

Alpha Oscillations and Feedback Processing in Visual Cortex for Conscious Perception

Tony Ro

Abstract

■ Variability in perception between individuals may be a consequence of different inherent neural processing speeds. To assess whether alpha oscillations systematically reflect a feedback pacing mechanism for cortical processing during visual perception, comparisons were made between alpha oscillations, visual suppression from TMS, visual evoked responses, and metacontrast masking. Peak alpha oscillation frequencies, measured through scalp EEG recordings, significantly correlated with the optimum latencies for visual suppression from TMS of early visual cortex. Individuals with shorter alpha periods

(i.e., higher peak alpha frequencies) processed visual information faster than those with longer alpha periods (i.e., lower peak alpha frequencies). Moreover, peak alpha oscillation periods and optimum TMS visual suppression latencies predicted the latencies of late but not early visual evoked responses. Together, these findings demonstrate an important role of alpha oscillatory and late feedback activity in visual cortex for conscious perception. They also show that the timing for visual awareness varies across individuals, depending on the pace of one's endogenous oscillatory cycling frequency. ■

INTRODUCTION

While watching a basketball game, one observer may miss a foul that another viewer readily detects, despite careful viewing of the play by both individuals. This type of variability in perception may be due to individual differences in neural processing within the alpha oscillatory frequency band (8–12 Hz; Haegens, Cousijn, Wallis, Harrison, & Nobre, 2014; Berger, 1929). Indeed, several studies have demonstrated that the amplitude of alpha oscillations affect perception (Thut et al., 2011; Romei, Gross, & Thut, 2009; Thut, Nietzel, Brandt, & Pascual-Leone, 2006; Worden, Foxe, Wang, & Simpson, 2000). More recently, the alpha phase has been shown to directly affect perception (Jaegle & Ro, 2014; Mathewson, Gratton, Fabiani, Beck, & Ro, 2009) and has been suggested to reflect pulsed inhibition of neural processing (Klimesch, 2012; Mathewson et al., 2011). Despite several studies replicating and extending this phase-specific influence of alpha oscillations on perception (Mathewson et al., 2012, 2014; Busch, Dubois, & VanRullen, 2009), other effects of the alpha oscillatory signal on perception, such as differences in peak frequency, are not well understood. The current study assessed the relationship between alpha oscillation frequencies and visual information processing in early visual cortex. Of particular interest was determining how differences in alpha oscillation frequencies might reflect the temporal dynamics of feedback processing in visual cortex for conscious perception.

An influential theory of consciousness has proposed that feedback from higher to lower cortical areas is essential for conscious perception (Super, Spekreijse, & Lamme, 2001; Lamme & Roelfsema, 2000). Indeed, several different types of visual masking phenomena, in which an object or a mask suppresses a preceding target stimulus from perception, have been suggested to reflect the suppression of feedback target activity by feedforward processing of the mask (Tapia & Beck, 2014; Fahrenfort, Scholte, & Lamme, 2007; Enns, 2004; Ro, Breitmeyer, Burton, Singhal, & Lane, 2003). Consistent with this feedback account of visual masking, studies have shown the importance of late feedback activity in visual cortex for visual awareness (Fahrenfort et al., 2007; Ro et al., 2003). More recent and compelling neurophysiological evidence for this feedback account comes from studies in nonhuman primates demonstrating late alpha band activity in V1 in cortical feedback layers (van Kerkoerle et al., 2014). Most convincingly, after microstimulation of V1, van Kerkoerle et al. recorded feedforward activity in the gamma oscillatory frequency band (40–200 Hz) in the input layers (i.e., layer 4) of V4 but feedback activity in the alpha oscillatory frequency band in feedback layers 1, 2, and 5 in V1 after stimulation of extrastriate visual cortex area V4. A recent study in humans has corroborated these findings using magnetoencephalography and Granger causality analyses, which suggest a neural distinction between feedforward activity in the gamma oscillatory frequency band and feedback in the alpha band (Michalareas et al., 2016). An fMRI study provides further evidence that contextual feedback

processing may occur in superficial cortical feedback layers (Muckli et al., 2015).

Based on these studies, and because alpha activity has long been implicated in perceptual selection, inhibition, suppression (Jensen & Mazaheri, 2010; Worden et al., 2000; Berger, 1929), and, more recently, feedback processing (van Kerkoerle et al., 2014), the main aim of the current study was to assess how differences in alpha oscillations between individuals may affect visual cortical processing times for conscious perception. If alpha oscillations reflect feedback activity that is essential for conscious perception, peak alpha frequencies should correlate with the timing of late information processing in early visual cortex. To measure alpha oscillatory activity and the timing of neural activity for visual awareness, scalp EEG activity was recorded while participants performed a target detection task during metacontrast masking, a type of backward masking by a visual stimulus that does not overlap spatially with the preceding target (Ogmen, Breitmeyer, & Melvin, 2003; Breitmeyer, 1984). To further assess the timing of information processing in early visual cortex and how it may relate to alpha oscillation frequencies, optimal latencies for visual suppression were parametrically measured using single-pulse TMS to early visual cortex. Additionally, because several studies have suggested an important role of the P1 component in visual perception (Klimesch, 2011; Thut et al., 2003), the P1 and subsequent P2 visual evoked potentials were also compared with alpha oscillation frequencies. As a further but more indirect measure of cortical feedback processing times (Enns, 2004), individual latencies for metacontrast masking were also computed and compared with alpha oscillations frequencies.

METHODS

Participants

Twenty adults with normal or corrected-to-normal vision were recruited to participate in this experiment. The participants were paid volunteers recruited from the Graduate Center of the City University of New York or via online advertisements. All 20 participants first completed the TMS session of the experiment. Fifteen of those 20 participants returned for a second session on a subsequent day, during which EEG data were recorded while participants performed a metacontrast masking target detection task. EEG data were not collected from five participants for the following reasons: There was an attrition of two participants, another two participants were excluded because visual suppression from TMS was not possible at maximum TMS output intensity, and one participant was excluded because she could not see any of the targets with TMS. An additional two participants were excluded from further data analyses because of high false alarm rates (>25%) on the masking task (28% and 39%), three other participants were excluded because of flat

masking functions across the target disk SOA conditions, and one participant was excluded because of excessive noise in the EEG data. The remaining nine participants (three women, six men; mean age = 26.56 years) met all inclusion criteria and are the focus of the remaining analyses.

Apparatus

All stimuli were presented through a Dell Optiplex 755 desktop computer with an ATI Radeon graphics card connected to a Dell Trinitron 53.3-cm cathode ray tube monitor. The monitor, cycling at a vertical synchronization rate of 100 Hz, was positioned at a viewing distance of 57 cm. Custom software written in C/C++ and DirectX libraries were used to control stimulus presentation and to trigger the TMS and EEG systems.

EEG Recordings

EEG activity was recorded from 12 electrodes that were each connected to analog Grass IP511 amplifier. The electrode coordinates for F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, Oz, and O2 were determined using the International 10–20 electrode placement system. Reference electrodes were placed over the left and right mastoids and electrooculograms were recorded from channels placed above and below the left eye and over the outer canthus of the right eye. Channel impedance was at or below 10 k Ω for all sessions. The continuous EEG activity was sampled at a rate of 1000 Hz with an on-line bandpass filter of 0.1–100 Hz. Activity was referenced online to the left mastoid and rereferenced offline to the average of both mastoids.

TMS Stimuli and Procedures

For TMS, we used a Cadwell MES-10 polyphasic stimulator attached to a circular coil that was 9 cm in diameter. The visual stimuli consisted of individual horizontal or vertical gray lines (6.36 cd/m²) that briefly appeared on a light gray background (14.18 cd/m²). At a viewing distance of 57 cm, the lines were either 0.25° × 0.05° or 0.05° × 0.25° of visual angle and were positioned 0.25° to the right of the fixation square, which was 0.25° × 0.25° in size and 6.36 cd/m² in luminance. For each trial, a line would appear on the screen for 10 msec and was followed by a single TMS pulse at varying latencies. The SOA between the visual stimulus and TMS ranged from 55 to 155 msec in steps of 10 msec and was randomized across trials (Figure 1).

