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RESEARCH NOTE

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The role of human extra-striate visual areas V5/MT and V2/V3 in the perception of the direction of global motion: a transcranial magnetic stimulation study

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Abstract Several published single case studies reveal a double dissociation between the effects of brain damage in separate extra-striate cortical visual areas on the perception of global visual motion defined by a difference in luminance (first-order motion) versus motion defined by a difference in contrast (second-order motion). In particular, the medial extrastriate cortical region V2/V3 seems to be crucial for the perception of first-order motion, but not for second-order, whereas a lateral and more anterior portion of the cortex close to the temporo–parieto–occipital junction (in the territory of the human motion area hV5/MT$^+$) seems to be essential only for the perception of second-order motion. In order to test the hypothesis of a functional specialization of different visual areas for different types of motion, we applied repetitive transcranial magnetic stimulation (rTMS) unilaterally over areas V2/V3, V5/MT, or posterior parietal cortex (PPC) while subjects performed a 2AFC task with first- or second-order global motion displays in the contralateral visual field. Results showed a comparable disruption of the two types of motion, with both rTMS over V2/V3 or over MT/V5, and little or no effect with rTMS over PPC. The results suggest that either the previous psychophysical results with neurological patients are incorrect (highly unlikely) or that the lateral and medial regions are directly connected (as they are in macaque monkeys) such that stimulating one automatically affects the other, in this instance disruptively

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Introduction

Evidence from a variety of sources—psychophysics, functional neuroimaging, clinical neuropsychology, single cell recording in macaque monkeys—indicates that different forms of visual motion are separately computed and that there is even evidence of gross regional segregation at the final stages of cortical motion processing (for reviews see Vaina 1998; Vaina et al. 1998a). Examples of different forms of visual motion are local, global, flow fields, biological, frontal, radial, motion discontinuity, first-order and second-order. This article is concerned solely with the latter two, which have received the most attention and whose psychophysical and anatomical substrates have been investigated in detail (Ledgeway and Smith 1994; Lu and Sperling 1995; Werkhoven et al. 1993; Clifford and Vaina 1999; Vaina and Soloviev 2004). In first-order motion we see real or apparent displacement of items defined by a luminance difference between the items and their surround, e.g. black dots on a bright background. In contrast, second-order motion consists of perceiving items whose mean luminance is the same as that of the surround, and that differ from the

background by some other "higher-order" feature such as contrast or texture (e.g. colour or moving micropatterns on a background of similar overall texture). Whereas first-order motion involves a directional shift in a luminance distribution, second-order motion has no overall luminance shift and the motion signal must be extracted by some non-linear processing of retinal illumination.

Although there is evidence from single cell recordings in monkeys and cats that some directionally sensitive cells respond better to one or other type of motion (Albright 1992; O'Keefe and Movshon 1996; Zhou and Baker 1993) the cells are not grossly regionally segregated, suggesting that both types of motion processing occur within the cortical visual areas from which they were recorded. Functional neuroimaging of subjects viewing first- and second-order displays has produced either no evidence (Somers et al. 1998; Sunaert et al. 1999) or slight evidence (Smith et al. 1998) or strong evidence (Dumoulin et al. 2003) for gross separation of the two mechanisms. Yet there is convincing evidence that a circumscribed brain lesion in humans can selectively disrupt one or the other (Vaina and Cowey 1996; Vaina et al. 1998b) and that the damage that impairs second-order motion is lateral and just dorsal to motion area V5/MT, but not within in, whereas the impairment of first-order motion was found in patients with medial occipital damage centred on areas V2 and V3 (Vaina et al. 1998b). A third patient, TF, who was selectively impaired on first-order motion had a small infarct principally in area V2. In all these patients the defect was confined to the visual field contralateral to the lesion.

