

The effects of transcranial magnetic stimulation on visual rivalry

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One extensively investigated form of perceptual bistability is binocular rivalry—When dissimilar patterns are presented one to each eye, these patterns compete for perceptual dominance. Here, we report that transcranial magnetic stimulation (TMS) over early visual areas induces alternations during binocular rivalry. The effect of TMS on binocular rivalry was retinotopic, suggesting that rivalry mechanisms are localized in the cortical representation of visual space. The timing of perturbations was highly dependent on individual differences in rivalry alternation frequencies, with more delayed effects found in slower alternators. This finding suggests that both binocular rivalry and TMS dynamics might be contingent on individual differences among observers. We performed an analogous set of experiments by replacing TMS with transient visual stimulation. The results, however, qualitatively and quantitatively differed from those reported with TMS. Finally, we found that TMS over early visual areas does not produce any time-locked effects on another dynamical process—eye-swapping stimulus rivalry. These findings constitute the first causative evidence that binocular rivalry is contingent on neural activity in early visual areas and suggest that binocular rivalry and stimulus rivalry have different neural correlates, supporting multilevel theories of visual rivalry.

Keywords: binocular rivalry, transcranial magnetic stimulation (TMS), stimulus rivalry, single pulse, bistable, neural excitability

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Introduction

Nonlinear dynamical processes are ubiquitous in physical and biological systems (Wilson, 1999), including the visual nervous system (Kleinfeld et al., 1994; Prechtl, Cohen, Pesaran, Mitra, & Kleinfeld, 1997). An actively studied dynamic brain phenomenon in human vision is binocular rivalry (Blake & Logothetis, 2002), the fluctuating states of visual awareness that occur when two eyes view different stimuli in corresponding regions of the retina. During rivalry, perception is bistable in that observers often perceive only one of two monocular stimuli, with perception switching to the other stimulus after some variable duration of dominance. A number of recent studies have focused on the statistical properties of rivalry dominance durations (Brascamp, van Ee, Pestman, & van den Berg, 2005; Kim, Grabowecky, & Suzuki, 2005; Mamassian & Goutcher, 2005) and on the neural events producing alternations in perception during rivalry (Carter & Pettigrew, 2003; Freeman, 2005; Kim et al., 2005; Lankheet, 2006; Wilson, 2003).

Perceptual bistability with dynamics comparable with conventional binocular rivalry can also be observed when dissimilar stimuli are swapped rapidly between the eyes (Lee & Blake, 1999; Logothetis, Leopold, & Sheinberg, 1996; Pearson & Clifford, 2005). This form of bistability cannot arise from competition between the two eyes because the durations of dominance of a given stimulus greatly exceed the period of stimulation of a single eye—for this reason, this form of bistability has been termed stimulus rivalry (in distinction to conventional binocular rivalry). Compared with conventional binocular rivalry, stimulus rivalry occurs under a more restricted range of stimulus conditions (Lee & Blake, 1999), and it behaves differently in response to variations in stimulus size and internal structure (Bonneh, Sagi & Karni, 2001). These differences have led to the *conjecture* that binocular rivalry and stimulus rivalry are implemented at different stages of neural processing within the visual pathways (Freeman, 2005; Wilson, 2003).

In a series of experiments, we investigated the effects of localized cortical stimulation on conventional binocular

rivalry and stimulus rivalry using transcranial magnetic stimulation (TMS; Hallett, 2000; Walsh & Pascual-Leone, 2003). TMS is associated with a relatively local, transient disruption of neural activity. Thus, TMS applied to a cortical region involved in visual rivalry might disrupt ongoing rivalry dynamics. Moreover, if conventional binocular rivalry and stimulus rivalry are indeed implemented at different stages of neural processing, then TMS over the early visual areas may have different effects on the two types of rivalry.

We show that TMS over early visual cortex (V1/V2) perturbs the dynamics of binocular rivalry in a retinotopically specific manner. The TMS-induced perturbations in binocular rivalry occurred between 0.6 and 1.8 s after the pulse. This variability in the temporal characteristics of the effects of TMS was correlated with the speed of rivalry alternations in different observers—a result linking TMS and individual differences in rivalry dynamics. Replacing TMS with a transient visual flash also perturbed binocular rivalry dynamics (cf., Kanai, Moradi, Shimojo, & Verstraten, 2005); however, this effect did not depend on the individual differences in rivalry. Finally, we found that TMS over the early visual areas did not produce any time-locked effects on the dynamics of eye-swapping stimulus rivalry, suggesting that the two phenomena differ in their neural mechanisms.

Methods

Stimuli were generated on a 21-in. linearized monitor (1,200 × 1,600 resolution; 75 Hz refresh rate) controlled by a Macintosh computer running MATLAB and the Psychophysics Toolbox (Brainard, 1997; Pelli, 1997). Dichoptic displays inducing rivalry were sinusoidal gratings appearing within a circular aperture 3.8° in diameter. One grating was green (CIE: $x = 293$; $y = 602$) and the other was red ($x = 632$; $y = 333$), and their orientations were $\pm 45^\circ$. The color and luminance of the background were the average of the two gratings (10.07 cd/m²). The spatial frequency of the gratings was 2 cycles/deg, and their Michelson contrast was 25% unless otherwise stated. The contrasts, when manipulated, were 10%, 40%, 70%, and 99%, which produced an approximately twofold range of alternation frequencies for each observer.

