



Original Article

Low Intensity TMS Enhances Perception of Visual Stimuli

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ABSTRACT

Background: Transcranial magnetic stimulation (TMS) is a popular functional mapping tool in cognitive and sensory neuroscience. While strong TMS typically degrades performance, two recent studies have demonstrated that weak TMS, delivered to visual cortex, can improve performance on simple visual tasks. The improvement was interpreted as the summation of visually-evoked and TMS-elicited neuronal activity in visual cortex, but the nature of this interaction remains unclear.

Objective: The present experiments sought to determine whether these weak pulses of TMS assist subjects to see the visual stimulus itself or create a distinct “melled” percept that may not be recognizable as the visual stimulus.

Methods: We measured contrast thresholds in an orientation discrimination task in which participants reported the orientation (left or right) of gratings tilted 45° from vertical.

Results: Weak TMS improved sensitivity for identifying gratings, suggesting that TMS sums with but preserves orientation information so that the subject can recognize the visual stimulus. We explain the effect using a mechanism of non-linear transduction of sensory signals in the brain.

Conclusions: The capability of low-intensity TMS to augment the neural signal while preserving information encoded in the stimulus can be employed as a novel approach to study the neural correlates of consciousness by selectively “pushing” an unconscious stimulus into consciousness.

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Introduction

In a “virtual lesion” paradigm, transcranial magnetic stimulation (TMS) is applied at a relatively high-intensity such that it impairs task performance, presumably by disrupting the orderly neural response that is required for the task [1–4]. In contrast to this approach, two recent studies have demonstrated the opposite effect – that TMS at low intensity can improve performance [5,6]. In both studies, low-intensity TMS was shown to enhance visual sensitivity. The improvement was interpreted as the summation of visually-evoked and TMS-elicited neuronal activity in visual cortex. However, both studies left open a possibility for alternative interpretations. Here we further explore the nature of this improvement. We asked if low-intensity TMS improves visual sensitivity while preserving information that can be used to identify the visual stimulus.

In the experiments by Abrahamyan et al. [5], subjects detected a visual stimulus (a plaid) by reporting which of two temporal intervals contained the stimulus. The contrast threshold at which the subjects could reliably detect the visual stimulus was reduced when they performed the task while receiving single pulses of TMS to occipital cortex, but only when TMS intensity was around 90% of the phosphene threshold. The effect was topographically specific, in that TMS improved sensitivity (reduced the detection threshold) when delivered to those cortical neurons that responded to the visual stimulus, but TMS did not have this effect when delivered to the corresponding region of visual cortex in the opposite hemisphere (ipsilateral to the visual stimulus).

In the experiment by Schwarzkopf et al. [6], a sequence of three pulses (20 Hz) of TMS to motion-sensitive area V5 improved subjects’ accuracy in discriminating the left-versus-right direction of motion of a display of moving dots. The effect was obtained when the intensity of TMS was low (60% of the threshold intensity to induce a phosphene from V5), but was not observed with TMS at higher intensities (80% and 100% of the phosphene threshold). Further, these weak pulses of TMS only improved motion discrimination when the

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motion coherence of the stimulus was very low, such that accuracy was at 60% (chance performance = 50%); there was no improvement in identifying the direction of motion in a display with a higher level of motion coherence that produced an accuracy rate of 85%.

The authors of these papers reached the same conclusion, that the weak magnetic stimulation excites visual neurons and this neural activity can sum with the activity elicited by a visual stimulus, such that the combined activation is above a perceptual threshold. The effect was described as a TMS-induced pedestal for the visual stimulus [5] or as stochastic resonance between the visual stimulus and TMS [6]. The implication of both of these interpretations is that perceptual information about the visual stimulus was sufficiently well preserved that TMS served to make an otherwise invisible stimulus visible.

The experiment by Abrahamyan et al. [5] used a simple detection task – subjects reported in which of two intervals they saw a visual stimulus. Normally, the threshold for detecting a simple visual stimulus, such as a grating, is equal to the threshold for identifying that grating (for example, recognizing its orientation as 45° left or right from vertical) [7]. However, this may not be true when subjects are detecting a stimulus while receiving weak pulses of TMS. In this case, the percept created by the sum of TMS-induced and visually-evoked neuronal activity may not resemble the visual stimulus, but instead have some unrecognizable form, or may even resemble the phosphene elicited by suprathreshold TMS intensities. Thus, it is important to determine the form of the visual percept when a weak pulse of TMS is combined with a subthreshold visual stimulus.

