

The Role of the Left Posterior Parietal Lobule in Top-Down Modulation on Space-Based Attention: A Transcranial Magnetic Stimulation Study

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Abstract: Converging evidence from neuroimaging as well as lesion and transcranial magnetic stimulation (TMS) studies has been obtained for the involvement of right ventral posterior parietal cortex (PPC) in exogenous orienting. However, the contribution of dorsal PPC to attentional orienting, particularly endogenous orienting, is still under debate. In an informative peripheral cueing paradigm, in which the exogenous and endogenous orienting can be studied in relative isolation within a single task, we applied TMS over sub-regions of dorsal PPC to explore their possible distinct involvement in exogenous and endogenous processes. We found that disruption of the left posterior intraparietal sulcus (pIPS) weakened the attentional effects of endogenous orienting, but did not affect exogenous processes. In addition, TMS applied over the right superior parietal lobule (SPL) resulted in an overall increase in reaction times. The present study provides the causal evidence that the left pIPS plays a crucial role in voluntary orienting of visual attention, while right SPL is involved in the processing of arousal and/or vigilance. *Hum Brain Mapp* 33:2477–2486, 2012. © 2011 Wiley Periodicals, Inc.

Key words: exogenous; endogenous; superior parietal lobule; intraparietal sulcus; cue validity; peripheral cueing

INTRODUCTION

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Directing attention in a voluntary way is referred to as top-down or endogenous orienting, and directing attention in a reflexive way irrespective of current goals is referred to as bottom-up or exogenous orienting. The relevant neuronal mechanisms have been widely studied, and a growing body of evidence supports a dissociation of the neural networks involved in the two types of orienting. Recent neuroimaging studies have shown that endogenous orienting mainly activates a bilateral dorsal frontoparietal network including the frontal eye field (FEF) and dorsal posterior parietal cortex (PPC), particularly the intraparietal sulcus (IPS) and superior parietal lobule (SPL) [Bressler et al., 2008; Carlson et al., 1998; Corbetta et al., 1993, 2000; Corbetta and Shulman, 2002; Hannula et al., 2010; Hopfinger et al., 2000; Kastner et al., 1999; Kincade et al., 2005; Nobre et al., 1997; Shulman et al., 2010; Sylvester et al., 2007; Wang et al., 1999; Woldorff et al., 2004], whereas exogenous

orienting employs not only part of the bilateral dorsal network involved in endogenous orienting but also a right lateralized ventral frontoparietal network, including the ventral frontal cortex (IFG) and temporoparietal junction (TPJ) [Arrington et al., 2000; Corbetta et al., 2000; Kincade et al., 2005; Macaluso et al., 2002; Mayer et al., 2004; Rao et al., 2003]. Neuropsychological studies of patients with left unilateral neglect also support this view, showing that patients with right ventral parietal cortex lesions, particularly those with damage at the TPJ, often had impaired performance when they were required to exogenously orient towards the left visual field [Driver and Vuilleumier, 2001; Mort et al., 2003; Posner et al., 1984, 1987; Vallar, 2001; Vallar and Perani, 1986]. Furthermore, recent transcranial magnetic stimulation (TMS) studies have found that application of TMS to the right PPC in normal human subjects induced exogenous deficits as seen in neglect patients [Bjoertomt et al., 2002; Brighina et al., 2002; Fierro et al., 2000, 2001; Hilgetag et al., 2001; Muri et al., 2002; Pascual-Leone et al., 1994; Walsh and Rushworth, 1999].

Therefore, converging evidence from neuroimaging, lesion, and TMS studies have suggested a crucial role of the right ventral PPC in exogenous orienting. However, with regard to endogenous orienting, neuroimaging and lesion studies yielded inconsistent results. While many neuroimaging studies have observed that the dorsal PPC is involved in endogenous orienting [e.g., Corbetta et al., 1993, 2000; Hopfinger et al., 2000; Kastner et al., 1999; Nobre et al., 1997], patients with lesions in PPC have shown relatively unimpaired endogenous processes [Bartolomeo and Chokron, 2001, 2002; Bartolomeo et al., 2001; Friedrich et al., 1998; Han et al., 2004; Ladavas et al., 1994; Posner et al., 1984; Smania et al., 1998]. Thus, it remains unknown whether dorsal PPC sub-regions (e.g., SPL, IPS) differentially contribute to attentional orienting, particularly endogenous orienting [e.g., Corbetta and Shulman, 2002; Thut et al., 2005]. In the present study, we combined repetitive TMS and an informative peripheral cueing paradigm to directly explore the different possible roles of the dorsal PPC sub-regions in endogenous and exogenous orienting.

