

Current Biology

Extinguishing Exogenous Attention via Transcranial Magnetic Stimulation

Highlights

- Investigated how TMS affects the typical benefits and costs of exogenous attention
- Identical TMS for all cueing conditions guided by individuals' phosphene mapping
- TMS to occipital cortex extinguished the perceptual effects of exogenous attention
- Causal link between V1-V2 and exogenous attention's effect on visual perception

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In Brief

Fernández and Carrasco show that TMS locked to stimulus onset after deployment of exogenous spatial attention extinguishes its typical benefits and costs on a visual discrimination task. Using a psychophysics-TMS protocol, the authors provide a causal link between early visual areas and exogenous attention's effect on visual perception.

Report

Extinguishing Exogenous Attention via Transcranial Magnetic Stimulation

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SUMMARY

Orienting covert exogenous (involuntary) attention to a target location improves performance in many visual tasks [1, 2]. It is unknown whether early visual cortical areas are necessary for this improvement. To establish a causal link between these areas and attentional modulations, we used transcranial magnetic stimulation (TMS) to briefly alter cortical excitability and determine whether early visual areas mediate the effect of exogenous attention on performance. Observers performed an orientation discrimination task. After a peripheral valid, neutral, or invalid cue, two cortically magnified gratings were presented, one in the stimulated region and the other in the symmetric region in the opposite hemifield. Observers received two successive TMS pulses around their occipital pole while the stimuli were presented. Shortly after, a response cue indicated the grating whose orientation observers had to discriminate. The response cue either matched—target stimulated—or did not match—distractor stimulated—the stimulated side. Grating contrast was varied to measure contrast response functions (CRF) for all combinations of attention and TMS conditions. When the distractor was stimulated, exogenous attention yielded response gain—performance benefits in the valid-cue condition and costs in the invalid-cue condition compared with the neutral condition at the high contrast levels. Crucially, when the target was stimulated, this response gain was eliminated. Therefore, TMS extinguished the effect of exogenous attention. These results establish a causal link between early visual areas and the modulatory effect of exogenous attention on performance.

RESULTS

Attention is a mechanism that enables the brain to optimize performance given metabolic constraints [3]. Covert spatial attention enhances stimulus processing at relevant locations in the visual field at the expense of stimuli at other locations via a push-pull mechanism [4]—improving visual processing at the attended location (benefits) and suppressing signals at unattended locations (costs) [e.g., 5–7]. There are two types of covert spatial attention [1, 2]. Exogenous attention is involuntary, stimulus driven, and rapidly deployed (~100 ms) in a transient manner. Endogenous attention is voluntary, goal driven, and more slowly deployed (~300 ms) in a sustained manner. Behaviorally, both types of attention enhance performance in tasks mediated by contrast sensitivity [1, 2, 5–7] and spatial resolution [8, 9]. Converging evidence from neuroimaging, electrophysiological, and neurophysiological studies also indicate that covert spatial attention affects contrast sensitivity [e.g., 10–18, 19].

Neural responses to stimuli of varying contrast are non-linear and follow a sigmoidal shape [20, 21], which characterizes the contrast response function (CRF). Psychophysical evidence suggests that both types of attention affect responses to contrast in a different manner. Endogenous attention predominantly affects responses via contrast gain, with a maximal attentional modulation within the dynamic range of the CRF.

Exogenous attention operates via response gain, increasing attentional modulation monotonically as a function of contrast [6, 22, 23].

Covert spatial attention modulates basic visual dimensions, suggesting a relation between spatial attention and early visual cortical areas. fMRI studies on endogenous and exogenous attention have characterized networks of brain regions within the frontal and parietal lobes and often assume similar effects in striate and extra-striate areas [24, 25]. A recent study, however, has shown differential effects [15]. Several studies [14, 15, 26] report modulations of exogenous attention on neural activity in visual cortex; fMRI cannot establish causality, as this technique records, but does not manipulate brain function.

Here, to establish a causal relation between early visual cortex and the perceptual modulations by exogenous attention, we applied TMS over the occipital pole while observers performed a visual task under different attentional states. When used on a cortical region, TMS can briefly and non-invasively disrupt the balance of excitation and inhibition at the targeted regions and is thus a very powerful tool for inferring the causal role of those regions [e.g., 27–30]. The TMS effect on performance depends on the brain activation state of the stimulated region [31–33]. Manipulating brain states via psychophysical protocols (e.g., adaptation or priming) enables informed predictions about the stimulation outcome [31–35].