The issues just raised for the experiments reported by Abrahamyan et al. [5] do not apply to the experiment by Schwarzkopf et al. [6] since their subjects performed a discrimination task on the visual stimulus. Therefore, the improvement in accuracy when the subjects received weak TMS must have reflected an improvement in their perception of the stimulus itself. However, the nature of the visual stimulus and TMS stimulation they used gives rise to two possible interpretations. Specifically, they found that weak TMS improved the subjects' ability to identify the direction of motion (left versus right) of a display of dots, but only when the motion coherence of the display was very low, and not when the coherence was higher. This manipulation of motion coherence confounds changes in signal strength (number of coherently moving dots) with changes in noise in the stimulus (number of randomly moving dots) because the total number of dots is held constant. That is, the low coherence stimulus had a weaker left or right motion signal than the high coherence stimulus, but it also had higher motion noise than the high coherence stimulus.

This confound in the way that Schwarzkopf et al. [6] created their stimuli means that the improvement in discrimination that they observed may have been due to TMS reducing the noise rather than improving the weak signal. Indeed, Schwarzkopf et al. [6] used triple-pulse sequences of TMS aligned with the stimulus onset and delivered at 20 Hz on each trial. In a recent study, Allen and colleagues [8] found a surprising improvement in subjects' detection accuracy when subthreshold TMS was delivered 0–40 ms after the visual stimulus onset. However, they were able to induce this improvement only when using a pair of TMS pulses presented at 25 Hz but not when using single-pulse TMS. In our previous study [5] we found that single-pulse subthreshold TMS can only improve detection when delivered 100 or 120 ms after the visual stimulus but not earlier. Therefore, using multiple pulses of TMS (pairs or triplets) could produce short-lived inhibition [9], which can improve discrimination by improving the signal to noise ratio. Indeed, Waterston and Pack [10] proposed that “offline” TMS may improve stimulus discrimination by reducing noise correlation as a result of neuronal inhibition. Thus, not controlling for the levels of

visual noise and using triple-pulse stimulation leaves open the question whether the improvement in the Schwarzkopf et al. [6] study was a result of interaction of TMS and signal strength (noise addition) or interaction of TMS and visual noise through noise suppression. We therefore use a single-pulse time-locked subthreshold TMS delivered 100 ms after the stimulus combined with simple oriented gratings to probe for improvement in orientation discrimination.

The present experiment further explored the effect of TMS on visual sensitivity to determine whether low-intensity TMS improves visual sensitivity while preserving information that can be used to identify the visual stimulus. We measured subjects' contrast thresholds as they performed a discrimination task in which they reported the orientation of a sinusoidal grating tilted to the left or right of vertical. If the summation of TMS-induced and stimulus-evoked neural activity preserves information about the visual stimulus, then subjects should be able to report the orientation of the stimulus even when the contrast of the tilted gratings is slightly below the detection threshold, due to the summed neural response crossing the detection threshold. In other words, their threshold to perform the discrimination task should be reduced by low-intensity TMS, which indicates an increase in visual sensitivity.

We measured the contrast threshold for the orientation discrimination as a function of stimulation intensity of TMS. Participants reported the orientation of briefly presented sinusoidal gratings tilted 45° to the left or right of vertical (orientation difference was 90°). A single pulse of TMS was delivered either to the hemisphere contralateral to the visual stimulus or to the opposite (control) hemisphere (ipsilateral to the stimulus). To ensure that the TMS stimulated the same neurons that responded to the visual stimulus, we presented gratings at the apparent location of visual phosphenes (determined at the start of the experiment). The contrast thresholds for the gratings were measured using a Bayesian adaptive staircase procedure [11], while the TMS intensity varied from 60 to 100% of phosphene threshold. We expected that the contrast threshold of orientation discrimination would be lower, compared with the control condition, when stimulation intensities are just below the phosphene threshold, as we previously found for a detection task [5].

Material and methods

Participants

Eleven volunteers, including the authors, participated in the experiment. Except the authors, participants were naïve to the purpose of the study. Participants were screened according to the TMS safety guidelines [12,13], had normal or corrected to normal vision, reported seeing visual phosphenes, and provided informed written consent (mean age 32 years; age range 24–44 years, 10 males). Experimental procedures were approved by the Human Research Ethics Committee at the University of Sydney.

Visual stimulus

The visual stimulus was a sinusoidal grating tilted either to the left or to the right of vertical. The stimulus had a spatial frequency of 1 cycle per degree and was modulated by a symmetric two-dimensional Gaussian contrast envelope to smooth sharp edges (peak contrast = 100%; full width at half-height 2.2° of visual angle).

Equipment

Visual stimuli were presented on a 19" cathode ray tube (CRT) monitor (BenQ P992) operating at 85 Hz refresh rate and 1024×768

screen resolution. We used a Bits++ digital video processor (CRS, Cambridge, UK) to increase the contrast range of the PC's graphics card from 8 bits (the default) to 14 bits. This extended the available luminance levels from 256 to 8192, allowing subtler changes in stimulus intensity and more accurate measurements of discrimination threshold. Gamma correction was applied using an OptiCAL photometer (CRS, Cambridge, UK) and a Matlab script to ensure a linear luminance profile. The participant's head was supported by chin and forehead rests at a viewing distance of 57 cm from the monitor. Visual stimulus presentation and synchronous triggering of the TMS pulse were programmed in Matlab (MathWorks) assisted by Psychtoolbox [14,15].