To ensure that participants could accurately detect the lines in the absence of TMS, familiarization and practice blocks were run before any TMS was introduced. For the familiarization block, participants simply advanced through the trials, viewing the stimuli, and performance was not recorded. In a subsequent practice block, participants' performance was recorded, and line discrimination

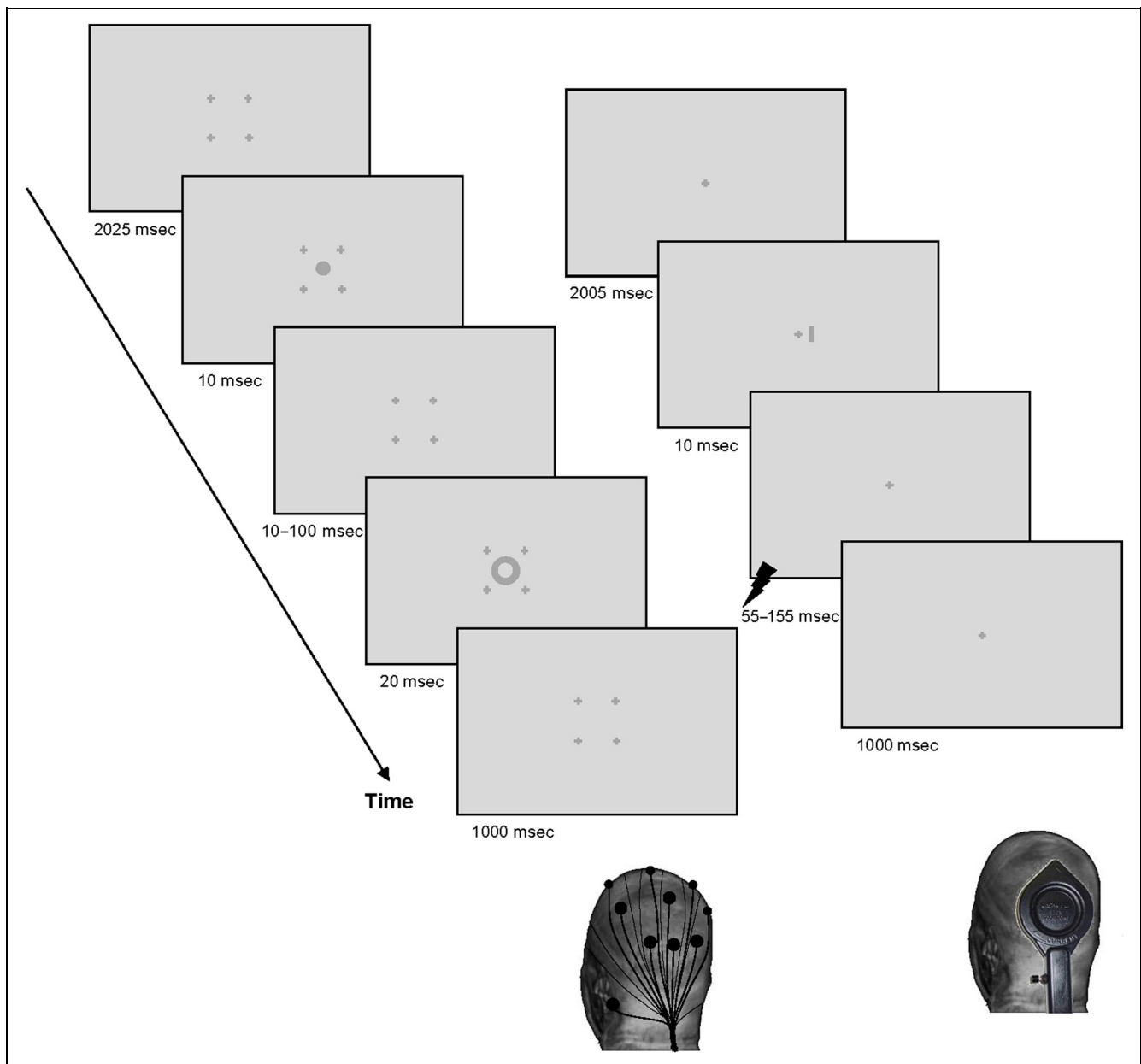


Figure 1. Stimuli and procedures. Left: Schematic depiction of the metacontrast masking stimuli and timing parameters during EEG recordings. After the prestimulus period on each trial, which was used to calculate alpha power and frequency, a circular target appeared at the center of the screen and was followed by a metacontrast mask at varying latencies. Right: Schematic depiction of the line detection task during TMS. After the prestimulus period on each trial, a horizontal or vertical line appeared at the center of the screen and was followed by a single TMS pulse at varying latencies.

accuracy had to be at least 80% for the experiment to continue.

Next, optimal TMS site and intensity for inducing visual suppression was determined by first positioning the base of the TMS coil 2 cm above and 1 cm to the left of the participant's inion, with stimulation intensity set to 50% (1.1 T). For each trial, a square identical in color and size to the fixation would appear for 10 msec with a TMS pulse delivered 95 msec after the visual stimulus onset. The location of the square on the screen was identical to the location of the line stimuli used for the detection

task. Participants reported if they could detect the square. The coil position and TMS intensity were adjusted incrementally until the participant reported not seeing the stimulus for three of five trials. The optimal location on the head was then marked to ensure identical stimulation throughout the session. The average threshold TMS intensity was 70.0% of maximum stimulator output intensity, with a range of 64–90%. TMS intensity during the line detection task was set at 10% above each individual's suppression thresholds. To familiarize participants with this 10% stronger stimulation intensity for the line

detection task, participants ran one practice block with TMS at this intensity before beginning the session.

For each trial of the TMS session, participants reported whether or not they saw the orientation of the line. Although horizontal and vertical lines were presented during the TMS, the performance measure of interest in this study was whether or not participants detected the line on each trial (i.e., a simple detection task). Twelve blocks of 22 trials were run for each session, yielding 24 total trials for each of the 11 SOAs. The suppression curve for each participant was derived from the percentage of trials across the SOAs in which the participant reported seeing the line orientation. The SOA with the smallest percentage of seen trials was determined to be the SOA of maximum suppression. All participants completed the TMS session on the first day of testing, which took a total of approximately 1.5 hr for the informed consent process, localizing visual cortex, practice on the task, frequent breaks to prevent overheating of the TMS coil, and the completion of a total 264 trials.

Metacontrast Masking Stimuli and Procedures

During the second session, approximately 1 week later, participants completed a metacontrast masking task while EEG activity was recorded. The stimuli were dark gray on a light gray background and consisted of surrounding fixation crosses, a target disk, and a surrounding mask (Figure 1). The fixation crosses, disk, and metacontrast mask had a luminance of 6.36 cd/m², and the background had a luminance of 14.18 cd/m². The diameter of the disk subtended 1° of visual angle, the metacontrast mask subtended 2°, and each of the fixation crosses subtended 0.5° and was positioned at the corners of an imaginary 2.0° × 2.0° square.

On 91% of the trials during the EEG and metacontrast masking session, the target disk appeared 2025 msec after the start of each trial and remained on the screen for 10 msec. This long prestimulus time window was used to increase the resolution of the frequency-based analyses. The SOA between target disk and metacontrast mask varied across 10 test conditions, in 10-msec intervals, from 20–110 msec. The mask appeared after the corresponding ISI (SOA minus target duration time of 10 msec) and remained on the screen for 20 msec. Trials with response latencies over 1000 msec with respect to target onset were not included for behavioral analysis. A control condition was also included (9% of the trials) in which no target was presented but a mask appeared 2025 msec after the start of the trial. Each condition consisted of 80 trials, for a total of 880 trials per session, which lasted approximately 1.5 hr when including time for EEG preparation, practice on the task, and breaks to prevent fatigue. Participants were instructed to fixate on the center of the screen and to report on each trial whether they saw a circular disk in the metacontrast masking task. The in-

structions were to press the left button of a mouse when the target disk was detected and to press the right mouse button when the target disk was not detected. A practice block was included to familiarize the participants with the task, but trials from this block were not included for analysis.