The gratings were presented one to each eye using a stereoscope, whose mirrors were carefully adjusted for each observer. A 0.5° bull's-eye fixation point and circular fusion locks (4° diameter) were used to stabilize binocular eye alignment. In the stimulus rivalry condition, the gratings were swapped between the eyes every 320 ms (1.56 Hz). In both the binocular and stimulus rivalry conditions, the stimuli flickered on–off at 18.7 Hz. We also ran binocular rivalry conditions without on–off flicker and found a similar pattern of results. The perceptual flash in the control experiments was a bright Gaussian blob (60 cd/m², $\sigma = 1.5^\circ$), presented during the off phase of the stimulus flicker.

While experiencing binocular and stimulus rivalry, observers tracked alternations in exclusive dominance by pressing and holding one key while the green grating was dominant and another key while the red grating was dominant. No key was pressed when observers experienced mixed (piecemeal) rivalry. Observers' native (no TMS) dominance durations were measured between TMS sessions with the air-cooling device running to equate auditory noise levels across conditions.

Experiments took place in a darkened room, and observers wore earplugs to reduce TMS noise. Observers sat on an unmovable chair, with their head supported by a chin rest and forehead supported by a padded support bar. For a given condition, each observer participated in three 3-min blocks, yielding a total of 54 min of rivalry tracking data in most conditions.

TMS methods

TMS was administered with a Magstim 2T Rapid stimulator (Magstim Company, UK; peak discharge = 1.8 kV; 70-mm figure-eight, air-cooled coil). The use of air-cooled coil allowed us to avoid stopping the experiment due to coil overheating and provided a steady noise source that likely masked some of the auditory effects associated with TMS pulses. TMS pulses were triggered remotely using a computer. The coil was carefully positioned for each observer, with placement dictated by the location of evoked phosphenes. Once the appropriate coil location was established, the coil's orientation was locked in place with the handle pointed upwards, at an angle of approximately 45° counterclockwise. Although varying slightly from person to person, coil location was approximately 1–3 cm above theinion (thus avoiding possible hemispheric effects; Miller et al., 2000), except during the peripheral phosphene experiment, wherein the position was 4–7 cm above theinion.

Phosphene thresholds were estimated using a modified binary search paradigm (Tyrell & Owens, 1988) that established the TMS intensity at which each observer reported a phosphene on 75% of stimulations. Coil position yielding a phosphene was localized with eyes open, after which TMS intensity was adjusted to 10% above the phosphene threshold. Across all observers, the stimulator intensity used ranged from 51% to 83% of the stimulator maximum. For central stimulation, coil position was adjusted until the reported phosphene was inside the circular fusion locks (i.e., within 2° from the fovea). Peripheral phosphenes were between 7° and 15° below the fovea, ensuring that the upper border of the phosphene was always below the area where the stimulus is presented. It should be noted, however, that observers did not report seeing the foveal phosphenes during rivalry tracking, likely because of the attentional demands of the rivalry task and the presence of a stimulus at the phosphene location (Rauschecker, Bestmann, Walsh, & Thilo, 2004). On the

other hand, in the peripheral condition, observers reported seeing phosphenes while they tracked rivalry alternations.

Observers

All procedures were approved by the Vanderbilt University Institutional Review Board, and all observers gave written informed consent.

Thirteen experienced psychophysical observers with either normal or corrected-to-normal vision were recruited for the study. Two observers were excluded because they had difficulty perceiving phosphenes at comfortable TMS intensity levels. One observer withdrew from the study because of discomfort. Two observers who could not perceive stimulus rivalry alternations were also excluded; that is, they frequently perceived perceptual alternations every 320 ms, the rate of the eye swaps. The remaining 8 observers (age = 19–33 years; 2 women; 6 naive) participated in the study.

Six observers (including two authors) participated in binocular rivalry experiments (e.g., Figures 1, 2A, and 3). Five out of six observers participated in stimulus rivalry experiments (Figure 4). Two of the authors and two additional observers naive to the experimental purpose participated in the experiment where stimulus contrast was manipulated (Figure 2B).

Analysis

Alternation probability functions were computed in the following way: All time points when an observer released one of two keys (indicating the end of a dominance duration) were taken to indicate perceptual alternations. For the data analysis, we counted all alternations that occurred in successive 213-ms bins following the TMS pulse (yielding 15 bins) and divided each sum by the total number of alternations for each observer. The average number of alternations used was 217 per observer (range: 90–307). The baseline probability for each bin is then .067 (1/15). These data were then smoothed with a [0.1 0.2 0.4 0.2 0.1] moving window. To improve the estimation of peak position (shown in Figures 2A and 2B), a weighted average of the peak and data points before and after the peak was taken.

To derive estimates of expected variability, we randomly shuffled each observer's dominance durations (thus removing any effects that are time locked to TMS pulse) and analyzed the data in the same way as the actual data. This was repeated 100,000 times, thereby yielding 100,000 alternation probability functions, from which we computed standard deviation that is plotted on the right y-axis in figures. A separate simulation was performed for each experimental condition and, where individual data are shown, for each observer. This analysis also yielded 100,000 peaks of the alternation probability functions (free from any time-locked effects), from which we

computed p values for experimentally observed peaks. Note that the smallest p value we can measure is 10^{-6} , which indicates that not a single peak from the 100,000 simulated alternation probability functions was larger than the experimentally observed data.