TMS was delivered with a Magstim Rapid2 system (Whitland, UK) and a 70-mm figure-eight coil held by an adjustable articulated arm (Manfrotto, Italy). To position the coil around the primary visual cortex, we combined structural MRIs and a real-time 3D neuronavigation system (Brainsight, Rogue Research, Canada). We were able to register coil position using the individual head scans of five participants; for the remaining participants, for whom we were not able to acquire MRI scans, we used an MRI that best matched the size of their head. For all subjects, the neuronavigation system was used to record the coil position for the experimental and control stimulation sites, in order to check that the subject's head remained in position relative to the coil throughout a session, and to assist in returning the coil to that same location for subsequent sessions.

Procedure

TMS hotspot and phosphene location

Sitting in a dimly lit experimental room, participants dark adapted for about 5 min. During the first day of testing, we located a TMS "hotspot" at the occipital pole by delivering single pulses with the coil initially placed 3 cm above and 2 cm lateral to theinion. We positioned the TMS coil tangentially to the scalp with the handle pointing either to the left or to the right of the participant for left and right occipital lobes, respectively. Such coil arrangement induces an electrical current that flows from lateral to medial, which is optimal for eliciting phosphenes [16]. The coil was moved in small steps (a few millimeters), assisted by the MRI and neuronavigation software, until the stimulation evoked bright phosphenes in the lower contralateral visual field away from the fovea. The coil was fixed in that "hotspot" with the articulated arm. The hotspot location was also saved within the neuronavigation system to track the position of the coil during the experimental session and to reposition the coil at the same area of the brain during each subsequent experimental session. For many subjects ($n = 9$) it was easier to elicit clear phosphenes at lower TMS intensities while stimulating the left occipital lobe while for some ($n = 2$) stimulation of the right hemisphere yielded the same effect (stimulation on the left side did not elicit clear phosphenes). To indicate the apparent location of a phosphene on the screen, participants fixated the center of the monitor and moved a circle on the screen using a mouse. The visual stimulus was then presented at this location for all experimental conditions. We ensured the precise position of the coil at a target brain area throughout all testing sessions using the real-time neuronavigation system.

Phosphene threshold

To estimate phosphene thresholds accurately, we used the "rapid estimation of phosphene thresholds" (REPT) procedure [17]. REPT programmatically adjusts the stimulator's pulse intensity based on a Bayesian adaptive staircase procedure [11] to estimate phosphene thresholds at 60%, which corresponds to the threshold parameter of a Weibull function fitted to the proportion

of phosphene responses between 0 and 1 with a lapse rate of 4%. Due to the asymmetric nature of the Weibull function used in the Bayesian adaptive staircase, the phosphene threshold is more accurately estimated at 60% rather than the more conventional 50% (this difference should be taken into account when intending to observe an effect with subthreshold stimulation). During phosphene threshold measurements, participants closed their eyes while maintaining their gaze at the remembered fixation position on the screen. We then asked participants to respond "No" (with the left "Shift" key) only when no change was present in the visual field and respond "Yes" (with the right "Shift" key) otherwise. As accurate estimation of the phosphene threshold was important for this study, it was calculated as the mean value of two or three phosphene threshold estimates. The mean phosphene threshold across all participants was 52% of stimulator output ($n = 11$, range: 38–70%).

Visual task

We measured the contrast threshold of orientation discrimination of sinusoidal gratings using a one-interval, two-alternative forced-choice orientation-discrimination task (Fig. 1A). The measured threshold values corresponded to Michelson contrast, which is the difference between the lowest and highest luminance values as a proportion of the full luminance range of the monitor. The monitor's background was uniformly gray with luminance equal to 77 cd/m², being the midpoint of the monitor's luminance range. The visual stimulus appeared on this background situated within a black circular ring (diameter 6.5° of visual angle) to help participants locate the target and therefore reduce spatial uncertainty [18]. Importantly, the grating was presented at the apparent location of the phosphene, to appear within the receptive field of the neurons targeted by TMS.

The beginning of each trial was marked by a central fixation cross (0.7° of visual angle) remaining on the screen for 353 ms. As a cue to the stimulus, the fixation cross changed to a square (0.2° of visual angle). After another 353 ms, a short beep was presented as an auditory cue, while the fixation square remained on the screen for a further 353 ms before the visual stimulus appeared on the screen. The stimulus was presented for 35 ms (3 frames). A single-pulse of TMS was delivered 106 ms (9 frames) after the stimulus onset. The fixation square disappeared after the TMS pulse, and participants had to press either the left or right "Shift" button to indicate whether the grating was tilted left or right, respectively. Each trial lasted for an average of 1.2 s.

