Extrageniculate mediation of unconscious vision in transcranial magnetic stimulation-induced blindsight

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The proposed neural mechanisms supporting blindsight, the above-chance performance of cortically blind patients on forced-choice visual discrimination tasks, are controversial. In this article, we show that although subjects were unable to perceive foveally presented visual stimuli when transcranial magnetic stimulation over the visual cortex induced a scotoma, responses nonetheless were delayed significantly by these unconscious distractors in a directed saccade but not in an indirect manual response task. These results suggest that the superior colliculus, which is involved with sensory encoding as well as with the generation of saccadic eye movements, is mediating the unconscious processing of the transcranial magnetic stimulation-suppressed distractors and implicate a role of the retinotectal pathway in many blindsight phenomena.

saccades | perception | consciousness | visual cortex | human

Blindsight refers to a condition in which patients with visual field deficits are able to perform at above-chance levels on visual discrimination tasks, despite being unaware of the visual stimuli (for reviews, see refs. 1 and 2). It has been suggested that the extrageniculate visual pathway from the retina to the superior colliculus, which is involved with sensory coding and the generation of saccadic eye movements, may be involved with this blindsight phenomenon (2–5). For example, Rafal *et al.* (3) showed visual distractor processing in the blind hemifield of hemianopic patients in a saccadic eye movement, but not in a manual button-press task, suggesting a role of the superior colliculus in blindsight. However, a more recent study was unable to replicate this saccade distractor effect in a larger group of hemianopic patients (6), whereas others have suggested that incomplete damage of the occipital lobes, or islands of spared cortex, rather than extrageniculate vision may be mediating the blindsight phenomenon in some patients (7, 8). Note that this latter hypothesis of islands of spared cortex has been ruled out in many blindsight patients based on behavioral/perimetric (9) and neuroimaging (10–12) findings.

This variability and inconsistency in measuring blindsight effects may be in part attributable to differences, as others also have suggested (e.g., see ref. 9), in the lesions of the patients, as well as possible differential reorganization of brain function between patients after visual cortex damage. In the current study, we tested whether blindsight may be mediated by the superior colliculus by inducing temporary and reversible scotomas with disruption of occipital cortex in normal observers by using transcranial magnetic stimulation (TMS) (13–15). Because of the transient nature of the TMS, as well as the precisely controlled location and timing of the scotoma, we were able the test the extrageniculate hypothesis of blindsight in normal subjects under more precisely controlled conditions and without the possibility of contamination caused by any reorganization of brain function.

Methods

Six neurologically normal, right-handed observers (four female, two male) completed the experiment after informed consent. The mean age of the observers was 20.8 years, ranging from 19 to 25 years. They were naïve to the purpose of the experiment, recruited from the Rice University campus, and were paid for their participation. The visual cortex first was systematically mapped in each observer with TMS. By using a Cadwell (Kennewick, WA) MES-10 polyphasic stimulator (16) with a circular coil measuring 9 cm in diameter, TMS intensity was set for the experiment at 10% above the visual suppression threshold for each observer. The mean intensity of the TMS used for the experiment was 62.5% of maximum output (2.2 T), ranging from 55% to 70%. A 9-cm circular coil was used because previous reports, including pilot studies in our laboratory, have been unsuccessful at inducing scotomas with more focal coils (see also ref. 17). The coil was placed on the scalp, with the handle positioned below the base of the coil and parallel to the sagittal plane. Initial current flow in the coil was in the clockwise direction. Optimal lateral-medial and rostral-caudal coil positioning and threshold intensity was defined as the location and intensity at which observers did not perceive at least three of five briefly presented (17-ms) visual stimuli when a TMS pulse was administered. None of the observers reported perceiving TMS-induced phosphenes (18–20) at these intensities when asked before commencement or at the end of the experiment.

After the TMS mapping, each observer completed two blocks, the order of which was counterbalanced across subjects, of a peripheral target localization task. In the saccade task, observers were asked to make a saccadic eye movement to the location of a peripherally presented target (0.2° of visual angle in size positioned 5° or 10° to the left or right of fixation). Eye position was monitored and recorded with an Applied Science Laboratories (Bedford, MA) model 504 eye tracker. In the manual task, observers pressed one of four horizontally aligned buttons with one of the four fingers of their dominant right hand to indicate the corresponding position of the target. The targets remained present until a response was made or for 1,000 ms. On half of the trials, a foveally presented distractor (0.2° in size) was presented simultaneously with the target but only for 17 ms. All stimuli were green presented on a gray background (see Fig. 1). A TMS pulse was administered on 75% of the trials, at optimal time intervals for producing visual suppression (83, 100, or 116 ms after the onset of the distractor), as determined in other studies (21, 22). To assess awareness of the foveally presented distractors, observers verbally reported after each trial whether the distractor was perceived. A total of 320 trials was completed by each subject for each of the two tasks.

