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TMS over right posterior parietal cortex induces neglect in a scene-based frame of reference☆

Neil G. Muggleton[a], Peggy Postma[b], Karolina Moutsopoulou[b], Ian Nimmo-Smith[b], Anthony Marcel[b,*], Vincent Walsh[a]

[a] *Institute of Cognitive Neuroscience & Department of Psychology, University College London, London, UK*
[b] *Medical Research Council Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 2EF, UK*

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Abstract

Although damage to right posterior parietal cortex (RPPC) produces bias in line bisection, Karnath et al. [Karnath, H.-O., Berger, M. F., Küker, W., & Rorden, C. (2004). The anatomy of spatial neglect based on voxelwise statistical analysis: A study of 140 patients. *Cerebral Cortex*, *14*, 1164–1172] claim that it plays little role in spatial neglect, which is better measured by target cancellation. We used a detection task (approximating cancellation in requiring detection) to investigate this claim by compromising the parietal cortex with transcranial magnetic stimulation (TMS). Two outline shapes, one on each side of fixation, were briefly displayed before a mask. The target was a discontinuity in the left or right of the outline of one of these perceptual objects. Subjects indicated position or absence of target as fast as possible. Stimulus–mask onset asynchrony was adjusted individually to yield 75% detection. TMS was delivered over left posterior parietal cortex (LPPC), RPPC and Vertex, with Sham TMS over RPPC as a baseline control. Target detection was near ceiling and fastest at central positions and worst and slowest at the far right. Detection was significantly reduced at the far left position by TMS over RPPC. No other effects were obtained and latency was not affected by TMS. Disruption of RPPC by TMS does produce left neglect as measured by detection. Given the pattern of performance and since it was disrupted on one side of the display rather than on one side of each shape, attention and neglect were in a scene-based rather than object-based reference frame.

Keywords: Transcranial magnetic stimulation; Spatial neglect; Parietal cortex; Visual search; Frame of reference

1. Introduction

Until recently, studies of spatial neglect have mostly been restricted to deficits in patients, and what underlies different types of neglect remains opaque, especially regarding specific lesion sites because most naturally occurring cases involve extensive non-focal stroke (Vallar & Perani, 1986). This is complicated by identification of lesion sites by structural imaging which is largely insensitive to diaschisis or to remote dysfunctioning due, for example, to hypometabolism (Robertson & Murre, 1999). An alternative approach that can be more selective anatomically is offered by transcranial magnetic stimulation (TMS), since it can mimic pathological effects in normal subjects by transitory local disruption of cortical function if appropriate tasks are used. Indeed, several reports have claimed to induce neglect in vision (Bjoertomt, Cowey, & Walsh, 2002; Brighina et al., 2003; Fierro et al., 2000). All these studies have used functional equivalents of horizontal line bisection and have successfully biased judgements comparable to those in neglect by repetitive TMS (rTMS) of right posterior parietal cortex (RPPC). However, with the exception of Ellison, Schindler, Pattison, & Milner (2004), there is a problem in what one can infer from such studies about the relation of the brain site to neglect. Karnath, Berger, Küker, & Rorden (2004) point out that deficits in line bisection are associated with more posterior damage than that in patients showing neglect assessed by cancellation tasks, and Ferber & Karnath (2001) found that line bisection is normal in up to 40% of patients with severe clinically manifest neglect. In fact, Karnath et al. found structural imaging revealed that in patients with neglect defined on their battery of tests the most frequent damage was to right superior

☆ The study was conducted at Institute of Cognitive Neuroscience, University College London, London, UK.

* Corresponding author. Present address: Psychology Department, University of Hertfordshire, UK/Department of Experimental Psychology, University of Cambridge, UK. Mailing address: Department of Experimental Psychology, Cambridge University, Downing Street, Cambridge CB2 3EB, UK.
Tel.: +44 1223 764414; fax: +44 1223 333564.
E-mail address: a.marcel@herts.ac.uk (A. Marcel).

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temporal cortex, insula and subcortically to the putamen and caudate nucleus. The upshot of Karnath et al.'s claim is that bisection bias is not a generalizable index of neglect and that one is left in doubt as to the role of RPPC in neglect. Therefore, it is important to assess the effects of TMS at different sites with a task that overcomes the problem of using line bisection. Given the previous reports cited above, it is appropriate to start with PPC. A target detection task where possible target locations extend across the visual field would be closer to cancellation in exploratory requirements than to bisection.