The grating contrast varied according to a Bayesian adaptive staircase procedure [11], which estimated the contrast threshold after 30 trials at an accuracy of 80.3% correct. Each experimental block consisted of two interleaved staircases (2 × 30 trials) which provided two threshold estimates for the same condition. We collected at least 4 measures of the threshold for each condition. Thus for each participant the contrast threshold for each condition was calculated as an average of several independent measures of the threshold. We ran an average of 4.2 staircases per condition (126 trials). In a small number of cases (9 cases across 6 subjects) one threshold measurement deviated substantially from the other three thresholds of that subject in that condition. Because there were only four measurements per condition, rather than omitting the outlier value, we obtained additional measurements to provide a more reliable estimate and to reduce the contribution of the outlier to the average threshold for that condition.

TMS

During the visual discrimination task, we applied single-pulse TMS either to the visual cortex contralateral to the visual stimulus, or to the control site in the opposite hemisphere which was ipsilateral to the visual stimulus. The control site was in the

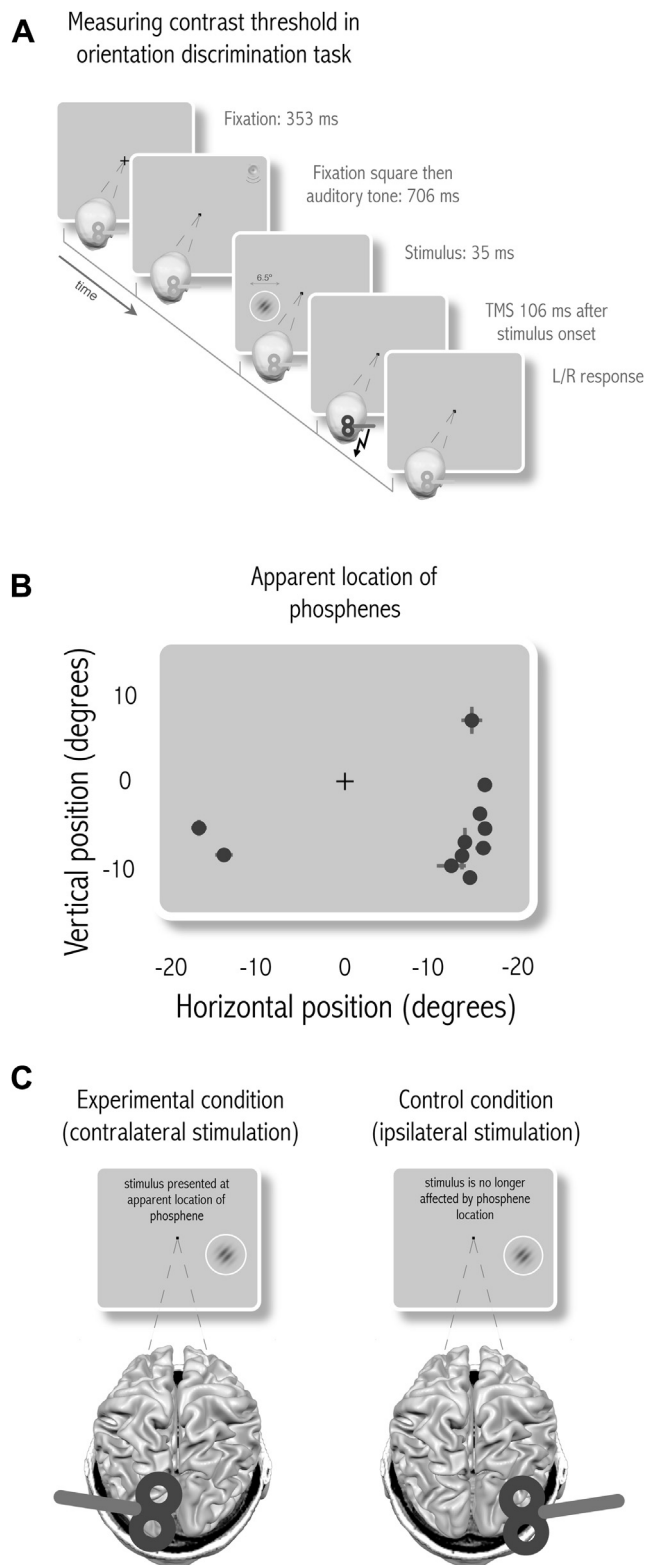


Figure 1. **A** Experiment design. Participants carried out a one-interval, two-alternative forced-choice task of discriminating the orientation (left or right) of the gratings. In each staircase, only one pair of oriented gratings was presented, while we manipulated the contrast of the gratings to find the subject's contrast threshold. At the beginning of each trial, participants fixated the cross at the center of the screen and were then presented with an auditory tone 353 ms before the appearance of the visual stimulus. The TMS pulse was presented 106 ms after the visual stimulus onset and delivered either to the contralateral (experimental) or ipsilateral (control) hemisphere relative to the visual stimulus. **B** Perceived location of phosphenes. Each dot shows individual

approximately symmetrical location in the opposite hemisphere to the coil position used for the experimental (contralateral) stimulation. The intensity of stimulation was subthreshold based on the phosphene threshold elicited from the contralateral site, and we ensured that subjects did not in fact perceive any phosphenes after changing the coil position to the ipsilateral stimulation site. The TMS pulse was delivered 106 ms after the onset of the visual stimulus in all TMS conditions. The latency was chosen based on the improvement of visual detection found previously [5] and is a commonly used TMS latency in visual suppression paradigms [2,4,19]. The exact value of 106 ms was used because this matched the start of a refresh cycle of the monitor and so made sure that the TMS pulse did not produce a visible artifact on the monitor while subjects were performing the task.