We also performed an analysis where we aligned the peaks from individual observers to time = 0 and then averaged the results (Figure 1B). Consequently, we performed an analogous simulation with the shuffled data. Note that peak aligning computation on the shuffled data yields a baseline that peaks at time = 0. This is because shuffled alternation probability functions also have peaks (albeit relatively small), which, of course, do not average out when peaks are aligned, as in Figure 1B. Moreover, variability near such peaks is smaller, as it is evident in the ± 2 SD band shown in Figure 1B.

All these analyses were performed on both smoothed and raw results, with only a negligible nonqualitative difference between the two. The p values reported in the text are from smoothed data to be in accord with figures.

Control experiments

We also ran control experiments assessing the potential effects of eye blink, auditory, or tactile artifacts of TMS. Three observers participated in these experiments. First, to control for the auditory (and some tactile) artifacts associated with TMS, we ran an experiment where the coil edge was positioned perpendicular to the skull at a location 3 cm above the inion.

Second, to examine whether TMS yielding foveal phosphenes also induced eye blinks, we used a ViewPoint eye tracker (Arrington Research, Scottsdale, AZ) to monitor eye blinks while observers tracked physical alternations between the two stimuli used in the binocular rivalry stimulus for a total of 18 min. Spatial and temporal resolutions were approximately 0.15° and approximately 30 Hz, respectively.

The experimental design was the same as in rivalry tracking experiments, except that observers tracked *physical* stimulus changes while TMS was applied every 3.2 s. We used simulated rivalry here because we could not accommodate the eye-tracking device within the constraints of our mirror stereoscope; simulated tracking is sufficient for our purpose, which is simply to measure the timing of blinks during the application of TMS while undertaking a tracking task. During the experiment, we recorded 202 blinks (about 11 blinks per minute).

Results

In the first experiment, we measured each observer's dominance durations during binocular rivalry without TMS.

Distributions of dominance durations measured without TMS confirmed that all observers showed the characteristic peak with skewness toward long durations (Levelt, 1965), with an average native dominance duration of 2.7 s ($SD = 1.3$ s). The distribution of normalized dominance durations was approximated well with a gamma distribution ($r^2 = .98$; Figure 1C, solid red line). Fitted scale (λ) and shape (r) parameters were 5.1 and 5.2, respectively.

The effects of TMS

Having established observers' binocular rivalry dynamics without TMS, we next investigated how event-related single-pulse TMS at regular intervals influences perceptual alternations during rivalry. First, we localized the scalp position of the TMS coil by systematically adjusting the position over the occipital lobe until observers reported a phosphene within 2° of fixation. In this condition, which we will call *central* stimulation, the rivalry stimulus always overlapped the location of the phosphene (see Methods section for details). Holding that coil position constant, a single TMS pulse was then delivered every 3.2 s while observers continually tracked perceptual alternations during binocular rivalry. Observers reported not seeing phosphenes during the tracking experiment. This is in accord with a study showing that stimulus presence increases phosphene thresholds (Rauschecker et al., 2004).

The application of TMS shortened dominance durations during binocular rivalry by about 300 ms, $t(5) = 2.99$, $p = .03$ (paired t test). This effect was significant in five out of six observers (all $t > 2.49$, all $df > 393$, all $p < .01$) and is evident in the slight leftward shift and sharpening of the gamma fit to the distribution of dominance durations ($r^2 = .97$; Figure 1C, dotted red line; normalized relative to non-TMS results for each observer). Fitted scale and shape parameters were 7.2 and 6.5, respectively. The magnitude of this dominance duration shortening, however, was relatively small, amounting to about a 10% decrease in observers' dominance durations. We suspect that a portion of this small increase in alternation frequency might be related to general elevation of arousal in the TMS condition (Carter, Pettigrew, et al., 2005; Carter, Presti, et al., 2005; George, 1936). For the sake of comparison, attending to rival stimuli can increase dominance durations by more than 50% (Chong, Tadin, & Blake, 2005).

The duration of mixed periods followed the same trend as dominance durations: When expressed in relation to the average dominance duration in a given condition, mixed period duration ranged between 6.9% and 7.4%. In other words, the addition of TMS did not change the proportion of mixed rivalry.

TMS, however, had a sizable effect on the timing of binocular rivalry alternations: A disproportionately large number of alternations occurred following TMS pulses. This effect was apparent in all observers (Figure 1A, solid blue circles). The timing of TMS-induced alternations

varied among observers, and it was followed by a period where perceptual alternations were less frequent, as evident by the dip following the peak in all observers.

The individual observers in Figure 1A are ordered by their native dominance duration. This reveals that the individual variability in the timing of TMS-induced alternations is related to the individual differences in binocular rivalry, with slower alternators exhibiting more delayed effects of TMS. We will return to this finding later in the article.

Next, we adjusted the position of the TMS coil systematically until observers reported a phosphene in the periphery of their visual field. In this *peripheral* condition, care was taken to ensure that phosphenes and binocular rivalry stimulus never overlapped in space. It should be reiterated that observers often perceived TMS-induced phosphenes in the peripheral condition while tracking rivalry alternations. Nevertheless, when we applied TMS at a peripheral location, we found a uniformly weaker effect that was significant in only two out of six observers (Figure 1A, open squares). Application of peripheral TMS had a only a small effect on observers' dominance durations (175 ms), $t(5) = 1.71$, $p = .15$ (paired t test; Figure 1C, dashed orange line). This result indicates some retinotopic specificity of the interaction between TMS and binocular rivalry, a result in accordance with other rivalry studies (Blake, Sobel, & Gilroy, 2003).