In an attempt to explain these differences we used an entirely different method of disrupting motion perception by applying transcranial magnetic stimulation (TMS) to different regions of extra-striate cortex in normal subjects while they performed first- and second-order motion tasks identical to those used previously with patients. The results indicate that TMS in the territory of human V5/MT or V2/V3 disrupts the perception of the direction of both types of global motion.

Materials and methods

Subjects

Six subjects, four male and two female, aged between 28 and 68 participated. Each subject performed 120 trials per experimental condition, in addition to a variable number of trials in pilot experiments. All experiments were approved by the local ethics committee (OxRec CO2.304) and were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All subjects gave their informed consent prior to their inclusion in the study. Four of the six subjects were experienced observers in visual psychophysical experiments involving TMS.

Apparatus and stimuli

The stimuli were the same as those used in Vaina et al. (1998b). Subjects sat at 60 cm from the monitor in a dimly lit room and fixated a small black fixation spot positioned 1° to the left and 1° above the top left corner of the virtual square delimiting the stimulus area. The position of the fixation point was chosen on the basis of the evidence that subjects, when stimulated either over left V2 + V3 or left hV5/MT^{+} with 80–90% of maximum output intensity, perceived phosphenes in most of or even more than the area corresponding to the stimulus position. Stimulus area subtended 10×10° arc, and was presented against a uniform grey background of 9.72 cd/m^2. The stimulus area was divided into a grid of 38×38 notional blocks, each subtending 16×16 arcmin. Each block is a dense random-dot microtexture consisting of pixels whose luminance is one of 256 possible gray levels. The number of light and dark dots within a block is equal. The block mean luminance is the average of its light and dark dots and its contrast is the ratio of the luminance difference between on and off dots divided by twice the mean luminance. A moving block can differ from the background either in mean luminance but not contrast (first-order motion), or in contrast but not in luminance (second-order motion). The assignment of a block to motion or background is carried out randomly at the beginning of each trial in such a way that tokens represent 42% of the total number of blocks throughout the test. The mean luminance of first-order motion blocks was 14.62 cd/m^2 and the contrast within the block was 0.2 (on dots: 17.47 cd/m^2, off dots: 11.55 cd/m^2), whereas the mean luminance of second-order motion blocks was 9.72 cd/m^2 and the contrast 0.54 (on dots: 15.17 cd/m^2, off dots: 4.54 cd/m^2). The mean luminance of the background was in both cases 9.72 cd/m^2 and the contrast 0.2 (on dots: 11.55 cd/m^2, off dots: 7.84 cd/m^2). An example of the two stimuli is illustrated in Fig. 1. Each motion stimulus consisted of 12 frames successively presented, each frame lasting 45 ms and with zero interframe interval. From one frame to the next, the token blocks are shifted either to the left or to the right with respect to the background. The texture pattern defining moving blocks and background is varied from frame to frame by randomly changing the component pixels from on to off and vice versa, while keeping their mean luminance and contrast identical throughout the trial. Although all such second-order displays necessarily contain some first-order energy, the latter is unsystematic with respect to correlated motion because the position of the light and dark pixels within a texture dot is randomised from frame to frame (Vaina and Cowey 1996).

In each trial a blank screen was presented for 1 s, then the moving stimulus display appeared for 536 ms, and a blank screen was presented again until the subject responded. The subject's response triggered the beginning of next trial. Subjects had to decide whether the stimulus was moving coherently left or right by pressing one of the direction keys on the computer keyboard.

