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23 November 2012

Version of attached file:

Accepted Version

Peer-review status of attached file:

Peer-reviewed

Citation for published item:

Lane, A.R. and Smith, D.T. and Schenk, T. and Ellison, A. (2012) 'The involvement of posterior parietal cortex and frontal eye fields in spatially primed visual search.', *Brain stimulation.*, 5 (1). pp. 11-17.

Further information on publisher's website:

<https://doi.org/10.1016/j.brs.2011.01.005>

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**The involvement of Posterior Parietal Cortex and Frontal Eye Fields in Spatially
Primed Visual Search.**

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Running title: PPC and FEF in Spatially Primed Search

Word counts: The manuscript contains 3999 words (Abstract: 247).

The manuscript contains 19 pages, and includes 0 tables and 4 figures.

Keywords: animal replacement technique; attention; transcranial magnetic stimulation;
visuospatial cognition

Abstract

Background

Right posterior parietal cortex (rPPC) and frontal eye fields (FEF) are known to be involved in processing visuospatial attention. However, the functional involvement of these areas in spatial priming in complex conjunction visual search has yet to be determined.

Objective

This study aimed to examine the roles of rPPC and bilateral FEF in conjunction search when spatial ambiguity was reduced by priming the target location.

Methods

Participants completed a conjunction search task whereby the target location was random or else repeated from the previous trial. Transcranial magnetic stimulation was delivered to each one of the three sites of interest at a time, and task performance was compared to a sham condition.

Results

Spatial priming occurred for all conditions: search times were faster for primed relative to non-primed trials. When the target appeared at a non-primed location, stimulation over any of the three sites increased reaction times relative to the sham condition. However, when the target location was repeated, reaction time was only significantly increased by stimulation over the right FEF.

Conclusions

rPPC and left FEF are only involved when the target location is random, suggesting that these areas are essential for resolving spatial ambiguity in order to localize targets. Conversely, right FEF contributes equally to visual search regardless of spatial priming. We propose that right FEF has a role in the integration of bottom up saliency and top down expectancy signals and is the node at which rPPC and/or left FEF is either recruited or not.

Introduction

It is now widely accepted that visual attention is a function that cannot be attributed to the processing of an isolated brain area. Historically, parietal cortex has been the key central region mainly identified from neuropsychological evidence⁽¹⁾ with support from neuroimaging.⁽²⁾ However, it is now known that other regions of the brain can be solely or equally involved in attentional tasks according to their functional specifications (e.g. V5⁽³⁾ and superior temporal gyrus^(4,5)).

The goal of the current study is to contrast the roles of right posterior parietal cortex (rPPC) and frontal eye fields (FEF); two regions known to be involved in aspects of attentional visual search tasks^(6,7). Given that both areas have been found to have similar roles in the orientation of spatial attention⁽⁸⁻¹⁰⁾, one way to compare their respective roles is to manipulate the ambiguity of the target location via priming. Although the involvement of these areas in priming in simple tasks has been investigated using fMRI,⁽¹¹⁾ their functional involvement in priming in more complex visual search tasks has yet to be determined. Ellison et al.⁽⁹⁾ found that TMS over rPPC disrupted performance for a task in which participants had to decide whether the single item presented was a target or not. However, this effect was limited to trials when the target location was unpredictable. The current study aims to expand this finding to a more ecologically valid conjunction visual search task, and will also seek to establish if FEF responds in the same way.

To achieve this, a priming paradigm is used in which the target location is either repeated in subsequent trials or is random (non-primed), whilst distractor positions are always random. If the main role of rPPC is target location, then this role becomes less important when the position is repeated. Therefore, based on previous findings with single item displays, we would expect that TMS over rPPC should have a greater disruptive effect on

non-primed than primed trials. At present, it is unknown what pattern of results may be seen for the FEFs, and this study will allow us to determine whether the role of FEFs in visual search is also intimately linked to target location identification. Hemispheric functional asymmetry has been demonstrated for several attentional tasks with regards to FEF^(8,12-14) and therefore we will also address how each FEF responds to spatially primed targets.