To factor out individual differences in the data, we aligned the peaks from different observers by taking the largest peak for each observer in central TMS condition and aligning it to time = 0 (Figure 1B). This also allows us to examine the relative timing of the effects of central and peripheral TMS. The average result once again reveals a highly significant effect of central TMS on the timing of binocular rivalry alternations ($p \ll 10^{-6}$). The effect of peripheral TMS is much weaker. This holds even when individual results are aligned relative to peripheral TMS peaks ($p = .01$; Figure 1B, solid gray square).

Figure 1B also shows that the effect of peripheral TMS is delayed relative to central TMS by about 200 ms. This delay might be due simply to a weaker effect of TMS yielding a peripheral phosphene. However, we speculate that at least a portion of the observed delay might reflect the time it takes for TMS-induced signals to propagate from the peripheral stimulation site to neural tissue mediating rivalry alternations. Although approximately 200 ms may seem long for signal propagation, similarly slow propagation speeds have been reported for "traveling waves" during binocular rivalry (Lee, Blake, & Heeger, 2005; Wilson, Blake, & Lee, 2001).

The individual results show that peaks in the alternation probability function differed considerably across observers, with peak timing ranging from 505 ms to 1.8 s. These individual differences, however, were correlated with each observer's native (non-TMS) mean dominance duration ($r = .93$, $p = .007$; Figure 2A, solid blue circles), with slower alternators exhibiting later peaks. This correlation