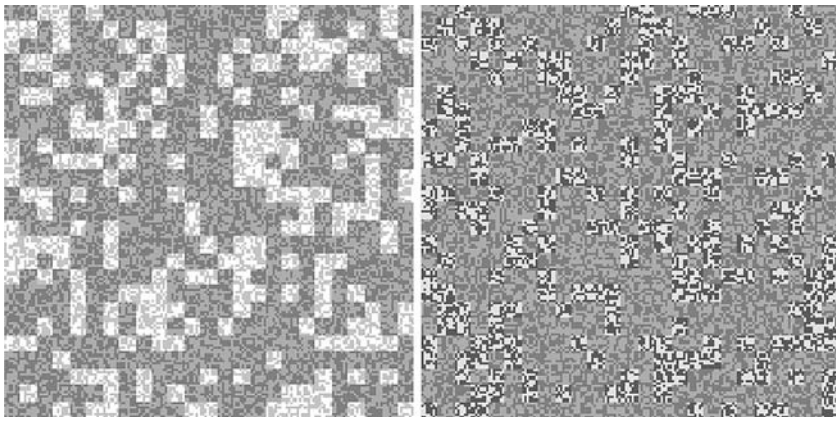

Fig. 1 *Left*: an example of one frame of the first-order motion display. The mean luminance of the moving blocks is higher than that of the background. Although many motion blocks necessarily touch each other in such a high-density display, they have a different relative spatial disposition in the next frame, which ensures that subjects cannot follow a particular cluster of blocks. *Right*: a similar representation of blocks in a second-order display. Each moving block has the same mean luminance as the background but has a higher mean contrast

Contrast, luminance and coherence (proportion of moving blocks moving coherently in one direction) were fixed for each subject. Coherence of moving dots was determined in advance with pilot experiments using an adaptive staircase procedure that determined the level of coherence for 75% correct. This value was then used with the method of constant stimuli to determine any effects of TMS on performance. The value of coherence used in the final experiment varied from subject to subject and was also different for the two types of motion, reflecting the fact that all subjects found the second-order motion more difficult to perceive. In this way we were able to equate the performance level for first- and second-order motion discrimination.

Gaze monitoring

Eye gaze was monitored and recorded in all sessions and for each subject with eye tracking equipment (iView RED-III) with a sampling rate of 60 Hz. This system comprised an infrared camera placed directly beneath the stimulus display and connected to an independent Pentium III PC. The system was re-calibrated before each session with each subject. In each session and for each subject eye gazes during a trial that deviated more than 1° of visual angle from fixation point were discarded and the trial was repeated.

Statistical analysis

We considered three independent variables: task (first- vs. second-order motion), stimulated site (V5/MT, V2/V3, and posterior parietal cortex, PPC) and TMS condition (TMS vs. baseline). The dependent variable was accuracy (percentage correct trials) in motion direction discrimination, which is an ordinal scale and therefore appropriate for non-parametric statistics. We were interested in testing whether rTMS over V5/MT or over V2/V3 could have different effects on first and second order motion discrimination, which can only be done by looking at the three-way interaction: task by stimulation site by TMS condition. Unfortunately there is no standard statistical non-parametric procedure for testing a within-subject three-way interaction. Therefore, as suggested by Conover (1998), we first performed the ANOVA on the raw data and then conducted the same procedure on the rank transformed data. Since these two procedures gave nearly identical results the assumptions underlying the usual analysis of variance were deemed reasonable and the regular parametric analysis is valid (Conover 1998). Within-subjects contrasts were performed in order to compare the effect of TMS in the three stimulated sites with the two different stimulus displays.

Results

As shown in Fig. 2, TMS impaired performance for both types of motion and at all three stimulation sites ($F_{1,5} = 88.5$, $P < 0.0001$). However, the difference in percentage correct between baseline and TMS condition was not equivalent at all sites ($F_{2,10} = 20.2$, $P < 0.0001$). The impairment was much more pronounced with TMS over V5/MT ($F_{1,5} = 29.9$, $P < 0.005$) and over V2/V3 ($F_{1,5} = 21.3$, $P < 0.01$) than with TMS over PPC. Neither stimulus task by stimulation site ($F_{2,10} = 1.3$, $P > 0.05$), nor stimulus task by TMS condition ($F_{2,10} = 1.1$, $P > 0.05$), nor the three-way interaction (stimulus by stimulation site by TMS condition: $F_{2,10} = 1.7$, $P > 0.05$) were significant. This indicates that TMS over V5/MT and over V2/V3 have a similar disrupting effect with either first- or second-order stimuli. Surprisingly, the factor stimulation site was also significant ($F_{1,5} = 8$, $P < 0.01$), and contrasts revealed that when TMS was (or was not, in the baseline condition) applied over PPC, performance was better than when TMS was (or was not) applied over V5/MT ($F_{1,5} = 13.8$,