Data Analyses

The continuous EEG data were segmented into 880 epochs from 2025 msec before the onset of the target stimulus to 1000 msec after target onset. Trials with artifacts greater than 100 μV were rejected before frequency analyses. To determine each participant's peak alpha-band frequency, a discrete Fourier transform was performed on the EEG data spanning a 2000-msec prestimulus time window that began at the start of the segmented epoch and ended at 25 msec before stimulus onset. Peak alpha frequency was defined as the frequency with maximum power for each participant in the 8–12 Hz range. Alpha frequency was converted into alpha period in milliseconds by the following equation: $T = 1/f \times 1000$, where T = alpha period and f = alpha frequency.

A regression analysis was initially conducted on the TMS visual suppression data. Further analyses were then conducted to determine the sources of any significant components. For comparisons between TMS suppression latencies, two-tailed t tests were used to assess significant differences in target visibility as a function of SOA. The mean peak TMS suppression latency was defined as the mean of the maximum suppression latency across participants.

The ERPs were extracted by first filtering the raw EEG with a Butterworth bandpass filter (0.1–30 Hz) and then segmenting the continuous data into epochs of 800 msec, with a 200-msec prestimulus baseline period used for baseline correction and a 600-msec poststimulus period. The latencies of the P1 visual evoked potentials to the target stimulus were computed across all SOAs and were defined for each participant as the peak positive inflection point within 75 and 175 msec after stimulus onset. The P2 component latencies were defined as the peak positive inflection point within 100 msec after the N1 component. The N1 component, defined as the peak negative inflection within a 100-msec window after each individual's P1 latency, was not analyzed further and was computed only to extract the P2 component.

To compute the metacontrast masking functions, the percentage of hits for target-present trials was calculated for each participant in each SOA condition. A logit function was then fit to each participant's data. This sigmoidal rather than a U-shaped function was used because the experimental design did not include any target-to-mask SOAs shorter than 20 msec, when metacontrast masking typically becomes less effective and results in quadratic-shaped functions (e.g., see Figure 2 of Boyer & Ro, 2007 and Figure 3 of Ogmen et al., 2003). Within the range of

SOAs used, masking effectiveness increases monotonically with SOA. Because the detection rate of some participants was around or above 50% at the shortest SOA, a 75% detection rate was computed as the masking latency from the fitted functions rather than an interpolated 50% threshold detection rate, which would have been estimated from missing data. Because performance increased monotonically across a window of SOAs, different threshold estimates (e.g., 50% vs. 75%) should not bias the results in any systematic way.

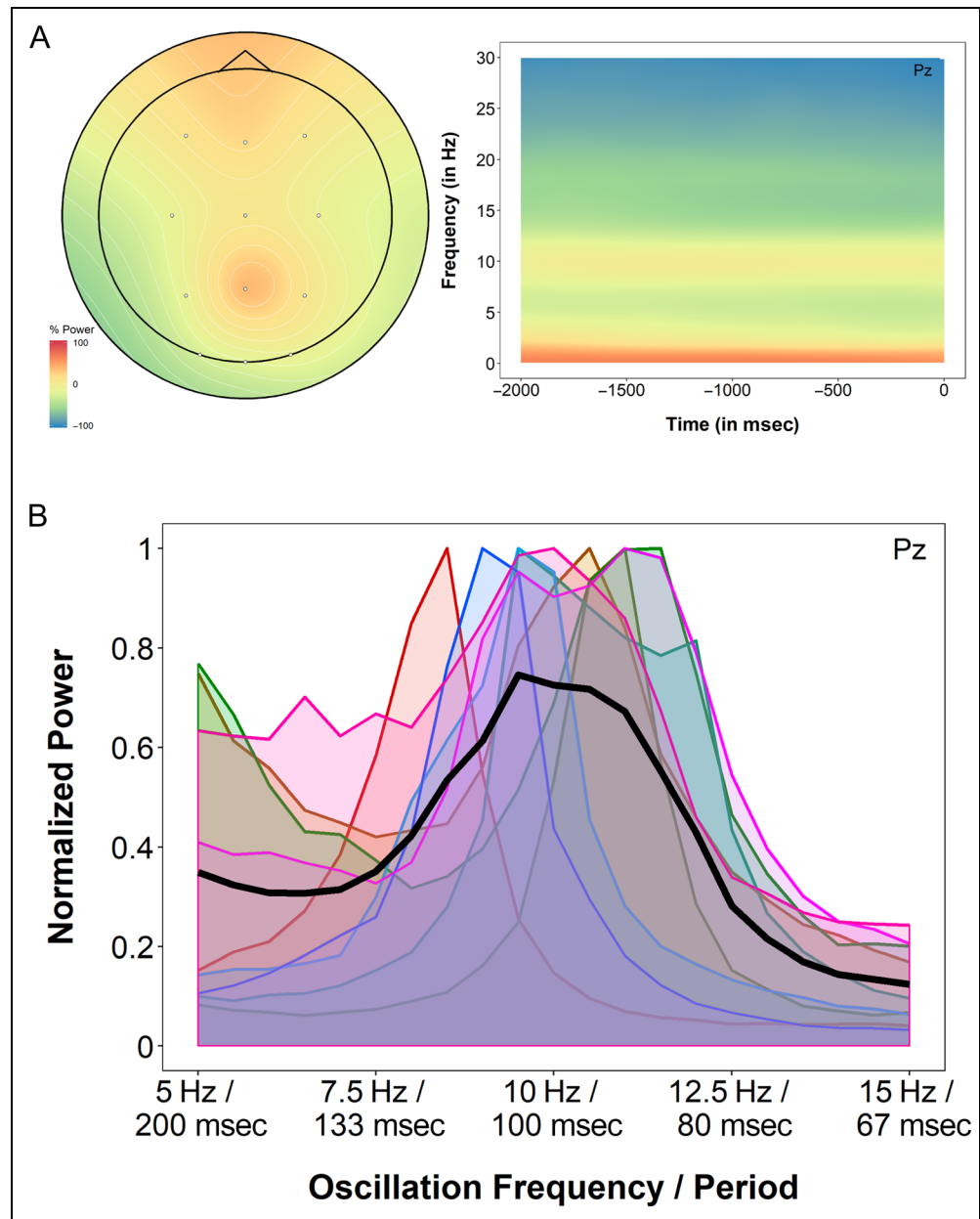
Pearson correlation coefficients, along with Bayes Factor correlation analyses, were computed to assess the relationships between alpha frequency, peak TMS suppression latencies, metacontrast masking threshold latencies, and early visual evoked responses (i.e., the P1 and P2). Because inverse relationships were expected

between alpha frequency and latencies measuring visual processing time in early visual cortex, as well as positive relationships between TMS suppression, masking thresholds, and visual evoked responses, one-tailed tests were employed. Post hoc Bayesian sequential analyses, which assess whether sufficient evidence has accumulated during sequential data collection and are often used as a stopping rule in clinical studies, were also conducted to indicate sufficient sample sizes for the significant correlations.

RESULTS

Scalp EEG activity was recorded while participants performed a metacontrast masking task, in which a briefly presented target stimulus precedes the presentation of

Figure 2. Normalized alpha power distributions. (A) The topographic map illustrates the spatial scalp distribution of alpha power (8–12 Hz) averaged across participants, whereas the spectrogram shows the normalized power across different frequency bands during the prestimulus interval from electrode Pz. Peak alpha power and frequency were extracted from a 2-sec window that ended 25 msec before target stimulus onset. (B) The thin colored lines represent each individual's normalized power from electrode Pz as a function of oscillation frequency (in Hz)/period (in msec). The thick black line represents the mean.