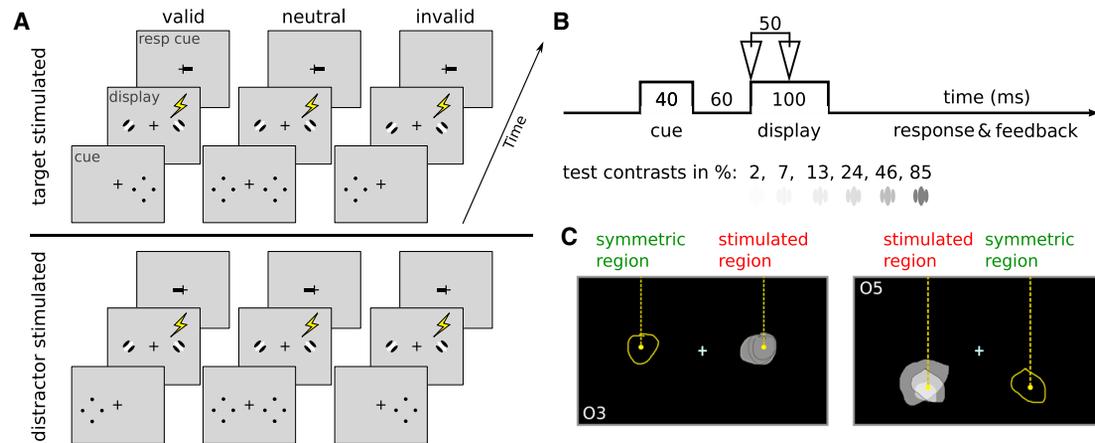


Figure 1. Psychophysics-TMS Task

(A) Task design: in a valid trial, the location indicated by the peripheral cue matched the response cue. In an invalid trial, the location indicated by the peripheral cue did not match the response cue. In a neutral trial, both the symmetric and stimulated region were peripherally cued, and the response cue was equally likely to point to either location. In the target-stimulated condition, the stimulated region matched the response-cued region. In the distractor-stimulated condition, the stimulated region was opposite to the response-cued region.

(B) Trial timeline: occipital TMS was applied at stimulus onset with a 50 ms delay between the two pulses. The main task tested six different contrast levels as depicted by the cartoon gratings.

(C) Phosphene mapping: observers were stimulated near their occipital pole and drew the outline of their perceived phosphene on the screen by using a mouse. The anatomical coordinates corresponding to this phosphene were tested at the start of each session. O3 and O5 are two representative observers, and the translucent shapes depict their drawings for each experimental session. The outlines in the symmetric region are only for visualization purposes.

Here, we stimulated primary visual areas while manipulating the observer's brain state by using a modified TMS-attentional cueing protocol [36] and assessed the benefits and costs of exogenous attention. Observers completed three simultaneous psychophysics-TMS sessions as detailed below:

Thresholding sessions proceeded as follows: (1) Observers received TMS near the occipital pole and drew the location of their phosphene (an illusory blob perceived in the contralateral hemifield); stimulation intensity was decreased until observers reported seeing a phosphene 50% of the time. (2) Observers performed the orientation discrimination task (I) without stimulation, (II) with only neutral cues, and (III) at the maximal contrast level (85%). Once the grating tilt required to achieve ~80% accuracy was determined, observers moved on to session one (same day).

Sessions 1–3 proceeded as follows: Observers performed an orientation discrimination task at six contrast levels (Figures 1A and 1B). After a peripheral valid, neutral, or invalid cue, two cortically magnified gratings were presented, one in each observer's phosphene region (stimulated region) and the other in the symmetric region in the opposite hemifield. On every trial, observers received double pulse TMS locked to stimulus onset. Shortly after, observers reported the orientation of the grating indicated by the response cue, which either matched—target stimulated—or did not match—distractor stimulated—the stimulated side. Both thresholds were checked at the start of each session to ensure that the observer's perceived phosphene had not moved significantly (Figure 1C) and to account for any learning effects in the orientation discrimination task.

We assessed (1) whether intact neural activity in early visual areas is needed for exogenous attention to modulate performance and (2) whether and how TMS affects the CRF when exogenous attention modulates the brain state. We compared six experimental conditions: valid, neutral, or invalid cue at the

stimulated cortical region corresponding either to the target—target stimulated—or to the distractor—distractor stimulated.