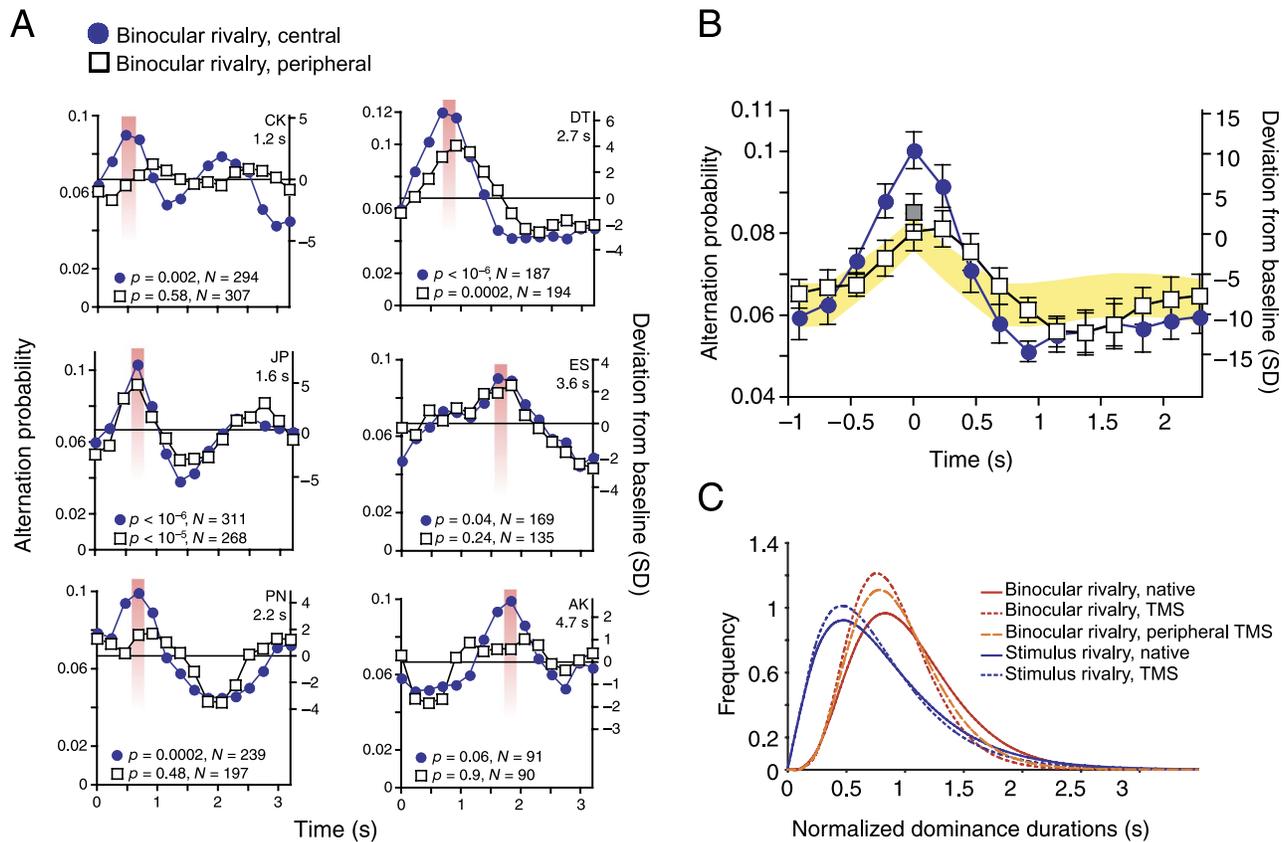


Figure 1. Effects of TMS on binocular rivalry. (A) Alternation probability function for individual observers. Alternation probability is shown as a function of time after TMS pulse ($N = 6$, see [Methods](#) section for detailed explanation). In the binocular rivalry, central condition, there is a clear peak in the alternation probability function for all observers (solid blue circles), but not when the TMS coil was positioned to evoke peripheral phosphenes (open squares). Light red bars mark peaks for each observer in the binocular rivalry, central condition. Note the individual differences in latency of the peak. N s in the panels refer to the number of perceptual alternations recorded for each observer in the two conditions. (B) Averaged data. Here, group result is computed by aligning each observer's central binocular rivalry peak to time = 0 and then averaging across observers. This figure shows the average size of the effect untainted by individual differences in timing and also shows the relative timing of the effects of central and peripheral TMS on binocular rivalry. The gray square indicates the result obtained by aligning each observer's peripheral binocular rivalry peak to time = 0 and then averaging across observers. Shaded area depicts ± 2 SD. (C) Gamma-distribution fits to distributions of dominance durations in different conditions ($f(x) = [(\lambda^r)/\Gamma(r)]x^{r-1}\exp(-\lambda x)$, with $\Gamma(r) = (r - 1)!$). The curve for each condition was obtained by normalizing dominance distribution for each observer relative to his or her mean dominance duration in binocular rivalry, native condition (two distributions are obtained for each observer, one for each rival stimulus) and fitting gamma distribution to the average across observers.

suggests that the time it takes for TMS to be reflected in a perceptual alternation depends on the unperturbed cortical processes mediating binocular rivalry.

To estimate the actual delay between the delivery of a TMS pulse and triggered perceptual alternations, observers' reaction times must be subtracted from the peak times. van Dam and van Ee (2006a, 2006b) reported reaction times to perceptual alternations clustering around 500 ms. Subtracting 500 ms from the results in [Figure 2A](#) reveals that TMS has almost an immediate effect for observers whose alternation frequency is very fast and that the effect of TMS is progressively delayed as one's alternation rate decreases. For slow alternators, TMS causes perceptual alternations well over a second after the administration of a TMS pulse.

These results indicate that the timing of the effect of TMS on rivalry is contingent on the alternation frequency of binocular rivalry. But why is the effect of TMS delayed in slow alternators? The relationship could indicate (a) an artifactual interaction between a periodic application of TMS and different rivalry alternation frequencies or (b) that both the effects of TMS and one's native alternation frequency depend on a factor that differs among individuals. We sought to distinguish these two alternatives by experimentally varying rivalry alternation frequency *within* an observer. If changes in one's alternation frequency affect the timing of the effect of TMS, then our result ([Figure 2A](#), solid blue circles) likely indicates an interaction between a periodic application of TMS and the alternation frequency of binocular rivalry.

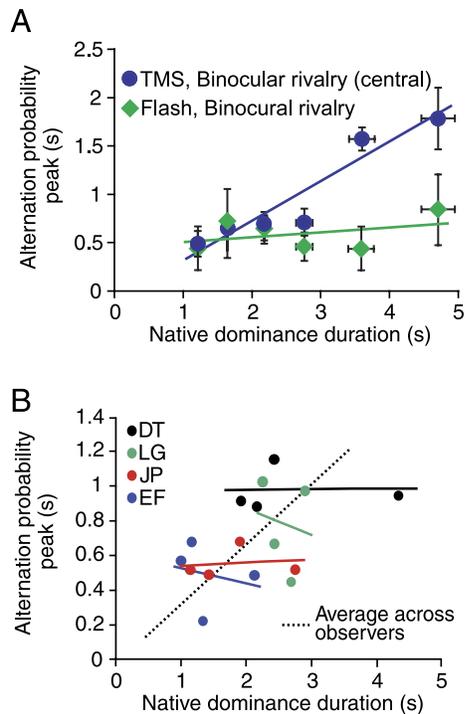


Figure 2. Relationship between dominance durations and alternation probability peaks. (A) Relationship between individual observers' native dominance duration (during binocular rivalry) and the timing of TMS- and flash-induced peaks in alternation probability functions. TMS-induced peaks correlate with observers' alternation rates, whereas flash-induced peaks do not. Straight lines are linear fits to the data. Error bars are *SEM*. (B) Relationship between contrast-induced changes in dominance durations and the timing of TMS-induced peaks in alternation probability functions. Solid lines are linear fits to each observer's data. The dashed line is a linear fit through the average results (one point for each observer).

On the other hand, if the timing of the TMS-induced peaks remains constant despite large changes in observers' mean dominance durations, then we can conclude that the individual variability in our TMS results and the differences in observers' rivalry alternation frequencies likely depend on some common factor.

An effective way to modulate alternation rate during binocular rivalry is to vary the contrast of the rival stimuli (Hollins, 1980; Mueller & Blake, 1989): Low-contrast stimuli produce slower alternation frequencies. By testing four observers, we measured an approximately twofold range of mean dominance durations *between* observers. Moreover, by testing a range of contrasts (10–99%) for each observer, we were also able to vary each observer's dominance duration over an approximately twofold range. Figure 2B shows the timing of the TMS-induced alternation probability peaks for a range of dominance durations. For each observer, the introduction of contrast-dependent changes in his or her average dominance duration had no effect on the timing of the effect of TMS

(average $|r| = .14$, $p = .86$). On the other hand, an approximately similar change in dominance durations driven by the individual differences (not contrast) had a significant effect on the timing of TMS-induced rivalry alternations ($r = .95$, $p = .046$; Figure 2B, dotted line), a result replicating the finding reported in Figure 2A. The linear fits to the results of the two experiments are also similar: $y = 0.40x - 0.08$ (Figure 2A) versus $y = 0.34x - 0.02$ (Figure 2B).

