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Abstract: A previous transcranial magnetic stimulation (TMS) study (Ellison & Cowey, 2006) showed that both the dorsal and ventral cortical visual processing streams are involved in the processing of a task in which judgement of relative spatial position is required. In order to determine whether both streams are active in a parallel or serial manner, a double pulse TMS (20Hz) experiment was carried out to expose peaks of disruption, indicative of when each of the areas under investigation is most potently involved. Results show that TMS over lateral occipital cortex produces greater disruption of performance than that provoked by TMS over posterior parietal cortex, significantly so when applied at 50 ms and 100 ms post visual array onset. Both areas showed peaks of disruption up to 350 ms after visual stimulus onset. The results are discussed with respect to why each of these areas is involved in this task and what the pattern of their involvement reveals.

Time course of the involvement of the ventral and dorsal visual processing streams in a visuospatial task.

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Abstract:

A previous transcranial magnetic stimulation (TMS) study (Ellison & Cowey, 2006) showed that both the dorsal and ventral cortical visual processing streams are involved in the processing of a task in which judgement of relative spatial position is required. In order to determine whether both streams are active in a parallel or serial manner, a double pulse TMS (20Hz) experiment was carried out to expose peaks of disruption, indicative of when each of the areas under investigation is most potently involved. Results show that TMS over lateral occipital cortex produces greater disruption of performance than that provoked by TMS over posterior parietal cortex, significantly so when applied at 50 ms and 100 ms post visual array onset. Both areas showed peaks of disruption up to 350 ms after visual stimulus onset. The results are discussed with respect to why each of these areas is involved in this task and what the pattern of their involvement reveals.

Keywords: Ventral Stream, Dorsal Stream, visual discrimination, transcranial magnetic stimulation.

Introduction

There is now abundant and incontrovertible evidence that the dorsal and ventral cortical visual processing streams differ in their relative processing specialisations (e.g. Avidan et al., 2003), although there is also evidence that both may be involved in the processing of a common task (Ellison & Cowey, 2006). This could indicate that some aspects of processing may be common to both streams and/or that there may be some interaction between the areas.

Neurological patients with damage to their dorsal stream are impaired on spatial tasks involving judgements of relative position or lateral extent, such as the landmark task (Harvey et al., 1995), but when asked to point to the middle of the screen or a shape, they are unimpaired (Bartolomeo et al., 2003), perhaps by recruitment of their intact ventral streams specialised for shape perception. A previous paper (Ellison & Cowey, 2006) investigated this paradoxical dichotomy and discovered that there was a clear dissociation between the two streams when processing a shape task, with only right lateral occipital (LO) cortex being involved but not right posterior parietal cortex (PPC). However, counter-intuitively, both right LO and PPC were involved in the processing of a visuospatial task concerning the relative position of items in the frontal plane. This finding is explicable if shape-based processing contributes to how the normal brain computes relative spatial distance. This is manifested by the finding of Bartolomeo et al. (2003) in which neurological patients with dorsolateral parietal damage and classical left hemineglect also have deficits in processing line bisection or landmark tasks but the ability to point to the middle of the screen or a shape is spared, presumably by making a discrimination based on shape rather than spatial extent and thereby recruiting their undamaged ventral stream. There is a possibility therefore that the dorsal and the ventral streams are processing the same task, but in different ways, i.e. PPC is basing its analysis on visuospatial properties, but LO is using shape information to complete the task. It is also possible however that the dorsal and ventral streams are interacting in order to process the task, with LO providing shape information and PPC spatial information. Both of these hypotheses are consistent with the behavioural effect of increased reaction times with TMS at either site.

If the relative timing of involvement of PPC and LO could be determined, the results should help in deciding between these two possibilities. If LO and PPC are active in parallel and simultaneously, both areas would seem to be processing the task according to their relative functional specialization, be it shape or space. If consecutive peaks of activation are seen, it is more likely that LO and PPC work in sequence in order to accomplish the task.

The same visuospatial distance task as was used in our previous study was used in the present investigation, but with double pulse TMS to provide a brief disruption window of 100 ms, allowing us to make inferences as to when each area of investigation is most involved in processing the task.