Results

Fig. 2*a* illustrates the mean latencies from the saccade task. Only trials in which accurate saccades were made and subjects reported being unaware of the distractor when TMS was given (78.5% of the trials) or were accurate in the distractor report when no TMS was administered (76.5% of the trials) were included in Fig. 2 and in the statistical analyses. As can be seen

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Abbreviations: TMS, transcranial magnetic stimulation; RT, reaction time.

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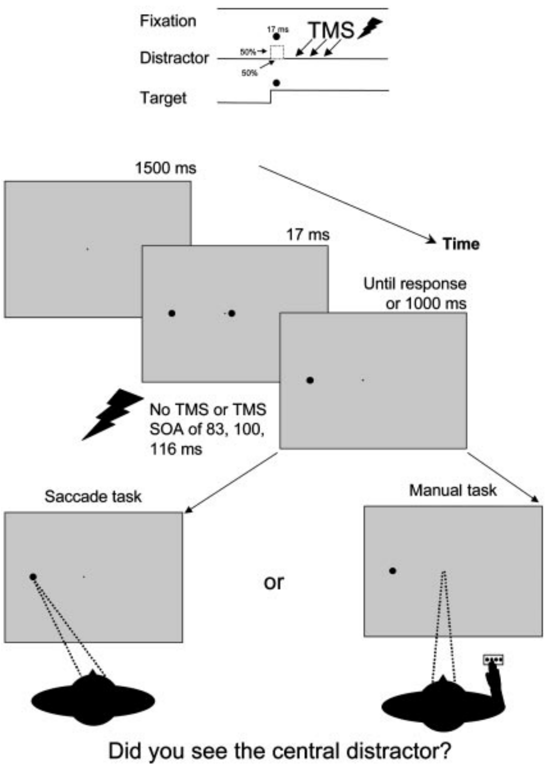

Fig. 1. The stimuli and timing used in this experiment. Distractors, when presented on 50% of the trials, were slightly offset to the right of fixation in each subject because this was the location that produced the most consistent and robust visual suppression with TMS, likely because of a further posterior extension of the left occipital lobe in humans (29).

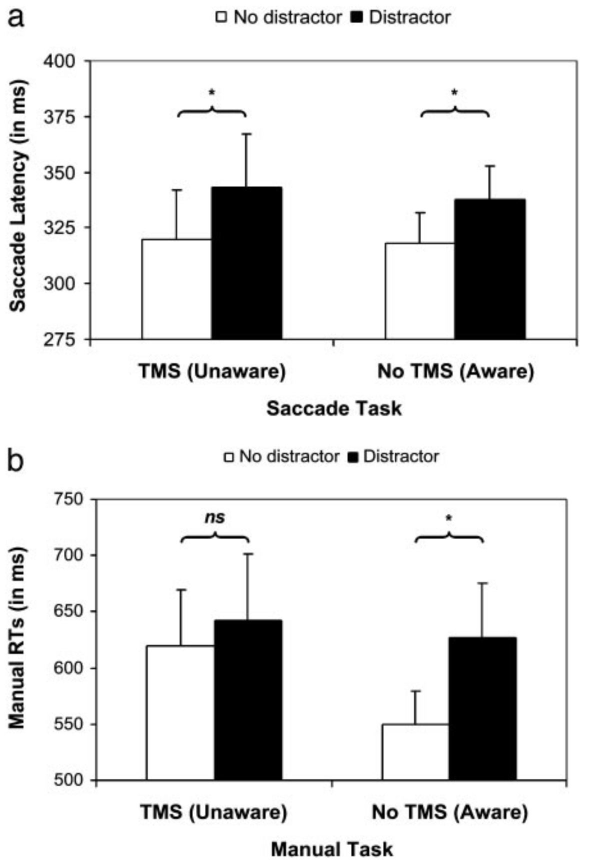

Fig. 2. The mean saccadic latencies for the TMS/unaware and no TMS/aware conditions (*a*) and the mean manual latencies for the TMS/unaware and no TMS/aware conditions (*b*). Note the change in scale in *b* to accommodate for the overall slower responses and larger difference on the aware trials in this task. Error bars represent one standard error of the mean. *, $P < 0.02$; ns, not significant.

in the left half of Fig. 2*a*, even though subjects were unaware of the distractors, and thus the distractor-present trials were phenomenally identical to the distractor-absent trials when TMS was delivered, subjects nonetheless were delayed in making saccades to peripheral targets when an unconscious distractor was presented. A two-way ANOVA, with distractor presence and TMS as the two within-subject factors, confirmed that there was a significant main effect of distractor presence ($P < 0.001$). The main effect of TMS was not significant ($P > 0.10$), and, most importantly, the distractor presence by TMS interaction also was not significant ($P > 0.10$). A two-tailed paired *t* test showed that when there was no TMS and subjects were aware of the distractor, saccade latencies were significantly slower than when no distractors were presented ($P < 0.02$). Critically, another two-tailed paired *t* test conducted on the TMS trials showed that even when TMS was administered and subjects reported being unaware of the foveally presented distractors, saccadic responses nonetheless were delayed significantly by these unconscious distractors as compared with when no distractor was presented ($P < 0.01$). All six observers had slower saccade latencies when a distractor was present in both the unaware/TMS and aware/no TMS conditions.

