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Dissociating the neural mechanisms of distance and spatial reference frames.

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ABSTRACT

This study investigated if the neural mechanisms involved in processing distance (near and far) and frame of reference (egocentric and allocentric) can be dissociated. 36 participants completed a conjunction visual search task using either an egocentric (deciding if the target was to their left or right) or an allocentric (deciding if the target was to the left or right of a reference object) frame. Both tasks were performed in near (57 cm) and far (171 cm) space conditions. Participants were separated into three groups, and each received transcranial magnetic stimulation (TMS) to a different site; right posterior parietal cortex (rPPC), right ventral occipital cortex (rVO), or right frontal eye field (rFEF) in addition to sham TMS. The results show that rFEF is critical in the processing of each search at each distance whereas, contrary to previous detection results, TMS over rVO did not affect performance for any condition. TMS over rPPC revealed that specialised egocentric processing in the parietal cortex does not generalise to far space, providing evidence of a separation of the reference frame/distance conflation in the literature.

Keywords:

Frontal Eye Fields. Parietal Cortex. Spatial processing. Transcranial magnetic stimulation. Ventral Occipital. Visual search.

1. Introduction

Our perception is seamless, without boundary or division. However, neuropsychology has revealed that it is possible to experience perceptual deficits in one region but not others. For example, patients can present with visual neglect that is restricted to near or far space (Berti & Frassinetti, 2000; Cowey, Small & Ellis, 1994, 1999; Halligan & Marshall, 1991; Mennemeier, Wertman & Heilman, 1992; Pizzamiglio et al., 1989; Vuilleumier, Valenza, Mayer, Reverdin & Landis, 1998). By association, it would seem reasonable to assume that different brain regions or networks of regions underlie normal visual perception in different spatial locations.

Taking this neuropsychological data together with that gathered from techniques including neuroimaging and electroencephalography, there is converging evidence that the dorsal stream including right posterior parietal cortex (rPPC) is important in near space, while ventral stream areas (such as right ventral occipital, rVO) are involved in far space processing (Bjoertomt, Cowey & Walsh, 2002; Butler, Eskes & Vandorpe, 2004; Halligan & Marshall, 1991; Mennemeier et al., 1992; Shelton, Bowers & Heilman, 1990; Valdés-Conroy, Sebastián, Hinojosa, Romá & Santaniello, 2014; Vuilleumier et al., 1998; Weiss et al., 2000). The frontal eye fields (FEF), known to be involved in the orientation of visual attention, have also been associated with far space processing (Cowey et al., 1994; Rizzolatti, Matelli & Pavesi, 1983). There is the suspicion however that dichotomies between theorised neural mechanisms may be driven by task characteristics (Aimola, Schindler, Simone & Venneri, 2012; Keller, Schindler, Kerkhoff, von Rosen & Golz, 2005; Van der Stoep et al., 2013).

To that end, a recent transcranial magnetic stimulation (TMS) study using neurotypical participants and a common conjunction visual search task in both near

and far space supported the rPPC and rVO dichotomy, but found that right FEF (rFEF) was involved in both near and far space (Lane, Ball, Smith, Schenk & Ellison, 2013). The dependant measure used in that study was the speed of detection of a target amongst distractors; *e.g.,* the target could be either present or absent. In search in everyday life we are not merely concerned with the presence or absence of an item, but also where it is located (for example, we would want to know where a predator is and not just whether or not there is one). When locating an item in our field of view, a further psychological coordinate system is employed; that of egocentric and allocentric space. An egocentric reference frame refers to space that is defined relative to the observer; an object is to the left or right of the individual (where is the predator compared to me?). Egocentric space can be further defined relative to the body part being used for reference such as the trunk, head, retina or limb (Behrmann & Geng; 2002, Ball, Smith, Ellison & Schenk, 2010). Space can also be defined independently of the observer; a so-called allocentric frame of reference. Allocentric processing can encompass both judgements based on the relative positions between two external objects (*e.g.,* predator relative to your partner), but also between two components of the same object (*e.g.,* the position of the claw with respect to the trunk).

