $Z(15) = -2.89$; $Z_{crit} = -2.75$; peak coordinates: -51/12/38), and in the right Parietal ROI in inferior parietal areas from 179-153ms and from 384-307 ms pre-target (peak $Z(15) = -2.87$; $Z_{crit} = -2.56$; peak time: -332 ms; peak coordinates: -49/-72/19). These differences occurred before a large and long-lasting difference in Alpha activity in the cuneus and dorsal extrastriate regions from 281-230 ms and from 25-0 ms prior to the target (peak $Z(15) = -3.25$; $Z_{crit} = -2.71$; peak time: 255 ms; peak coordinates: -3/-71/42).

We next visualized the distribution and depth of the cuneus Alpha effect by focusing on the temporal peak of the effect at 255 ms prior to target onset. Figure 6.5A shows this activity enlarged from the axial and coronal views, with six red vertical lines indicating the horizontal

slices shown below in Figure 6.5B. Evident is a widespread difference in EROS Alpha power

that extends throughout the width and depth of the precuneus and cuneus areas. Crucially, the

difference in EROS Alpha power between detected and undetected targets at the cuneus peak at

255 ms pre-target was correlated across subjects with the difference in EEG Alpha power over

visual areas during the pre-target period which peaked at a similar time (~300 ms; $r = .47$; $t(15)$

$= 2.02$; directional $p < .05$). This indicates the correspondence between the EEG and EROS

measures of Alpha activity, and reveals a likely underlying source of the scalp measured

differences in Alpha.


*EROS Sorted by EEG Alpha*

As an additional window into the brain areas associated with modulations in Alpha

activity, we next sorted the broadband unfiltered EROS activity by the simultaneously measured

single-trial EEG Alpha power used to compute the data in Figure 6.3A. Figure 6.6A shows the

average over the pre-target period of the areas of the brain whose EROS activity correlated

positively (red) or negatively (blue) with the single trial EEG Alpha power. Evident are three

areas in the frontal lobes that correlated with Alpha activity. Since no activity in the right frontal

ROI reached significance, more specific ROI's were constructed around areas known to correlate

with Alpha modulation in the frontal eye field (FEF) and anterior PFC (He et al., 2007;

Shadaghiani et al., 2010; Figure 6.6.C). The more activity there was in medial prefrontal cortex

(PFC), the higher Alpha power was on a given trial (peak $Z(11) = 2.80$; $Z_{crit} = 2.57$; peak

coordinates: -3/34/34). Conversely, EROS activity was negatively correlated with the single trial

Alpha power in both the right anterior PFC (peak $Z(11) = -2.47$; $Z_{crit} = -2.35$; peak coordinates:

27/49/26) and the right FEF (peak $Z(11) = -2.43$; c = -2.18; peak coordinates: 39/-1/45). Two

representative sagittal slices crossing the clusters of activation reveal the depth of the Alpha

correlations in Figure 6.6B.

*Lagged Cross Correlation*

Finally, in order to identify the network of brain areas whose activity preceded and

predicted the EROS and EEG Alpha modulations, we computed lagged cross correlations from a

seed in the point of maximal Alpha difference in the cuneus region from Figure 6.5. First, Figure

6.7A shows the backwards-lagged cross-correlations between the EROS Alpha activity in the

cuneus and the same time-frequency transformed EROS Alpha activity in all other brain areas.

There were significant correlations between EROS Alpha activity and preceding and

simultaneous activity in a number of the ROIs. Figure 6.7A and 6.7B show the peak correlation

in each ROI as a colored circle corresponding to the respective ROI (Figure 6.7C). First, as

implied by this method, there was an auto-correlation in the cuneus region from 51-0 ms (peak

$Z(15) = 6.114$; $Z_{crit} = 2.80$; peak lag: 0 ms; peak coordinates: -3/-78/38). There was also a

*negative* lagged autocorrelation in the cuneus from 204-153 ms prior to its Alpha modulation

effect (peak $Z(15) = -4.02$; $Z_{crit} = -2.71$; peak lag: 179 ms; peak coordinates: -6/-86/25).

Going backward from the peak of cuneus activity (lag 0), to the last 50 ms prior to the

Alpha detection effect, there was a positive correlation with FEF activity (peak $Z(15) = 2.67$; $Z_{crit}$

$= 2.28$; peak lag: 0 ms; peak coordinates: 34/-3/51), and a negative correlation with activity in

the right inferior parietal lobe (peak $Z(15) = -3.712$; $Z_{crit} = -2.81$; peak lag: 25 ms; peak

coordinates: 44/-88/56). Earlier in time, there was a positive correlation from 128-102 ms with

activity in left parietal lobe (peak $Z(15) = 3.19$; $Z_{crit} = 2.61$; peak lag: 128 ms; peak coordinates:

-33/-66/47). There was a long lasting positive correlation with right frontal activity in the 153 ms

prior to the Alpha effect (peak $Z(15) = 3.55$; $Z_{crit} = 2.85$; peak lag:152 ms; peak coordinates: 39/29/33), preceded by an earlier negative correlation from 204 to 153 ms lags with left frontal activity ms (peak $Z(15) = -4.68$; $Z_{crit} = -2.75$; peak lag: 179 ms; peak coordinates: -21/24/43), and with medial PFC activity (peak $Z(15) = -4.76$; $Z_{crit} = -2.81$; peak lag: 179 ms; peak coordinates: -18/27/45). A summary of the temporal progression of this modulatory activity is presented in Figure 6.7D with the colour of the box and text corresponding to the ROIs shown in Figure 6.7A-C. Evident is a clear temporal order of correlations from frontal and medial areas to right parietal areas, to subsequent Alpha modulation in the cuneus.

As a second investigation of the network of brain areas correlated with the modulation of Alpha activity we correlated the seed activity from the cuneus region with unfiltered broadband temporal domain EROS activity (Figure 6.7B). Since areas that modulate Alpha oscillations must not necessarily themselves oscillate in the Alpha range, this analysis is more sensitive to possible modulatory influences. There were positive correlations 25 to 0 ms in both the right FEF (peak $Z(15) = 2.84$; $Z_{crit} = 2.27$; peak lag: 25 ms; peak coordinates: 32/9/51) and in the right inferior parietal lobe (peak $Z(15) = 3.20$; $Z_{crit} = 2.76$; peak lag: 25 ms; peak coordinates: 54/-78/85). Earlier, there was a negative correlation from 127-76 ms in the left superior parietal ROI (peak $Z(15) = -3.29$; $Z_{crit} = -2.58$; peak lag: 102 ms; peak coordinates: -33/-58/51),  a positive correlation in right anterior prefrontal areas (peak $Z(15) = 2.47$; $Z_{crit} = 2.44$; peak lag: 102 ms; 34/47/27), and a positive correlation in left frontal areas (peak $Z(15) = 2.92$; $Z_{crit} = 2.77$; peak lag: 127 ms; peak coordinates: -36/27/38). Finally there was a positive correlation between EROS Alpha band activity in the cuneus and the broadband EROS activity in the medial prefrontal lobe 179-153 ms earlier ($Z(15) = 3.34$; $Z_{crit}$ 2.82; 179 ms; -13/47/35).