Attentional orienting is commonly studied through a cueing paradigm, in which a cue provides relevant information about the location of a following target [Posner, 1980]. In a typical cueing experiment, subjects are asked to fixate on the central fixation point and to respond upon detection of a target appearing in one of two laterally placed boxes. Each target is preceded by a cue that indicates which of the two boxes is likely to hold the upcoming stimulus. Cues can be either central (e.g., an arrow presented to the fovea) or peripheral (e.g., a flash or an abrupt onset in the periphery). Reaction times (RTs) have been found to be shorter for targets appearing at the cued location (valid trials) than for those appearing at the uncued location (invalid trials), suggesting that cues activate an orienting response and facilitate the subsequent processing at that cued location [Abrams and Law, 2000; Briand, 1998; Cheal and Lyon, 1994; Posner, 1980]. Endogenous and exogenous orienting

are often studied using central and peripheral cues, respectively. However, these approaches for dissociating endogenous and exogenous orienting may introduce potential confounds because recent evidence has shown that central cues could also elicit reflexive attention orientation, even when the cues carry no predictive information concerning target location and are to be ignored [Hommel et al., 2001; Pratt and Hommel, 2003]. In addition, peripheral cues have been found to trigger both a fast-acting exogenous and a slow-acting endogenous orienting process [Muller and Findlay, 1988; Muller and Rabbitt, 1989]. Therefore, central and peripheral cueing cannot simply correspond to endogenous and exogenous orienting, respectively. In light of this concern regarding the separation of endogenous and exogenous processes, in the current study, we adopted an informative peripheral cueing paradigm designed by Egly et al. (1994), in which two rectangles with equal length and distance from each other were presented in the background. After an informative (70% of the time) peripheral cue flashed at one end of one of the rectangles, subjects were asked to detect a target that appeared 300 ms later either at the cued location (valid condition), at the uncued location within the same rectangle (intra condition), or at the equally distant uncued location within the uncued rectangle (inter condition). RTs for the valid condition were shorter than those for the intra and inter conditions, reflecting a space-based attentional effect (SAE). RTs for the intra condition were shorter than those for the inter condition, which has been referred to as an object-based attentional effect (OAE). By manipulating cue validity (the percentage of valid trials in the total target-present trials), which affects only the voluntary mechanism but not the reflexive one, previous studies have found that the magnitude of SAE is affected by cue validity, suggesting that SAE reflects an endogenous orienting mechanism which requires spatial expectancy based on the information of most probable target onset location. However, the magnitude of OAE is not affected by cue validity, suggesting that OAE reflects an exogenous orienting mechanism triggered by the abrupt onset of the cue [He et al., 2004, 2008]. Hence, by adopting this double-rectangle peripheral cueing design, attentional effects of both endogenous and exogenous processing, reflected by the magnitudes of SAE and OAE respectively, can be simultaneously studied in relative isolation from one another within a single task.

First, in Experiment 1, we further confirmed that SAE and OAE can reflect, respectively, the endogenous and exogenous processing. Then in Experiment 2, by applying left or right parietal stimulations, we explored the possible role of left and right parietal regions in endogenous processes, as compared to exogenous processes.

EXPERIMENT 1

Previous study [He et al., 2004] has shown that SAE and OAE were both present under high cue validity, whereas under low cue validity, SAE was absent but OAE still existed.