Dorsal, ventral and frontal regions have also been implicated in the processing of these reference frames, with evidence that the dorsal stream may be specialised for egocentric and the ventral stream for allocentric processing (Committeri et al., 2004; Grimsen, Hildebrandt & Fahle, 2008; Hillis et al., 2005; Honda, Wise, Weeks, Deiber & Hallett, 1998; Medina et al., 2009; Neggers, Van der Lubbe, Ramsey & Postma, 2006; Vallar et al., 1999; Verdon, Schwartz, Lovblad, Hauert & Vuilleumier, 2010). There may also be a particular role for associated

frontal areas, including the rFEF, for egocentric space (Grimsen et al., 2008; Neggers et al., 2006; Vallar et al., 1999). However, there is also evidence for considerable overlap in the areas associated with egocentric and allocentric processing, particularly within the right frontoparietal network (Chechlacz, Rothstein, & Humpreys, 2012; Committeri et al., 2004; Galati et al., 2000; Zaehle et al., 2007).

Evidence pointing to these regions common to both near and far space and egocentric and allocentric coding is conceptually intuitive. It is reasonable to imagine that near space may be processed in an egocentric manner since successful interactions with the nearby environment (*e.g.,* picking up an object) rely upon knowing the position of objects relative to oneself (Kosslyn, 1994). Conversely, far space processing may be more allocentric in nature; for example, perceiving that the bank is to the left of the bakery (Kosslyn, 1994). This model does have the consequence of conflating near with egocentric space, as well as far with allocentric space, and therefore it is important to establish the association (or lack thereof) of neural correlates related to distance and reference frame.

By dissociating these spatial aspects in a factorial design using conjunction visual search and TMS, it is possible to design a task that can be completed in either an egocentric or allocentric manner and displayed in near and far space. Thus the current study sought to define the precise role of these regions in near and far space for both egocentric and allocentric coding, unencumbered by task variability, correlative measures or imprecise location issues.

2. Method

2.1. Participants

The study was conducted with the approval of Durham University Ethics Advisory Committee and in accordance with the Declaration of Helsinki. The sample included 36 neurologically healthy participants (21 males) aged between 18 and 53 years (mean: 25.8 years). Participant recruitment criteria complied with the current guidelines for repetitive TMS research (Rossi et al., 2009), and all had normal or corrected-to-normal vision. Informed consent was obtained and participants could withdraw at any point. Participants were separated into three groups (n = 12), with each group receiving TMS over a different site (rPPC, rVO or rFEF). The TMS site was chosen as a between-subjects variable in order to minimise practice effects. The participants in the three groups did not differ significantly with regards to sex (χ^2(2, N = 36) = 2.06, p = .358) or age ($F_{(2, 33)}$ = 2.50, p = .098).

2.2. Stimuli and Procedure

There were two types of search tasks which had different reference frames: egocentric and allocentric. In the egocentric task participants were required to decide as quickly and accurately as possible whether the target stimulus was to their left or right. In the allocentric condition they had to decide whether the target stimulus was to the left or right of a reference marker (a blue square).

E-Prime 2.0 (Psychology Software Tools Inc., Pittsburgh, PA, USA) was used to present the tasks and remotely trigger the TMS. The random search arrays for each task were created using Matlab (The Mathworks Inc., Cambridge, UK) and then loaded into E-Prime as .jpg files. Search arrays consisted of ten non-overlapping items, one of which was always the target, and there was never more than one target presented per trial. The target was a red forward-slash (/) and the distractors were five green forward-slashes and four red backward-slashes (\). All items were

approximately 2.5° of visual angle in length and 0.5° in width. The stimuli were presented against a black background and matched for photometric luminance within and between items across the display.

In the egocentric task a dark grey screen was presented for 500 ms at the start of each trial and participants were informed to use this as a cue to re-fixate the centre of the screen. This was used rather than a central fixation cross to prevent participants from making a judgement about the target position relative to a remembered location. This was followed immediately by the presentation of the search array, which remained present until the participant made a button-press response (see Figure 1a). The target appeared equally often to the left and right of the screen / participant's sagittal midline. Participants were free to move their eyes whilst searching and were asked to respond with their right hand, which was ipsilateral to the TMS. Participants decided whether the target was to their left or right and made the response using a corresponding button press, using their index and middle fingers for the two choices (left and right respectively). The inter-trial interval was 3500 ms, during which time a blank black screen was presented.

In the allocentric task, the dark grey fixation screen (presented for 500 ms) contained a fixation cross (+, 1.5°) which appeared along the horizontal midline either 8° to the left or to the right of centre. The location of the fixation cross matched the position at which the reference marker (blue square, 1°) would appear in the subsequent array. Participants were required to decide whether the target was to the left or right of the reference marker. The search array was presented until the participant made a button-press response (as above; see Figure 1b) and during the inter-trial interval (3500 ms) a blank black screen was presented. Presenting the

reference marker ahead of the search array ensured that in the allocentric task participants did not first have to locate the marker before searching for the target.