It is evident that the same summary in Figure 6.7D corresponds just as well to this way of considering the correlations with sensory Alpha modulations, given the order of correlation in each ROI. Together, these cross-correlations provide further evidence that the fronto-parietal attention network is related to modulations in posterior Alpha activity, which predicts subsequent awareness.

**Discussion**

Here we find that the power of Alpha oscillations, as measured by either EEG or EROS, predicts subsequent visual awareness and that these modulations are related to top-down activity in fronto-parietal areas. Detection performance of the brief circular target is hindered by the subsequent metacontrast mask. Our moderate $d'$ levels (1.81) show that this masking is not complete, providing us with an opportunity to compare trials when the target was and was not detected. The low level of false alarms associated with this performance precluded any analysis of brain activity preceding spurious detection.

A large number of studies have shown that EEG Alpha oscillations preceding the onset of sensory stimuli predict subsequent stimulus processing (Mathewson et al., 2009; Ergenoglu et al. 2004; Hanslymayr et al., 2007; Palva et al., 2005; Romei et al., 2008a; 2008b; Van Dijk et al., 2008; Babiloni et al., 2006). Here we replicate this result in our EEG data, finding that Alpha power differed between detected and undetected masked visual targets with a maximum difference at a frequency of around 11-12 Hz and a peak around 300 ms prior to the onset of the target (Figure 6.3A). Interestingly, the topography of our observed differences in EEG Alpha showed differences in Alpha all over the brain. However, the small number of EEG channels in

the current experiment prevented us from analyzing the underlying sources of these differences in EEG Alpha activity.

Other studies have attempted to spatially localize sources of variations in EEG Alpha power measured on the scalp using a combination of EEG and fMRI. These studies have found large negative correlations between Alpha and hemodynamic activity in areas around the interparietal sulcus (Babiloni et al., 2009; Sadaghiani et al., 2010), the inferior parietal lobe (Laufs et al., 2002; Moosmann et al. 2003), and the superior parietal lobe (Laufs et al., 2002; Sadaghiani et al., 2010). Additional negative correlations have been found in frontal areas (Moosmann et al., 2003; Laufs et al), and in dorsal and lingual extrastriate visual areas (Moosmann et al., 2003; Sadaghiani et al., 2010). Normally, only small positive correlations are found between EEG Alpha power and hemodynamic activity, and these have been restricted to areas of the thalamus (Goldman et al., 2002) and cingulate areas (Laufs et al., 2002; Sadaghiani et al., 2010). These studies of the relationship between EEG Alpha power and functional neuroimaging suffer from the limitation that the fMRI activity is much too slow to directly measure Alpha oscillations and thus a power envelope in the EEG data must be used as a regressor for the BOLD signal. This analysis thus reveals areas whose activity is modulated as a function of the overall power of Alpha, and not areas whose activity is oscillating at 8-12 Hz per se.

In order to overcome these limitations we combined EEG measurement with *simultaneous* fast optical imaging using EROS (Gratton & Fabiani, 2010). By measuring scattering changes associated with membrane depolarization, EROS provides a window onto neuronal activity itself that is both spatially and temporally precise and related in source to the oscillatory activity of the EEG. EROS has a significant history of being used for studies of both

visual sensory processing (e.g., Gratton et al., 1995; 1997; 1998; 2000; 2006; Fabiani et al., 2003) and of task preparation (Low et al., 2006; 2009). Importantly, it has recently been shown that transformation of the optical signal into the frequency domain can provide accurate estimations of the oscillatory activity in the underlying brain areas (Tse et al., 2010). Here we extend this result, showing for the first time the ability to measure task- relevant oscillatory activity from the whole brain with EROS.

Here we also performed the EROS experiments to record simultaneously from the whole head, complementing our EEG recording. We visualized the interrogated brain areas and found that the measures covered the entire parietal and visual cortices, as well as most of superior frontal areas and some temporal cortex (e.g., Figure 6.2, 6.6). This wide coverage allowed for a test of the cortical correlates of Alpha oscillations, using both time-frequency analysis of the EROS signal itself, as well as EEG-Alpha-based sorting of the EROS data. Our method also differs from those of past attempts to measure functional correlates of Alpha oscillations, in that we are using a task setting instead of a resting or passive state. We did this to provide a measure of behavioral outcome associated with fluctuations in Alpha oscillations. It is of note that since EROS does not have the penetration into midbrain areas, we are unable to measure any activity in the thalamus, which is an important modulator of sensory Alpha activity (e.g., Lopes de Silva, 1991). Combination of EROS and fMRI recording may be useful to illuminate the relationship between our results and modulatory thalamic activity.

We employed a series of methods for finding areas of the brain that either oscillated at 8-12 Hz or modulated Alpha oscillations. First, we measured the oscillatory EROS Alpha activity by computing a time-frequency transform of the time-domain EROS data and reconstructing the progression of EROS Alpha power. A number of areas were found in Frontal, Parietal, and

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Visual cortices whose EROS Alpha power was lower before detected targets (blue color on maps). Around 350 ms prior to target onset, the left dorsolateral prefrontal and the right inferior parietal lobe have less Alpha power prior to detected targets. This is followed around 255 ms before the onset of the target by a large area in the cuneus and dorsal extrastriate visual areas. This cuneus activity was widespread and robust (Figure 6.5), and lasted for around 100 ms. This was consistent with the time course of the Alpha effect in the EEG data. In fact, the difference in EEG Alpha was correlated with the difference in EROS Alpha across subjects, confirming this cross-modal relationship. The left frontal and right parietal areas preceding the cuneus activity may represent control areas or modulators of the 12-Hz signal.

Furthermore, in the 200 ms prior to the onset of the target, widespread areas in ventral and lateral occipital and right inferior parietal cortex have less Alpha power prior to detected targets, but these effects were not as robust (Figure 6.4B, bottom rows). Interestingly, there is also an area of the left inferior temporal lobe that appears to have more Alpha power prior to detected targets. This is consistent with recent findings from intracranial EEG in humans of a similar inverse relationship between Alpha and detection in inferior temporal lobes, whereas decreased detection was found for increased Alpha power in extrastriate visual areas (Mo et al., 2004; Bollimunta et al., 2008; 2011).