Materials and methods

Participants

24 healthy participants (9 males, 15 females) aged between 18 and 51 years (median age: 22 years), with normal or corrected-to-normal vision, participated in the experiment. Each experimental session (in which TMS was delivered to a different stimulation site) was carried out by 14 participants, with some participants completing more than one session. One participant was excluded from each session due to difficulties accurately localising the TMS site. Therefore, the final sample for each session included 13 participants. Participants gave their signed informed consent in accordance with the Declaration of Helsinki⁽¹⁵⁾ and with the approval of Durham University Ethics Advisory Committee, and could withdraw at any point. Participant selection complied with current guidelines for repetitive TMS research⁽¹⁶⁻¹⁷⁾.

Stimuli

All stimuli were presented on a 32 cm x 24 cm VDU driven by a Pentium-4 PC, and programmed in E-Prime (Psychology Software Tools, Inc., Pittsburgh, PA, USA). Participants sat 57.5 cm away from the screen which was centred at eye level. The participant's head and trunk sagittal midline were aligned with the centre of the screen, and head position was maintained using a chinrest. Except for the light from the PC the room was darkened.

Visual Search Tasks

Each trial began with a white central fixation cross (subtending $0.5^\circ \times 0.5^\circ$ of visual angle) against a black background presented for 500 ms, followed immediately by the search array. The search display comprised a 10×6 virtual array, which subtended $32^\circ \times 24^\circ$ of visual angle. The task involved a conjunction visual search in which the target was a red slash (/) and the distractors were green slashes and red backslashes (\). All stimuli subtended $2^\circ \times 2^\circ$ of visual angle, were presented against a black background and were matched for luminance within and between items across the display. The array comprised 12 items: 11 distractors plus the target (target-present condition) or 12 distractors (target-absent condition). The target was present in 50% of trials and there was never more than one target. Participants had to determine as quickly and accurately as possible whether the target was present or absent, and press a keypad button accordingly. The array remained present until response and the intertrial interval was 4000 ms. Participants were free to move their eyes during trials but were instructed to return fixation to the centre at the start of each trial. Eye-movements were not monitored during the experiment.

Trials were presented in blocks of 28. Each block contained 8 target-absent trials and 20 target-present trials. These 20 target-present trials included 8 trials where the target location was not repeated (*random trials*) and 6 pairs of trials where the same target location was used twice in a row. Distractor positions were randomized. Targets were presented with equal frequency to the left and right. Six blocks were presented for each TMS condition. This resulted in a total of 168 trials per condition: 48 target-absent, 48 random, 36 first presentation and 36 second presentation trials.

Transcranial Magnetic Stimulation

A Magstim™ SuperRapid magnetic stimulator (Magstim, Whitland, Carmarthenshire, Wales) was used to apply 5 pulses at 10 Hz from visual stimulus onset, at 65% of the stimulator's maximum power (*i.e.* 1.3 Tesla). This level of stimulation is just greater than that required to induce movement (when applied over motor cortex) or the perception of phosphenes (over primary visual cortex).

TMS was applied over one area of interest (right FEF (rFEF), left FEF (lFEF) or rPPC) in each experimental session. For participants who completed more than one session the order of sessions was counterbalanced. Participants performed only one session per week. FEF was stimulated using a 50 mm figure-of-eight coil with the windings perpendicular to the mid-sagittal plane resulting in an anterior-posterior magnetic field. rPPC was stimulated using a 70 mm coil placed tangential to the skull, with the handle pointing backwards, parallel to the mid-sagittal plane. The experimenter held the coil in place.

A hunting procedure with a conjunction search task, as described by Ashbridge et al.⁽¹⁸⁾, was used to identify the rPPC location. Briefly, 10 trials of TMS were given to each site in a 3 x 3 matrix (with each adjacent point 1 cm apart), the centre of which was 9 cm dorsal to the mastoid inion and 6 cm lateral towards the right. The selected site was the one which demonstrated an approximate 100 ms increase in response time (RT) relative to no-TMS trials. This location was correlated with cortical position (angular gyrus) using BrainSight software (Rogue Research™, Montreal, Quebec, Canada), in which each participant's anatomical MRI scan was co-registered with their skull anatomy (as shown in Figure 1).