There were six subtypes of allocentric array; the target could be to the left or to the right of the reference marker, in addition to which the target could be congruent with the egocentric position (*i.e.,* to the left of the reference marker and the viewer, or the right of both marker and viewer), incongruent (*i.e.,* leftwards of the reference marker but to the right of the viewer, or right of the marker and to the left of the viewer) or straight ahead and thus truly allocentric (*i.e.,* left or right of the reference marker and directly in front of the viewer). See Figure 1c for examples of each condition of congruence.

< Insert Figure 1 >

The search tasks were completed under two distance conditions: *near* and *far*. In both conditions the stimuli were back-projected onto a blank screen using an Epson EMP-74 projector, and the room was darkened except from the light from the projector. In the near condition participants were seated approximately 57 cm from the screen, whilst in the far condition this was extended to approximately 171 cm. The displays in both conditions subtended the same visual angle to ensure identical retinal size irrespective of viewing distance. Participants were presented with a central fixation cross at the start of each block to ensure that their head and trunk sagittal midline was aligned with the centre of the screen, and the centre of the presented array was at eye-level. Participants were encouraged to remain as still as possible in order to maintain a stable viewing distance.

Each participant completed two sessions; one with egocentric and one with allocentric tasks, the order of which were counterbalanced. Each testing session lasted no longer than two hours. There were twelve blocks of trials per session, with 48 trials per block; 24 where the response was left and 24 where the response was right (8 for each of the congruent, incongruent and ahead allocentric trials). The twelve blocks included six blocks of trials in the near condition and six in the far condition, half of which were completed with TMS (delivered to rPPC, rVO or rFEF depending on group) and the other half with sham-TMS. The TMS and sham-TMS blocks were interleaved, with half of the participants starting with TMS.

2.3. Transcranial Magnetic Stimulation and Site Localisation

Five pulses of TMS were delivered at 10Hz at the onset of the visual array using a Magstim™ Rapid (Magstim, Whitland, Carmarthenshire, UK) at 65% of the maximum machine output (*i.e.,* 1.3T). TMS was applied over one area of interest (rPPC, rFEF or rVO; Figure 2). For rFEF, each participant's skull was co-registered with their own MRI brain scan using BrainSightTM frameless stereotaxic software (Rogue Research, Montreal, Quebec, Canada) and the site was located anatomically. The chosen site was the intersection of the precentral and superior frontal sulci, a location that has repeatedly been used with TMS and confirmed as a functional locus (Grosbras and Paus, 2002; Paus, 1996; Ro et al., 1999). The rVO site was determined using the averaged scalp co-ordinates reported by Bjoertomt et al. (2002), who also used this same site to examine near and far space processing. They stated that for an inion–nasion distance of 35 cm, VO is located 1.5 cm dorsal and 2.25 cm lateral to the inion. As the parietal region is large, and the precise locus of involvement varies across subjects, in the case of rPPC, we used a method of

localisation that examined functional effects (see Sack et al. (2009) for a discussion of the relative merits of localisation methodologies). We therefore functionally localised this site using the conjunction search hunting procedure first described by Ashbridge et al. (1997). This meant that the area of cortex stimulated was the region within rPPC that was specifically involved in the processing of conjunction search, which was the experimental task. Briefly, the procedure involved 10 trials of TMS being given to each site in a 3x3 matrix, with each adjacent point 1 cm apart. The central point was located 9 cm dorsal to the mastoid inion and 6 cm lateral. The selected site was the one which demonstrated a 100 ms increase in RT relative to no-TMS trials. For each brain area, once the site was established the position was recorded and marked with a sticker on a tightly fitting lycra swimming-cap.

< Insert Figure 2 >

A 50 mm figure-of-eight branding iron coil was used to stimulate rFEF and rVO to minimise twitches, with coil angle adjusted for each individual in order to prevent peripheral nerve stimulation or eye-blinks. For rPPC, a 70 mm the coil was placed tangential to the skull, with the handle pointing backwards, parallel to the mid-sagittal plane. Coil selection was in accordance with previous TMS investigations of these regions (e.g. Lane et al., 2013, Mahayana et al., 2014). In all conditions the coil was held in place by the experimenter. For sham-TMS blocks an active coil was placed in close proximity to the participant whilst an inactive coil was positioned over the relevant site. Therefore, the subjective sensation of coil position and auditory effects were comparable to those experienced in the TMS blocks, but no active stimulation was delivered.