The results provide additional evidence of the involvement of the fronto-parietal network in Alpha modulation. These data also provide interesting contrast to the literature correlating EEG Alpha power with modulations in hemodynamic activity. Some of the areas in parietal and frontal cortices are those same that have been implicated to correlate with fluctuations in EEG Alpha power during passive tasks (Laufs et al., 2002; Moosmann et al., 2003; Sadaghiani et al., 2010). Specifically, dorsal visual areas have been found to correlate with EEG Alpha power in a

passive task (e.g. Sadaghiani et al., 2010). Further, inferior parietal and dorsolateral prefrontal areas have also been shown to correlate with resting EEG Alpha power (e.g., Laufs et al., 2002). Importantly, however, we here provided a window into the underlying brain areas oscillating at ~10 Hz in a task preparation setting where the oscillatory activity has behavioural relevance.

It should be noted that some attempts have been made to model the source of underlying alpha oscillations using inverse reconstruction from MEG or EEG oscillatory activity on the scalp. For example, van Dijk and collegues, (2008) found increased MEG Alpha prior to the onset of correctly discriminated visual targets. The source of this difference in Alpha was estimated to a location along the parieto-occipital sulcus, were similar in location to the maximal 10-Hz difference in EROS activity in the cuneus in Figure 6.5.

It is of note that we measured the power of oscillatory EROS activity in the trial averaged data, as an estimate of the amount of phase-coherent oscillatory activity. Given the fixed inter-stimulus interval of our task, as well as the fixation warning stimulus, we predicted that enough of the preparatory activity would be phase-locked for us to reliably measure the Alpha activity in the average. Indeed, we were able to reliably measure difference in EROS Alpha power between detected and undetected targets (Figure 6.5). In the future, single trial time-frequency analysis of the EROS data and subsequent averaging may reveal important information both about the oscillatory activity that is not phase locked across trials, and of the locking of the phase of oscillatory activity around events of interest and between areas.

In order to better compare our results with those of previous findings correlating fMRI BOLD signal with the EEG Alpha power envelope, we also re-sorted the EROS data as a function of the simultaneously measured single trial Alpha power prior to the onset of the target. We considered these data without regard to the subsequent behavioural outcome, in order to

consider areas of the brain whose activity correlates with Alpha power. We also averaged the resultant contrast over the entire pre-stimulus period, for better comparison with hemodynamic functional activations. Given that these modulatory areas represent those whose EROS activity correlated with the EEG Alpha power envelope, it is not surprising that the results differed from the previous analysis of the oscillatory information in the EROS signal alone. We believe that this analysis provides a measure of the modulatory influences on Alpha oscillations prior to stimulus onset that do not oscillate in the Alpha range.

We found two areas in the right prefrontal cortex whose activity negatively correlated with EEG Alpha, of note one of them in the FEF. The FEFs have been implicated in the top-down modulation of attention as part of the dorsal attention network (Corbetta & Shulman, 2002; He et al., 2007). Also of interest was a large area over medial prefrontal and dorsal cingulate cortex where activity positively correlated with Alpha oscillations. Interestingly, this medial prefrontal area, along with the cuneus (where the largest EROS Alpha modulation was observed) have been implicated as part of the network of brain areas more active during resting or task irrelevant processing, the so called default mode network (Raichle et al., 2001; 2007; Buckner et al., 2008). Alpha oscillations have previously been implicated as relating to activity of the default mode network (e.g., Ben-Simon et al., 2008). The extent to which this network is active prior to the onset of the target seems to predict subsequent lapses in awareness, indicating a *disengagement* from task processing. This finding opens the possibility of monitoring in real time the vigilance state of the individual based on optical activation in the medial prefrontal and cuneus areas, as well as EEG and EROS Alpha oscillations.

We finally wanted to test the extent to which these modulatory areas form a network to control Alpha oscillations. We tested this by using the EROS Alpha activity in the cuneus as a

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seed for correlation with all other areas, both coincident in time and at various negative lags, such that we highlighted activity that predicted *subsequent* Alpha modulation. We considered the correlation between cuneus activity and preceding activity in the EROS signal both specific to Alpha oscillations, and in the broad time-domain EROS signal, using the same cuneus Alpha seed. In both cases we found a progression of correlated areas in the frontal and parietal cortex that predicted subsequent Alpha range modulatory activity in the cuneus.

Figure 6.7D shows the apparent progression of correlations between these regions and Alpha activity. Coincident with the Alpha modulation, areas of the FEF and IPS are correlated with its magnitude. Prior to this co-modulation, areas in the left superior parietal lobe, and left and right superior frontal lobes predict the Alpha modulation occurring around 100-125 ms later. Earlier yet, a correlation is found with medial prefrontal regions at a lag ~179 ms before the Alpha modulation. This progression of negatively lagged correlations reveals the network of brain areas modulating the subsequent Alpha power differences in sensory cortices. We are now in the process of probing with single pulse TMS over these areas during these time-intervals to examine the causal relationship between activity in these areas and subsequent Alpha and detection modulations.

In summary, here we illuminate the relationship between top-down modulations from the fronto-parietal attention network, fluctuations in oscillatory Alpha activity in sensory areas, and subsequent awareness. We report on techniques used for the first time to correlate differences in EEG Alpha oscillations with temporal-spatial information from the EROS. We measured with high spatial and temporal resolution the power of Alpha oscillations in the EROS data, and identified a large area in the cuneus where 10-Hz oscillations differed between detected and undetected targets. Across three analyses Alpha oscillations correlated with activity in the fronto-

parietal network. Importantly, we show that these Alpha EEG differences have important behavioral consequences, predicting the level of subsequent visual awareness. Further, we advance knowledge of the underlying brain network associated with changes in Alpha power, by corroborating past findings of brain areas whose activity correlates with the envelope of EEG power, and also breaking new ground by measuring the temporal relationship between these areas and the progression of this preparatory activity. These data provide important information on the cortical areas that control our preparatory Alpha activity and the point in time at which they become relevant for processing. These findings support the predictions of the pulsed inhibition account of Alpha oscillations (Mathewson et al., 2011) in which top-down preparation from the fronto-parietal attention network is proposed to modulate the sensory relevant inhibitory Alpha activity. The extent to which these differences in Alpha relate to previous findings of additional influences of the *phase* of ongoing Alpha oscillations in processing and performance (e.g. Mathewson et al., 2009) remain the topic of future research.