This result indicates that the relationship between the timing of the effect of TMS and observers' native dominance duration is not merely a product of an interaction between the periodic application of TMS and changes in the alternation frequency of binocular rivalry because changes in the alternation frequency within an observer had no effect on the timing of the effect of TMS. Evidently, the individual differences that govern each observer's alternation frequency also determine the timing of temporal interactions between TMS and rivalry.

TMS controls

Besides its direct cortical effects, TMS is also associated with tactile, auditory, and motor effects. These peripheral effects must also be considered. In particular, it is important to rule out eye movements as a possible explanation of our results because of a known link between microsaccades and perceptual alternations during binocular rivalry (van Dam & van Ee, 2006a). van Dam and van Ee showed that microsaccades and associated retinal image changes are highly correlated with perceptual alternations during binocular rivalry. Thus, it is important to consider whether the potential eye movement artifacts of TMS can explain our findings. However, several aspects of our results are incompatible with the eye movement hypothesis and other peripheral artifacts of TMS. First, a positive correlation between microsaccades and binocular rivalry alternations is observed just before perceptual alternations (van Dam & van Ee, 2006a). However, in our results, we show that the effect of TMS can be observed well over a second after a pulse. Thus, we can rule out the contribution of microsaccades, which are associated with rivalry alternations on a much shorter timescale.

Second, the retinotopic specificity of the effects of TMS also serves as an experimental control for the peripheral effects of TMS because such artifacts should not exhibit substantial dependency on cortical retinotopy. That is, a small change in the location of the TMS coil is unlikely to have a considerable effect on the auditory, tactile, and motor effects of TMS. Finally, the absence of phosphenes during the tracking task also eliminates potential problems associated with an abrupt and presumably attention-drawing perceptual experience. For example, attentional shifts are linked with microsaccades (Engbert & Kliegl, 2003; Hafed & Clark, 2002; Laubrock, Engbert, & Kliegl,

2005), which, in turn, are associated with perceptual alternations during rivalry (van Dam & van Ee, 2006a, 2006b).

In addition, we ran two standard control experiments. In the first experiment, the coil was positioned perpendicular to the skull. Such placement can isolate the auditory effects of TMS associated with a loud click. The results showed that TMS pulses delivered with the coil in this configuration had no significant effect on binocular rivalry ($p = .14$). In the second control experiment, we monitored observer's eye blinks while they tracked simulated rivalry alternations. Results showed no increase in the frequency of blinks immediately following the TMS pulse ($p = .18$). No (macro) saccades were detected during this task either. Given that observers engaged in an attentionally demanding tracking task and that TMS occurred at predictable intervals along the occipital midline (i.e., far from the efferent pathway to the eyelids), this result, although gratifying, is not surprising.

The effect of visual flash

Are the observed results specific to TMS or do they generalize to other forms of transient perturbations? To explore that possibility, we replaced the TMS pulse with a bright (60 cd/m^2), centrally presented Gaussian-shaped flash (approximately 27 ms; see Methods section) superimposed at the location of the rivalry stimuli. Like TMS, this flash was delivered every 3.2 s, always during an off phase of the 18.7-Hz on–off flicker. This external stimulation should create transient activity propagating throughout the visual pathways, thus potentially disrupting binocular rivalry.

Indeed, a visual flash affected the timing of rivalry alternations (Figure 3; $p < 10^{-6}$). The magnitude of these flash-induced peaks was similar to that of TMS-induced peaks, $t(5) = 0.81$, $p = .45$ (paired t test). Importantly, the effects of the flash on binocular rivalry, unlike TMS, were not correlated with observers' native dominance durations ($r = .38$, $p = .45$; Figure 2A, green diamond symbols). In contrast with TMS, a visual flash produced a more immediate effect on rivalry that did not depend on individual differences in rivalry dynamics. The flash-induced rivalry alternations peaked about 630 ms after the flash (Figure 3), which is earlier than the TMS results but in agreement with other psychophysical results (Kanai et al., 2005).

To ensure that the lack of dependence between flash-induced peaks and observers' native dominance durations was not due to a ceiling effect, we repeated the above-described experiment with a weaker flash (10 cd/m^2). Four of the original six observers participated in this control experiment. On average, reducing flash luminance resulted in an approximately 25% reduction in the alternation probability peak, whose timing changed by

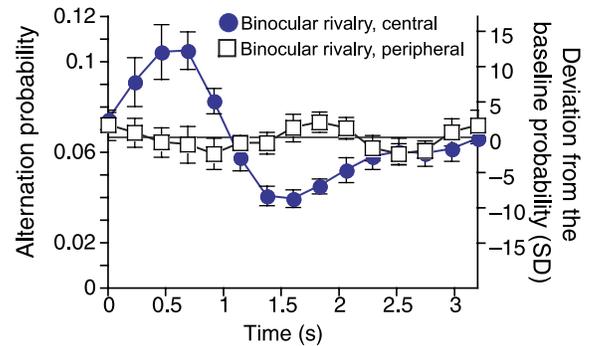


Figure 3. Alternation probability as a function of time after a transient visual flash presented either centrally (blue symbols) or at 10° eccentricity (open symbols).

only 8 ms. More importantly, the timing of individual flash-induced peaks remained uncorrelated with observers' native dominance durations ($r = .25$, $p = .68$).