3. Results

Analyses were only concerned with response times (RTs) for the trials in which the correct response was given; incorrect responses accounted for less than 5% of the data (mean accuracy was 95.90**%**) and were removed. Non-parametric tests were conducted to investigate the effect of Site, Distance and Frame on accuracy and no significant differences across the conditions were found ($p \geq .053$). Since there were no significant effects observed for the accuracy data then any effects observed for RT can be interpreted independently of this. Furthermore, outliers (RTs which were more than two standard deviations away from the mean) were also removed on an individual participant basis (2.6% of correct trials).

The mean correct RT data was subjected to a 2 (*Frame*: allocentric vs. egocentric) x 2 (*Distance*: near vs. far) x 2 (*TMS*: TMS vs. sham-TMS) x 3 (*Site*: rPPC, rFEF and rVO) mixed-model ANOVA, with Site as the between-subjects factor. This revealed a significant main effect of Distance ($F_{(1,33)} = 98.71$, $p < .001$); participants were quicker to respond when tasks were performed in far space ($M = 875.33$ ms, $SD = 197.15$) than in near space ($M = 930.83$ ms, $SD = 207.65$). The Frame by Distance interaction was also significant ($F_{(1,33)} = 9.50$, $p = .004$). Following up this significant interaction, when the task was performed in near space participants were slower in the allocentric condition ($M = 937.58$ ms, $SD = 226.49$) than the egocentric one ($M = 922.87$ ms, $SD = 188.10$), although this difference was non-significant ($t_{(35)} = -.67$ $p = .51$). Conversely, although again non-significant, when the search was completed in far space the reverse was observed in that participants were faster in the allocentric ($M = 866.23$ ms, $SD = 213.56$) relative to the egocentric condition ($M = 883.19$ ms, $SD = 178.86$), ($t_{(35)} = .851.13$, $p = .40$). There was also a

significant interaction effect between TMS and Site ($F_{(2,33)}$ = 7.33, p = .002) and individual ANOVAs were performed for each site separately to investigate this further, as detailed below (Sections 3.1 – 3.3). No other main effects or interactions reached significance ($p \geq$ .09). Importantly, there was no main effect of Site (p = .754), indicating that the performance of participants in each of the three groups was equivalent.[1]

3.1. rPPC:

The results of the 2 (Frame) x 2 (Distance) x 2 (TMS) repeated-measures ANOVA revealed a main effect of Distance ($F_{(1,11)}$ = 25.95, p <.001), with participants responding more quickly in far space than near space (see Figure 3a). The three-way interaction between Frame, Distance and TMS was also significant ($F_{(1,11)}$ = 8.46, p =.014). There were no other main effects or interactions ($p \geq$.062). Paired samples t-tests were performed to investigate the conditions in which TMS affected performance, and these were adjusted for multiple comparisons using a Bonferroni correction (adjusted alpha = .013). These tests revealed a significant difference between the sham and TMS conditions only for the egocentric task in near space ($t_{(11)}$ = -3.65, p = .004), with RTs being slower in the TMS condition. All other comparisons failed to reach significance ($p \geq$.307).

3.2. rVO:

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[1] For each of the three sites individually additional mixed model ANOVAs were conducted in order to investigate if TMS specifically affected certain subtypes of trials. For egocentric tasks the side of space in which the target was presented (left / right) was examined, and importantly the interaction between Side and TMS was not significant for any stimulation site (p >.094). For the allocentric tasks both side of response (left / right) and congruence with egocentric position (congruent, incongruent and ahead; see Figure 1c for stimuli examples) were considered. Of note, none of the interactions involving Side and/or Congruence with TMS were significant for any stimulation site (p >.091).

The 2 x 2 x 2 repeated-measures ANOVA for the stimulation site of rVO revealed a signifant Distance effect ($F_{(1,11)}$ = 36.22, p <.001); participants had faster RTs in far space (see Figure 3b). There were no other significant main effects or interactions ($p \geq$ .081) and therefore no further analyses were performed.