The FEF site was anatomically located using BrainSight software, and was determined as the intersection of the precentral and superior frontal sulci in each hemisphere. This site was functionally verified using the procedure described by Ro et al.⁽¹⁹⁾ In short, 3

TMS pulses at 25 Hz were delivered at display onset, and the effect of stimulation on saccade latency was measured. Eye-movements were measured with the Video Eyetracker Toolbox (CRS, Rochester, Kent, UK). A 3 x 3 matrix of stimulation sites (with the anatomically localized site at the centre and adjacent points 1 cm apart) was examined. The stimulation site that resulted in the highest mean latency-increase was chosen as the FEF. The scalp position of this site was on average 2.5 cm anterior and 2 cm lateral to the vertex in each hemisphere.

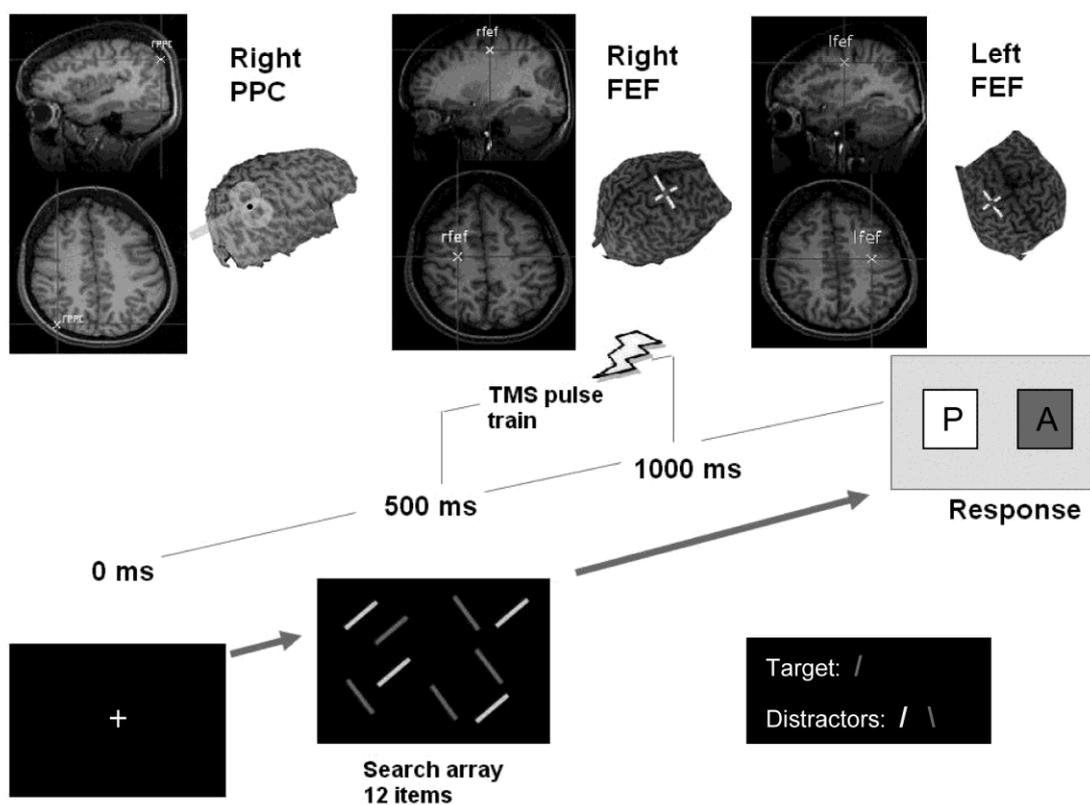


Figure 1. A schematic of the location of the areas of interest (rPPC, rFEF and lFEF) to which TMS was applied and the trial progression. A central fixation cross was presented for 500 ms. This was followed immediately by the search array which remained present until a button-press response was made. TMS was delivered at 10Hz for 500 ms from the beginning of array onset.

There were three experimental sessions; one when TMS was applied to rFEF, one with TMS applied to lFEF and one when TMS was applied to rPPC. In each of these sessions there were six TMS blocks and six sham blocks, in which a non-discharging coil was placed over the area of interest while a discharging coil was placed in close spatial proximity. Therefore the sensation of coil position and auditory effect were comparable but no magnetic pulse was applied. Within each session the order of blocks (TMS/sham) was alternated and counterbalanced across participants. Each testing session usually lasted no longer than 1.5 hours.