TMS has been used to investigate the role of RPPC in visual search (i.e. detection). Walsh and co-workers have shown using TMS that a region of RPPC may be involved in conjunction search but not in feature ("pop-out") search (Ashbridge, Walsh, & Cowey, 1997); and Ellison, Rushworth, & Walsh (2003) showed that TMS over RPPC had no effect on a single-feature search task even if it was difficult, nor did it disrupt a conjunction decision if it did not require spatial search. However, it is still moot whether TMS at RPPC will affect detection of a single-feature target if target discriminability is low and requires spatial search. Moreover, in these studies, the measure has been reaction time with displays whose viewing time is not curtailed. That is, the role of PPC and the effect of TMS, if brief displays are pattern masked, is unknown. The reason that such a paradigm, as used in this paper, is relevant is that it requires temporal and spatial distribution of visual processing. Parallel search (e.g. for a single-feature target) over spatial locations per se does not discriminate the time required at different locations across the task-relevant field. Increasing the attentional demands of a task by reducing the viewing time may make performance more susceptible to disruption by TMS.

If the possible positions of targets are located on the right or left side of perceptual objects, a detection task can also be used to assess the spatial frame of reference underlying performance and in which any evident neglect is occurring. A frame of reference, by which location is specified, is either a coordinate system defined by point of origin, a structural description, or defining extremities. Regarding left neglect, some cases have been reported where patients neglect whatever is on their egocentric left, while others have been reported where patients neglect the left side of objects irrespective of the objects' location from the patient's viewpoint. Although dissociations are found in individual patients (Humphreys & Riddoch, 1995), Baylis, Baylis, & Gore (2004) point out that in many patients the apparently deficient reference frame may be due to the task used for testing. They found that the same patients showed scene-based or object-based neglect according to task (Is a target present on the screen? versus Is a target present in one of the two shapes displayed on the right and left?). Indeed, there may be no qualitative difference between these kinds of reference frame: objects and scenes may correspond to the width of the "attentional frame", i.e. the task-relevant area. (Strictly speaking, what Baylis et al. were addressing was not frame of reference in the conventional sense, but rather what defines the "frame" of attention, what one is attending to, which in their case defines the width of spatial attentional focus.) However, there is an alternative to Baylis et al.'s theory. The extent of attentional frame may be created either by the structure of the environment or by what the subject attends to, and in neglect there may be damage to whatever instantiates certain particular reference frames. Thus, some patients may show neglect in whatever frame is task-relevant, while others may be selectively deficient in certain frames (e.g. they may be unable to widen or narrow their attentional frame at will). Whichever is the case, different brain structures may underlie (a) body-centred space versus the space of an object irrespective of its egocentric location, or (b) the ability to attend to objects within a larger scene versus to a scene containing objects within it.

In a display containing two laterally aligned perceptual objects, a discontinuity can occur on either the left or right side of the left or right object or can be absent. If left neglect, manifested as detection failure, is scene-based, then detection should be a monotonic function across the whole display field. If it is object-based, then detection should be a function of the side of one or both objects. One might suppose that in the latter case detection should show the same pattern for both objects. However, if the display necessitates a serial search, say from left to right, and display time is too short for exhaustive search, then object-based left neglect would present as superior performance for the right compared to the left side of the left object but performance inferior to both of these for the two locations on the right object. It is important that features of the task should minimise ceiling effects. Crucially this means that control conditions should not permit all target locations to be at ceiling. With short presentations this can occur if targets are such as to allow rapid detection irrespective of number of distractors (a.k.a.: "pop-out"; Egeth, Jonides, & Wall, 1972).

It is common for TMS to affect latency. However, whether TMS affects latency, bias or sensitivity may depend on which components of a task are disrupted (Walsh & Cowey, 1998; Walsh & Pascual-Leone, 2003). Indeed, in some cases, disruption by TMS of one brain region may disinhibit a competing region, leading to paradoxical functional facilitation (Walsh, Ellison, Battelli, & Cowey, 1998). Given what we have said about the effects of TMS on latency, it is possible that (a) any of the patterns of performance sketched above might be manifested in latency in addition to or instead of in accuracy, (b) latency might be independent of accuracy, or (c) especially where masking curtails a perceptual representation, as here, latency might be unaffected.

The task design proposed also permits one to assess the presence of another feature of neglect. It is frequent in neglect that patients show allochiria (Bisiach & Berti, 1995). Contralesional perceptual content (stimuli, features or sensations) experientially migrates to the ipsilesional side of space (i.e. to the focus of attention). Indeed, Marcel et al. (2004) have argued that this is a central feature of much neglect and extinction. In the case where targets may appear at one of a number of horizontal locations, allochiria would manifest as mislocation of a target when presented at an affected location to a position where it is reported at a rate greater than reported for that position on trials with no target. To assess this, as well as for a check on spuriously correct detections, it is necessary for subjects to report target location as well as presence. The present task was designed to address the foregoing issues.

Our predictions were that TMS over RPPC would impair target detection on the left, but that TMS over left posterior parietal cortex (LPPC) would do so on the right less or not at all. Since 'left' and 'right' are relative to frame of reference, this transforms into two sets of predictions as follows. For a scene- or space-based reference frame, 'left' and 'right' refer to space across the whole display; for an object-based reference frame, 'left' and 'right' refer to the space of each outline figure. Our prediction was that TMS over PPC would induce neglect in a scene-based frame. We had no predictions regarding latency.