Critically, because TMS was locked to stimulus onset, observers had already deployed their exogenous spatial attention, which takes ~100 ms [1, 2, 5–9], by the stimulation time; thus, we could make informed predictions, given activity-dependent effects with TMS [31–35], about attention's effect on stimulus processing (Figure 2). We expected the typical response gain with exogenous attention in the distractor-stimulated condition; an increase in the upper asymptote with the valid cue (benefits) and a decrease with the invalid cue (costs) in relation to the neutral cue. If early visual areas underlie exogenous attention, then disrupting their function should abolish response gain. Therefore, we predicted that in the target-stimulated condition TMS would effectively eliminate response gain modulations by bringing the valid and invalid functions closer to the neutral function. These predictions were motivated by contrast gain changes with contrast adaptation [37, 38]. When adapted prior to stimulation, TMS alters performance via contrast gain [31], suggesting that TMS modifies the ongoing cortical computation (i.e., gain). Given that we manipulated exogenous attention, which operates via response gain, we hypothesized that TMS would modulate the upper asymptote of the CRF.

TMS Effects on Attention

Most observers (70%) perceived a phosphene when their right hemisphere was stimulated; we grouped the data regardless of the stimulated hemisphere. In a study using a similar task and stimulation protocol, there were no differences in performance regardless of which hemisphere was stimulated [36].

To answer whether early visual areas mediate exogenous attention's effect on performance, we conducted a three-way [stimulated region (target/distractor) X attentional state (valid/

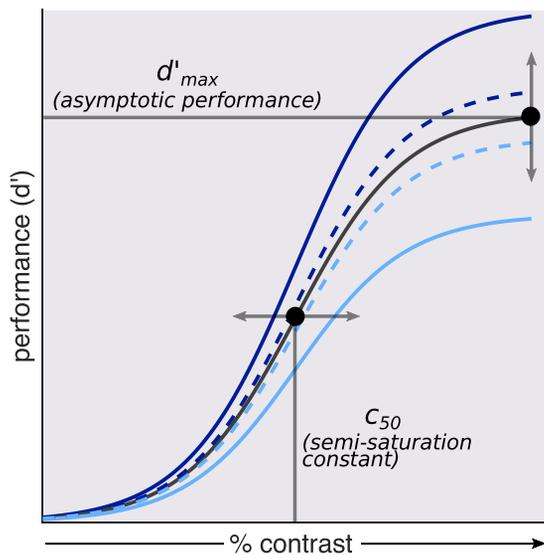


Figure 2. Predicted Results

In the distractor-stimulated condition (solid lines), we expected response gain, an upward shift of the upper asymptote of the valid CRF and a downward shift of the upper asymptote of the invalid CRF in relation to the neutral curve. In the target-stimulated condition (colored dashed lines), we expected the valid (dark blue) and invalid (light blue) curves to shift toward the neutral (black) curve, effectively eliminating the differences in asymptotic performance. The gray dashed arrows represent the possible directions of change for parameters c_{50} and d'_{max} in the CRF. Importantly, d'_{max} shifts along the y axis (performance), whereas c_{50} shifts along the x axis (contrast). A leftward shift of c_{50} would indicate that observers required a lower contrast stimulus than in the neutral condition to reach the same performance level; a rightward shift of c_{50} would indicate that observers required a higher contrast stimulus than in the neutral condition. An upward (downward) shift of d'_{max} would indicate that at the same contrast level observers performed better than in the neutral condition in the task; a downward shift of d'_{max} would indicate that at the same contrast level observers performed worse than in the neutral condition.

neutral/invalid) X contrast] repeated-measures ANOVA on performance (indexed by d'). Performance increased as a function of contrast ($F(5,45) = 120.3$; $p < 0.001$; $\eta^2_G = 0.68$) and was modulated by attention ($F(2,18) = 46.74$; $p < 0.001$; $\eta^2_G = 0.10$). Critically, there was a significant three-way interaction ($F(10,90) = 3.570$; $p = 0.002$; $\eta^2_G = 0.03$) that emerged because attention and contrast significantly interacted in the distractor stimulated condition ($F(10,90) = 5.315$; $p < 0.001$; $\eta^2_G = 0.10$), but not in the target stimulated condition ($F(10,90) = 0.180$; $p = 0.314$). Indeed, the attentional effect, valid minus invalid performance across contrast levels, was significantly greater for the distractor- than the target-stimulated condition ($t(9) = 4.707$; $p = 0.001$; $d = 2.1$).