The purpose of the experiment was to establish if subthreshold TMS can lead to improvement in visual sensitivity when using a discrimination task. We measured the contrast threshold of oriented gratings which were tilted 45° left or right from vertical (90° orientation difference). We manipulated the intensity of the magnetic field delivered to the visual cortex. Magnetic field values were 60, 70, 80, 90 and 100% of phosphene threshold in the experimental condition, and 80 and 90% in the control condition. We limited the control stimulation to just two intensities in order to reduce the amount of stimulation being delivered to the subjects through the course of the experiment, and based on our previous evidence showing that these two intensities were the most effective at improving visual sensitivity when the TMS pulse was delivered 100 ms after the stimulus onset [5]. To prevent presentation order artifacts, blocks of trials at each TMS intensity and stimulation site (as well as no-TMS condition) were randomly intermixed. We also measured the contrast threshold without applying TMS (no-TMS condition) to acquire participants' baseline measure of performance.

Results

We varied the intensity of TMS from 60 to 100% of phosphene threshold for each participant. In the control condition, we delivered TMS to visual cortex ipsilateral to the visual stimulus (Fig. 1C) at intensities 80% and 90% of the phosphene threshold. The distribution of contrast thresholds was positively skewed (skew = 3.56) with a large kurtosis (kurtosis = 16.09). Positively skewed contrast thresholds are not uncommon [20] and in our case could have been linked to differences between subjects in the spatial location of the visual stimulus which depended on the apparent location of phosphenes (Fig. 1B). We therefore transformed our data by computing contrast sensitivity, which is the reciprocal of threshold ($1/\text{threshold}$) and a conventional measure of visual sensitivity [21]. This data transformation reduced the skew (skew = -0.65) and kurtosis (kurtosis = 0.49) considerably, thus bringing the distribution of the data much closer to normal. Contrast sensitivity scores were then averaged across two separate sessions and then across all participants. The grand averages are presented in Fig. 2A with error bars showing within-subjects standard error of the mean [22]. Article data together with R code to reproduce the results and figures can be accessed here: <http://bit.ly/1qkA69v>.

average position of phosphenes as reported by subjects. The phosphene position is shown relative to the fixation cross in degrees of visual angle. Visible error bars show the standard error of the mean. **C** TMS coil position during experimental (contralateral to visual stimulus) and control (ipsilateral to visual stimulus) conditions. The visual stimulus was presented at the apparent location of phosphenes to appear within the receptive field of the neurons targeted by TMS during the experimental condition but not during the control condition.

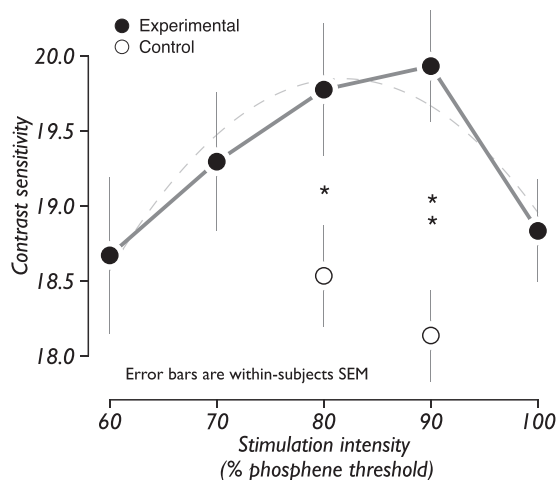


Figure 2. Changes in visual sensitivity during orientation discrimination as measured using Bayesian adaptive staircase. The dashed line shows a quadratic trend in visual sensitivity as a function of TMS intensity in experimental condition. There was also significant improvement in visual sensitivity relative to control conditions demonstrating that low-intensity TMS can improve visual sensitivity.