2. Method

2.1. Subjects

Ten healthy subjects participated, six male and four female, with an age range of 21–42 years. All were right handed and all had normal vision. All subjects had previous experience participating in TMS experiments.

The study was approved by the Oxford Research Ethics Committee (OXREC) and the Institute of Neurology, University College London, and exclusion criteria conforming to current guidelines for rTMS research were applied (Wasserman, 1998). The procedure was explained to subjects and they were told that they were free to withdraw from the experiment at any stage.

2.2. Stimuli

Stimuli were presented on a 40 cm × 30 cm computer screen (resolution: 1024 × 768) at a viewing distance of 57 cm. They consisted of a pair of outline shapes each with four "petals" at 12, 3, 6 and 9 o'clock, one to each side of central fixation (see Fig. 1). The width and height of each outline figure was 6° visual angle and its centre was 6° from fixation. Thus, the total stimulus display subtended 18°. A target was a discontinuity or "gap" in the outline, where a section of the black outline of 1.2° was a light grey. The aim, refined over piloting, was to achieve a target discriminability low enough to avoid "pop-out" (Egeth et al., 1972), such as to require focal attention and to necessitate search. Targets could appear at one of four horizontal locations, each on one of the horizontal-pointing petals: far left, mid left, mid right and far right, at 4° and 10° eccentricity. Each could appear at either the top or bottom of the petal. Gaps never appeared in the outline of vertical-pointing petals. The high and low positions were introduced following piloting to increase spatial uncertainty and therefore overall task difficulty. Since the aim was to investigate horizontal location, we were concerned with only the horizontal target locations. There were also trials with no target. The duration of the stimulus display was set by individual subjects' sensitivity. A post-stimulus pattern mask, consisting of scrambled segments of the outline of the stimuli, extended just beyond the area of the stimuli in a rectangle shape. The mask remained on the screen until subjects made a response and was followed by a blank screen which remained blank throughout the intertrial interval. The stimulus–mask stimulus onset asynchrony (SOA) was determined individually for each subject (see Section 2.4).

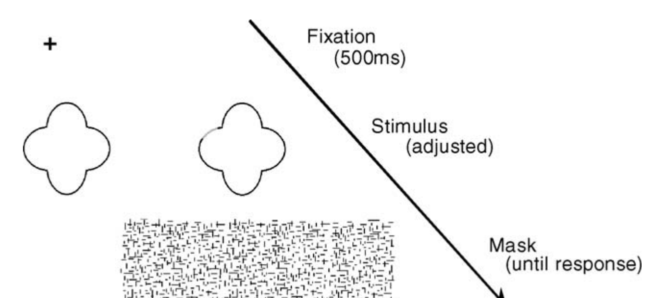

Fig. 1. Sequence of events on a trial, illustrating the fixation cross, the stimuli with a target 'gap' and the mask. Size is not to scale.

2.3. TMS

A Magstim Super Rapid Stimulator (Magstim, UK) was used to deliver TMS via a figure-of-eight coil with a diameter of 70 mm. Its maximal output was 2 T. TMS was delivered at 65% of maximal stimulator output, with the coil handle pointing upwards and parallel to the midline. A single intensity was used for all subjects because it is known that neither motor thresholds nor phosphene thresholds are reliable indicators of PPC excitability (Stewart, Walsh, & Rothwell, 2001). This level was suprathreshold for phosphene and motor thresholds for all subjects. On blocks of trials with TMS, test stimuli were presented during 500 ms rTMS with onset concurrent with the onset of the visual stimuli. TMS frequency was 10 Hz.

2.3.1. Stimulation sites and control

FSL software (FMRIB, Oxford) was used to transform coordinates for LPPC and RPPC for each subject individually. This procedure involved normalising each subject's MRI scan against a standard template. The description of each resulting transformation was then used to convert the appropriate Talairach coordinates to the untransformed (structural) space coordinates, yielding individual specific localisation of the sites. These coordinates were then used to guide the frameless stereotaxy.

In addition to Sham rTMS, rTMS was administered to three sites: Vertex, left posterior parietal cortex and right posterior parietal cortex. Sites were localised using MRI scans obtained for each subject in conjunction with the Brainsight frameless stereotaxy system (Rogue Research). The site that was identified as the RPPC was that used in the studies of Bjoertomt et al. (2002) and Goebel, Walsh, & Rushworth (2001) and, as such, the coil was centred on the Talairach coordinates 42, 58, 52 (see Fig. 2). The LPPC was therefore equivalent to −42, 58, 52. Vertex was used as a control site for potential non-specific effects of TMS such as noise and tactile sensation.

Sham rTMS was used as a baseline condition. This was done by holding the edge of the coil on the RPPC such that the current was directed away from the brain. This site was chosen for Sham TMS since it was a site from which a TMS effect might be expected, and so allowed more direct control for non-specific effects of TMS such as the acoustic artefact.