Statistical Methods

RTs were collapsed across all non-primed trials (comprising the random and first presentation trials), and the primed trials consisted of those trials in which the target location was repeated from the previous trial. Mean target-present RT was subjected to a 2 (*TMS*: TMS vs. sham) x 2 (*Presentation*: non-primed vs. primed) repeated-measures ANOVA, with site (lFEF, rFEF or rPPC) as a between-subjects variable since only a subset of participants completed more than one session. To further explore the relationships between the conditions of TMS and priming, 2 (*TMS*) x 2 (*presentation*) repeated-measures ANOVAs and paired-samples t-tests were conducted. The two t-tests for each site were adjusted for multiple comparisons using a Bonferroni correction, resulting in an alpha-level of 0.025.

Lastly, TMS effects were computed for all three stimulation sites by calculating the difference between TMS and sham trials. This was done separately for the non-primed and primed trials. Independent samples t-tests were then conducted on the TMS effects in order to examine whether or not the three sites play different roles in visual search when target location is primed or not.

Results

For each condition there were 84 non-primed and 36 primed trials. Search times for each hemifield were compared for each participant in each TMS condition. No significant differences were obtained and the data from the two hemifields was therefore pooled for increased statistical power. Results from the target-absent trials were not analysed for simplicity. Incorrect responses accounted for less than 3% of data points and were removed from the analysis.

The RT for each presentation of the target and for the sham and TMS conditions at each site are shown in Figures 2-4. Sham reaction times were compared (via univariate ANOVA) across site for both non-primed ($F_{(2, 36)} = 0.39$; $p = 0.682$) and primed trials ($F_{(2, 36)} = 0.98$; $p = 0.386$) and revealed no significant differences, thereby demonstrating performance consistency across experimental sessions.

The results of the 2 (*TMS*) x 2 (*Presentation*) repeated-measures ANOVA with site as a between-subjects variable revealed a significant effect of presentation ($F_{(1, 36)} = 102.26$; $p < 0.001$). This demonstrates a significant priming effect, such that RT was reduced on trials where the target was presented for a second time at the same location relative to the non-primed trials. There was no significant interaction between presentation and site ($F_{(2, 36)} = 0.09$; $p = 0.912$) or presentation and TMS ($F_{(1, 36)} = 3.34$; $p = 0.076$), therefore the priming effect was preserved regardless of condition: at no site did the TMS overcome the effects of spatial priming.

The analysis also revealed a significant TMS effect ($F_{(1, 36)} = 45.43$; $p < 0.001$), such that TMS led to an increase in RT relative to the sham condition. Furthermore, there was a significant two-way interaction between TMS and site ($F_{(2, 36)} = 5.52$; $p = 0.008$) and a three-way interaction between presentation, TMS and site ($F_{(2, 36)} = 4.17$; $p = 0.024$). This indicates

that the TMS effect was different for the two presentation types and the different stimulation sites. To further examine these interactions 2 (*TMS*) x 2 (*Presentation*) ANOVAs were performed for each site individually.

The results for rPPC revealed significant main effects of presentation ($F_{(1, 12)} = 19.09$; $p = 0.001$) and TMS ($F_{(1, 12)} = 15.22$; $p = 0.002$), as well as a significant interaction between presentation and TMS ($F_{(1, 12)} = 4.75$; $p = 0.005$). Paired-samples t-tests were conducted to further examine the interaction effect, revealing that TMS significantly increased RT for the non-primed trials ($t_{(12)} = -5.44$; $p < 0.001$) but not for the primed ones ($t_{(12)} = -1.32$; $p = 0.212$) as demonstrated in Figure 2.