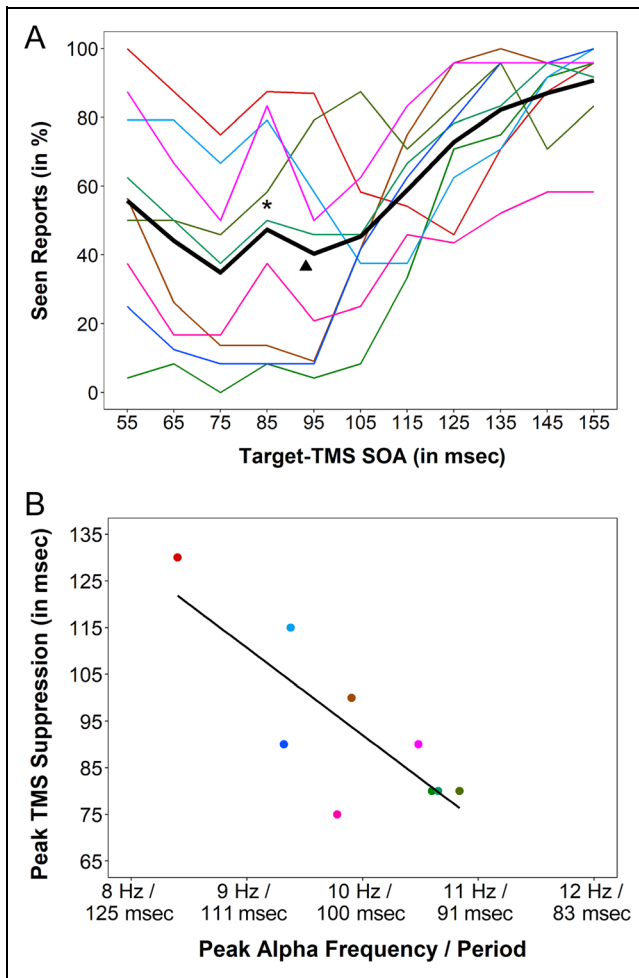


Figure 3. Visual cortex suppression from TMS and its relationship to alpha oscillation frequency. (A) The TMS visual suppression functions for each individual (thin colored lines with the same color coding as Figure 2) and the mean suppression function across individuals (thick black line). The arrowhead indicates the mean peak suppression latency, which is in a second window of suppression that is separated from an earlier window by a significant increase in detection, as indicated by the asterisk. (B) There is a highly significant relationship between individual alpha frequency/period and peak TMS visual suppression latency.

a subsequent mask (Figure 1). As with other forms of backward masking, this form of masking has been suggested to be effective because the feedforward activity from the mask interferes with feedback processing of the target in early visual cortex (Enns, 2004; Ro et al., 2003). In addition to recording alpha oscillatory and visual evoked responses with EEG, single-pulse TMS was applied at varying intervals after the brief presentation of a target to further assess processing times in early visual cortex. Comparisons of peak alpha oscillation frequencies, TMS suppression latencies, the latencies of visual evoked responses, and metacontrast masking functions were made to assess whether alpha oscillations reflect the timing of specific neural processes in visual cortex.

The peak alpha oscillation frequency was calculated for each participant by computing a discrete Fourier transform¹ for a 2-sec time window that ended 25 msec before stimulus onset. Although the mean peak alpha oscillation amplitude was largest over Pz and the mean peak alpha oscillation frequency/period across individuals was 9.93 Hz/101 msec ($SD = 0.80$ Hz/8.75 msec, range = 8.40–10.84 Hz/92.3–119.0 msec), there was considerable variation in peak alpha frequency/period across participants (Figure 2).

A regression analysis on the TMS suppression data revealed a significant quartic (W-shaped) function ($R^2 = .62$, $p < .001$) because suppression from TMS was at its maximum in two time windows: the first between 65 and 75 msec and the second between 95 and 105 msec (Figure 3A). To statistically confirm that these two time windows are distinct, post hoc t tests were used to compare detection performance at sequential SOAs. There was a significant increase in detection rates between the peak suppression latency of 93.3 msec ($SD = 18.54$ msec, range = 75–130 msec) and the preceding SOA, $t(8) = 3.67$, $p = .006$, further demonstrating that there are two windows of visual suppression from TMS. Maximum TMS suppression latency was defined as the interval between visual stimulus onset and the TMS SOA that produced the largest magnitude of reported misses, regardless of suppression window. For two participants who had two adjacent SOAs meeting this criterion (pink and light blue lines in Figure 3A), the average of the two SOAs was used as the participants' maximum suppression point. As with peak alpha oscillation frequency, there was considerable variability in the maximum suppression time of the TMS.

To assess whether alpha oscillation frequency/period may reflect the pace of feedback processing, the relationship between alpha oscillations and maximum TMS suppression latencies was assessed. As can be clearly seen in Figure 3B, peak alpha oscillation frequency/period was significantly correlated with maximum TMS suppression latency ($r = -.81$, $p = .004$; $BF_{10} = 15.64$). This strong negative correlation, which remained significant after a false discovery rate correction for multiple comparisons, indicates that participants with slower peak alpha oscillation frequencies had longer maximum TMS suppression latencies and that participants with faster peak alpha oscillation frequencies had shorter maximum TMS suppression latencies. In other words, higher alpha oscillation frequencies, which have shorter time intervals between complete cycles, reflect faster processing times that result in earlier maximum TMS suppression latencies. A post hoc Bayesian sequential analysis, which indicated that this correlation remained “strong” after only four participants, provides evidence that the sample size of nine participants was more than sufficient to demonstrate this effect. Furthermore, this correlation between alpha peak frequency and maximum TMS suppression latencies remains statistically significant in a larger sample

size of 14 participants ($r = -.67, p = .009$), which includes the additional five participants who were excluded from the main data analyses because of their inadequate performance on the masking task (see the Methods section). It

is also significant using a Spearman's correlation analysis ($\rho = -.63, p = .016$).

Whereas the mean ERPs to the target were reliably measured with little influences from the subsequent mask