We also conducted an experiment where the TMS pulse eliciting peripheral phosphenes was replaced with a brief peripheral flash (60 cd/m^2) presented at 10° eccentricity. The experimental methods were otherwise the same as in the above-described visual flash experiment. This peripheral visual perturbation had no effect on binocular rivalry dynamics ($p = .31$; Figure 3, open squares)—a finding mirroring those reported for other forms of perceptual bistability (Kanai et al., 2005).

Stimulus rivalry results

Stimulus rivalry is a perceptual phenomenon resembling conventional binocular rivalry (Logothetis et al., 1996). It is still unknown, however, to what degree these two forms of visual rivalry share common neural mechanisms. This motivated us to investigate whether the effects of TMS on stimulus rivalry are different from its effects on binocular rivalry. Therefore, we ran experiments analogous to those described above, except that in the place of conventional binocular rivalry, we presented eye-swapping stimulus rivalry. As with conventional binocular rivalry, our observers showed the characteristic peak with skewness toward long durations for stimulus rivalry (Levelt, 1965; Logothetis et al., 1996). The distribution of dominance durations was fit well with the gamma distribution ($r^2 = .94$), with scale and shape parameters (4.5 and 4.4, respectively) consistent with those previously reported (Logothetis et al., 1996).

The average dominance duration during stimulus rivalry was 2.09 s ($SD = 0.25$ s), about a second shorter than that for binocular rivalry, 2.93 s ($SD = 1.2$ s). This is evident when dominance duration distribution for stimulus is shown relative to that for binocular rivalry (Figure 1C, solid blue line). Analyzing results separately for each person, three out of five observers exhibited significantly

longer dominance durations during binocular rivalry (all $t > 3.47$, all $df > 605$, all $p < 10^{-3}$), and one observer had a longer dominance duration during stimulus rivalry, $t(902) = 4.48$, $p < 10^{-5}$; for the remaining observer, the difference between the two conditions was nonsignificant.

We then applied TMS over a scalp position yielding central phosphenes while observers tracked stimulus rivalry alternations. Application of TMS shortened stimulus rivalry dominance durations in two out of five observers (all $t > 3.1$, all $df > 546$, all $p < .002$) and had no effect on the remaining three observers. On average, this dominance duration shortening was relatively small (180 ms; Figure 1C, dotted blue line) and nonsignificant at a group level, $t(4) = 2.25$, $p = .09$ (paired t test).

TMS applied at the scalp location eliciting *central* phosphenes, however, had no effect on the timing of stimulus rivalry alternations ($p = .12$; Figure 4A, red diamonds), that is, the same TMS site that *did* influence binocular rivalry. In other words, TMS at the same location and intensity, although inducing alternations in binocular rivalry, did not induce any time-locked effects on the perceptual alternations of stimulus rivalry. We also analyzed the individual results (as in Figure 1A) and found no significant alternation probability peaks in all five observers (all $p > .34$). Based on this null result, we suspect that the small and, more importantly, non-time-locked increase in alternation frequency for two observers could be related to a general elevation of arousal during the TMS experiment (e.g., Carter, Pettigrew, et al., 2005; Carter, Presti, et al., 2005; George, 1936).

We next attempted to perturb stimulus rivalry by replacing TMS pulses with visual flashes. A transient visual flash should send a propagating signal throughout the different stages of the visual system, and thus, we hypothesized that it should disrupt not only binocular rivalry but also stimulus rivalry. Indeed, unlike TMS, the visual flash affected stimulus rivalry ($p < 10^{-5}$; Figure 4, open diamonds). We also examined the relationship between the timing of flash-induced effect on stimulus

rivalry and individual observers' native dominance duration for stimulus rivalry but found no correlation ($r = -.49$, $p = .51$), a result mirroring those for binocular rivalry (Figure 2A). The susceptibility of stimulus rivalry to visual flash transients indicates that the null result with stimulus rivalry and TMS (Figure 4A) is not attributable to a general insensitivity of stimulus rivalry to transient events but perhaps to stimulus rivalry not being contingent on the neural areas that we stimulated with TMS.

Discussion

Our findings indicate that TMS applied over early visual areas disturbs the ongoing neural dynamics that normally produce spontaneous alternations in perceptual states during binocular rivalry. The magnitude and timing of this effect varied with TMS coil position in such a way that when the phosphene overlapped with the rivalry stimulus, the effect was more immediate and larger in magnitude. However, the effect of a transient visual flash alone, unlike the effect of TMS, did not correlate with individual observers' alternation frequencies. The contingency of the temporal relationship between TMS and perceptual alternations suggests that the speed at which a TMS pulse can manifest its effect on perception is dependent on some underlying factor, different in each individual.

The retinotopic specificity of the effect of TMS on binocular rivalry suggests that the neural correlate of binocular rivalry includes mechanisms localized in the cortical representation of visual space. In contrast, TMS had essentially no time-locked effects on the dynamics of stimulus rivalry, a form of perceptual competition that resembles binocular rivalry in several other ways (Bonneh et al., 2001; Lee & Blake, 1999; Logothetis, et al., 1996; Pearson & Clifford, 2005). Although the present results do not allow us to ascertain the actual neural loci of these two forms of rivalry, we can conclude that the two are mediated, at least in part, at different stages of processing. This conclusion squares with the emerging view that rivalry transpires within multiple stages of the visual hierarchy (Blake & Logothetis, 2002; Tong, Meng, & Blake, 2006), a notion that has been formally embodied in several recent theories of rivalry (Freeman, 2005; Wilson, 2003).