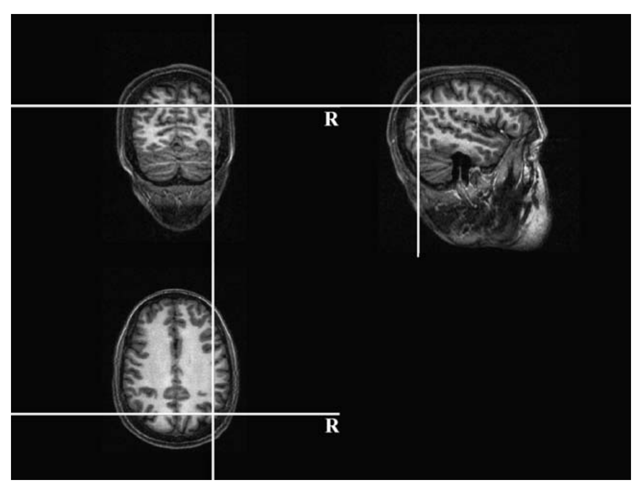

Fig. 2. TMS site localisation. The vertex was defined as a point midway between the inion and the nasion and equidistant from the left and right intertragal notches. The posterior parietal cortex site was localised using the Brainsight TMS–MRI co-registration system (Rogue Research, Montreal, Canada), utilizing individual high resolution MRI scans for each subject. The right and left posterior parietal cortex were marked using transformed Talairach coordinates for each individual scan. The location to be stimulated thus lay in the region of angular gyrus immediately lateral to the intraparietal sulcus. In the right hemisphere, this was equivalent to the site stimulated by Bjoertomt et al. (2001) which induced neglect on a line bisection task. This site was also in the same area in which TMS stimulation has resulted in deficits in visual search tasks (e.g. Ashbridge et al., 1997; Ellison et al., 2004). A typical stimulation location for right posterior parietal cortex for one subject is illustrated.

2.4. Procedure

Subjects were seated with their eyes 57 cm from the computer screen with their heads stabilised on a chinrest. During the experiment the room was darkened, such that the only illumination was from the computer screen. Subjects were shown examples of the stimuli and were told that the task was to detect whether a 'gap' was present or not and, if so, to report its location. They were asked to respond as fast as possible using allocated keys on a standard computer keyboard. They were instructed to indicate detection and location of the gap as follows: far left – 'r' (using left middle finger); mid left – 't' (left index finger); mid right – 'y' (right index finger); far right – 'u' (right middle finger). If no gap was present, they were asked to respond by pressing the spacebar with their thumb(s). It was made clear that they were not required to distinguish between vertical positioning of gaps (i.e. whether it appeared on the upper or lower outline of horizontal petals). Subjects received a block of 40 trials to familiarise them with the stimuli and with the task.

Each trial started with the presentation of a fixation cross in the centre of the screen for 500 ms. The stimulus was then displayed briefly and was immediately followed by the mask. The stimulus–mask SOA was established for each subject by a thresholding procedure (see below). The mask remained until the subject responded. Stimuli and presentation were programmed in E-Prime version 1.1. The sequence of events on a trial is illustrated in Fig. 1.

There were 8 blocks of trials, with 40 trials per block. Each block had 8 'no-gap' trials and 32 'gap' trials, consisting of 8 trials with a gap at each of the 4 possible horizontal target locations. Trial types appeared in random order throughout each block. Of the eight gaps at each of the horizontal locations, four appeared in the 'higher' location and four in the 'lower' location. There were two blocks of each of the four TMS conditions: Sham, Vertex, LPPC and RPPC. Order of condition was established for each subject (randomized) for the first four blocks, this order was then repeated in the next four blocks.

For each subject pre-mask SOAs were determined by a thresholding procedure which uses a Bayesian adaptive psychophysical routine where the data are evaluated against a psychophysical function (according to Kontsevich & Tyler, 1999). The threshold was determined for 75% accuracy in terms of the presence or absence of the target. (This added to the practice received by subjects.) Following this, the first four blocks of trials were run. Then a second thresholding session was run to control for any reduction in critical SOA, following which pre-mask SOAs were adjusted accordingly if necessary, and the next four blocks were run. The range of SOAs was 80–260 ms; individual subject values were 80, 90, 100, 120, 160, 170, 180 and 260 ms (mean: 132.5). Trial onset and the delivery of TMS were all controlled automatically by the E-Prime software, such that stimulus and TMS onset were concurrent.

3. Results

The logic of the design allowed us to conduct a phased analysis of both the accuracy data and the latency data. If the two control conditions, Sham TMS and TMS over Vertex do not differ, this permits us to exclude one of these from further analyses. This has two effects: (a) it increases the power of the statistics and (b) it reduces the degrees of freedom, producing a more conservative criterion. It was decided beforehand that, if the two control conditions did not differ, it is more appropriate to exclude Sham TMS because TMS over Vertex (a) is the critical intervention at a location for which a null or non-differential effect is reasonably expected for the present task and (b) controls for cortical stimulation and both auditory and tactile artefacts whereas Sham TMS controls only for auditory artefacts.