Methods

Subjects

Ten healthy subjects, aged 19-26, with normal or corrected to normal vision (all right handed; 6 female, 4 male), each participated in two experimental sessions. Subjects gave their signed informed consent in accordance with the Declaration of Helsinki and with the approval of Durham University Ethics Advisory Committee, and could leave the experiment at any time. Subject selection complied with current guidelines for rTMS research (Wassermann, 1998).

Stimuli

All stimuli were presented on a 32 cm x 24 cm VDU driven by a Pentium-4 PC programmed in E-Prime (Psychology Software Tools, Inc). Subjects were seated comfortably 57.5 cm away from the screen with the centre of the screen at eye level. The subjects' head and trunk sagittal midline was aligned with the centre of the screen, and head position was controlled by a chinrest.

Visual Task

The distance discrimination task directly replicated that used by Ellison & Cowey (2006), in which subjects had to judge which of two eccentric and identical green (11 cd/m^2) squares (1º x 1º in size, 5º to the left of the vertical midline) in the left hemifield was closer to a third identical square at the fixation point. One square (either the top or the bottom) was always 3º above or below the horizontal midline. The other square was initially presented at a vertical eccentricity of 4 degrees from the horizontal meridian and progressively it approached it in 0.2º steps until the threshold for 80% correct was reached according to the following rule. Difficulty was changed after each set of five trials. After five consecutive correct responses difficulty was increased by one step. If two or more incorrect responses out of five were made, the difficulty was decreased by one step. Performance was deemed stable when performance reached 80% correct (four out of five) in two subsequent sets.

Every trial began with a 500 ms central fixation cross (0.5º x 0.5º) after which the three stimuli were presented for 500 ms, one of them replacing the fixation cross. The background colour was a uniform grey with a luminance of 30 cd/m^2. There was a 5 second interval between trials. The experimental value of the distance of the furthest object from the centre was set at 0.2º greater than the threshold value. The subject was asked to indicate which item was closer to the item in the centre by pressing the bottom button on a keypad if the bottom item was closest and the top button if it was the top item. The top square was the closer item in 50% of trials, at random.

FIGURE 1 ABOUT HERE

TMS

A Magstim™ Rapid Model was used to apply 2 pulses at 20Hz (50 ms apart) at 65% of the stimulator's maximum power (*i.e.* at 1.3 Tesla) using a 70 mm figure-of-eight coil placed tangential to the skull, with the handle pointing backward, parallel to the horizontal and the mid-sagittal plane and held in place throughout by the experimenter. The magnetic intensity used is greater than the threshold intensity required to induce movement (over motor cortex) or the perception of phosphenes (over primary visual cortex, V1) in all of the subjects but did not produce phosphenes when delivered over LO or PPC. The TMS train of 2 pulses began at 8 onset times, namely: 0, 50, 100, 150, 200, 250, 300, and 350 ms after the onset of the visual array.

Two sites of stimulation were used, as by Ellison & Cowey (2006), a right ventral stream site (LO) and a right dorsal stream site (PPC). The dorsal site was chosen as an area of posterior parietal cortex (PPC) known to be involved in difficult conjunction visual search tasks that engage dorsal functions, and was identified by using a hunting procedure with the hard conjunction task, as described in Ashbridge *et al.* (1997). The ventral site was chosen in relation to area right V5 (generally corresponding to 3 cm above the mastoid-inion and 5 cm lateral to the right) which was precisely identified by localising the area where a train of TMS pulses (10 Hz, 500 ms) repeatedly elicited the strongest and most salient moving phosphenes (see Schenk *et al.*, 2005) at the lowest TMS intensity. The ventral site LO was then calculated to be 1-1.5 cm caudal on the skull in a direct line towards the inion. This area corresponds well with lateral occipital cortex, LO (see figure 1).

Trials were administered in six blocks of 40 trials (per task) each block randomised across subjects to minimise either order or practice effects; four blocks with TMS over the experimental site (LO or PPC) on each trial, and two blocks of sham TMS with a non-discharging coil held over the experimental site and a second coil discharged a few cm above the skull on the subjects' right so that the subjective experience of the noise associated with a TMS pulse was the same, as was the tactile experience of the silent coil placed on the head. However, no effective pulse was administered to the brain. Two testing sessions were required, one for each experimental site (PPC or LO) and the order of sessions was the same for each session within subject but randomised across subjects. Each testing session usually lasted no more than 1 hour.