3.3. rFEF:

The results of the 2 x 2 x 2 ANOVA for rFEF revealed a significant effect of Distance ($F_{(1,11)}$ = 39.70, p <.001); participants were faster to respond in the far space condition than the near (see Figure 3c). The Frame by Distance interaction effect was significant ($F_{(1,11)}$ = 7.87, p =.017). To follow up this significant interaction, two comparisons were performed: in near space there was a trend for participants to be slower in the allocentric condition (M = 951.99 ms, SD = 281.37) relative to the egocentric condition (M = 915.18 ms, SD = 242.55); however, this slowing was not statistically significant ($t_{(11)}$ = 1.16, p = .272). Conversely, in far space, while again not statistically significant, reaction times showed the opposite pattern: search times in the allocentric condition (M = 875.74 ms, SD = 263.13) were faster than those in the egocentric condition (M = 885.20 ms, SD = 233.87), ($t_{(11)}$ = -.28, p = .787). A significant effect of TMS was found ($F_{(1,11)}$ = 8.47, p =.014), with RTs being slower in the TMS condition as compared to the sham one. There were no significant interaction effects involving TMS ($p \geq$ .092), indicating that the TMS effect occurred in both the allocentric and egocentric tasks when performed in near and far space; this can be seen in Figure 3c. No other main effects or interactions were significant ($p \geq$ .092).

< Insert Figure 3 >

4. Discussion

The experiment reported here sought to understand if the neural substrates of the visual processing of both near and far space and egocentric and allocentric coding are separable. Whilst historically, and intuitively, egocentric coding has been associated with near space and allocentric coding with far space (Kosslyn, 1994), no neurotypical evidence has hitherto existed to understand if brain mechanisms support this conflation. Our central question was whether our three regions of interest were driven by distance, spatial reference frame or a subset of these. We found that rPPC is highly selective and is only involved in near space perception when egocentric processing is required. Conversely, rFEF is involved regardless of distance or frame of reference. Finally, despite previously demonstrating involvement of rVO in the detection of the presence of targets in far space (Lane et al., 2013), rVO may not be involved when a judgement about the spatial location of the target is required at either distance.

The role of rPPC in processing near space is in accordance with previous research (Bjoertomt et al., 2002; Halligan & Marshall, 1991; Lane et al., 2013; Mennemeier et al., 1992; Weiss et al., 2000), as is its relationship with egocentric processing (Committeri et al., 2004; Galati et al., 2000; Hillis et al., 2005; Medina et al., 2009; Neggers et al., 2006; Vallar et al., 1999). Neuropsychological research has indicated that the right hemisphere is involved in egocentric processing in near space (Iachini, Ruggiero, Conson & Trojano, 2013), although this finding was based on extensive fronto-parietal lesions in only four patients making it difficult to determine the precise brain area underlying their impairment . In that study however, the tasks in near and far space were not matched for visual angle, and relied upon

visuospatial memory rather than being purely perceptual. As far as we are aware, the study we present here is the first dissociating these spatial components using visual search and demonstrating the specific involvement of rPPC for near, egocentric spatial processing only and not egocentric coding *per se.*

However, a recent TMS study has reported conflicting results in relation to the contribution of rPPC. Mahayana et al. (2014) found that rPPC was critically involved in search in far but not near space. This difference in the proposed role of rPPC could be explained by the nature of the task used: Mahayana and colleagues used a structured visual search whereby search items appeared at set locations around an ellipse. This configuration reduces spatial variability as compared to typical random arrays, including those used here. We know that if the spatial component of the task decreases, for example by priming the target location, rPPC involvement is reduced, at least for near space conjunction search (Lane, Smith, Schenk & Ellison, 2012). Indeed, there is evidence for the speciality of right superior temporal gyrus, and not rPPC, for structured searches within near space (Schindler, Ellison & Milner, 2008). Similarly, if the visuomotor component of a search task in near space is increased by asking individuals to touch the target location then rPPC becomes necessary for feature search tasks for which it is otherwise not critical (Lane, Smith, Schenk & Ellison, 2011). Taken together with the data presented here, the involvement of rPPC appears to be highly task specific.

Our previous work (Lane et al., 2013) supported the finding that rVO of the ventral stream is involved in far space processing but not near (Bjoertomt et al., 2002; Butler, Eskes & Vandorpe, 2004; Halligan & Marshall, 1991; Mennemeier et al., 1992; Shelton, Bowers & Heilman, 1990; Valdés-Conroy, Sebastián, Hinojosa, Romá & Santaniello, 2014; Vuilleumier et al., 1998; Weiss et al., 2000). Specifically,

Bjoertomt et al. (2002) revealed a significant involvement of rVO in a landmark task in far space, which could be identified as an allocentric task albeit not involving visual search. Contrary to this, here TMS to rVO did not disrupt spatial processing in far space. Changing the question from 'is the target present or absent?' to 'is the target to the left or right of the marker?' increases the spatial demands of the response required to a visual search task. This transforms the task from a one-step process to a more complex two-step process: first the participant has to identify the target from the distractors before making a decision about its location relative to themselves/the landmark. This additional processing is reflected in response times being longer here than in Lane et al. (2013).