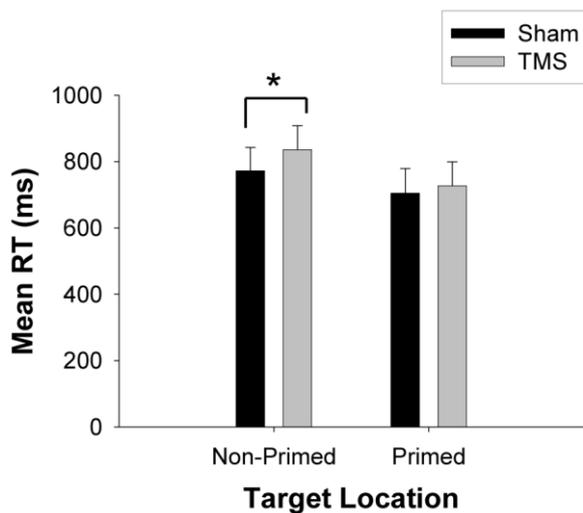


Figure 2. Bar-graph depicting the mean RT in milliseconds (\pm SEM) in the rPPC condition for the non-primed and the primed location trials, separately for the TMS and the sham conditions. An asterisk denotes significant to $p < 0.05$.

Similarly to rPPC, the results for IFEF revealed significant main effects of presentation ($F_{(1, 12)} = 59.98$; $p < 0.001$) and TMS ($F_{(1, 12)} = 12.88$; $p = 0.004$), and a significant interaction effect ($F_{(1, 12)} = 5.38$; $p = 0.039$). As highlighted in Figure 3, RT was

significantly increased by TMS for the non-primed location trials ($t_{(12)} = -3.81$; $p = 0.002$), whilst the TMS did not significantly affect RT for the primed trials ($t_{(12)} = -1.85$; $p = 0.089$).

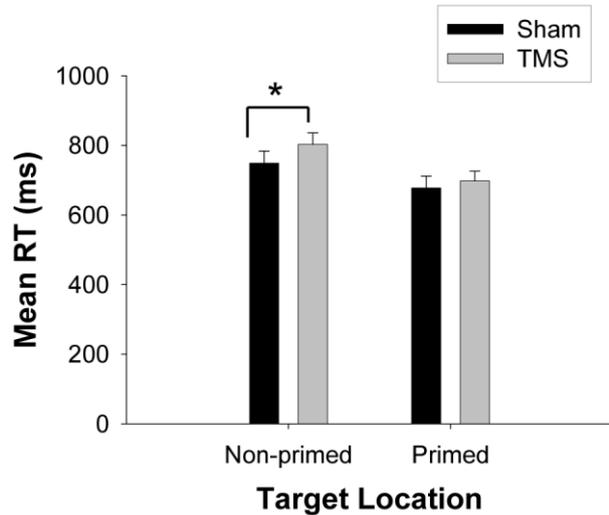


Figure 3. Bar-graph depicting the mean RT in milliseconds (\pm SEM) in the IFEF condition for the non-primed and the primed location trials, separately for the TMS and the sham conditions. An asterisk denotes significant to $p < 0.05$.

A 2 x 2 ANOVA for rFEF revealed a significant main effect of presentation ($F_{(1, 12)} = 48.78$; $p < 0.001$) and also of TMS ($F_{(1, 12)} = 20.90$; $p = 0.001$). However, the interaction between presentation and TMS was not significant ($F_{(1, 12)} = 1.68$; $p = 0.220$): TMS significantly increased RT for both non-primed ($t_{(12)} = -4.35$; $p = 0.001$) and primed trials ($t_{(12)} = -4.29$; $p = 0.001$; Figure 4).

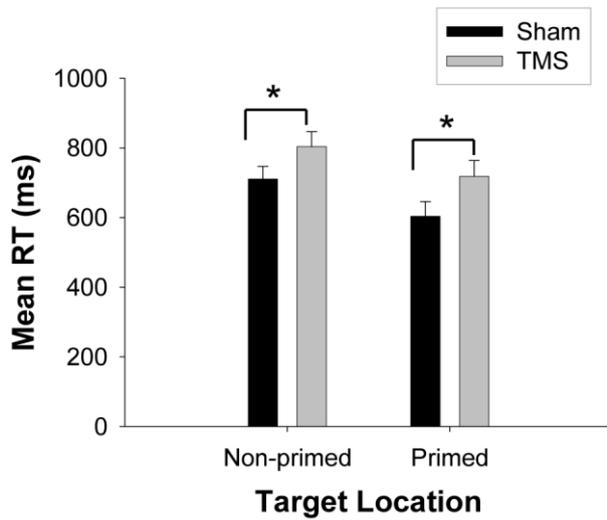


Figure 4. Bar-graph depicting the mean RT in milliseconds (\pm SEM) in the rFEF condition for the non-primed and the primed location trials, separately for the TMS and the sham conditions. An asterisk denotes significant to $p < 0.05$.