**Tables**

Table 6.1. Talairach Coordinates of Regions of Interest

| ROI | $X_L, X_R$ / $Y_P, Y_A$ / $Z_I, Z_S$ | References |
|---|---|---|
| rSFG/MFG | 20,50 / 5,45 / 10, 40 | Moosmann et al., 2003; Sadaghiani et al., 2010; Low et al., 2006; 2009; He et al., 2002 |
| lSFG/MFG | -20,-50 / 5,45 / 10, 40 | Moosmann et al., 2003; Low et al., 2006; 2009 |
| rTPJ/IPS | 30, 60 / -90, -50 / 0, 30 | Laufs et al., 2002; Moosmann et al., 2003; Sadaghiani et al., 2010; He et al., 2002; Copotosto et al., 2009; Hamidi et al., 2009 |
| lTPJ/IPS | -30, -60 / -90, -50 / 0, 30 | Laufs et al., 2002; Moosmann et al., 2003; Sadaghiani et al., 2010 |
| Cuneus/Precuneus | -20, 20 / -100, -70 / 15, 45 | Moosmann et al., 2003; Talairach & Tournoux, 1988 |
| Medial PFC | -20, 20 / 20, 50 / 25, 45 | Sadaghiani et al., 2010; Laufs et al., 2002 |
| rFEF | 25, 45 / -10, 10 / 40, 60 | He et al., 2002; Copotosto et al., 2009; Hamidi et al., 2009 |
| rAnterior PFC | 25, 45 / 30, 50 / 10, 30 | Shadaghiani et al., 2010 |

ROI, region of interest; X, Y, Z are Talairach coordinates; L/R, left/right; P/A, posterior/anterior; I/S, inferior/superior; r/l, right/left hemisphere; SFG, superior frontal gyrus; MFG, middle frontal gyrus; TPJ, temporoparietal junction; IPS, inferior parietal sulcus; PFC, prefrontal cortex; FEF, frontal eye field
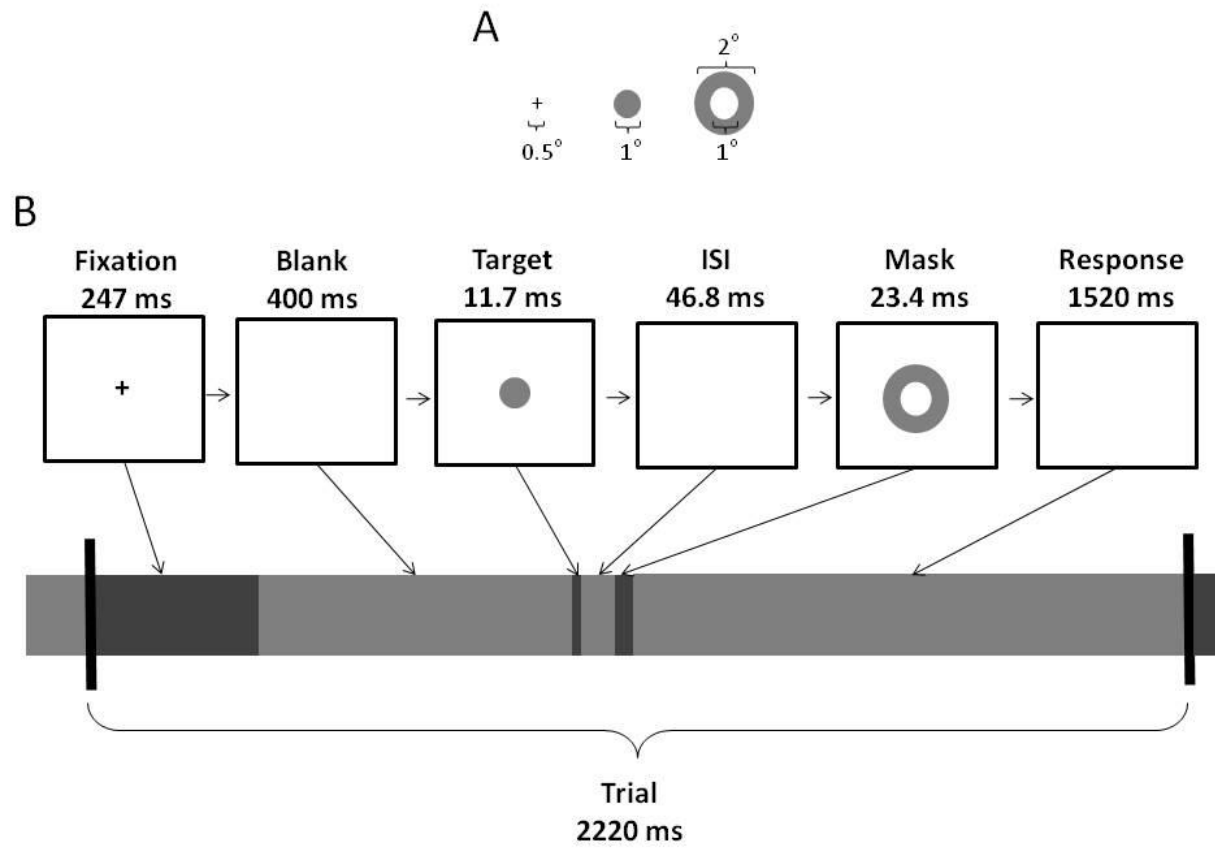
**Figures**