In contrast to the results obtained with the saccadic eye movement task, the manual reaction times (RTs) showed a very different pattern of results (see Fig. 2*b*). In particular, when subjects were unaware of the foveal distractors caused by the TMS of the visual cortex, there was no influence of these unconscious distractors on the manual button-press responses made to the peripheral targets. As with the saccade data, only trials with accurate button-press responses and unaware distractor trials with TMS (82.6% of the trials) and accurate distractor report trials without TMS (84.8% of the trials) were included in Fig. 2 and in the statistical analyses. The main effect of distractor presence was significant ($P < 0.025$). The main effect of TMS was marginally significant ($P = 0.059$), as there was a tendency for overall slower responses when a TMS pulse was delivered, even for the no-distractor conditions. However, and most importantly and unlike with saccades, the distractor presence by TMS interaction was significant ($P < 0.05$). Two-tailed paired *t* tests demonstrated that this interaction was caused by there being a significant effect of the distractor when no TMS was delivered and subjects were aware of the distractor ($P < 0.02$), but no effect of the distractor when TMS was administered and subjects were unaware of the distractor ($P > 0.10$). Although all six observers had slower manual RTs when they were aware of the distractor with no TMS, only four of the six observers responded more slowly when unaware distractors were presented.

Although the three-way Distractor × Task × Awareness interaction was significant ($P < 0.05$) in the omnibus ANOVA, which further suggests that the unconscious distractors had differential effects in the manual vs. the saccade task, the absolute magnitude of the unconscious distractor effect (distractor-present minus distractor-absent conditions) was similar between the two tasks (see Fig. 2). However, note that the overall RTs for the manual task were nearly twice as large as those for the saccade task, and that the distractor effect in the manual task when subjects were aware of the distractor was more than three times as large as for the saccade task. Thus, to test for proportional differences in the magnitude of the unconscious distractor effect between the saccade and manual tasks, the RT data from each subject in each condition were subjected to a logarithmic transformation. A two-tailed t test on the difference scores (i.e., the distractor effect) revealed a significantly greater unconscious distractor effect in the saccade task than in the manual button-press task ($P < 0.05$). This finding is consistent with the claim that unconscious distractors influence saccades but not manual button-press responses.

Discussion

We induced a transient scotoma in normal observers by applying TMS over the visual cortex and showed that responses to visual stimuli within the scotoma were affected in tasks more directly relying on the superior colliculus. Specifically, we induced a form of blindsight in the saccadic eye movement task but not in the manual button-press, target-localization task. Interestingly, RTs in the TMS trials for the manual task were slightly longer overall in comparison to the no TMS trials, regardless of whether a distractor was presented. This slowing for the TMS trials in the manual response task may have been attributable to a general delay and interference introduced by the TMS pulse, which was not present for the saccadic eye movement task. This lack of a general disruptive effect of the TMS on the saccadic eye movement task further suggests that the saccade task was less influenced by higher cognitive and/or cortical activity and mediated by the subcortical retinotectal pathway, which may be more reflexive.

Previous studies have demonstrated accurate pointing responses to unseen visual targets in hemianopic patients (4, 23). Furthermore, other studies have reported *faster* response times from redundant stimuli in the blind hemifield in simple manual RT tasks (24, 25). The manual RT task used in the current study, however, involved a discrimination of spatial positions and an indirect spatial mapping and transformation between target locations on a computer monitor and button positions on a response pad that was on a table in front of the observers. It therefore is likely that the manual task we used involved more perceptual/cognitive resources that relied on the retinogeniculostriate pathway and hence was less subject to the influence from unconscious distractors. In other words, although the retinotectal pathway projects from the superior colliculus via the pulvinar into the dorsal pathway (26), which has been suggested to be involved with directed manual-reaching responses (27, 28), the indirect manual task that was used in this study unlikely involves this subcortical pathway. Future studies using this TMS-induced blindsight paradigm with a directed reaching task are planned to determine whether such manual tasks that are likely to rely more heavily on the dorsal stream are more affected by unconscious stimuli.

Taken together, these results demonstrate unconscious influences of visual distractors specifically on saccadic eye movements, which are directly mediated by means of the superior colliculus. With the visual processing disruptions in the occipital cortex after TMS, these results suggest an active role of the retinotectal pathway, frequently conceived of as a vestigial visual system, in visually guided behaviors. The transient nature of the single-pulse TMS used in this study also rules out these effects, as well as many blindsight effects observed in patients with visual cortex lesions, as being caused by plasticity and reorganization of brain function. Our results further suggest that extrageniculate vision, with its pathways projecting into the dorsal stream, may play a prominent role in many of our automatic and visually guided behaviors without awareness (27).

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