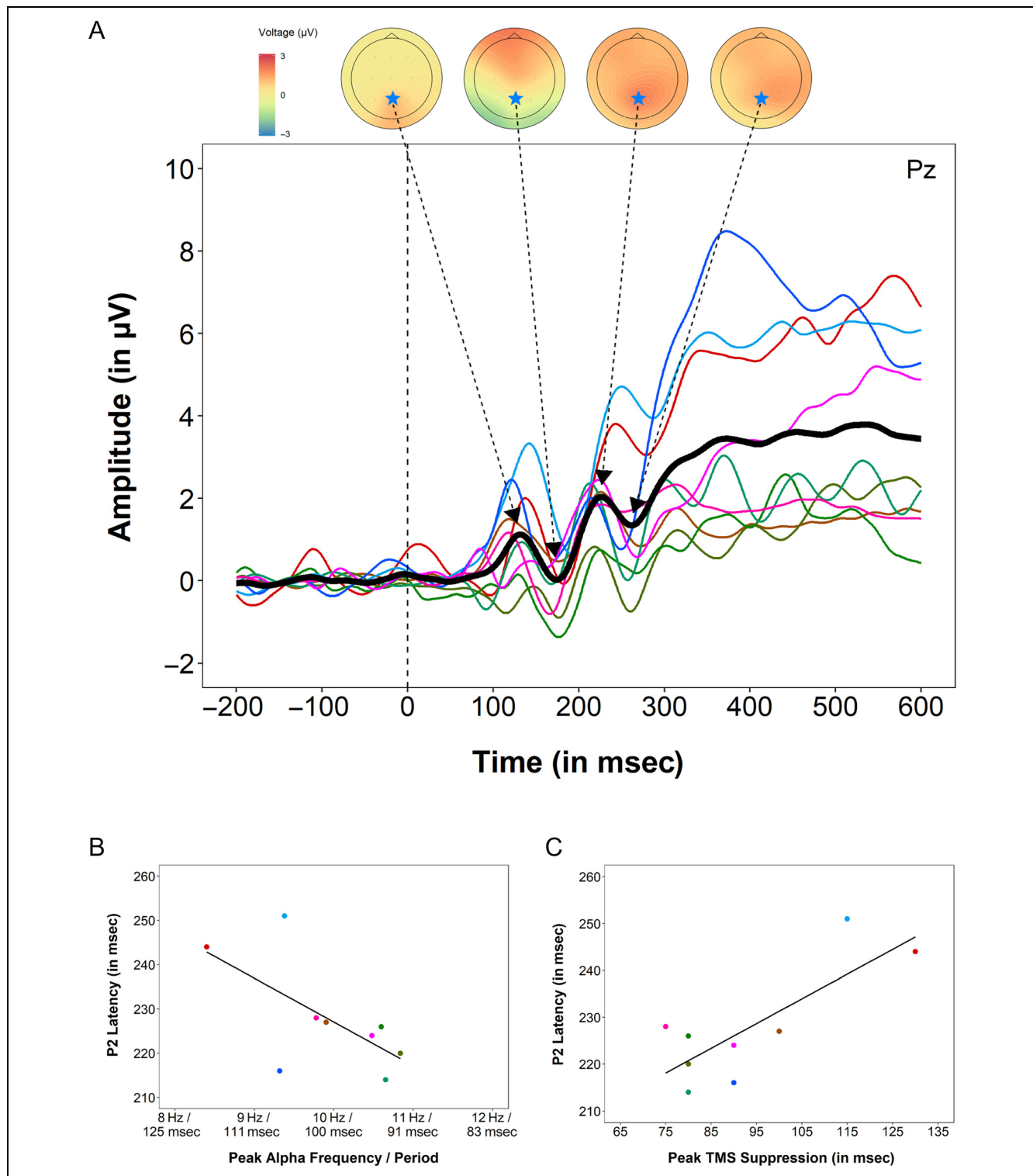


Figure 4. ERP responses to masked targets and their relationships to peak alpha frequency. (A) ERP responses to masked targets for each individual participant (thin colored lines with the same color coding as in Figures 2 and 3) and the mean ERPs across individuals (thick black line). (B) Peak alpha frequency/period is significantly correlated with the P2 ERP component peak latency in response to the target stimulus. (C) Peak TMS suppression time is also significantly correlated with the P2 ERP peak latency.

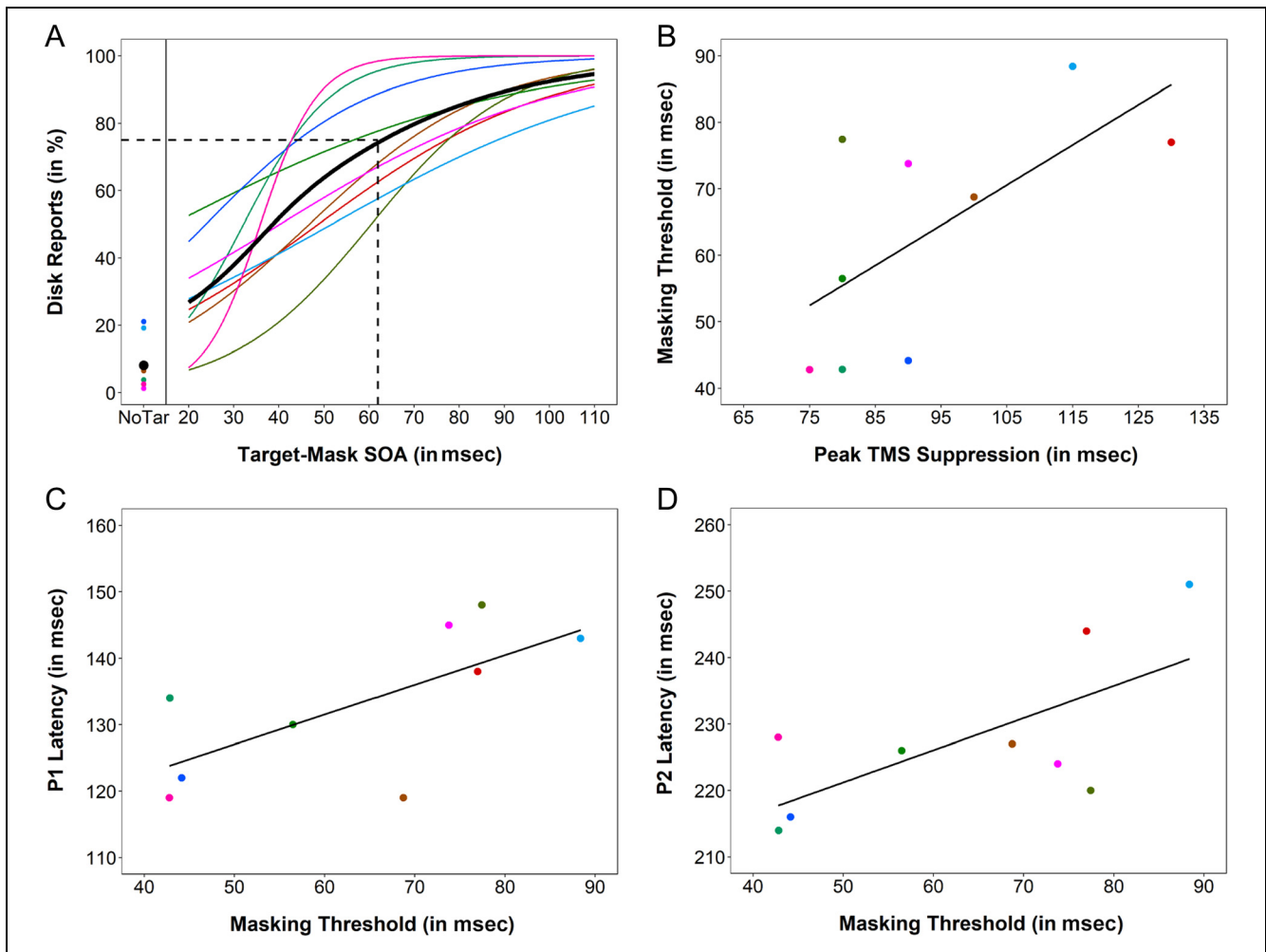


Figure 5. Metacontrast masking and its relationship to TMS suppression and ERPs. (A) The individual (thin colored lines) and mean (thick black line) metacontrast masking functions. The scatterplots illustrate significant relationships between each individual's mean threshold masking latency and (B) TMS suppression latency, (C) the P1 ERP component, and (D) the P2 ERP components. Color coding as in Figures 2 through 4.

(Figure 4A), ERPs to the masks were minimal and strongly affected by the preceding target stimulus (Supplementary Figure 1A²).³ Note that, in contrast to our previous study (Mathewson et al., 2009), which used only one target-to-mask SOA of 58.5 msec and equal proportions of mask-only and target-only trials, the current study used a range of target-to-mask SOAs that spanned from 20 to 110 msec and included 1/11th mask-only trials but not a target-only condition. Therefore, the mask-related activity could be estimated from either the ERPs time-locked to mask onset (Figure S1A) or from the mask-only trials (Figure S1B). In both cases, the subtraction procedure produces systematic decreases in ERP amplitudes, especially for the later components, and negligible shifts in latency (Figure S1C and D). Because the effects of the mask cannot be accurately isolated in the presence of a preceding target and also because the different mask-related activity extraction methods result in different estimations of the effects of the mask, the minimally influential mask-related activity was not subtracted from the subsequent target-related ERP analyses.

The P1 and P2 ERP component latencies to the targets were defined as the time after target onset when the first and second positive potentials were at their peak.⁴ Both peak alpha frequencies/periods and maximum TMS suppression latencies were significantly correlated only with the later P2 (Figure 4B and C) but not the earlier P1 ERP latencies. The significant negative correlation between peak alpha frequencies and the P2 component ($r = -.64, p = .03; BF_{10} = 3.57$) but not the P1 component ($r = .21, p = .30; BF_{10} = 0.63$) indicates that participants with faster peak alpha frequencies/periods had earlier P2 component latencies whereas participants with slower peak alpha frequencies/periods had later P2 components. Similarly, the P2 ($r = .80, p = .005; BF_{10} = 13.68$) but not the P1 ($r = .23, p = .27; BF_{10} = 0.67$) visually evoked response component latencies were significantly correlated with TMS suppression latencies (Figure 4C). Participants with earlier P2 component latencies had earlier maximum TMS suppression latencies, and vice versa. A post hoc Bayesian sequential analysis showed that this alpha frequency correlation

with P2 latencies was “moderate” after three participants, dropped to “anecdotal” after six participants, and then was “moderate” again after eight participants, demonstrating some variability in this relationship. The post hoc Bayesian sequential analysis on the TMS suppression latencies correlation with P2 latencies showed that this relationship remained “strong” after six participants. These post hoc Bayesian sequential analyses provide evidence that the sample size was sufficiently large to demonstrate these effects.