Results

Thresholds:

The mean threshold achieved across subjects in the distance task was a difference of 0.42 ± 0.10º for 80% correct. This led to a fixed distance of 0.62 ± 0.10º for the furthest square in the experimental task.

Effect of TMS:

A two-factor repeated measures general linear model (GLM) comparing reaction times for sham and PPC stimulation over all time bins ($TMS_{[PPC,\ sham]}$ x $TMStime_{[8\ SOAs]}$) revealed a significant main effect of TMS ($F_{(1,\ 9)} = 9.056$, $p = 0.015$) and a main effect of TMS time ($F_{(7,\ 63)} = 2.711$, $p = 0.016$) with no interaction effect ($F_{(7,\ 63)} = 1269.964$, $p = 0.779$). As PPC and LO sites were tested in separate sessions, the same analysis was performed for the LO TMS reaction times and the corresponding sham reaction times. This revealed a main effect for TMS ($F_{(1,\ 9)} = 14.078$, $p = 0.005$) and TMS time ($F_{(7,\ 63)} = 7494.714$, $p < 0.001$) but with no interaction ($F_{(7,\ 63)} = 1855.94$, $p = 0.363$).

Separate one-factor repeated measures GLMs at each time point revealed that TMS had a significant effect on reaction time when TMS was applied over PPC at 50+100 ms ($F_{(1,\ 9)} = 5.230$, $p = 0.048$), 250+300 ms ($F_{(1,\ 9)} = 6.018$, $p = 0.037$), and 350+400 ms ($F_{(1,\ 9)} = 13.214$, $p = 0.005$). When TMS was applied over LO, reaction times were significantly increased over sham reaction times at 0+50 ms ($F_{(1,\ 9)} = 8.565$, $p = 0.017$), 50+100 ($F_{(1,\ 9)} = 10.556$, $p = 0.010$), 100+150 ($F_{(1,\ 9)} = 24.463$, $p = 0.001$), 150+200 ($F_{(1,\ 9)} = 8.357$, $p = 0.018$), 200+250 ($F_{(1,\ 9)} = 7.820$, $p = 0.021$) and 350+400 ($F_{(1,\ 9)} = 10.409$, $p = 0.010$).

FIGURE 2 ABOUT HERE

PPC vs LO

In order to compare the effect of TMS at PPC and LO, TMS reaction times were normalised with respect to each session's sham condition. Data were normalised according to the formula (TMS-sham)/sham, therefore positive values denote an increase in reaction time with TMS at that particular SOA. A two-factor repeated-measures GLM ($\text{TMS}_{[\text{PPC, LO}]}$ x $\text{TMStime}_{[8\ \text{SOAs}]}$) was then performed using the normalised effect of TMS at each SOA for each site. There was no main effect of TMS ($F_{(1,\ 9)} = 2.545$. $p = 0.145$). However, there was a main effect for TMStime ($F_{(7,63)} = 4.766$. $p < 0.001$) with no interactions ($F_{(7,63)} = 0.923$. $p = 0.495$). This pattern of significances suggests that although there is no overall difference in how TMS affect performance at each site, there is a difference in its effects in different time bins. As visual information from the eye first reaches occipital cortex, including area V1, at about 40 ms after stimulus onset and subsequent feedback information reaches extra-striate visual areas at around 90-100 ms (reviewed by Corthout et al., 2007) we would expect differences in activations between PPC and LO temporally early in visual processing (as can be seen in Figure 2B). Therefore, we compared the effects of TMS delivered over LO and PPC at 50 and 100 ms. There was a significant difference between these sites when double pulses of TMS were applied at SOAs of 50 ms (*$t = -2.677$, $df = 9$, $p = 0.025$*) and 100 ms (*($t = -2.861$, $df = 9$, $p = 0.019$*). There was no reason to expect any difference at other SOAs and indeed there were none.