3.1. Target detection

For each of the four target locations, the data were calculated for each TMS condition in terms of percent gaps correctly detected, percent gaps reported in the wrong location and percent gaps missed. For trials with no gaps, the data were calculated in terms of percent correct reports (i.e. gap absent) and percent false detections by location. Percent correct detections per location for each TMS condition are shown in Fig. 3.

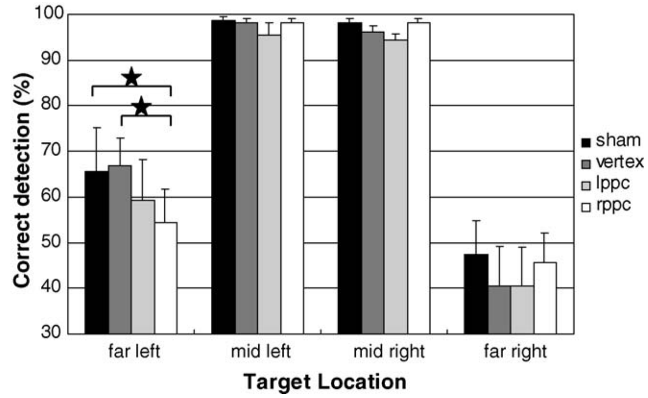

Fig. 3. Percent correct detection and standard errors at each position for each TMS condition. Differences between TMS conditions ($p < 0.02$) are indicated on the graph.

Considering overall performance irrespective of TMS, it is clear from Fig. 3 that detection at the two central locations was near ceiling and that it is at the eccentric locations that subjects fail to detect targets.

3.1.1. Phase 1

For completeness, we report a 4 × 4 repeated measures ANOVA with the factors of target location and TMS, each with four levels. The main effect of target location was significant ($F(2.6, 23.0) = 30.6$, $p < .001$). There was no main effect of TMS ($F(3, 27) = 1.79$, $p = .173$) and there was no interaction of TMS condition with target location ($F(4.6, 41.7) = 1.56$, $p = .196$).

A 2 × 4 repeated measures ANOVA comparing Sham TMS with TMS over Vertex across the four target locations was then conducted. There was a significant effect of target location ($F(2.6, 23.5) = 29.1$, $p < .001$). There was no main effect of TMS ($F(1, 9) = 0.67$, $p = .435$) nor was there any interaction ($F(2.7, 24.4) = 0.72$, $p = .538$).

3.1.2. Phase 2

Given no difference between Sham TMS and TMS over Vertex, we excluded Sham TMS from further analyses for the reasons given above and because TMS over Vertex controls for everything that Sham TMS does (cf. first paragraph of Section 3).

A 3 × 4 repeated measures ANOVA was performed with the factors of TMS (Vertex, LPPC, RPPC) and target location. There was a significant effect of target location ($F(2.4, 21.2) = 31.1$, $p < .001$). There was no main effect of TMS ($F(1.4, 12.3) = 0.709$, $p = .460$). There was a significant interaction between TMS and target location ($F(6, 54) = 2.5$, $p = .032$). This interaction justifies comparisons of TMS conditions at each target location.

3.1.3. Phase 3

Target location. Simple main effects of TMS conditions were analysed, for each target location separately, using paired *t*-tests. Where there are directional a priori predictions (e.g. that TMS at RPPC will adversely affect detection of gaps at far left), the corresponding *p*-value for the *t*-statistic is the usual one for a one-tailed test. For the remaining comparisons for which there were no predictions, a Bonferroni correction was applied following the convention that raw *p*-values are multiplied by the number of comparisons so that these adjusted *p*-values may then be compared with conventional critical *p*-values, e.g. .05, .01 or .001. This use of separate *t*-tests follows the current multivariate approach to repeated measures ANOVA (Howell, 1992; Maxwell & Delaney, 1990) rather than the classical univariate approach (Winer, Brown, & Michels, 1971). The multivariate approach gives greater weight to the issues of non-homogeneity and non-sphericity of variance. Moreover, it accepts a trade-off between loss of power and increased validity of tests based on just the variability within the subset of data that relates to each individual comparison. Families of comparisons for testing simple main effects of TMS conditions were made separately for each target location because comparisons across different target locations have no relevance here. Following Howell (1992), unadjusted significance tests were made for planned (a priori) comparisons, and family-wise adjustments were made for the remaining comparisons of the simple main effects.