In the present study we asked a more spatially determined question, and neural interference by TMS to rVO no longer had any significant detrimental effect on performance, indicating that this area is not critically necessary for this task. Whilst it seems clear that rVO is involved in object identification (James, Culham, Hupmhrey, Milner & Goodale, 2003), the current task places more emphasis on object localisation with the consequence that rVO becomes less important in the processing of the task. There is precedence for uncovering such dichotomies using TMS; for example, a conjunction visual search task requiring attention to motion does not recruit rPPC as one would expect, but rather V5 is sufficient for performance owing to its specialisation for processing moving stimuli (Ellison, Lane & Schenk, 2007). In the current task there is no uncertainty regarding target presence (it is always there) as there would be in a pure detection task, and thus while object identification is a diminished component of the task processing, spatial localisation is increased. In this case, it may be that the neural noise associated with the application of TMS over rVO can be overcome by the continued processing within brain areas (such as FEF)

with a greater involvement in the enhanced localisation task requirements. Of course, the limited disruption introduced to rVO does not discount the possibility of relative compensation by the opposite hemisphere, however it seems more likely that as the dependant measure was not directly related to rVO function, TMS effects are difficult to uncover. Regardless, our results suggest that rVO is not critical in the processing of such spatially specific tasks in either near or far space.

It is possible that the absence of a TMS effect for the rVO condition could be related to the anatomical localisation of this area (in contrast to the functional localisation of rPPC). However this seems unlikely as the coordinates used here are well established (c.f. Bjoertimt et al., 2002; Lane et al., 2013) and have been used by us before to establish significant effects in a variant of this same task as already discussed.

A further possibility exists in that carrying out a spatial localisation in far space is easier, and therefore performance may have been at ceiling leading to a lack of TMS effect over rVO, which is in contrast to our previous findings (Lane et al., 2013). However, this is not thought be the case given that TMS did slow reaction times when applied over rFEF. It is also worth noting that the mean far space reaction times were over 900ms in the rVO group, slower than those in the rFEF group where differences were established. Therefore, the lack of rVO effect still presents a novel puzzle relating to the involvement of rVO, thought to be representative of the ventral stream's involvement in far space. However, if an area is no longer required for the processing of the task, it is reasonable to assume that this may contribute to a speeding of reaction time.

In contrast to rVO, rFEF is consistently involved across all conditions of frame and distance. This result with regards to distance is in keeping with earlier TMS

studies (Lane et al., 2013; Mahayana et al., 2014), and although rFEF has been specifically associated with egocentric processing by some (Grimsen et al., 2008), other studies have demonstrated overlapping activation in such frontal regions between egocentric and allocentric tasks (Chechlacz et al., 2012; Committeri et al,. 2004; Galati et al., 2000; Zaehle et al., 2007). This is however the first study to demonstrate the critical involvement of rFEF in both of these components of spatial processing in the same task. Since rFEF is one brain area which integrates input from both the dorsal and ventral streams (Schall, Morel, King & Bullier, 1995), it is perhaps not surprising that it serves a function in the processing of space regardless of distance or reference frame. The involvement of this region could be explained by its proposed role in controlling spatial attention (Grosbras & Paus, 2002; Smith, Jackson & Rorden, 2005; Szczepanski, Konen & Kastner, 2010), a process which is essential for all conditions of conjunction visual search as investigated here. Specifically, rFEF could mediate target selection, possibly by acting as a salience map indicating the possible target locations and using top-down information to effectively filter out non-target distractors (Hung, Driver & Walsh, 2011; Thompson, Bichot & Schall, 1997).

An alternative explanation of the role of rFEF relates to oculomotor behaviour, since this area has also been implicated in the generation of eye movements (Juan et al., 2008; Juan, Horter-Jacob & Schall, 2004) and TMS delivered to rFEF can disrupt eye movement behaviour (Müri, Hess & Meienberg, 1991; Thickbroom, Stell & Mastaglia, 1996). Whilst eye movements were not recorded in this study, saccades were permitted post-fixation. Saccade metrics were the same across all conditions due to a fixed visual angle, and therefore any effect of TMS owing to eye movements would be constant across distance and reference frames, in accordance

with the results observed. However, it is unlikely that TMS effects on reaction time following rFEF stimulation are due to an effect on eye movements alone as studies where eye movements are not permitted also show rFEF involvement (*e.g.,* Mahayana et al., 2014, Muggleton, Juan, Cowey & Walsh, 2003), pointing to a role of rFEF in the orientation of attention independent of saccades.