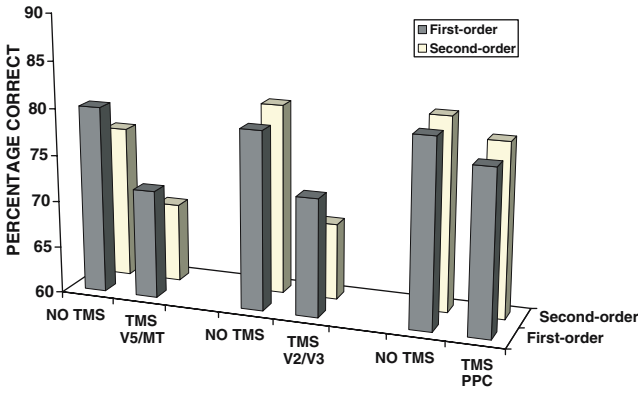

Fig. 2 Percentage correct performance with and without transcranial magnetic stimulation (TMS) at three different stimulation sites. TMS had almost no effect when delivered over the left posterior parietal cortex but impaired performance on both first- and second-order motion when applied above area V5/MT or dorsal V2/V3

$P < 0.05$) or V2/V3 ($F_{1,5} = 9.3$, $P < 0.05$). This reflects the small effect that TMS had over PPC, having as a result a general increase in performance in the PPC stimulation condition.

Discussion

The results show that the dorsal PPC is not necessary for, and might not even be involved in, the processing of either first- or second-order motion, whereas both V5/MT and V2/V3 are importantly involved in the analysis of moving stimuli, whether they are defined by luminance (first-order) or contrast (second-order) differences.

At first sight the outcome of the experiment indicates that both regions are involved in processing both types of motion and that the results obtained with neurological patients, where a lesion of one or other region impairs only one or other type of motion are incorrect or unreliable. However, this apparent paradox has a simple but important resolution. It is sometimes said, although not by the authors of the phrase (Walsh and Cowey 2000; Walsh et al. 1998) that TMS is just like a reversible lesion of the area stimulated and that during the stimulation and its aftermath the subject is a "virtual patient". Indeed this is the rationale behind many TMS experiments. A major problem with this view of TMS is that it ignores any neuronal activity that is propagated from the stimulated region. That the latter occurs is now well documented by recording field potentials distant from the stimulated region. (e.g. Ilmoniemi et al. 1997). The present data show that the effects of real and virtual lesions can differ greatly and that in interpreting their comparative effects it is important to evaluate the different mechanisms of the two interventions. The effects of TMS can occur at the primary site of stimulation and also at secondary sites that are anatomically connected it. In some studies the effects of secondary stimulation may be to enhance sensitivity, as we showed in a previous TMS experiment on motion perception (Walsh et al. 1998). In other studies the effects of secondary activation may be to increase the effects of disruption of the primary target, as in the current study. As V5/MT is extensively reciprocally connected with V2 and V3 (Van Essen and DeYoe 1995) the repetitive stimulation used here may have stimulated these connected sites. We have shown elsewhere that connected sites can be dissociated most effectively when single or double pulse TMS is used, and the current data show that PPC, although it too is reciprocally connected with V5/MT, is not involved in first or second order motion processing. We can draw two competing conclusionsfrom these data. Either the segregation of first- and second-order motion processing in neuropsychological patients reflects selective reorganisation in the motion system following lesions, or both V2/3 and V5/MT are equally involved in the two processes. Single pulse TMS studies of first- and second-order processes may well yield a closer correspondence between real and virtual lesions.

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