Far left. The comparison of correct detection rates between TMS conditions showed that RPPC was significantly lower than Vertex ($t(9) = 2.74$, $p = .011$, one-tailed). LPPC was no different from Vertex ($t(9) = 1.08$, $p = .619$ corrected) and RPPC was no different from LPPC ($t(9) = .98$, $p = .702$ corrected). (The last two comparisons were non-significant even when Bonferroni correction was not applied.) Thus, TMS over RPPC causes a reduction in correct detection at the far left location compared to other TMS conditions. (Note that the equivalent comparison between RPPC and Sham TMS when Vertex was excluded was similarly significant ($t(9) = 2.42$, $p = .019$, one-tailed), as indicated in Fig. 3.)

Mid left, mid right, far right. No comparisons between TMS conditions for any of these locations were significant for percentage correct.

3.1.4. Mislocations

There were very few mislocations. Since correct detection approached ceiling in the central locations, the issue of mislocations is inapplicable for those locations. Between 3.5% and 9% of targets at the far right were mislocated to the mid right position, the highest percentage being with TMS over RPPC. Between 2.5% and 6.9% of targets at the far left were mislocated to the mid left position, the highest percentage being with TMS over LPPC.

Far left. A 4 × 3 repeated measures ANOVA was performed with the factors of TMS (Sham, Vertex, LPPC, RPPC) and position of mislocation (mid left, mid right, far right). There was a significant difference between positions of mislocation ($F(2, 18) = 4.72$, $p = .023$) with most targets being mislocated to the mid left. There was no main effect of TMS ($F(3, 27) = 0.735$, $p = .541$) and no interaction between TMS and position of mislocation ($F(6, 54) = 1.01$, $p = .427$).

Far right. A 4 × 3 repeated measures ANOVA was performed with the factors of TMS (Sham, Vertex, LPPC, RPPC) and position of mislocation (far left, mid left, mid right). There was a significant difference between positions of mislocation ($F(1.2, 10.4) = 3.98$, $p = .037$) with most targets being mislocated to the mid right. There was no main effect of TMS ($F(3, 27) = 0.541$, $p = .659$) and no interaction between TMS and position of mislocation ($F(6, 54) = 1.84$, $p = .109$).

Although there were only a few significant effects concerning mislocations, it is worth noting that those that did occur were from eccentric positions to the adjacent central position on the same side, and that there was a tendency (though non-significant) for their frequency to be amplified by TMS over ipsilateral PPC. However, compared with the rates of false alarms on no-gap trials (see below), TMS over PPC had no selective effect on mislocations (i.e. the rate at which targets were mislocated to each location did not differ from the rate at which false alarms were assigned to the respective locations).

3.1.5. Misses

Since the only significant number of misses was at the far locations, an ANOVA was performed on only these locations. A 2 × 4 repeated measures ANOVA was performed with the factors of TMS (Sham, Vertex, LPPC, RPPC) and target location (far left, far right). There was no main effect of TMS ($F(3, 27) = 0.53$, $p = .664$). However, there was a significant effect of target location ($F(1, 9) = 5.4$, $p = .045$), and a significant interaction between TMS and target location ($F(3, 27) = 3.12$, $p = .042$).

Simple main effects of TMS conditions were analysed for each target location separately, using paired *t*-tests. No differences were found when the target was on the far right. However, in the far left target conditions TMS over RPPC produced significantly more misses than TMS over Vertex ($t(9) = 3.72$, $p = .029$, two-tailed corrected).

Therefore, independently of any effect on mislocation, TMS over RPPC led to more missed targets on the far left than did Vertex or Sham (although the difference between RPPC and Sham TMS did not survive Bonferroni correction).

3.1.6. No-gap trials

Correct reports of target absent for the TMS conditions were as follows: Sham 91%; Vertex 86%; LPPC 87%; RPPC 88%. False alarms were slightly more prevalent at the mid right (3–7%) and far right (3–5%) positions. But there was no statistical effect of TMS on correct reporting of no-gap trials, of position of false alarms, nor of TMS on position of false alarms.

3.2. Reaction times

Fig. 4 shows the means of median reaction times and the effects of TMS conditions for correct target detection for the four locations and for correct reports of target absent. (Medians minimise the effect of long-tailed distributions found with RTs.)

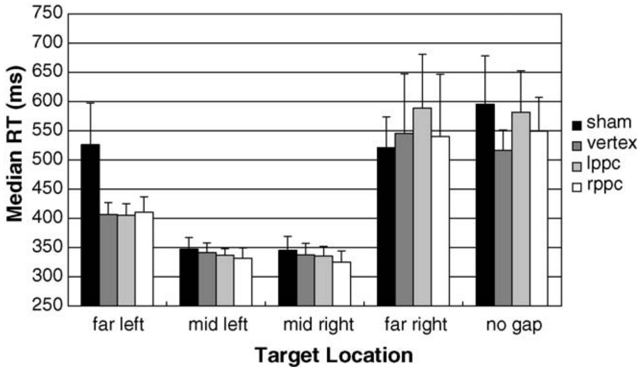

Fig. 4. Means of median reaction times for correct detection, standard errors at each position, and reports of target absence for each TMS condition.