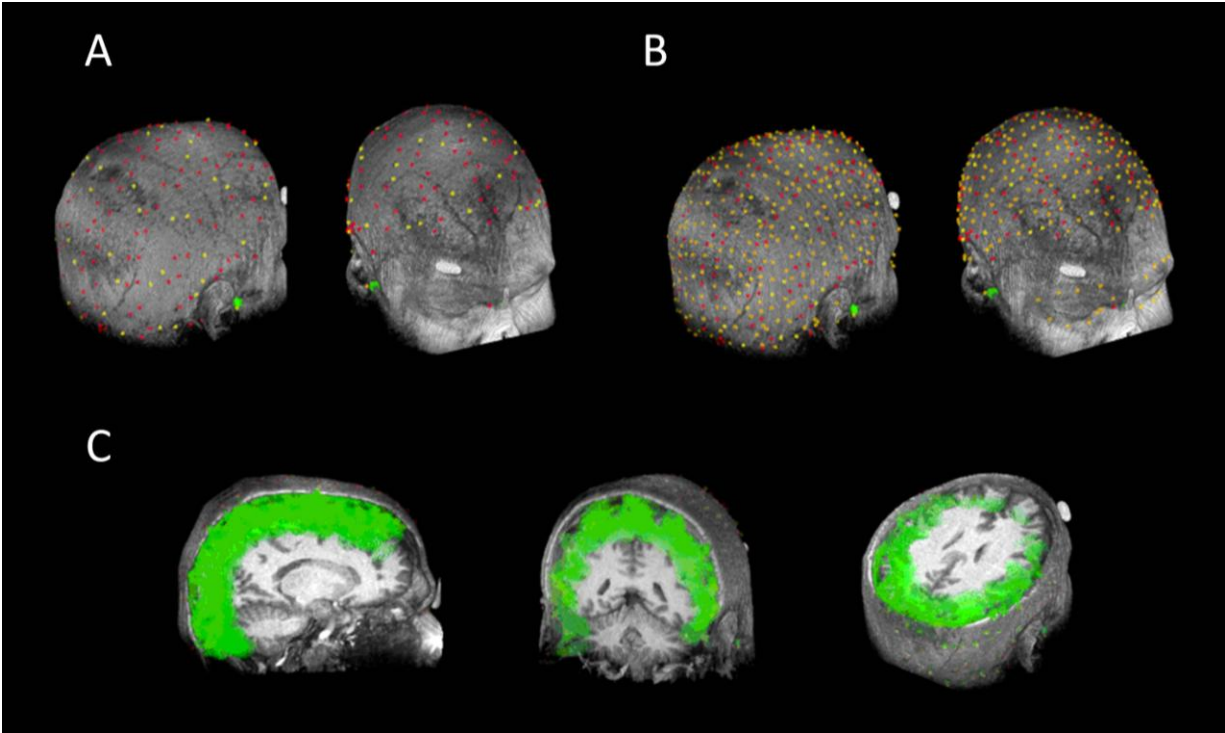Figure 6.1. Stimulus dimensions (A) and trial timeline (B).

Figure 6.2. Montage, Co-registration, and 3D reconstruction. (A) Position of each of the sources (red) and detectors (yellow) across both sessions co-registered with the individuals structural magnetic resonance image (MRI) for a single representative subject. (B) In addition to the 128 sources and 48 detectors, the locations of an additional 500 points, including nasion and pre-aricular common fiducial landmarks (green dots), on the scalp and face were used to enhance the co-registration process, and are shown here for the same subject. (C) Three-dimensional reconstruction of the estimated light path of each optical channel between a source and detector in A are shown as green ellipsoids for each channel between 1.5 and 6.0 cm, again overlaid on the structural MRI of the same subject from three oblique angles, showing the consistent and widespread coverage by the optical imaging montage.
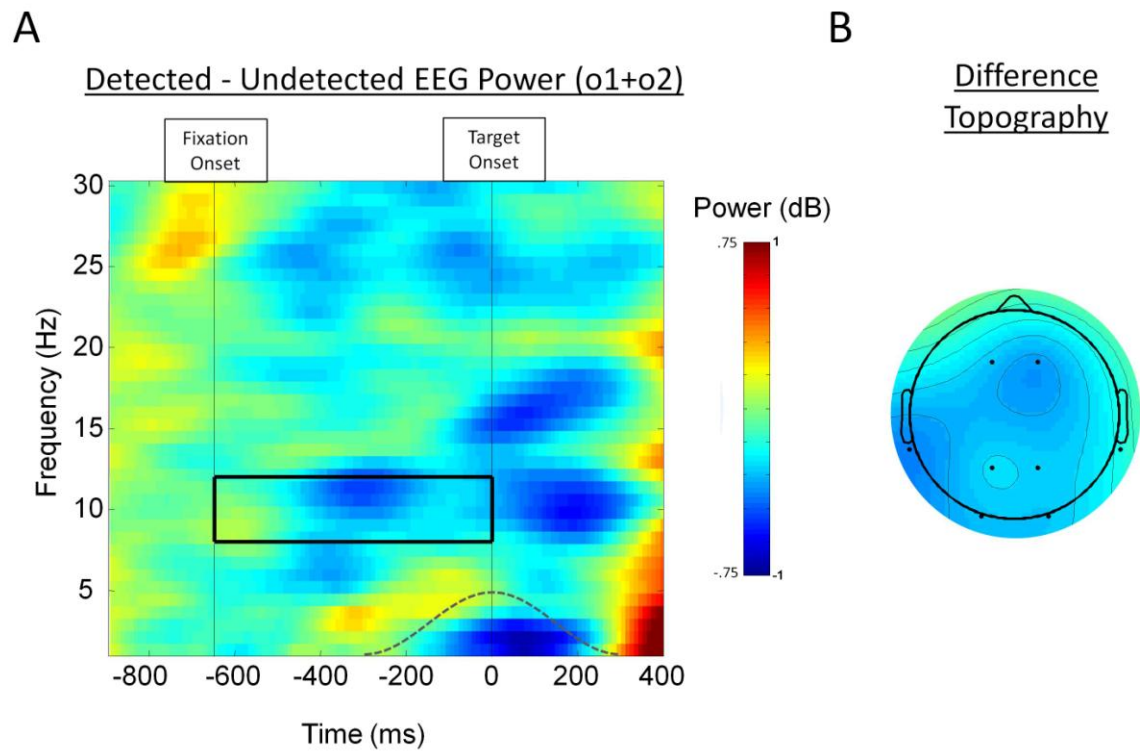
Figure 6.3. EEG Alpha (A) The event-related spectral power for detected targets subtracted from that for undetected targets revealed a difference in EEG Alpha oscillations between 200 and 400 ms prior to the onset of the target. Shown is this difference over frequency and time, averaged together from the two occipital electrodes. The dashed line represents the size and shape of the moving Hamming window FFT used to compute the data. (B) The distribution of this difference in EEG Alpha activity is shown over the scalp using a Laplacian transform of the difference in voltage at each electrode. Evident are right frontal and left occipital maxima.
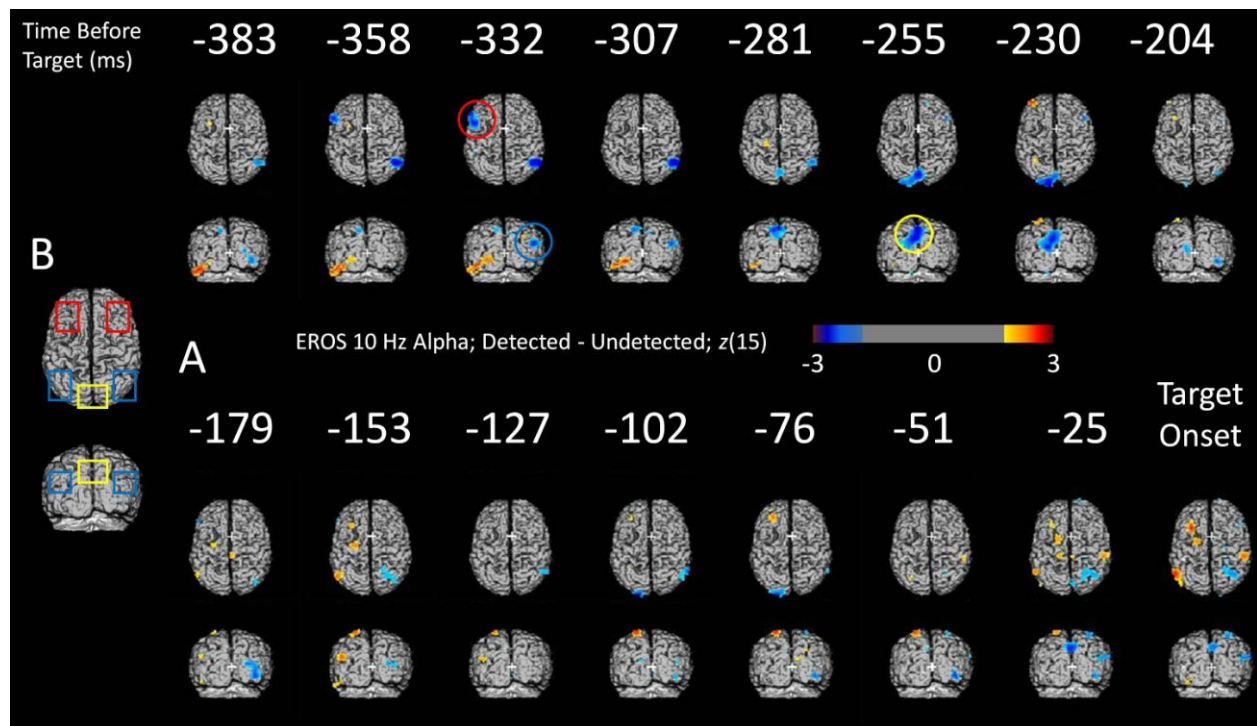
Figure 6.4. EROS Alpha. (A) Statistical parametric maps of the $Z$-score difference in EROS Alpha power between detected and undetected targets (detected – undetected) for every 25.6 ms of the 400 ms prior to the onset of the masked target. The difference in EROS is shown projected orthogonally onto a common template of the superior axial (top) and a posterior coronal (bottom) surfaces of a brain in Talairach space. Only $Z$ scores greater than ±2 are plotted. Coloured circles represent the moment in time and location at which a significant difference in EROS Alpha power peaked in the colour-corresponding region of interest (ROI) shown in (B). Bilateral frontal (Red), bilateral inferior parietal (blue), and cuneus (yellow) regions of interest were considered.