The ANOVA results described above revealed a significant interaction effect between presentation, TMS and site. Therefore, to further examine the differences across the three sites, for each site a TMS-effect was calculated (difference in RT between TMS and sham conditions, divided by sham RT) separately for the non-primed and primed trials. These TMS effects were then compared across sites using independent samples t-tests. The results revealed that for the non-primed trials the TMS effect at rPPC was not significantly different to that at lFEF ($t_{(24)} = 0.39$; $p = 0.700$) or rFEF ($t_{(24)} = -1.33$; $p = 0.196$), and similarly the TMS effects at both FEF sites were comparable ($t_{(24)} = -1.49$; $p = 0.150$). With regards to the primed trials, the TMS effects at rPPC and lFEF were not significantly different ($t_{(24)} = 0.17$; $p = 0.871$). However, rFEF was significantly different to rPPC ($t_{(24)} = -2.89$; $p = 0.008$) and lFEF TMS effects ($t_{(24)} = -3.23$; $p = 0.004$).

To summarize these results, when the target location was not primed the TMS significantly increased RT to a comparable extent when delivered to rPPC, lFEF or rFEF. When the target location was primed however, rFEF TMS continued to increase RT whilst TMS over rPPC or lFEF no longer produced a significant effect.

Discussion

The findings of this study contribute to the evidence that rPPC and both FEFs are functionally involved in visual search; however, it is still unclear what each of these regions offers to the processing of space. Therefore, this study examined the role of rPPC and bilateral FEFs in a task in which the target location was either primed or unprimed. There was a significant priming effect that was robust to TMS at all sites, such that search time decreased across two consecutive presentations of the target at the same location. TMS therefore did not affect the priming effect *per se*. Consequently it would seem that complex visual displays are not conducive to the demonstration (using single site event-related TMS) that these regions are (or are not) involved in the priming effect (the decrease in reaction time with repetition of stimulus features) as has been reported elsewhere with simpler tasks (e.g. for FEF: O'Shea et al.⁽¹⁴⁾) and using earlier performance indicators such as eye-movements. Due to the distributed nature of visual processing in the brain, it would seem impossible to localize one region “responsible” for the priming effect during complex visual search (see Kristjánsson & Campana⁽²⁰⁾ for review). In contrast, the testing of each area's involvement in the processing of primed and unprimed trials is valuable evidence in the investigation of specificity of these areas' roles and their interaction.

Therefore, the crucial contrast in this study was the effect that TMS had on reaction times for trials in which the target location was primed and unprimed. The main finding of interest is that rFEF is dissociated from lFEF and rPPC with regards to their involvement in

primed trials: TMS over rPPC or IFEF did not have a significant effect, however TMS over rFEF significantly increased search time. This indicates that rPPC and IFEF are not involved in such tasks when the target location is repeated and more predictable, whilst rFEF remains critically involved.

With the target at a non-primed position, TMS over rPPC, rFEF and IFEF increased reaction times significantly relative to the sham condition, suggesting that all three areas are involved in conjunction visual search when target location is unpredictable. This is in accordance with established roles of these areas in visual processing; FEFs in saccade initiation and fast sensory processing^(8,21) and rPPC in visuospatial orientation and feature binding.^(2,9) In visual search for conjunction targets it is possible that output from rPPC and FEFs needs to be integrated before the button-press response regarding target presence can be made.