A phased analysis of the latency data similar to that for detection was conducted. However, there were five target conditions because latency for no-gap trials was included.

3.2.1. Phase 1

Again for completeness, we report a 4 × 5 repeated measures ANOVA performed on median RTs with the factors of TMS (Sham, Vertex, LPPC, RPPC) and target condition (far left, mid left, mid right, far right, no-gap). There was a significant effect of target condition ($F(2.0, 15.0) = 7.51$, $p = .005$). There was no effect of TMS condition ($F(3, 14) = 1.73$, $p = .187$) nor was there any interaction between factors ($F(3.0, 23.9) = 1.54$, $p = .230$).

A 2 × 5 repeated measures ANOVA comparing Sham TMS with TMS over Vertex across the five target conditions showed a significant effect of target condition ($F(3.2, 28.7) = 7.30$, $p < .001$). There was no difference between the TMS conditions ($F(1, 9) = 2.98$, $p = .118$) nor was there an interaction between factors ($F(1.8, 16.4) = .151$, $p = .249$).

3.2.2. Phase 2

Again, given no difference between Sham TMS and TMS over Vertex, we excluded Sham TMS from further analyses for the reasons given above (cf. first paragraph of Section 3).

A 3 × 5 repeated measures ANOVA was performed with the factors of TMS (Vertex, LPPC, RPPC) and target condition. There was a significant effect of target location ($F(1.4, 12.9) = 7.46$, $p = .011$). There was no effect of TMS ($F(2, 18) = 1.43$, $p = .265$) nor was there an interaction between factors ($F(3.9, 35.0) = 0.82$, $p = .517$).

3.2.3. Phase 3

Although the above analyses yielded non-significant results regarding TMS, for completeness we analysed simple main effects of TMS conditions for each target location. No comparisons between TMS conditions for any target location or for the no-gap condition showed any significant difference.

4. Discussion

While, in accordance with our predictions, TMS affected target detection (TMS over RPPC reduced detection at the far left position), TMS had no effect on latency. We made no predictions regarding latency. But in view of the fact that RTs are frequently most sensitive to TMS (though in many instances errors, bias or d′ have been the appropriate and effective dependent variable), the absence of latency effects of TMS warrants a comment. In the present procedure, the display was brief and followed by a mask. The purpose of the mask was to limit duration of availability of the perceptual representation. The effect of TMS was plausibly to compromise the perceptual representation or to delay it such that the remaining time before the mask was too brief for detection. If the result of this was that subjects failed to detect a target or failed to do so before a subjectively criterial time, then we would not expect TMS either to delay correct detection or to produce longer erroneous "No" RTs than correct "No" RTs. If on any trial TMS failed to compromise or delay the perceptual representation sufficiently, then one would not expect delayed correct detections.

The main result was the effect of TMS on target detection. Compared to the control conditions, Sham TMS and TMS at Vertex, stimulation of RPPC impaired detection of targets at the far left position, but nowhere else. Stimulation at LPPC had no statistically significant effect compared to the control conditions. This is an important result. Karnath et al. (2004) have suggested that neglect is appropriately measured by detection tasks (e.g. target cancellation), and that neglect measured thus is associated with lesions more anterior than posterior parietal cortex. In their terms, we have produced neglect by TMS at right posterior parietal cortex. One might argue that while this affects healthy participants, it is not the same as the effect of a lesion at relevant sites. However, given the lateral asymmetry of right versus left brain damage in producing contralateral neglect, the same asymmetry in our results, and the good correspondence between real lesions and TMS intervention (Walsh & Pascual-Leone, 2003), this argument becomes implausible. Therefore, in spite of the fact that Karnath et al. found that structural imaging revealed a statistical preponderance of lesions elsewhere to be associated with neglect, one seems justified in concluding that perturbation of RPPC can and does produce effects equivalent to neglect. However, it is the case that not all cases of damage to RPPC produce obvious neglect (Karnath et al., 2004). But this is also true of damage to other sites. Indeed, the question arises of why this is the case. At this point in our knowledge one can only speculate whether the relevant factor in producing clinical neglect, given damage at a particular site, is extent or volume of lesion, diaschisis encompassing some other necessary structure, or even some individual predisposing factor. Indeed, Marcel et al. (2004) have reported a high susceptibility to allochiria (spatial migration of sensations or percepts) in a proportion of the healthy population that suggests an individual difference in premorbid susceptibility to deficits associated with neglect.

The level of detection performance across the display area in the present experiment makes further inferences difficult. Target detection at the central positions was almost at ceiling for the mid left position and at near ceiling for the mid right position. Our procedure to determine SOA was based on 75% correct detection over all target positions and was thus insensitive to performance level at specific positions. Inspection of Fig. 3 makes it clear that what contributed overwhelmingly to threshold determination were errors at the outer locations. Since performance at the near left location was almost at ceiling, it is difficult to tell whether RPPC TMS would have affected performance at that location as well as at the far left position.