To identify a pedestal effect produced by TMS, we needed to show that the change in sensitivity was itself a function of TMS intensity. To this end, we fitted a linear and quadratic trend models to the data using mixed-modeling approach. We found that quadratic trend fitted the data better than linear trend ($\chi^2(1) = 5.22$, $P = 0.022$) describing the change in the subjects' performance as a function of TMS intensity (dashed line in Fig. 2). Because the ipsilateral control condition was only tested at two TMS intensities (80 and 90% of PT), we performed a 2×2 repeated measures ANOVA comparing the location of the TMS coil (experimental vs control) and stimulation intensities (80 and 90%). This analysis confirmed that there was a significant main effect for the location of the TMS coil ($F(1,10) = 33.45$, $P < 0.001$, partial $\eta^2 = 0.77$). However, the main effect of stimulation intensity was not significant, indicating no difference between 80 and 90% intensities ($F(1,10) = 0.10$, $P = 0.76$, partial $\eta^2 = 0.009$). Further, there was no interaction between TMS location and stimulation intensity ($F(1,10) = 0.50$, $P = 0.49$, partial $\eta^2 = 0.05$). Follow up paired t -tests showed significant differences between experimental and control conditions at both 80% and 90% stimulation (80%: $M_{\text{diff}} = 1.24$, $t(10) = 2.65$, $P = 0.02$, Cohen's $d = 0.27$; 90%: $M_{\text{diff}} = 1.80$, $t(10) = 3.80$, $P = 0.003$, Cohen's $d = 0.47$).

We compared sensitivity in the ipsilateral (control) condition (the average of the 80% and 90% intensities) with sensitivity measured during blocks of trials without TMS. This revealed that sensitivity was significantly worse in the ipsilateral condition than with no-TMS ($M_{\text{diff}} = 1.09$, $t(10) = 2.63$, $P = 0.025$, Cohen's $d = 0.27$), indicating that TMS at this control location did have some negative impact on the subjects' performance. As a result, the improvement observed in the experimental condition with 90% TMS intensity was not significantly greater than the no-TMS condition ($M_{\text{diff}} = 0.5$, $t(10) = 0.8$, $P = 0.43$, Cohen's $d = 0.12$). Given that the control stimulation site was specifically chosen because the neurons affected would not contribute to identification of the visual stimulus (the stimulus did not fall within their receptive fields), we think it unlikely that this difference reflects a specific effect of the TMS on the neuronal processing of the stimulus. Indeed, in previous work we have shown that TMS delivered to ipsilateral visual cortex, in the same manner described here, does not impair visual sensitivity relative to another active control condition in which TMS is delivered to Cz, on the top of the head far away from visual areas [5].

Thus, we think the difference in sensitivity between the ipsilateral condition and the no-TMS blocks reflects non-specific interference effects from TMS, such as resulting from the auditory click and tactile sensation produced by the magnetic pulse. Indeed, it is for this reason that we have adopted a control condition that involves active stimulation on the head of the subject in order to control for these non-specific effects. Nonetheless, the difference in performance between ipsilateral TMS and no-TMS may question whether the difference between the ipsilateral and contralateral conditions reflects an improvement in performance resulting from weak stimulation of contralateral cortex or an impairment in performance resulting from weak stimulation of ipsilateral cortex. In this regard, the additional evidence presented here—that the effect of TMS to contralateral cortex depends on the intensity of TMS, as seen from the quadratic trend on Fig. 2—establishes that the main effect we report here is due to stimulation to contralateral visual cortex rather than an effect of stimulation to ipsilateral cortex.

Discussion

Our study demonstrates that a low-intensity TMS pulse can significantly improve *identification* of visual stimuli that are otherwise too faint to be reliably identified. The improvement manifested as lowering of contrast thresholds required to identify the orientation of leftward or rightward tilted visual gratings. This happened when TMS was applied 106 ms after the visual stimulus onset at TMS intensities set slightly below the phosphene threshold. We found that low-intensity TMS assisted in discriminating orientation differences for gratings that differ by 90° (tilted 45° left or right from vertical). Our results demonstrate that low-intensity TMS boosts the neural signal evoked by a subthreshold visual stimulus in a manner that preserves information for identification of that stimulus.

These results are consistent with findings recently reported by Schwarzkopf et al. [6]. They found that low, but not high, intensity TMS to motion-sensitive area V5 increased subjects' accuracy in discriminating the left-versus-right direction of motion in a display of moving dots. This effect was only evident when the motion coherence of the dots was very low; there was no beneficial effect of the TMS for stimuli with higher motion coherence. Thus in that study, as in the present one, TMS served to improve identification of the stimulus. The explanation offered by Schwarzkopf et al. [6] and Abrahamyan et al. [5] for the improvements in visual sensitivity with weak TMS relies on the idea that neuronal activity must exceed some threshold for perception to occur. TMS adds a small amount of neuronal excitation that helps to push activity in visual cortical neurons over this threshold and allows perception of a visual stimulus that would otherwise fall below threshold. However, we note that correct discrimination does not necessarily mean that subjects perceive the original stimulus but that the percept contains sufficient information to aid discrimination. Both our and Schwarzkopf et al. [6] experiments cannot determine the veridical percept experienced by subjects.

Correct discrimination does not necessitate that the resultant percept is exactly the same as the stimulus, but only that there is enough difference between two possible percepts to support discrimination. What that difference is cannot be determined from this experiment. I don't think that this takes away much from the main conclusions of the paper, but this caveat should be acknowledged.