The mean masking latency for a 75% detection rate across participants was 63.5 msec ($SD = 17.35$ msec, range = 42.81–88.40 msec; Figure 5A). Mean masking latency was not significantly correlated with peak alpha frequencies ($r = -.19, p = .31; BF_{10} = 0.60$). However, masking latencies were significantly correlated with maximum TMS suppression latencies (Figure 5B; $r = .65, p = .03; BF_{10} = 3.63$), consistent with previous suggestions that these two types of disruptions on visual processing may be highly related (Breitmeyer, Ro, & Ogmen, 2004). A post hoc Bayesian sequential analysis, which indicated that this effect became “moderate” after eight participants, provides evidence that this sample size was sufficient to demonstrate this effect. Both the P1 and P2 visual evoked response latencies were also significantly correlated with threshold masking latencies ($r = .69, p = .02; BF_{10} = 4.94$ and $r = .68, p = .02; BF_{10} = 4.721$, respectively; Figure 5C and D). Post hoc Bayesian sequential analyses, which indicated that the masking threshold correlations with the P1 latencies became “moderate” after eight participants and that the masking threshold correlations with the P2 latencies became and remained “moderate” after six participants, provide evidence that there was a sufficient number of participants to demonstrate these effects.⁵

Table 1 provides a summary of the different correlational analyses and shows clear relationships between alpha oscillatory activity, neural processing times in visual cortex as indexed by TMS suppression times, and late (P2) visual evoked responses. Together, these results

Table 1. Pearson Correlation Matrix for the Different Latency Variables

	Mean (msec)	Correlations			
		TMS	Masking	P1	P2
Alpha	9.93 Hz/101	-.81**	-.19	.21	-.64*
TMS	93.3	–	.65*	.23	.80**
Masking	63.5	–	–	.69*	.68*
P1	133.1	–	–	–	.25
P2	227.8	–	–	–	–

* $p < .05$.

** $p < .05$, false discovery rate-corrected.

suggest that alpha oscillations may reflect an important role of late feedback activity on visual awareness.

DISCUSSION

The main results of this study show systematic relationships between peak alpha-band oscillatory frequency of parietal EEG activity, maximum TMS visual suppression times, and late visual (P2) evoked responses. In addition to a strong inverse relationship between peak alpha frequency and maximum TMS visual suppression latency, there was a significant positive relationship between TMS suppression latency with the later P2 ERP component, but not the earlier P1 component. There were also positive relationships between alpha frequency and the later P2 component, as well as a positive relationship between metacontrast masking threshold latencies and the optimal interval for suppressing visual perception with TMS of early visual cortex (Railo & Koivisto, 2012; Breitmeyer et al., 2004), but these were not statistically significant after false discovery rate corrections for multiple comparisons.

Alpha Oscillations and the Timing of Visual Perception

Alpha oscillation cycle durations systematically varied between participants. Individuals with faster alpha oscillation cycles had faster visual cortical relay times, as assessed with TMS over visual cortex. This shows a direct relationship between the duration of an alpha period and the timing of visual processing in visual cortex. Although this relationship may imply that the alpha oscillation frequency reflects a static processing time for cortical processing and subsequent perception, it is important to note that alpha oscillation frequencies are not static. For example, several recent studies have now shown that alpha oscillation frequency can change depending on the task (Webster & Ro, submitted; Wutz, Melcher, & Samaha, 2018; Haegens et al., 2014). Therefore, rather than a static duration of alpha oscillation periods and cortical processing times within a given individual, it is more likely that the timing of visual perception varies as a function of changing alpha frequencies that may be dependent on cognitive state. Regardless of the mechanisms that may change alpha frequencies within a given individual across time and cognitive tasks, these results provide indirect but converging evidence and add to a growing body of literature that demonstrates that alpha oscillations reflect feedback processing in visual cortex (Michalareas et al., 2016; Muckli et al., 2015; van Kerkoerle et al., 2014).

Mechanisms of TMS-induced Visual Suppression

The mean maximum TMS suppression latency was within a later TMS suppression window, suggesting that TMS is

most effective at disrupting conscious visual perception when applied to early visual cortex predominantly during feedback processing. Note that the mean TMS suppression latency is later than the earlier strongest suppression latency because, although suppression was overall larger and more consistent at the shorter SOAs, thereby producing a larger suppression trough, there was maximum suppression at much later SOAs in some participants (e.g., light blue and red lines in Figure 3A). The earlier intervals of suppression may reflect TMS disruption of predominantly feedforward processes, whereas the later intervals of suppression may reflect more TMS-induced disruption of feedback processing. This result is consistent with previous studies that have also demonstrated two visual suppression peaks from TMS of visual cortex (Corthout, Uttl, Ziemann, Cowey, & Hallett, 1999), albeit with slightly different latencies.

Although the maximum TMS suppression interval was within a second suppression window and later than typical latencies measured for the C1 ERP component (approximately 70–80 msec), the mean maximum TMS visual suppression latency of 93.3 msec after stimulus onset may seem too early to directly affect feedback processing in visual cortex. However, the effects of the TMS over visual cortex may last about 50 msec, as estimated from the extent of visual suppression across SOAs. Further, yet indirect, support that the TMS may be acting more on later, feedback processes in visual cortex comes from the significant correlation between the maximum TMS latency for producing maximum visual suppression and the P2 ERP component. This latter correlation suggests that if late feedback activity is essential for conscious perception, then single-pulse TMS specifically at the P2 component latencies might also disrupt conscious perception.

Previous studies have demonstrated that TMS produces visual suppression independently from masking due to phosphenes (Kammer, Puls, Strasburger, Hill, & Wichmann, 2004) and that the TMS threshold intensity for phosphene perception is lower compared with that for visual suppression (Kammer, Puls, Erb, & Grodd, 2004; Kastner, Demmer, & Ziemann, 1998). Furthermore, Kastner et al. (1998) report that phosphenes are not reliably induced at higher TMS intensities that produce visual suppression. The TMS intensities for the current study were set at 10% above the threshold for visual suppression. Therefore, it is unlikely that participants may have perceived many phosphenes in this study. However, albeit a remote possibility, phosphenes from TMS could have interfered with target detection on a small proportion of trials in this study.

The P1 Component: Inhibition or Alpha Synchronization?

Although one study has suggested that TMS at the latency of the P1 component may maximally interfere with

visual processing (Thut et al., 2003), that was not the case in this study. Instead, the mean peak latency of the P1 component (133 msec) was found to be later than the mean peak latency for maximum TMS visual suppression (93.3 msec). Another study using combined TMS and EEG has also shown that the P1 response can peak at a later time interval than optimal TMS suppression latencies (Wokke, Sligte, Steven Scholte, & Lamme, 2012). Based on these previous and current results, the P1 ERP component may not be a direct reflection of the timing of feedback neural activity. Rather, it may reflect a combination of inhibition of task-irrelevant neural structures and networks, inhibition in task-relevant networks to increase signal-to-noise inhibition, and a delayed post-synaptic potential response that includes both feedforward as well as feedback responses (Wokke et al., 2012; Klimesch, 2011). This interpretation of the P1 is consistent with findings that show that both the amplitude and latency of the P1 component are influenced by cognitive states and tasks (Klimesch, 2011, 2012). It may also explain the lack of a correlation between the P1 and alpha frequencies, TMS suppression latencies, and the P2 component.

Another intriguing possibility is that the P1 may reflect the synchronization of ongoing alpha oscillations with evoked responses, which would be affected by prestimulus alpha amplitude and phase, but not frequency. The correlation between the P1 and the metacontrast masking latencies provides some indirect support for this possibility because metacontrast masking effectiveness at intermediate SOAs varies across trials, likely reflecting variations in the timing of feedforward and feedback processing that is dependent on the alpha oscillation phase (Jaegle & Ro, 2014; Mathewson et al., 2011). This account of the P1 would also explain its variable onset latencies across different studies and the lack of a correlation with the P2 latencies and alpha oscillation frequencies/periods. In line with this interpretation, peak alpha frequency/period, although not significantly correlated with the P1 component latency, was found in a post hoc analysis to be significantly correlated with the P1–P2 difference latency over Pz ($r = -.71$, $p = .016$; $BF_{10} = 5.83$). This suggests that the P1 and P2 components likely reflect one complete alpha cycle of processing, with the duration between these components equal to the participants' inherent oscillation frequency but a variable poststimulus cycle onset latency that is dependent on prestimulus alpha oscillation power and phase. Future studies manipulating prestimulus alpha oscillation power and phase may determine whether alpha can systematically affect the P1 amplitude and its onset latency.