We obtained CRFs by fitting Naka-Rushton functions [20] to the data. We assessed response gain by comparing asymptotic performance (d'_{max}) across observers by using a two-way (stimulated region X attentional state) repeated-measures ANOVA. Asymptotic performance depended on the attentional state (Figure 3) ($F(2,18) = 67.94$; $p < 0.001$; $\eta^2_G = 0.12$) and this effect interacted with the stimulated region ($F(2,18) = 13.01$; $p < 0.001$; $\eta^2_G = 0.09$). The interaction effect was driven by modulation of the upper asymptote in the distractor-stimulated condition

($F(2,18) = 51.20$; $p < 0.001$; $\eta^2_G = 0.34$) but not in the target-stimulated condition ($F(2,18) = 0.197$; $p = 0.823$). This effect was consistent for all but one observer, as shown in the scatterplot of attentional effects (valid-invalid d'_{max} values) for distractor-versus target-stimulated conditions (Figure 4). Additionally, stimulation predominantly affected attention (valid and invalid cue), as the neutral d'_{max} for target- and distractor- stimulated conditions did not significantly differ ($t(9) = 0.206$; $p = 0.842$).

A contrast gain modulation would be indexed by a shift in the semi-saturation constant (c_{50}). A two-way (stimulated region X attentional state) repeated-measures ANOVA on the semi-saturation constant yielded no significant main effects of attentional state ($F(2,18) = 1.664$; $p = 0.217$) or stimulated region ($F < 1$), and no interaction between them ($F < 1$).

DISCUSSION

We manipulated exogenous attention by using a well-established psychophysical protocol [1, 2, 5–7, 14, 15, 39] and applied non-invasive brain stimulation (TMS) to alter its effects on visual perception. We assessed (1) whether intact neural activity in early visual areas is needed for exogenous attention to modulate performance and (2) how TMS affects the CRF when exogenous attention modulates the brain state. Consistent with other studies [1, 2, 5–7, 22, 23], when the distractor was stimulated, we obtained benefits at the attended location and costs at the unattended location, via response gain. Critically, when the target was stimulated, both benefits and costs were extinguished. These novel findings reveal a causal link between early visual cortical areas and exogenous attention's modulatory effect on performance.

The phosphene mapping procedure [36, 40, 41] coupled with neuro-navigation, enabled us to specifically manipulate brain function in the retinotopic area processing the target or distractor, and to precisely target the same cortical region across sessions (Figure 1C). Phosphene induction is linked to stimulation of visual cortex (V1 [42, 43]; V1–V3 [44–46]). Given our coil position, we are confident that TMS was over the occipital cortex (V1–V2), and likely over surrounding visual area V3 (given that TMS can affect interconnected areas [47, 48]). All experimental conditions involved the same stimulation protocol; trial-wise fluctuations were cue type (valid, neutral, or invalid), location (target or distractor region), and grating contrast. This optimal control cannot be achieved with sham stimulation, commonly used in TMS research, which simulates some but not all TMS sensations [30].

The CRFs of the target stimulated condition confirmed our hypothesis. Response gain was practically eliminated as indicated by a lack of differences in d'_{max} values (Figure 3). The best fit curves to the valid and neutral conditions overlapped, illustrating that stimulation extinguished attentional benefits. In the invalid condition, costs were severely diminished as illustrated by the overlapping error bars with those of the other functions. Importantly, these effects were due to attention and not to the neutral condition, given that d'_{max} was similar for both neutral functions (distractor versus target stimulated). This similarity also rules out possible masking or phosphene-induced effects. Had TMS masked the stimulus, performance would have been impaired in the target in relation to distractor stimulated condition, and all cue conditions would have been impaired. However, TMS