Our study is not the first to use TMS to perturb binocular rivalry. Using a circular coil, which stimulates a much larger area of tissue than the figure-eight coil used here, Miller et al. (2000) applied TMS pulses in the direction of the left temporoparietal areas. The authors report that this lateralized stimulation, when coincidental with a binocular rivalry switch, had a tendency to reverse that switch; Miller et al. did not include any stimulation of early visual areas or stimulus rivalry among their test conditions. These authors interpreted their results as evidence for the involvement of interhemispheric

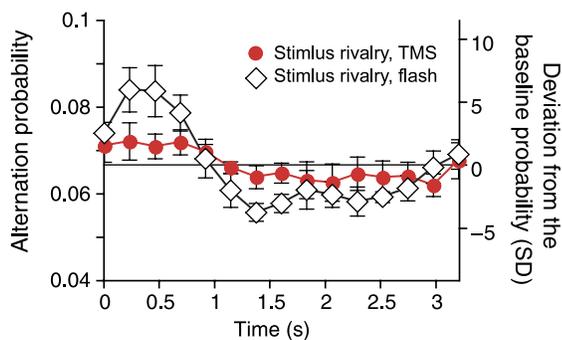


Figure 4. Stimulus rivalry results. The effects of TMS and visual flash on stimulus rivalry dynamics. Unlike the visual flash, the application of TMS did not result in an increase in alternation probability function beyond ± 2 SD.

competition in binocular rivalry, perhaps driven by a subcortical neural oscillator. This hypothesis, however, remains controversial (O’Shea & Corballis, 2003, 2005).

Functional imaging studies have found that activity in the frontoparietal areas of the human brain correlates with perceptual reports of alternations in rivalry (Lumer, Friston, & Rees, 1998, Lumer & Rees, 1999). Hence, it seems plausible that these frontoparietal areas play a role in governing changes in visual awareness during rivalry and, for that matter, other forms of bistable perception (Kleinschmidt, Buchel Zeki, & Frackowiak, 1998; Meenan & Miller, 1994; Ricci & Blundo, 1990). The general notion of high-level involvement in binocular rivalry is not incompatible with our results. One could easily imagine early visual areas, within the striate and extrastriate cortex, establishing and maintaining the neural representations corresponding to the perceptual content of the binocular rivalry stimuli, with “higher” cortical areas involved in attentional control contributing to the ongoing endogenous selection process characteristic of binocular rivalry.

Why does TMS targeting the V1/V2 area induce a change in perceptual state during binocular rivalry? The present results do not provide the exact answer. We know, of course, that TMS induces a brief pulse of electrical current in the volume of tissue beneath the coil, with this field extending a few centimeters into the depths of the underlying cortex (Cowey, 2004). The current pulse depolarizes nerve cells and, if sufficiently strong, produces a train of action potentials that can outlast the pulse itself by an order of magnitude. However, in this study, the effects of TMS, even when reaction times are taken into account, took over 1 s for some observers. Perhaps, TMS triggers a cascade of neural events that eventually cause a perceptual alternation during binocular rivalry.

There is some evidence that a single TMS pulse can induce a burst of synchronized neural activity in the beta wave range (15–30 Hz), as evidenced by EEG recordings over motor cortex during TMS stimulation (Paus, Sipila, & Strafella, 2001). Increased synchronicity (in the γ -frequency) has been observed when the corresponding pattern dominates during binocular rivalry (Fries, Roelfsema, Engle, Konig, & Singer, 1997). If ongoing phase-locked activity in higher frequency bands (40–60 Hz) is important during binocular rivalry and TMS can temporarily disrupt or slow this activity, then it is interesting to speculate that this might be the means by which TMS induces perceptual alternations during binocular rivalry.

TMS affects perception more quickly for faster binocular rivalry alternators than for slower alternators. However, when alternation frequencies are modulated within a single observer by changing the stimulus contrast, the timing of the effect of TMS remains constant. This suggests that it is not the binocular rivalry dynamics *per se* that modulate the temporal relationship between TMS and rivalry dominance. Whatever the effect of TMS on

binocular rivalry, it is dependent on neural events that govern individual differences in the rate of alternations in rivalry, differences that may have something to do with neuronal transmission speeds or individual differences in neurochemical components at the synaptic level (Carter, Pettigrew, et al., 2005; Carter, Presti, et al., 2005; George, 1936).

Future research might investigate the effect of frontoparietal stimulation during stimulus rivalry. If frontoparietal areas do indeed play a role in orchestrating endogenous modulations of visual awareness, then one might hypothesize that frontoparietal TMS stimulation should result in the perceptual perturbation of stimulus rivalry.

Finally, it is worth reiterating that TMS has a markedly different visual consequence on rivalry than an externally delivered visual flash does. This suggests that the rivalry perturbations observed here were not solely the result of the visual transient associated with a phosphene but most probably the consequence of neuronal depolarization in the tissue embodying the neural representation of the binocular rivalry content. In any case, in the current context, the effects of TMS on early visual processing cannot be veridically mimicked with transient visual stimulation.

In summary, the current work has produced the first causal evidence that the neural processing of binocular and stimulus rivalry might indeed reside in different neural locations. This provides strong empirical support for multilevel theories of visual rivalry (Freeman, 2005; Wilson, 2003).

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