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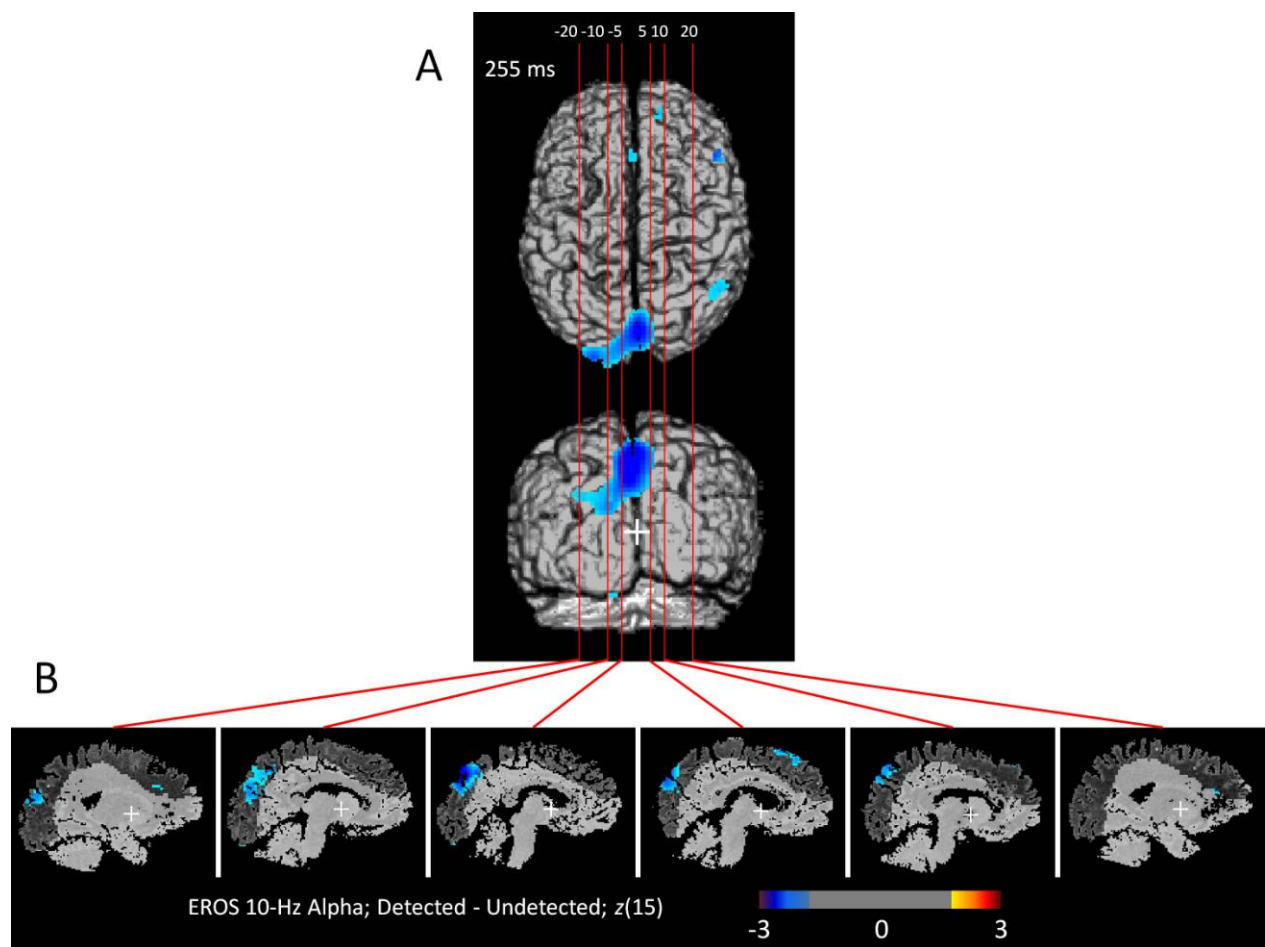
Figure 6.5. EROS Alpha cuneus difference. (A) A surface projection of the difference in EROS Alpha power from Figure 6.4 is shown from two orthogonal angles, only for the time period of maximal difference in the cuneus ROI. Vertical lines indicate the six Talairach X planes from which the sagittal sections were taken. (B) Sagittal slices through the template brain with the difference in EROS Alpha power from that hemisphere projected, indicating the horizontal extent and depth of the differences in oscillatory activity. Dark grey areas indicate cortical regions interrogated by the optical sources for at least 4 subjects, indicating widespread and deep coverage of parietal and frontal areas.
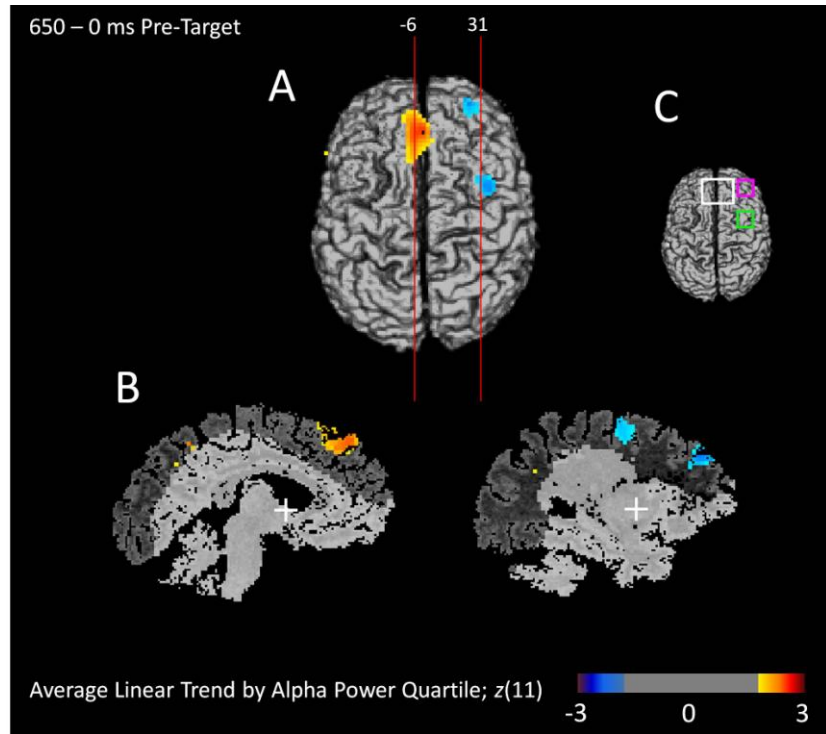
Figure 6.6. EROS Sorted by EEG Alpha . (A) The linear trend of EROS activity as a function of increasing single trial EEG Alpha power is shown projected onto a superior axial surface template. The average linear trend was computed throughout the 650 ms pre-target period. Red areas increase their activity as single trial EEG Alpha power increases, while blue areas do the opposite. Vertical lines represent the X-plane from which the Sagittal slices in (B) were taken. (B) Representative slices through the areas of significant difference at the two X-planes shown in (A), indicating the depth of spatial extent of the effects. (C) The three additional ROIs used for analysis of these differences. Medial Prefrontal cortex (white), right anterior prefrontal cortex (pink) and right frontal eye fields (FEF; green).