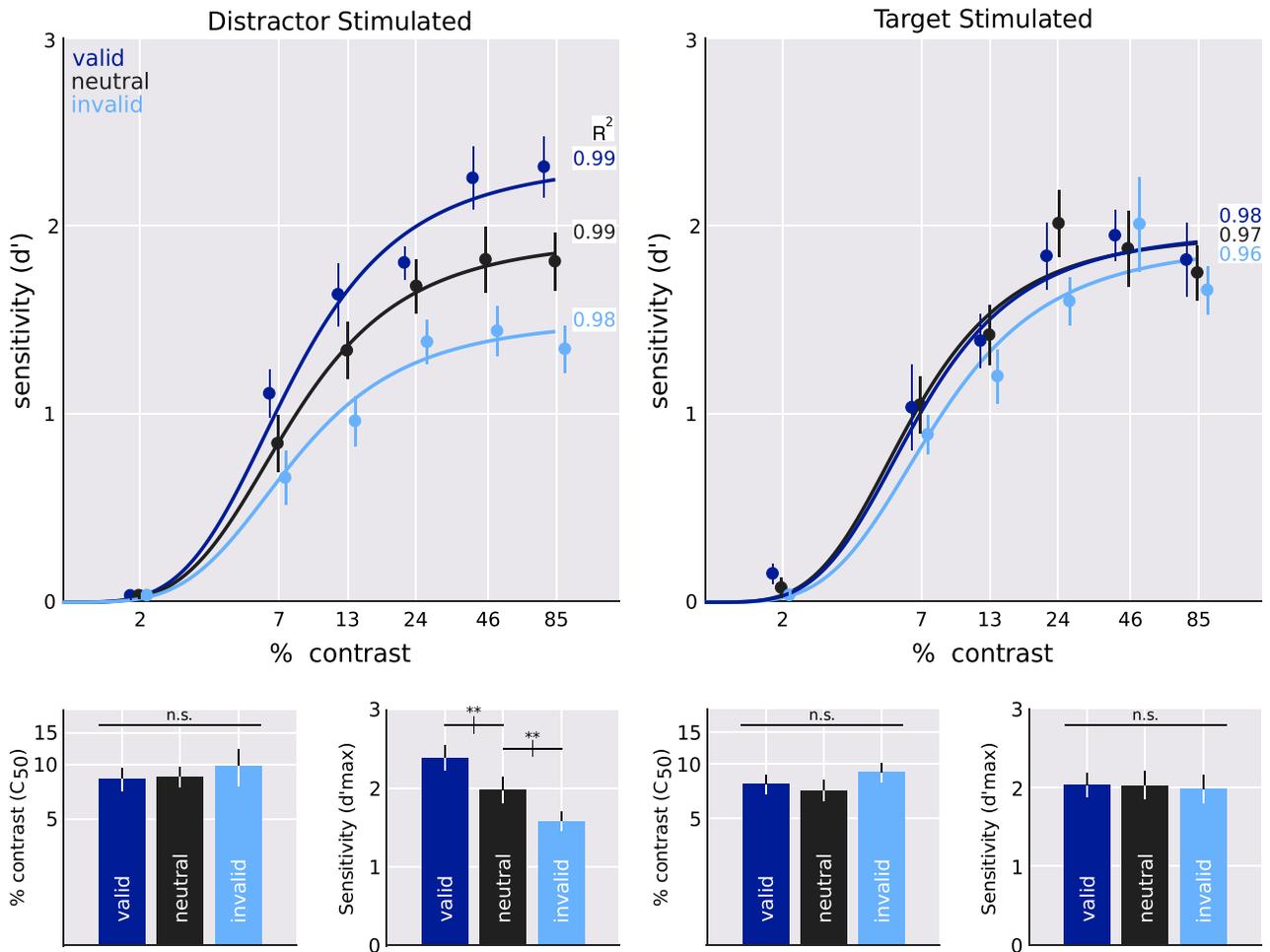


Figure 3. Contrast Response Functions

Mean CRFs across observers for distractor- (left) and target-stimulated (right) conditions. Data points are jittered horizontally around neutral (black) to avoid error bars from overlapping. Bottom bar plots represent mean parameter estimates for c_{50} and d'_{max} for their respective condition. Error bars are ± 1 SEM. $**p \leq 0.001$

impaired valid-cue trials but improved invalid-cue trials, indicating that TMS disrupted attention in particular rather than visual processing in general.

The results in the distractor-stimulated condition confirmed that our internal experimental control worked. Had trial-wise stimulation affected both hemifields, distractor- and target-stimulated conditions would have yielded the same results. However, performance in the distractor-stimulated condition followed the typical response gain of exogenous attention [1, 2, 6, 22, 23], benefit at the attended location, and cost at the unattended location. These benefit and cost effects also indicate that TMS neither masked stimuli nor disrupted all visual processing.

In a study testing the effect of TMS on the CRF, the semi-saturation constant was significantly altered [31]. Here, this was not the case between the neutral target- and distractor-stimulated conditions. The inconsistent findings could be because of protocol differences. We employed double pulse TMS with intensities ranging from 59% to 65% of maximum stimulator output, whereas that study employed a single pulse protocol at higher

intensities (70%–80%). Possibly, stimulation intensity interacts with contrast sensitivity thereby affecting the CRF. Moreover, because we expected response gain changes, we sampled the upper asymptote more finely than the dynamic range. But we doubt that finer sampling would yield contrast gain as our contrast levels are similar to those of that study.