Discussion:

The results confirm the finding of Ellison & Cowey (2006), that rTMS of right PPC and LO increases reaction time in a task requiring visuospatial discrimination of relative distance. The current experiment, however, sought to determine the temporal pattern of activation of right PPC and right LO in the processing of this task. There was no overall difference in how TMS impaired reaction times between PPC and LO but the TMS effect differed across stimulation times with significant differences when double pulses were applied at 50 ms and 100 ms. At both of these times TMS at LO had a significantly greater effect. PPC stimulation and LO stimulation also induced a similar and large increase in response latency at the later time point of 350 ms. These later impairments have not been explored.

These findings indicate that the ventral stream has a greater earlier involvement in the processing of this task, consistent with our previous conclusion that the involvement of LO in this task is based on the shape processing for which the ventral stream is specialized (Kourtzi & Kanwisher, 2001; Malach et al., 1995). In contrast the involvement of the dorsal stream is based on its established visuo-spatial specialisation (Avidan et al., 2003; Ellison et al., 2003; Bjoertomt et al., 2002).

Corthout et al., (2007) have recently delineated the arrival time of visual information in extra-striate visual cortex, whether feed-forward or feed-back, as between 50 and 100ms. This finding is supported by our results which show that although the involvement of the ventral and dorsal streams largely mirror each other, LO has a significantly more crucial role in early processing of visual information in our task. This is also in line with fMRI and ERP evidence that show the relative activation of these regions within this timescale (Vanni et al., 2004; Jiang & Han, 2005). However, it remains possible that the dorsal stream depends upon input from the ventral stream in order to adequately process the task, and that is why disruption of either area lengthens reaction time. A necessary interaction between the streams for the completion of this task will also explain why parietal patients cannot usually carry out such visuospatial tasks using their intact ventral streams alone (e.g. Harvey et al., 1995).

The much later, and unexpected, peaks of disruption when TMS is applied at 350 ms after visual stimulus onset may point to the activity of other reciprocal interactions. Although a model for such an interaction, mediated by V1, does exist (Deco & Lee, 2004), further work must be carried out to determine the functional specificity and timing of such associations and the nature of their connections. It is also possible that magnetically induced stimulation of both LO and PPC are impeding, and therefore slowing down, preparation for a motor response. The role of the dorsal stream in visuomotor transformations is clear from neuropsychological (James et al., 2003), functional imaging (Culham et al., 2006) and TMS (Ellison et al., 2003) studies. But this alone does not explain the involvement of PPC in the visuospatial task used in this study as PPC was not involved in a shape discrimination where the same visuomotor transformation was required in our previous paper (Ellison & Cowey 2006). However, it is even less clear why disruption of the ventral stream should lengthen a motor response. With respect to area V5, Schenk et al (2005) found that magnetic stimulation here can lengthen the execution of the action of catching a moving object. In contrast, a combined neuropsychological and fMRI study by James et al. (2003) shows a clear dichotomy between the ventral and dorsal streams for object recognition and object directed grasping. Nevertheless, in normal human subjects a much more integrative approach may be involved in processing tasks like the present one, in which reciprocal interactions which involve earlier perceptual processes may be concerned either with perceptual issues or response issues in the task. This important matter has yet to be addressed.

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Figure legend

Figure 1: Left, the visuospatial task in which subjects were asked to decide which item was closer to the central item and, right, the anatomical localisation of magnetic stimulation sites (right LO and right PPC).

*Figure 2***:** Normalised effect of TMS at each stimulus onset asynchrony at both right PPC and LO sites. Each SOA represents the time of the first pulse, with the second pulse 50 ms later. * indicates that the difference between the effects of TMS over LO and PPC is significant to the $p < 0.05$ level, **, significant to the $p < 0.01$ level. It should be noted that the effect of TMS at both sites was greatest at 350 ms, but there was no difference between the effect seen at LO and PPC.

Figure1

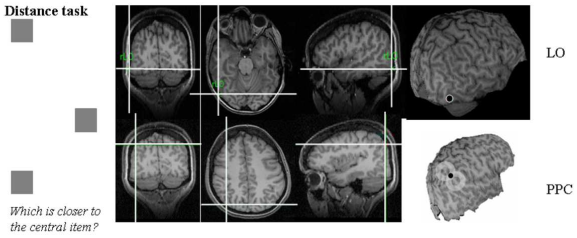
Distance task
Which is closer to the central item?
rLO
rLO
rLO
LO
PPC

Figure2

Click here to download high resolution image