At first sight, this drawback makes it seem impossible to address the issue of the frame of reference in which neglect effects were occurring. That is, to distinguish scene-based from object-based neglect, the obvious distinctive patterns of target detection reflecting such reference frames are a monotonic decrease across the whole field versus left–right asymmetries of detection for each outline figure. However, the obtained pattern of detection and the obtained spatial location of the TMS effect are informative. In all TMS and control conditions, detection falls off at the two outer locations. Given that these target locations were at about 10–11° eccentricity and the inner locations were at about 5–6° eccentricity, the pattern of detection performance appears to be primarily due to better contrast discrimination in the central than the peripheral visual field. Our piloting and design were intended to avoid a "pop-out" effect (Egeth et al., 1972), and they undoubtedly succeeded since detection of targets at the outer locations was not at ceiling. Indeed, since the SOAs for all but one subject (who had an SOA of 260 ms) precluded effective eye movements, the pattern of detections across the field must reflect some process that involves either different weightings of attention, selection or decision making. In this sense, especially given that the target was a single feature, one might infer a parallel search. One possibility that is supported by the latency data is that the pattern of detection reflects a scene-based reference frame, and it is in that frame that the effect of TMS in producing neglect was operating. TMS had no effect on latency. More relevantly the only latency effect was that correct detections on the far right were longer (far right RT = 549 ms; far left RT = 437 ms; mid left and mid right RT = 338 ms). This is highly unlikely to be due to either hemisphere or hand dominance, given the latencies for the other target locations. The far right position also produced more misses. A search model that would produce this pattern is one of a parallel search but where discrimination in the periphery, but particularly at the far right position, takes longer to terminate and is curtailed by the mask. Again, this entails parallelism across the whole display field of the screen. This implies that the reference or attentional frame was the outer limits of the stimulus shapes.

If it is appropriate to characterise the present performance as scene-based, two alternative explanatory hypotheses present themselves. One is that there was nothing in the present procedure or design to induce subjects to focus attention to one or other outline figure at a time. This is essentially in accord with the approach advocated by Baylis et al. (2004). The other hypothesis is that TMS over RPPC induces neglect in a scene-based frame and that TMS over another site might reveal a pattern of compromised detection consistent with object-based or object-centred neglect. The present data per se do not warrant speculation, but the literature encourages two conjectures concerning the association of brain sites with frames of reference. Parietal cortex is associated with representation of the body and its spatiality (Bisiach & Berti, 1995), and space- or scene-based neglect is body-centred or egocentric. Simultanagnosia consists in the restriction of conscious perception to one object at a time with a lengthened time needed for such perception (Farah, 1990). One variant of this is associated with dorsal stream lesions (usually bilateral) of superior parietal or superior occipital cortex (Rizzo & Hurtig, 1987). Another variant is associated with ventral stream lesions in the (usually left) inferior temporo-occipital region (Kinsbourne & Warrington, 1962). First, dorsal sites might be a candidate for object-based neglect, where the left of an object is from the viewer's perspective. Second, the temporal lobe is associated with object recognition. Therefore, occipito-temporal sites, as a path to object recognition, might be candidates for object-centred (as well as object-based) neglect, where the left of an object is defined intrinsically by a structural description independent of viewpoint or orientation. Indeed, this conception invites the hypothesis that the different sites associated with neglect emphasised by Karnath et al. (2004) and Vallar & Perani (1986) underlie neglect primarily, though not necessarily exclusively, in different reference frames. But if one is to produce object-based or object-centred neglect by TMS, one either has to induce a strategy of attention to one object at a time or use a display where perception of one object interferes with that of another, such as overlapping line-drawn figures as used by Duncan (1984) or Tipper (1985).

The present task was able to reveal allochiria. Targets in certain locations could be mislocated in a constant direction or to particular locations. However, (a) incorrect localisations were very few compared to omissions, and (b) there was little tendency for mislocations to occur more with TMS or to migrate to contralateral positions. The only slight tendency was for targets to migrate to an adjacent more central position. If the present results represent canonical neglect, they might cast doubt on the generality of Marcel et al.'s (2004) suggestion that allochiria may be central to at least some cases of neglect. But in both Marcel et al.'s and Manly, Woldt, Watson, & Warburton's (2002) research, migrations of stimuli from unattended locations only occurred if there was a target on the attended side. Therefore, the predominance of omissions rather than migrations in the present study may be due to absence of any feature to which targets could migrate. More pertinently, the near-ceiling detection at central positions plausibly represents the focus of attention, and both Marcel et al. and Manly et al., as well as most studies of perceptual migration, have found migrations are to the attentional focus. Therefore, the present directional tendency suggests that if candidate non-targets were also present, the balance of errors in an otherwise equivalent procedure would shift from omissions to migration.

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