Although rFEF continued to be critical when the target appeared in the primed position, rPPC and IFEF were not necessary. Using the same arrays but with three distractor set sizes, a pilot experiment established that search rates do differ significantly between randomly located targets and primed targets (*Non-primed*: $\bar{x} = 20.47$ ms/item, SEM = 4.69; *Primed*: $\bar{x} = 8.73$ ms/item, SEM = 2.75; $t_{(5)} = 2.95$; $p = 0.032$). However, the simple fact that the target “pops-out” in primed trials does not explain why rPPC is uninvolved in primed trials. Ellison et al.⁽⁹⁾ established that rPPC is involved in conjunction search even when the search function is parallel. It is much more likely, given what we know about rPPC’s role in visual search, that this area is no longer required due to the lesser requirement for spatial processing, strengthening the previous finding for one item displays⁽⁹⁾. Our data suggest that once there is increased expectancy regarding the likely target position, the spatial priming signal is capable of replacing the contribution of IFEF and rPPC, thereby reducing their involvement in the task. This theory has support from an fMRI study by Krisjansson and

colleagues⁽²²⁾ who found a decreased BOLD signal in parietal cortex following priming of either target form or location, whilst the same effect was found in FEF when both were primed (as is the case in the current experiment). The decrease in BOLD signal can be taken as evidence of less activity in the pertinent neurons from an elegant fMRI and electrophysiology investigation in monkeys by Shmuel et al.⁽²³⁾ This suggests that the role of rPPC and IFEF lies in spatial disambiguation.

The observed finding of a functional asymmetry between rFEF and IFEF is not new^(8,12-14), however there is much ambiguity over what these differences mean with respect to the role of FEFs in spatial orientation of visual resources. Some studies seem to suggest that disruption of IFEF will result in a significantly reduced priming effect⁽¹⁴⁾ in a feature search task, albeit finding no involvement of IFEF for non-primed trials. In addition, the performance indicator which they used was saccade latencies, a low level indicator of that region's involvement in one aspect of the visual search task. More recently, and conversely, Muggleton et al.⁽²⁴⁾ have shown that IFEF is preferentially involved when a target attribute such as colour is switched and it is not involved in primed trials. This finding, more parsimonious with our own, was achieved using a simple four item, fixed space array and so comparisons should be drawn lightly. The novelty of our study lies in the use of a difficult visual search in distributed space and can ask questions about how disruption of one area involved in spatial vision affects the processing of all task demands (search, localization, identification and response).

The fact that in the present study rFEF is still necessary once the location is primed shows that this area has a different role to play, and that it makes a contribution to the task which the primed signal cannot replace. It has previously been suggested that rFEF is involved in saccadic programming^(21,25-26) and that disrupting this process with TMS interferes with the ability to visually localize the target prior to making a button-press

response, a process that would be required regardless of spatial priming. The decrease in reaction time seen in primed trials has been attributed to the re-using of the same saccadic programme as used on the previous trial.⁽²⁷⁾ If this were the sole function of rFEF, then we would expect disruption here to negate the priming effect. However, for reasons already explained, our experimental design, dependant measure and event-related disruption may not uncover this. There is also no reason to assume that the same saccadic programme would be used in a primed trial. Nevertheless, it is now apparent that motor preparation is only part of rFEF's role⁽²⁸⁾. Evidence supporting a visual selection role for rFEF stems from a recent study by Liu and colleagues⁽²⁹⁾, who used theta-burst TMS to show that disruption of rFEF affected saccades to a greater extent when the probability of target location was high in a singleton-type display. They conclude that along with the accepted role of FEF in saccade initiation, rFEF plays a critical role in modulating the effects of location probability on saccade production.

Taken together with our results it seems that rFEF may act as a “puppet master” for deployment of resources during visual search. In a non-primed trial, the target location is random and so the full spatial attentional resources of the network are required (including rPPC and lFEF). However, if the target has been primed, it is only rFEF which is required to integrate top down and bottom up saliency information without recourse to rPPC and lFEF. This may manifest behaviourally as a faster reaction time for primed trials, and a parallel search rate whereby the target appears to pop out. If rFEF is the gate or decision maker as to whether or not to recruit rPPC and/or lFEF, then disruption here would merely lengthen reaction times with respect to the baseline of the primed trials by increasing such decision time, not negate the priming effect, which indeed is what we see. This theory is supported by Kalla et al.⁽⁶⁾ who found that FEF processing in visual search occurs earlier than PPC, and can

be further tested by investigating the contingency of rPPC activity on rFEF processing (and vice versa), which we next propose to do.

Acknowledgements

This work was supported by the Dr. Hadwen Trust for Humane Research – the UK’s leading medical research charity funding exclusively non-animal research techniques to replace animal experiments.

Financial Disclosures

There are no biomedical financial interests or potential conflicts of interest.

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