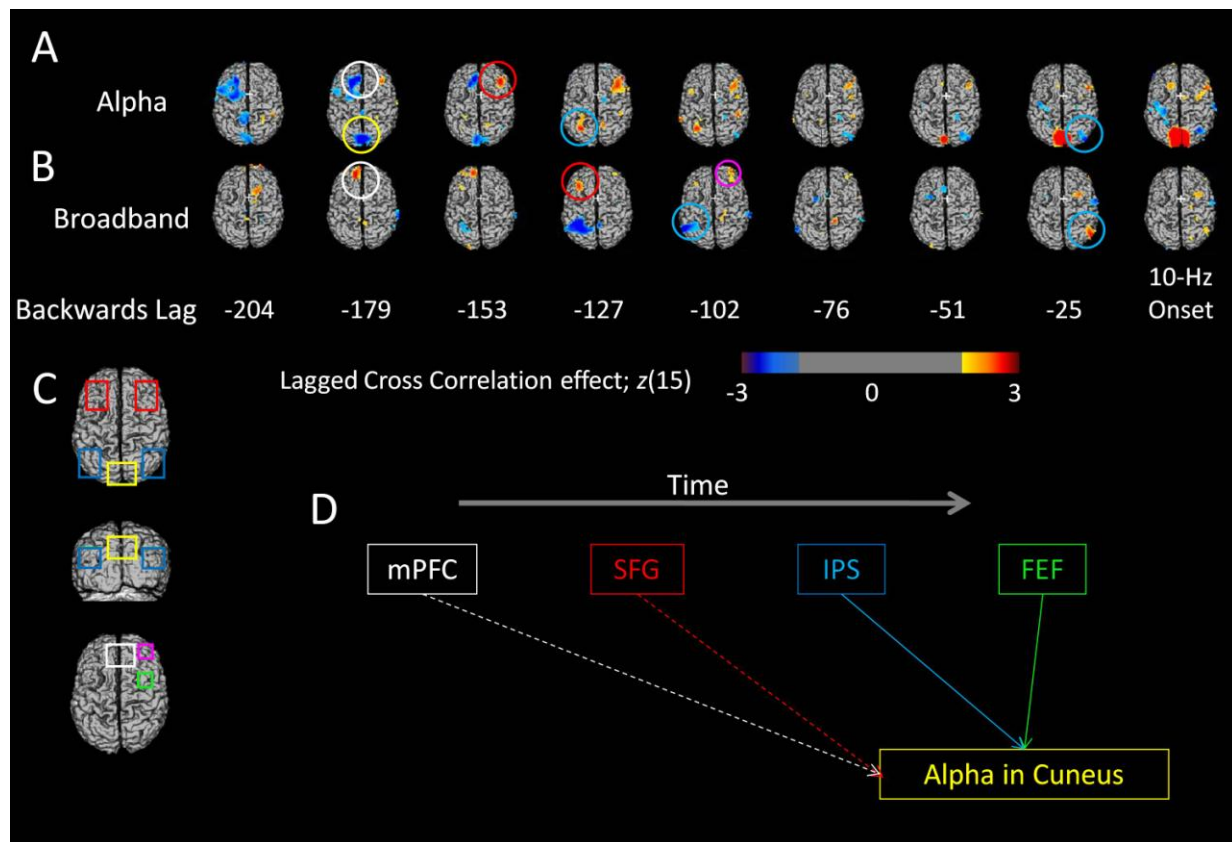Figure 6.7. Lagged Cross Correlation. (A) The results of a lagged cross-correlation analysis using the seed point of maximal EROS Alpha difference in the cuneus from Figure 6.5. Shown is the correlation between the average time course of activity from the coronal projection in the cuneus and the 10-Hz EROS Alpha activity for each other voxel, both at lag 0, and with the two time courses shifted such that areas of the brain thatcorrelate with *subsequent* differences in EROS Alpha activity in the cuneus are shown. Red colours indicate areas where 10-Hz EROS activity correlates positively with subsequent or concurrent 10-Hz cuneus differences, while blue areas represent those whose activity negatively correlates. Coloured circles represent the area and time point of maximal correlation in each of the given ROIs shown in (C). (B) Shows a similar lagged cross-correlation between the coronal projection of 10-Hz EROS Alpha difference in the cuneus ROI with activity in each of the other brain area, but this time considering the time-domain broadband EROS signal, instead of merely the 10-Hz activity. Again, areas were found whose broadband EROS activity negatively and positively correlated with subsequent modulations in 10-Hz EROS Alpha in the cuneus. (D) Shows the apparent progression of correlations between each of the ROIs and the modulation of posterior Alpha activity, considering the progression of lags at which each ROI was maximally correlated with subsequent Alpha modulations. Solid lines indicate areas that correlated at Lag 0 and thus may directly communicate with cuneus areas, while dashed lines were correlated at lags greater than 100 ms and may thus reveal more indirect connections. Horizontal arrows represent a hypothetical flow of information as these correlations were not tested.