In more precise terms, the concept of a threshold can be formally described in terms of a non-linearity in the transduction between input and response. The relationship between the intensity of sensory input and the neural response (Fig. 3B) shows an upwards inflexion around the detection threshold; the

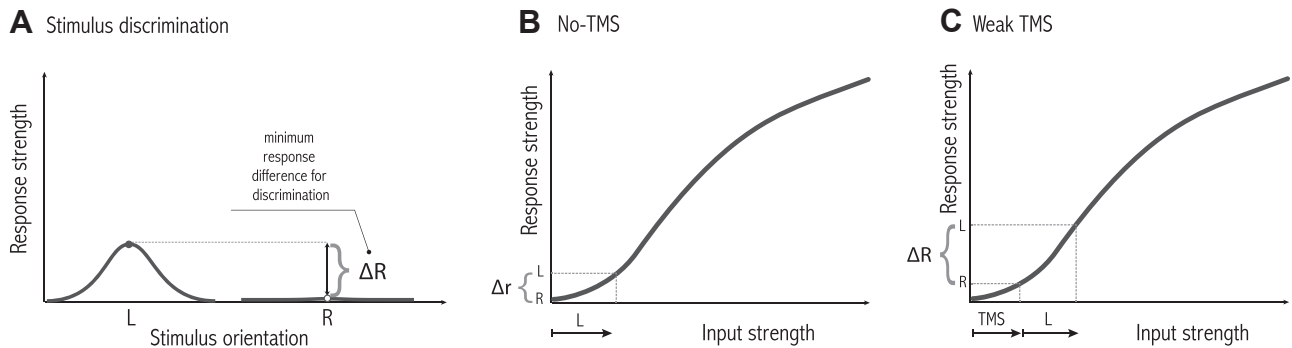


Figure 3. The contribution of weak TMS to improving contrast threshold of orientation discrimination. **A** shows the minimum response strength ΔR (or “just noticeable difference”, jnd) required to reliably discriminate the left-vs-right orientation of a 45° tilted grating. In this example, the subject is comparing the neural response, in left-preferring versus right-preferring channels, evoked by the left-tilted grating. Because -45° and $+45^\circ$ gratings have no overlapping response channels, discrimination of this coarse orientation difference requires contrast intensities close to the detection threshold. **B** Without TMS, the weak left-oriented grating evokes a small response in the left channel but the difference between this and the baseline activity in the right-preferring channel (Δr) is too small to be perceived. **C** a weak pulse of TMS adds input (a pedestal) to both left and right channels. At this point, the effect of input from the left grating on activity in the left channel is now large, due to the upward inflexion of the input–output function, so that ΔR is now much larger than in **B**.

inflexion then reverses (the curve gradually flattens) when stimulus intensities rise above the detection threshold [23–25]. Constrained by the interfering presence of sensory noise, a reliable discrimination between two stimulus intensities requires a minimal perceptual difference to occur (Fig. 3A). Therefore, when stimulus intensity is around the detection threshold, corresponding to the upward inflexion point of the input–response function, a small signal increment relative to the base intensity produces a sufficient perceptual difference to enable detection. In other words, a small increase in input can push the response over the threshold (Fig. 3C).

In the experiment by Schwarzkopf et al. [6], TMS selectively improved motion discrimination for stimuli with low motion coherence but not for stimuli with high coherence. This result is consistent with the explanation offered above in terms of a non-linear (sigmoidal) relationship between input and response strength: at low coherence the motion signal (left or right) is weak and therefore benefits from a small TMS-induced increment in input because this shifts the total input towards the steeper (more sensitive) part of the input–response function. However, it should be noted that the manipulation of motion coherence in that experiment confounds differences in signal strength with changes in stimulus noise: low coherence means both low signal and high noise, while high coherence means both high signal and low noise. In addition, it is not clear what is the effect of the triple-pulse TMS aligned with the visual stimulus onset used in that study. Recently, while studying mechanisms of blindsight with TMS, Allen and colleagues [8] found that only twin-pulses but not single-pulses of TMS delivered at the stimulus onset produce improvement in detection accuracy. It is known that twin-pulses produce a brief inhibition [9]. Neural inhibition, Waterston and Pack [10] argue, can reduce the neural noise and result in improved orientation discrimination. Thus, it remains unclear from Schwarzkopf and colleagues study [6] if the triple-pulse stimulation boosted the visual signal by adding noise into the visual system (stochastic resonance) or suppressed high levels of noise that was introduced into low-coherence motion stimulus.