The P2 Component: Feedback Processing and Conscious Perception

The P2 component was significantly correlated with optimal TMS suppression times, and it correlated with alpha

oscillation frequencies and metacontrast masking latencies before corrections for multiple comparisons. These relationships suggest that the P2 may reflect late, feedback processes that are crucial for visual perception and may indicate the time at which an observer consciously perceives a visual stimulus. If such is the case and based on the findings that (1) P1 latency does not correlate with either the alpha oscillation period or the P2 latency and (2) alpha oscillation period does correlate with the P2 latency as well as the P1–P2 latency difference, then the following equation may best summarize the time to visual awareness: $P2_{\text{latency}} = P1_{\text{latency}} + \alpha_{\text{period}}$. Given the variable nature of P1 onset latencies as well as fluctuating durations of alpha periods, future studies that directly manipulate cognitive tasks and states that change P1 latencies and alpha periods will be able to test whether this equation derived from the current results is generalizable.

Metacontrast Masking: Inhibition of Feedforward and Feedback Processes

Unlike with alpha frequency, ERPs, and TMS suppression, where a clear and distinct peak, maxima, or minima could be computed, the metacontrast masking latency at which target detection was at 75% reflects only one point within a larger time window of masking. If a mask appears at any time within approximately 20–100 msec after a target stimulus, the target may be effectively masked and undetected. In other words, although a masking “threshold” can be reduced to a single number, this threshold is unlikely to fully capture the extent of masking effectiveness. Furthermore, metacontrast masking may involve not only feedback inhibition but also inhibition of feedforward processes, such as transient on sustained inhibition (Breitmeyer, 1984) and inhibition of offset responses (Macknik & Livingstone, 1998). As a result, an effective masking temporal window likely includes masking due to both lateral and/or feedforward-only interactions at the earlier SOAs as well as target feedback inhibition from feedforward mask activity at the later SOAs. Consistent with this interpretation that masking may result from a range of interacting neural processes, both the P1 and P2 components were significantly correlated with masking latency.

Not only were threshold metacontrast masking latencies significantly correlated with both the P1 and P2 ERP components but they were also significantly correlated with maximum TMS suppression latencies. Together, these correlations suggest that metacontrast masking and likely other types of visual masking affect perception not only through suppression of feedback target-related activity by the mask but also through suppression of feedforward responses, lateral inhibition, as well as interactions between sustained, transient, and/or on/off responses (Macknik & Livingstone, 1998; Breitmeyer, 1984). These multiple factors that likely

contribute toward effective metacontrast masking may explain why there was also only a moderate relationship between TMS suppression latencies and metacontrast masking, as well as why alpha oscillation frequencies were not directly correlated with masking latencies. Further studies using types of metacontrast masking that produced a U-shaped nonmonotonic function, rather than the Type A monotonic type of function measured here, may demonstrate a more direct relationship between alpha oscillations and visual masking.

Conclusion

Taken together, these findings are consistent with several recent studies that indicate a causal relationship between alpha oscillations and perceptual awareness. For example, modulations of alpha power with rhythmic TMS at an alpha oscillation frequency affects visual detection (Thut et al., 2011) and parietal cortex alpha entrainment affects perception in a phase-dependent manner (Jaegle & Ro, 2014). In the alpha frequency domain, Cecere, Rees, and Romei (2015) demonstrated a link between peak alpha frequency of occipital EEG activity and the duration of perception for the audio-visual double-flash illusion and showed that entrainment of neural activity at different alpha frequencies via transcranial alternating current stimulation lengthens and shortens the duration of the illusion dependent on the frequency of stimulation. Similar results have been obtained with two-flash fusion (Samaha & Postle, 2015) and illusory jitter (Minami & Amano, 2017). Interestingly, recent findings even suggest that perceptual processing speeds may vary depending on alpha oscillation frequencies that may be modulated according to task demands (Wutz et al., 2018). Together, these results demonstrate that alpha oscillations are causally linked to the temporal constraints of perceptual awareness.

Given this abundance of evidence demonstrating a direct role of alpha oscillations in modulating perception and that late neural activity in the alpha oscillatory band reflects feedback processing for visual awareness (van Kerkoerle et al., 2014; Lamme & Roelfsema, 2000), the current findings indicate that visual information processing is modulated at an alpha frequency. They demonstrate a strong relationship between the timing of visual processing in early visual cortex and suggest that alpha oscillations reflect the sampling and filtering of external input for our conscious perception. Importantly, this peak alpha oscillation frequency varies between individuals, as well as within individuals under different contexts (Webster & Ro, submitted), which may explain why some individuals may sometimes be better at detecting visual events than others. Together, these results suggest that the frequency of alpha oscillations reflect a neural processing clock speed that paces visual processing in early visual cortex for visual perception.

Acknowledgments

This research was funded by NSF BCS grant 1358893/1561518. I thank Miriam San Lucas for assistance with data collection and Dr. Jeremy Fesi for data acquisition and preliminary data analyses. Dr. Fesi is now at the U.S. Marine Corps Behavioral Health Branch, which restricts coauthorship because of potential competing interests.

Reprint requests should be sent to Tony Ro, Programs in Psychology and Biology, The Graduate Center, City University of New York, 365 Fifth Avenue, New York, NY 10016, or via e-mail: tro@gc.cuny.edu.

Notes

1. Nearly identical results were obtained using a wavelet analysis.
2. Supplementary material for this paper can be retrieved from http://rolab.ws.gc.cuny.edu/files/2019/03/Ro_JOCN_2019_SFigs.pdf.
3. Several previous studies have also shown that both response (Fehrer & Biederman, 1962; Fehrer & Raab, 1962) and ERP (Bridgeman, 1986; Jeffreys & Musselwhite, 1986; Andreassi, De Simone, & Mellers, 1976; Vaughan & Silverstein, 1968; Schiller & Chorover, 1966) latencies to targets in metacontrast masking are independent from conscious target detection and minimally influenced by the mask.
4. ERP responses to detected and undetected targets were not significantly different (Supplementary Figure 2).
5. An analysis was also conducted on the slopes of the psychometric functions. However, the slopes of the masking functions did not correlate with alpha frequencies/periods or any other measure. This result should be interpreted with caution however, because the full psychometric function and hence its slope could not be estimated in most subjects given their considerably high detection rates even at the shortest SOA (Figure 5A).