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# CHAPTER 7

## CONCLUSIONS

This thesis highlights the important role that Alpha oscillations have in modulating sensory input. More generally, it suggests that Alpha oscillations may be an important mechanism by which inhibitory influence and attentional control are exerted over different cortical activities. Alpha oscillations are in large part determined by interactions between thalamo-cortical and intra-cortical neuronal populations. Specifically, they may be due to the activity of GABAergic inhibitory interneurons, which may themselves receive input from excitatory output neurons. The manifestation of this circuitry is oscillatory activity, which modulates cortical excitability. This mechanism may be ubiquitous throughout the cortex, although the frequency of the oscillation may perhaps vary from area to area.

According to this view, the appearance of the Alpha rhythm is not merely a correlate of a state of low cortical activation, but rather a mechanism in itself, by which low cortical excitability is enabled. Maintaining low excitability in an extended portion of the cortex probably serves a very important adaptive role, in that it allows for crucial information processing to occur undisturbed by irrelevant and secondary processes. At the same time, the oscillatory nature of the Alpha rhythm allows for some of the unattended information to filter through; this may be of critical importance in cases in which the unattended information may be valuable. This is the sense in which we have drawn an analogy between the Alpha-based mechanism for dealing with irrelevant information and the "anti-lock brake" (ABS) system of a car, in which some level of contacts with the road surface (in our case, the external environment) is maintained by applying pulses of braking rather than by braking continuously.

Chapter 4 and Chapter 5 suggest that this pulsed inhibition can become entrained to rhythmic external stimulation. This can be easily accounted for by the neuronal mechanisms that we have postulated to be at the bases of Alpha. Interestingly, they suggest that Alpha oscillations may be part of a general temporal tuning mechanism, by which our brain can exploit regularities in the environment to optimize processing.

Chapter 6 presented exciting new evidence of the modulators of this pulsed inhibitory Alpha activity. The fronto-parietal attention network seems to modulate the power of sensory Alpha oscillations, leading to the fluctuations in visual processing and awareness that are commonly observed under a variety of task settings. This same system is likely also involved in the directed orienting of attention, and the subsequent modulations of inhibitory Alpha activity that bias processing as a result.

A number of questions, however, remain open. For instance, what is the relationship between Alpha and other types of oscillatory activity described in the brain? Electrophysiologists have long described a number of other rhythms characterized by other frequencies (such as beta, theta, gamma and delta), and often correlated them with similar concepts such as perception, attention, and consciousness (Monto et al., 2008). The literature suggests that our brains can pick up on this wide range of frequencies. A question then follows: Is Alpha special, or just one of the many rhythms at which cell ensembles can operate? Or, are different types of cell ensembles involved in different oscillations, and, if so, do they bring forth special types of brain states when their oscillations are triggered?

What is the relationship between brain oscillations and consciousness? In 1890 William James wrote that consciousness: **"…**does not appear to itself be chopped up in bits. Such words as 'chain' or 'train' do not describe it fitly … It is nothing jointed … it flows. A 'river' or a

'stream' are the metaphors by which it is most naturally described". Since James' proposal that

our conscious stream is not jointed but flows (1890), many have proposed that in fact our

perception of the world is more discrete and quantized (Efron 1970a, 1970b; Dehaene, 1993;

Van Rullen et al., 2003; Smith et al., 2006; Pöppel, 2009). Some have proposed that this

quantized nature may account for some common illusions. The discrete frames of our visual

perception, perhaps related to the phase of ongoing excitability cycles, may create an aliasing

during certain motion perception (VanRullen et al., 2005; 2006; Simpson et al., 2005; Andrews

& Purves, 2005). Indeed, fluctuations in the illusory motion percepts are shown to correlate with

changes in Alpha oscillations (VanRullen et al., 2006; but see Kline et al., 2005, for an

alternative account). We predict that the pulsed inhibition of Alpha oscillations may be the

underlying cause of these so called perceptual moments.

The present thesis summarized the evidence that, at least in some cases (such as when

Alpha power is high) our perception of the visual world may be discontinuous in nature.

Specifically, during particular phases of the Alpha oscillations, information is shown to be very

poorly processed, while at other times information processing is enhanced. We summarized the

evidence that sensory processing is gated by the phase of ongoing oscillations in baseline brain

activity, creating oscillating periods of high and low neural excitability. We also described how

these oscillations in cortical excitability are associated with concomitant fluctuations in our

visual awareness; targets presented at particular phases of these oscillations do not reach

awareness. We propose that these cycles of excitability act as a pulsed inhibition on ongoing

processing and that this inhibitory processing mode is common across many brain areas. We

reviewed evidence that the timing of the preferential phases of processing can be entrained to

rhythmic stimuli in the environment, providing a possible mechanism for temporal attention in

the brain. Finally, we show new evidence revealing the network of sensory brain areas oscillating in Alpha frequencies, as well as a top-down attention network whose activity modulates this Alpha activity. Together, this evidence points to a role for Alpha oscillations in the brain as a general inhibitory mechanism, not as a static modulator of processing, but as a pulsed inhibition, allowing the world to only come through in waves.

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