One additional finding from this study was that for all TMS sites and both the egocentric and allocentric tasks, participants responded significantly faster in far space than in near space. This is a novel finding (c.f. Mahayana et al., 2014; Valdés-Conroy et al., 2014) and one which was not observed in our previous study investigating distance (Lane et al., 2013). One difference between our previous and current experiments is that in the current study the images in both conditions were projected, whereas previously CRT monitors were used for near space. Accordingly, one possible explanation for the distance effect is tied to image resolution and a visual phenomenon known as fixed pattern noise (Cain, Hayat & Armstrong, 2001), resulting in the intensification of image pixellation in the near condition relative to far when the image is projected. Subjectively this does appear to be the case. Such increased pixellation could make it harder to visually resolve and thus identify the target thereby slowing RTs in the near space condition. In support of this theory is data we collected in a pilot study to demonstrate search performance equivalency for the allocentric and egocentric tasks (see Supplementary Material A). This experiment also demonstrated a trend for shallower search slopes, and thus greater search efficiency, in far space relative to near space.

Alternatively, it may be that when perceptual localisation tasks are conducted in near space, and thus within reach, irrelevant visuomotor processing is carried out which has the consequence of delaying the reaction time (Cosman & Vecera, 2010).

However, one might expect a greater detriment to egocentric data since these co-ordinates are those used for visuomotor transformations (Kosslyn, 1994), but this is not in evidence here. Despite this, asking participants to localise targets that are within reach may elicit the same visuomotor processing for both allocentric and egocentric frames of reference, accounting for the overall slowing in near space.

The finding that rPPC is selective for egocentric coding but only in near space could have ramifications for patients with damage to this region displaying symptoms of neglect. If patients were encouraged to define their co-ordinate space in an allocentric manner (*e.g.,* where is the cup with respect to the plate, as opposed to where is the cup with respect to me), or to locate objects in far space (as opposed to near space), their behavioural deficits may be reduced. However, this strategy may be limited if damage extends to rFEF, as our data have shown that when TMS is applied to rFEF spatial processing, irrespective of frame of reference and distance, is disrupted. In theory, a spared rFEF should be able to compensate for the egocentric processing that is impaired in near space following rPPC damage in isolation. Nevertheless, a recent study utilising transcranial direct current stimulation and functional magnetic resonance imaging demonstrated diminished bilateral frontal lobe involvement when the signal from rPPC is decreased (Ellison et al., 2014). Given that the current study has established a role for rFEF regardless of distance or spatial reference frame, any compensatory paradigm aimed at improving function in patients with parietal lesions would have to take this into account.

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animal research techniques to replace animal experiments. We would also like to thank James Dowsett for his assistance with data collection.