Despite differences in task and TMS protocol, our results support the hypothesis that occipital TMS has an activity-dependent suppressive effect [31]. The authors of that TMS adaptation study proposed that TMS alters the balance of excitation and inhibition by predominantly affecting the more active neural populations, where TMS can suppress excitatory inputs (resulting in performance decrement) or further suppress inhibitory activity leading to disinhibition (resulting in performance increment). TMS should alter gain modulations at the attended and unattended locations, given that attention is selective and considered to operate via gain control [7, 8, 16, 17, 49]. In our study, given that stimulation occurred after attentional deployment, in the target-stimulated condition TMS extinguished attentional benefits and weakened attentional costs, providing converging

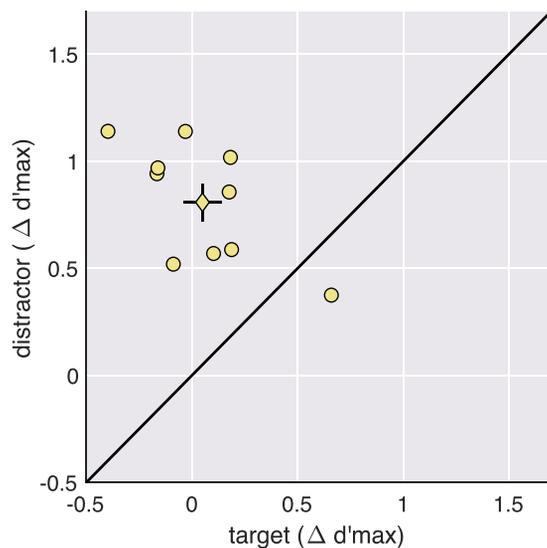


Figure 4. Attentional Effects

Valid-invalid asymptotic performance (d' max) averaged across observers (diamond) and for each individual observer (circles). Errorbars are ± 1 SEM.

evidence for the push-pull mechanism between the attended and unattended locations [4–6].

Specifically, conditions were as follows: (1) in the target-stimulated valid condition, exogenous attention was deployed to the task-relevant location (target stimulus) thereby increasing neural gain; TMS then suppressed this gain, negating the excitation provided by attention. (2) In the target-stimulated invalid condition, exogenous attention reduced neural gain at the non-stimulated side (distractor stimulus); TMS then further suppressed this less active neural population, leading to disinhibition, which brought invalid performance closer to neutral. (3) In the neutral condition, exogenous attention could have been evenly distributed to both hemifields, remained at fixation, or observers could have randomly chosen to attend to one location or to the other, all of which would yield similar curves in both the distractor- and target-stimulated conditions because they would predict symmetric or averaged gain for both hemifields. (4) In the distractor-stimulated valid condition, exogenous attention was deployed to the non-stimulated task relevant (target) location, leading to the typical benefits in performance. (5) In the distractor-stimulated invalid condition, exogenous attention was deployed to the non-task-relevant (distractor)-stimulated location, leading to performance costs.

A concurrent TMS-fMRI study of exogenous attention stimulated the right angular gyrus (parietal cortex) [50]. On the basis of improved performance in invalidly cued ipsilateral targets and increased BOLD response in contralateral angular gyrus and remote interconnected areas (e.g., V1 and V2), the authors concluded that stimulation facilitates rightward attentional reorienting—processing of the right stimulus when the left is cued. This explanation based on parietal TMS cannot account for our results because observers could not reorient during stimulus presentation; they did not know whether the trial was valid or invalid until after stimulus offset. Moreover, TMS not only extinguished attentional costs but also benefits, for which there was no reorienting.

There has been debate regarding whether the effects of exogenous attention are found for signals generated in striate cortex. Some electroencephalogram (EEG) studies report changes in the P1 ERP components, which indexes activation in extrastriate cortex, but not in the C1 component, which indexes striate cortex [e.g., 51, 52]. But another study using a similar task has reported changes in C1 with exogenous cueing [53], and a discussion paper reviews several studies on the topic and concludes that exogenous cueing, among other factors (e.g., stimulus location and distractors presence) contributes to the presence of spatial attention's effect on the C1 component [54]. Likewise, fMRI [14, 15] and TMS-fMRI studies [50] have suggested a link between V1-V2 and exogenous attention via changes in the BOLD signal. The inconsistent results are likely because of the sensitivity of different brain recording protocols as well as to different cue and stimulus parameters [54–56]. In any case, given that the present TMS study manipulates brain function by altering cortical excitability, it indicates that the effects of exogenous attention are indeed mediated by signals generated in striate cortex.