REFERENCES

- Andreassi, J. L., De Simone, J. J., & Mellers, B. W. (1976). Amplitude changes in the visual evoked cortical potential with backward masking. *Electroencephalography & Clinical Neurophysiology*, *41*, 387–398.
- Berger, H. (1929). Über das Elektroenkephalogramm des Menschen. *Archiv für Psychiatrie und Nervenkrankheiten*, *87*, 527–570.
- Boyer, J., & Ro, T. (2007). Attention attenuates metacontrast masking. *Cognition*, *104*, 135–149.
- Breitmeyer, B. G. (1984). *Visual masking: An integrative approach*. New York: Oxford University Press.
- Breitmeyer, B. G., Ro, T., & Ogmen, H. (2004). A comparison of masking by visual and transcranial magnetic stimulation: Implications for the study of conscious and unconscious visual processing. *Consciousness & Cognition*, *13*, 829–843.
- Bridgeman, B. (1986). Visual evoked potentials: Concomitants of metacontrast in late components. *Perception & Psychophysics*, *43*, 401–403.
- Busch, N. A., Dubois, J., & VanRullen, R. (2009). The phase of ongoing EEG oscillations predicts visual perception. *Journal of Neuroscience*, *29*, 7869–7876.
- Cecere, R., Rees, G., & Romei, V. (2015). Individual differences in alpha frequency drive crossmodal illusory perception. *Current Biology*, *25*, 231–235.
- Corthout, E., Uttl, B., Ziemann, U., Cowey, A., & Hallett, M. (1999). Two periods of processing in the (circum)striate visual cortex as revealed by transcranial magnetic stimulation. *Neuropsychologia*, *37*, 137–145.
- Enns, J. T. (2004). Object substitution and its relation to other forms of visual masking. *Vision Research*, *44*, 1321–1331.
- Fahrenfort, J. J., Scholte, H. S., & Lamme, V. A. (2007). Masking disrupts reentrant processing in human visual cortex. *Journal of Cognitive Neuroscience*, *19*, 1488–1497.
- Fehrer, E., & Biederman, I. (1962). A comparison of reaction time and verbal report in the detection of masked stimuli. *Journal of Experimental Psychology*, *64*, 126–130.
- Fehrer, E., & Raab, D. (1962). Reaction time to stimuli masked by metacontrast. *Journal of Experimental Psychology*, *63*, 143–147.
- Haegens, S., Cousijn, H., Wallis, G., Harrison, P. J., & Nobre, A. C. (2014). Inter- and intra-individual variability in alpha peak frequency. *Neuroimage*, *92*, 46–55.
- Jaegle, A., & Ro, T. (2014). Direct control of visual perception with phase-specific modulation of posterior parietal cortex. *Journal of Cognitive Neuroscience*, *26*, 422–432.
- Jeffreys, D. A., & Musselwhite, M. J. (1986). A visual evoked potential study of metacontrast masking. *Vision Research*, *26*, 631–642.
- Jensen, O., & Mazaheri, A. (2010). Shaping functional architecture by oscillatory alpha activity: Gating by inhibition. *Frontiers in Human Neuroscience*, *4*, 186.
- Kammer, T., Puls, K., Erb, M., & Grodd, W. (2004). Transcranial magnetic stimulation in the visual system. II. Characterization of induced phosphenes and scotomas. *Experimental Brain Research*, *160*, 129–140.
- Kammer, T., Puls, K., Strasburger, H., Hill, N. J., & Wichmann, F. A. (2004). Transcranial magnetic stimulation in the visual system. I. The psychophysics of visual suppression. *Experimental Brain Research*, *160*, 118–128.
- Kastner, S., Demmer, I., & Ziemann, U. (1998). Transient visual field defects induced by transcranial magnetic stimulation over human occipital pole. *Experimental Brain Research*, *118*, 19–26.
- Klimesch, W. (2011). Evoked alpha and early access to the knowledge system: The P1 inhibition timing hypothesis. *Brain Research*, *1408*, 52–71.
- Klimesch, W. (2012). Alpha-band oscillations, attention, and controlled access to stored information. *Trends in Cognitive Sciences*, *16*, 606–617.
- Lamme, V. A., & Roelfsema, P. R. (2000). The distinct modes of vision offered by feedforward and recurrent processing. *Trends in Neuroscience*, *23*, 571–579.
- Macknik, S. L., & Livingstone, M. S. (1998). Neuronal correlates of visibility and invisibility in the primate visual system. *Nature Neuroscience*, *1*, 144–149.
- Mathewson, K. E., Beck, D. M., Ro, T., Maclin, E. L., Low, K. A., Fabiani, M., et al. (2014). Dynamics of alpha control: Preparatory suppression of posterior alpha oscillations by frontal modulators revealed with combined EEG and event-related optical signal. *Journal of Cognitive Neuroscience*, *26*, 2400–2415.
- Mathewson, K. E., Gratton, G., Fabiani, M., Beck, D. M., & Ro, T. (2009). To see or not to see: Prestimulus alpha phase predicts visual awareness. *Journal of Neuroscience*, *29*, 2725–2732.
- 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 Psychology*, *2*, 99.
- Mathewson, K. E., Prudhomme, C., Fabiani, M., Beck, D. M., Lleras, A., & Gratton, G. (2012). Making waves in the stream of consciousness: Entraining oscillations in EEG alpha and fluctuations in visual awareness with rhythmic visual stimulation. *Journal of Cognitive Neuroscience*, *24*, 2321–2333.

- Michalareas, G., Vezoli, J., van Pelt, S., Schoffelen, J. M., Kennedy, H., & Fries, P. (2016). Alpha-beta and gamma rhythms subserve feedback and feedforward influences among human visual cortical areas. *Neuron*, *89*, 384–397.
- Minami, S., & Amano, K. (2017). Illusory jitter perceived at the frequency of alpha oscillations. *Current Biology*, *27*, 2344–2351.
- Muckli, L., De Martino, F., Vizioli, L., Petro, L. S., Smith, F. W., Ugurbil, K., et al. (2015). Contextual feedback to superficial layers of V1. *Current Biology*, *25*, 2690–2695.
- Ogmen, H., Breitmeyer, B. G., & Melvin, R. (2003). The what and where in visual masking. *Vision Research*, *43*, 1337–1350.
- Railo, H., & Koivisto, M. (2012). Two means of suppressing visual awareness: A direct comparison of visual masking and transcranial magnetic stimulation. *Cortex*, *48*, 333–343.
- Ro, T., Breitmeyer, B., Burton, P., Singhal, N. S., & Lane, D. (2003). Feedback contributions to visual awareness in human occipital cortex. *Current Biology*, *11*, 1038–1041.
- Romei, V., Gross, J., & Thut, G. (2009). On the role of prestimulus alpha rhythms over occipito-parietal areas in visual input regulation: Correlation or causation? *Journal of Neuroscience*, *30*, 8692–8697.
- Samaha, J., & Postle, B. R. (2015). The speed of alpha-band oscillations predicts the temporal resolution of visual perception. *Current Biology*, *25*, 2985–2990.
- Schiller, P. H., & Chorover, S. L. (1966). Metacontrast: Its relation to evoked potentials. *Science*, *153*, 1398–1400.
- Super, H., Spekreijse, H., & Lamme, V. A. (2001). Two distinct modes of sensory processing observed in monkey primary visual cortex (V1). *Nature Neuroscience*, *4*, 304–310.
- Tapia, E., & Beck, D. M. (2014). Probing feedforward and feedback contributions to awareness with visual masking and transcranial magnetic stimulation. *Frontiers in Psychology*, *5*, 1173.
- Thut, G., Nietzel, A., Brandt, S. A., & Pascual-Leone, A. (2006). Alpha-band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. *Journal of Neuroscience*, *26*, 9494–9502.
- Thut, G., Northoff, G., Ives, J. R., Kamitani, Y., Pfennig, A., Kampmann, F., et al. (2003). Effects of single-pulse transcranial magnetic stimulation (TMS) on functional brain activity: A combined event-related TMS and evoked potential study. *Clinical Neurophysiology*, *114*, 2071–2080.
- Thut, G., Veniero, D., Romei, V., Miniussi, C., Schyns, P., & Gross, J. (2011). Rhythmic TMS causes local entrainment of natural oscillatory signatures. *Current Biology*, *21*, 1176–1185.
- van Kerkoerle, T., Self, M. W., Dagnino, B., Gariel-Mathis, M. A., Poort, J., van der Togt, C., et al. (2014). Alpha and gamma oscillations characterize feedback and feedforward processing in monkey visual cortex. *Proceedings of the National Academy of Sciences, U.S.A.*, *111*, 14332–14341.
- Vaughan, H. G., Jr., & Silverstein, L. (1968). Metacontrast and evoked potentials: A reappraisal. *Science*, *160*, 207–208.
- Webster, & Ro. (submitted). Visual modulation of resting state alpha oscillations.
- Wokke, M. E., Sligte, I. G., Steven Scholte, H., & Lamme, V. A. (2012). Two critical periods in early visual cortex during figure-ground segregation. *Brain and Behavior*, *2*, 763–777.
- Worden, M. S., Foxe, J. J., Wang, N., & Simpson, G. V. (2000). Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. *Journal of Neuroscience*, *20*, RC63, 1–6.
- Wutz, A., Melcher, D., & Samaha, J. (2018). Frequency modulation of neural oscillations according to visual task demands. *Proceedings of the National Academy of Sciences, U.S.A.*, *115*, 1346–1351.