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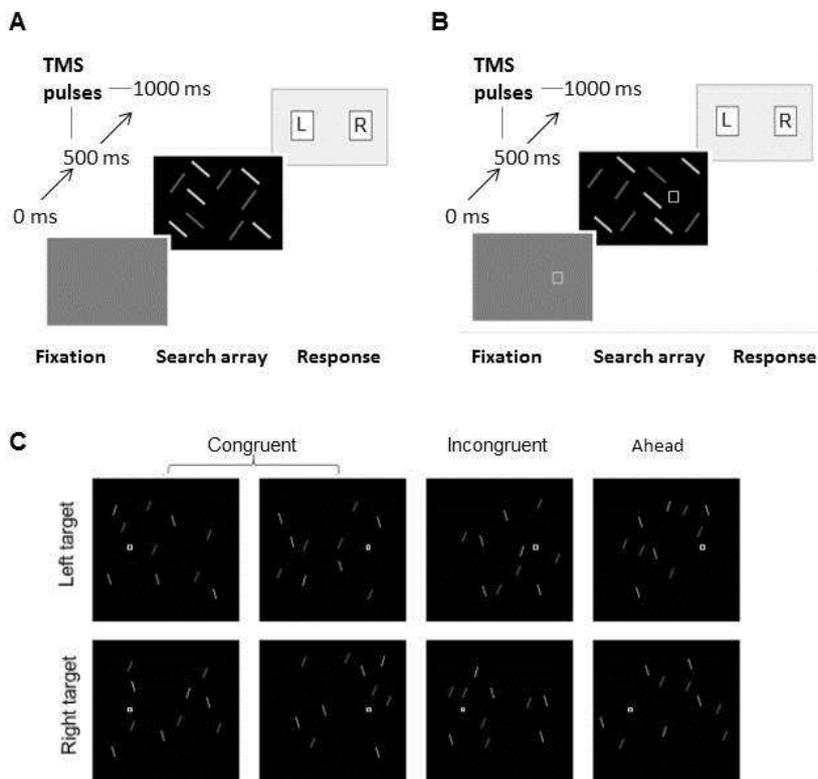
Figure 1. Diagrams depicting the trial progression for the egocentric (a) and allocentric (b) tasks. In each condition a re-fixation screen was presented for 500 ms, followed directly by the search array. This remained until the participant responded using a button-press (left or right); in the egocentric task participants had to decide if the target was to the left or right relative to them as the viewer, whereas in the allocentric task they had to decide if the target was to the left or right of the reference marker (blue square). TMS was delivered at 10Hz for 500 ms from the beginning of the array onset. Figure 1c gives examples of the different types of allocentric array; the target could be left or right of the reference marker, and this could be either congruent or incongruent with the egocentric position, or the target could be central to the viewer (labelled ahead).
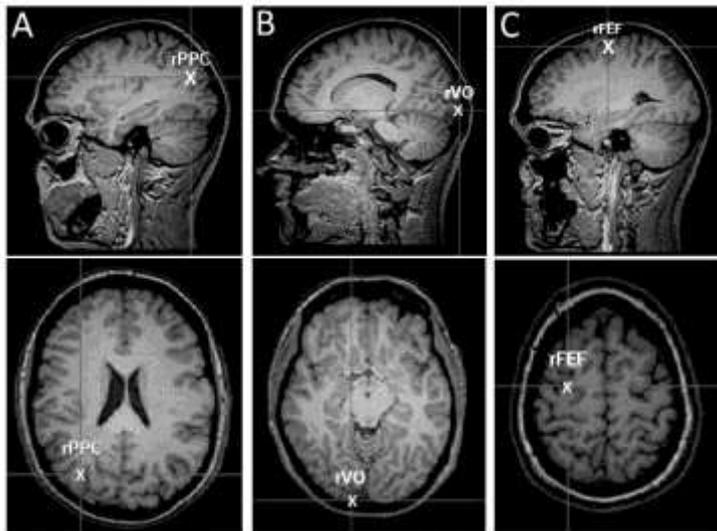
Figure 2. Diagram showing the approximate location of each of the three stimulated sites: rPPC (a), rVO (b) and rFEF (c).
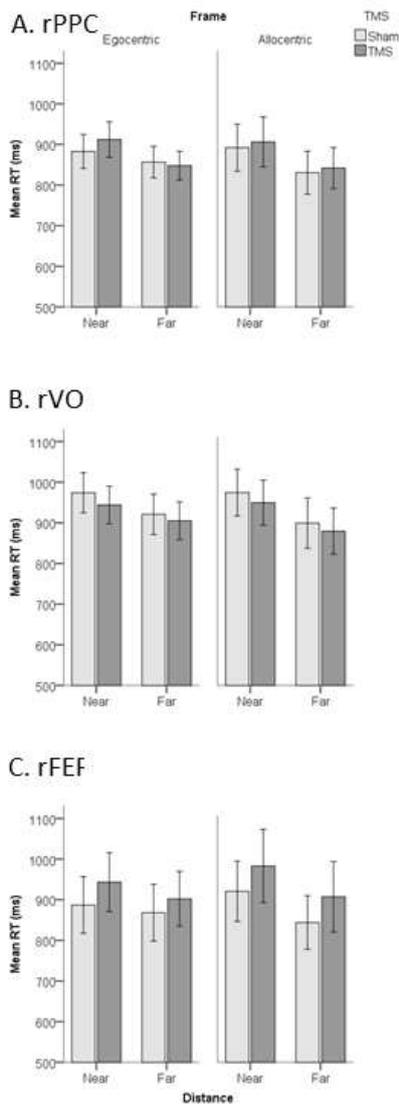
Figure 3. Graphs showing the mean RT (ms) for each condition of Frame, TMS and Distance. Different graphs are presented for each of the three stimulation sites: rPPC (A), rVO (B), and rFEF (C). Error bars represent the standard error of the mean. TMS over rPPC significantly increased RT in the egocentric, near-space condition only ($t_{(11)}$ = -3.65, p = .004; see panel A). There was a significant main effect of TMS over rFEF ($F_{(1,11)}$ = 8.47, p =.014; see panel C).