To conclude, here, we established a causal link between primary visual areas and exogenous attention's modulatory effect on visual perception. We used a psychophysics-TMS protocol to measure performance in orientation discrimination, an objective and criterion free task, and included a neutral condition to assess both benefits and costs of attention. This protocol allows us to relate our findings to well-established effects in visual perception and attention [1, 2, 5–7, 17, 22, 23]. TMS near the occipital pole after attentional deployment significantly altered task performance by eliminating the typical benefits and costs brought about by exogenous attention. Thus, these novel findings reveal that early visual cortical areas play a critical functional role in exogenous attention.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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AUTHOR CONTRIBUTIONS

A.F. and M.C. conceived the study; A.F. collected and analyzed the data; A.F. and M.C. wrote and revised the manuscript; M.C. provided funding.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Deposited Data		
code and data files	This paper	https://doi.org/10.17605/OSF.IO/B76JS
Software and Algorithms		
MATLAB	MathWorks	https://www.mathworks.com/ ; RRID: SCR_001622
R	[57]	https://www.r-project.org/ ; RRID:SCR_001905
Psychtoolbox	[58, 59]	http://psychtoolbox.org/ ; RRID: SCR_002881
Palamedes toolbox	[39]	http://www.palamedestoolbox.org/ ; RRID: SCR_006521
Brainsight	Rogue Research	https://www.rogue-research.com/tms/brainsight-tms/ ; RRID: SCR_009539

RESOURCE AVAILABILITY

Lead Contact

For further information and resources request, Lead Contact will be Antonio Fernández (antonio.fernandez@nyu.edu).

Materials and Availability

This study did not generate new materials.

Data and Code Availability

Datasets and code generated during this study are available on OSF <https://doi.org/10.17605/OSF.IO/B76JS>.

EXPERIMENTAL MODEL AND SUBJECT DETAILS

A total of eighteen observers participated in the phosphene session, out of the 18, 16 perceived phosphenes and 10 met the criterion for participation (8 females; mean age: 24.4 ± 3.6). To be included, observers' phosphene had to be between 4 and 12 degrees of visual angle (dva) away from fixation and subtend a diameter of at least 2 dva. The experimental protocol was in accordance with the safety guidelines for TMS research and was approved by the University Committee on Activities Involving Human Subjects at New York University. All observers provided informed consent and had normal or corrected-to-normal vision. Prior to their first session, observers were screened for TMS counter-indications.

METHOD DETAILS

Stimuli

Observers sat in a dark room with their head firmly positioned on a chin-rest 57cm away from a gamma calibrated ViewPixx/EEG LCD monitor (120Hz refresh rate; 1920×1080 resolution). A Linux desktop machine was used to control stimulus presentation and collect responses. Stimuli were generated using MATLAB (MathWorks, Natick, MA) and the Psychophysics toolbox [58, 59]. A black fixation cross (0.25 dva long perpendicular lines) was displayed in the center of the screen throughout the experiment. Stimuli consisted of two 2 cycles per degree Gabors. The eccentricity of the Gabors was determined by the center of the observers' perceived phosphene (6.22 ± 1.22 dva on average). Gabor size was adjusted according to the Cortical Magnification Factor: $M = M_0(1 + 0.42E + 0.000055E^3)^{-1}$ [60]. The attentional cues consisted of 4 black dots (2 above/below; 2 right/left of stimulus; 0.1 dva wide) that were 1 dva away from the Gabor edge. The response cue consisted of a black rectangle (0.3 dva long) that replaced

the left or right arm of the fixation cross (Figure 1). An EyeLink 1000 Desktop Mount (SR Research) recorded right eye position at 1000 Hz. Stimulus presentation was contingent upon fixation. If observers broke fixation (deviation > 1 dva) or blinked the trial was stopped and repeated at the end of the experimental block.

TMS machine and Neuro-navigation

Observers were stimulated using a 70 mm figure-of-eight coil positioned over occipital cortex with the handle oriented perpendicular to the sagittal plane. TMS pulses were applied using a Magstim Rapid Plus stimulator (3.5 T) and triggered with MATLAB using an Arduino board. We defined stimulation thresholds as the machine intensity required for each observer to perceive a phosphene 50% of the time. Stimulation intensity remained constant throughout all experimental sessions for each observer (mean intensity: 62% ± 3% of max stimulator output). Prior to their first session, observers' head was calibrated to match Brainsight software's built in 3D head template (Rogue Research). With Brainsight we were able to record coil position on the observer's scalp with millimeter precision, allowing us to precisely target the same region across sessions.

Phosphene Mapping

The same phosphene mapping procedure used here has been used successfully in other studies [36, 40, 41, 61]. Observers were seated in a dark room and asked to fixate on a dark blue fixation cross in the center of a black screen. A train of 7 TMS pulses at 30Hz and 65% of maximal machine intensity was applied on the scalp over the assumed phosphene region (2.87cm ± 1.46cm above the inion and 2.65cm ± 0.75cm away from the midline). If observers reported a phosphene, they were asked to draw the outline of the perceived phosphene on the screen using their mouse and coil location was recorded. To ensure the outline was a correct depiction of their perception, observers were allowed to repeat the trial until they were certain.