The forgoing discussion describes the effect of weak TMS as a visual pedestal, elevating the visual response towards the observer’s detection threshold. The pedestal effect is typically observed when the “pedestal” is a subthreshold copy of the target stimulus. Low-intensity TMS to the early visual cortex, however, is unlikely to produce a subthreshold copy of the visual stimulus, given that at higher stimulation intensities phosphenes are

described as composite complex visual percepts [26]. How then can low-intensity TMS act as a pedestal? Recent psychophysical experiments have demonstrated that visual noise used as a pedestal can produce a pedestal effect and improve visual sensitivity [27,28]. Similarly, low-intensity TMS could elicit a uniform response across all sensory channels. For example, when the visual stimulus is oriented to the left, low-intensity TMS provides input to both left and right oriented channels indiscriminately acting as a “noisy pedestal” that shifts sensory activity towards the detection threshold. However, because the transduction of input to output is non-linear (see Fig. 3C), the subthreshold TMS will have a greater impact on neuronal activity in one set of channels (those that preferentially respond to the left-tilted visual stimulus) than in the other set of channels (that would preferentially respond to a right-tilted stimulus). This asymmetric increase helps the left-tilted stimulus to be discriminated even though TMS also stimulates right channels. On the other hand, when TMS is applied at suprathreshold intensities, the high-intensity broadband excitation of channels crosses the detection threshold and can produce a visual phosphene that can serve as a suprathreshold pedestal. However, pedestals above the detection threshold are subject to Weber’s law that requires increasingly high discrimination thresholds and produce masking rather than a pedestal effect. This description of the effect of TMS as a noisy pedestal is equivalent to the description offered by Schwarzkopf et al. [6] in terms of stochastic resonance [29,30]. However, it is possible that due to different qualitative effects of low and high intensity TMS, the underlying shape of the transducer function can have an atypical form compared to those reported in vision experiments.

Our results are also consistent with neurophysiological findings of the acute effects of TMS in the visual cortex of cat. Moliadze and colleagues [31] reported that weak single-pulse TMS can enhance visually-evoked neural responses up to 200 ms after the onset of the TMS. This enhancement was corroborated by results we reported here as well as previous two studies that used low-intensity TMS [5,6]. On the other hand, Moliadze et al. [31] found that a high-intensity TMS pulse suppresses visual-stimulus evoked neural activity from about 100 to 200 ms following TMS onset, probably due to the acute activation of inhibitory interneurons, which may respond more readily to high-intensity stimulation than excitatory neurons. The behavioral evidence seems to support this hypothesis: high-intensity TMS has been reported to suppress visual perception in human participants [1,2,19,32].

Studies that applied “offline” repetitive TMS to visual or somatosensory areas have also reported improvements in discrimination of visual or tactile stimuli [10,33,34]. Similar to our findings, Waterston and Pack [10] showed that visual sensitivity during the coarse orientation discrimination of gratings separated by 90° was improved. While their and our results are similar, it is likely that the effects of TMS are different. Waterston and Pack [10] applied theta-burst TMS stimulation to the visual cortex, effectively inducing prolonged change in cortical excitability, after which subjects’ sensitivity was found to improve. The authors [10] contended that “offline” TMS might reduce neural noise correlation that can increase sensitivity by improving the signal to noise ratio [35] of the whole occipital cortex and last for an hour. The theta-burst protocol applied in their study was designed to have a protracted inhibitory effect on neuronal populations across the whole occipital cortex. Similarly, “offline” repetitive stimulation of the motion area MT led to improvement in motion direction discrimination of large stimuli, effectively lifting spatial suppression occurring with sufficiently large stimuli [33]. On the other hand, the single-pulse subthreshold TMS used in our study is designed to have a localized and acute effect at the target stimulation site. Moreover, single-pulse subthreshold stimulation is likely to have an excitatory effect [31] rather than the inhibitory effect induced by theta-burst stimulation. Thus, the subthreshold TMS used in our study is likely to improve visual sensitivity by providing a weak input to all channels to act as a pedestal instead of globally inhibiting the neural population.

Low-intensity TMS is a novel and powerful approach to explore the functioning of the brain [36]. Here we demonstrated that low-intensity TMS augments the neural signal evoked by a faint visual stimulus such that information about the stimulus orientation is retained. We contend that low-intensity TMS can amplify information to become available to other feature detectors that identify spatial frequency, size, colour or form. Therefore, low-intensity TMS has the potential to become a novel method for unraveling neural correlates of consciousness [37]. Indeed, current methods to study neural correlates of visual consciousness often employ contrasting conscious and unconscious neural footprints generated by a visual stimulus that alternates between “below awareness” and “above awareness” states [38]. Tracing when alternations between these two states occur, such as in the binocular rivalry paradigm, is not a trivial task. Low-intensity TMS, on the other hand, offers precise control over the timing of when an unconscious stimulus is “pushed” into conscious perception. Moreover, low-intensity TMS provides a methodology to amplify the neural signal non-invasively through cortical stimulation, without the need to change the intensity of the visual signal. This amplification can be applied to various parts of the neural architecture that is involved in generating awareness of a visual stimulus, such as to substructures of the occipito-parietal (dorsal) visual pathway. Thus, low-intensity TMS can provide a new approach for studying the neural correlates of consciousness.

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