The center of the drawing was then used as the coordinates for the Gabors in the psychophysics-TMS task. One Gabor was placed inside the phosphene region—stimulated region, the other was placed in the symmetrical region on the other hemifield—symmetric region (Figure 1C). If observers did not report seeing a phosphene or the perceived phosphene did not meet the requirements for inclusion the coil was moved, and the procedure was repeated until a suitable phosphene was found. Next, phosphene thresholds were derived by using the same stimulation scheme in the main task, two pulses spaced 50 ms apart, (Figure 1B) and manipulating stimulator output until observers reported a phosphene 50% of time. Stimulation intensity remained constant throughout the entire TMS portion of the study for each observer (range 59%–65% of the maximal stimulator output). The same phosphene mapping procedure was repeated at the start of each experimental session using the recorded coil location from session one; perceived phosphenes were consistent across experiments sessions (Figure 1C).

Psychophysics-TMS task

Each observer participated in three psychophysics-TMS sessions, 2–3 h per session, for a total of 6–9 h. At the start of their first session we localized and recorded the observer's phosphene. If the observer did not perceive a phosphene they were excluded from further sessions.

After phosphene localization, observers practiced the psychophysical task and a Gabor tilt-threshold was determined via an adaptive staircase procedure [39, 62]. Threshold was determined as the tilt required for each observer to discriminate the orientation of an 85% contrast Gabor at 80% accuracy. After phosphene mapping and tilt thresholding was completed observers moved on to the main task.

Observers performed three sessions of a two-alternative forced-choice orientation discrimination task (Figure 1A). After a variable fixation window (1,250, 1,650, or 2,250 ms) a peripheral (valid/invalid) or distributed (neutral) cue was presented for 40 ms. All cues were equally likely; therefore, the cue was uninformative. Following a 60 ms blank period two Gabors were presented on the screen for 100 ms, one in the phosphene region and the other in the symmetric region. Importantly, the first TMS pulse was time-locked to Gabor presentation, followed by another pulse 50 ms later (Figure 1B). The timing between the cue onset and stimulus presentation was optimal for exogenous attention to be deployed [1, 2, 8, 9]. After another brief blank period of 60 ms a response cue was presented in the center of the screen pointing to a hemifield. If the response-cued location matched the precue this was considered a valid trial. If the response-cued location did not match the precue this was considered an invalid trial. Importantly, if the response cue matched the stimulated region the trial was labeled as target stimulated, otherwise distractor stimulated. The response cue remained on the screen until response. Observers received feedback on incorrect trials in the form of a tone. Each observer completed a total of 2880 trials: 80 trials per data point x 6 contrast levels x 6 conditions (3 attention conditions: valid, neutral, invalid X 2 stimulated sites: target, distractor).

This design was optimal in that the same stimulation protocol was used across all tested experimental conditions. This optimality could not have been achieved with other commonly used protocols such as sham stimulation, which simulate some but not all sensations brought about by TMS.

QUANTIFICATION AND STATISTICAL ANALYSIS

Repeated-measures ANOVAs were used to assess statistical significance. If the sphericity assumption was violated, Greenhouse-Geisser correction was applied [63]. We report effect sizes in terms of generalized eta-squared (η^2_G) [64]. ANOVAs were computed in R [57]. Psychometric functions and parameter estimates were generated using the MATLAB `fmincon` function.

Task performance [indexed by d' : $z(\text{hit rate}) - z(\text{false alarm rate})$] was measured as a function of stimulus contrast. We considered correct discrimination of clockwise trials as hits and incorrect discrimination of counter-clockwise trials as false-alarms [7, 65, 66]. To account for cases in which observers did not false alarm we adopted the log-linear approach [67]. Performance was measured using the method of constant stimuli (interleaved six contrast levels; Figure 1B). To obtain contrast response functions we fit each observer's data with Naka-Rushton functions [20]:

$$d'(c) = d'_{max} \frac{c^\eta}{c^\eta + c_{50}^\eta} \quad (1)$$

and minimized the error using a least-squares criterion, where $d'(c)$ represents performance as function of contrast, d'_{max} is asymptotic performance in the high contrast range, c_{50} is the semi-saturation constant (contrast at which half the asymptotic performance is reached), and η determines the slope of the psychometric function. During optimization, d'_{max} and c_{50} were allowed to vary freely while η was fixed. As contrast is a log scale, we log transformed the values of contrast levels prior to fitting.

We report attentional effects as the difference in valid-invalid performance (Figure 4).