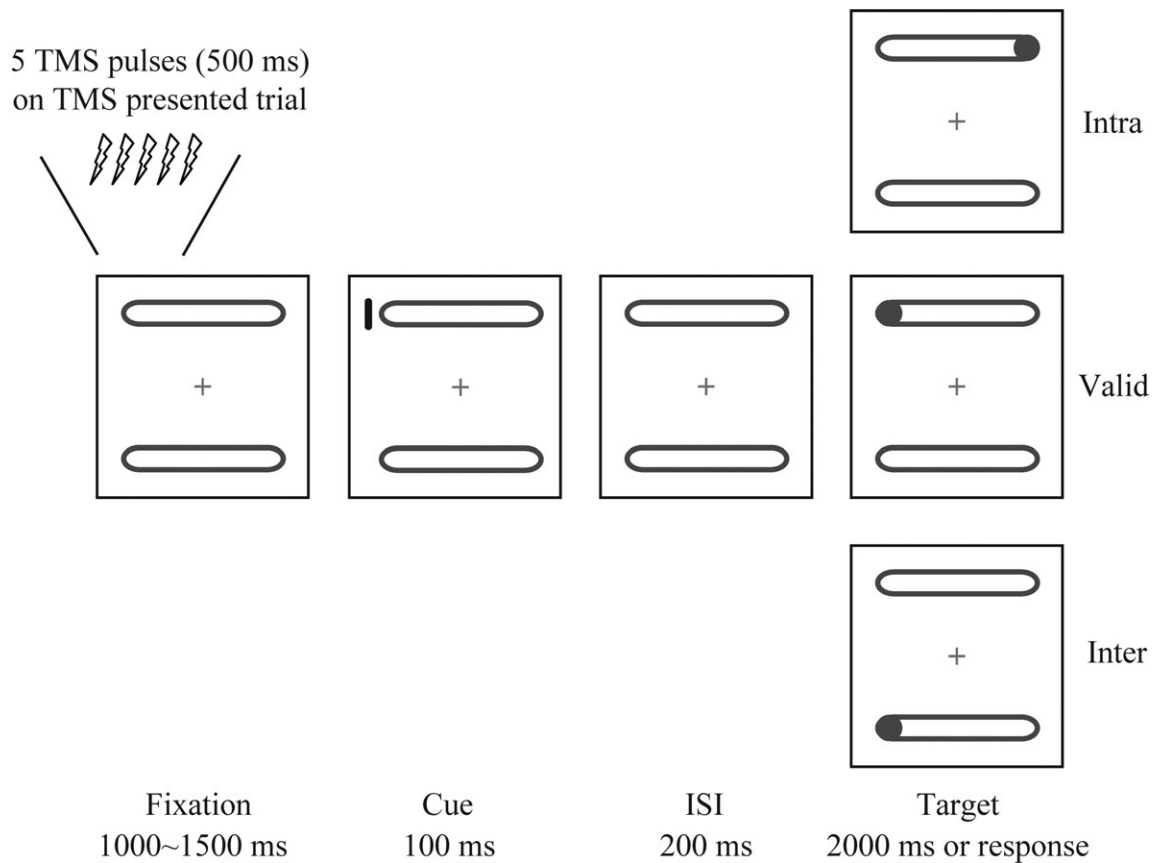


Figure 1.
Schematic depiction of the stimuli and procedure

They inferred that SAE, and not OAE, reflected the endogenous orienting mechanism. However, there was a lack of direct comparisons between the high and low cue validity for both SAE and OAE in their analysis, leaving open the possibility that target detectability may vary across the two cue validity conditions. Thus, the purpose of Experiment 1 was to confirm whether SAE and OAE could be used to reflect the endogenous and exogenous processing correspondingly, by comparing the cue validity effects on the magnitudes of SAE and OAE, within a same group of subjects.

MATERIALS AND METHODS

Subjects

Thirteen subjects (6 males and 7 females aged 19–27 years; all right-handed) participated in Experiment 1. All subjects had normal or corrected-to-normal vision and were naïve to the purpose of the experiment.

Stimuli and Procedure

All stimuli were white drawn on a black background, except for the fixation point. The fixation point was a

green plus sign (+) subtending $0.5^\circ \times 0.5^\circ$. Two outlined, rounded rectangles ($8.3^\circ \times 1.4^\circ$, 0.2° line width) appeared either above/below or to the left/right of the fixation point. Each of the rounded rectangles (4 cd/m^2) was 3.55° away from the fixation point (center-to-center). The cue was a light gray (14 cd/m^2) solid bar ($1.2^\circ \times 0.3^\circ$) placed at one of the four ends of the two rounded rectangles. The target was a gray (4 cd/m^2) solid disk ($1.2^\circ \times 1.2^\circ$). The rectangles were horizontally placed in half of the trials and vertically placed in the other half.

As illustrated in Figure 1, each trial began with a background containing the fixation point and two rounded rectangles. Subjects were instructed to focus their gaze on the fixation point. The trial continued after the subject signaled readiness to proceed. The cue was presented for 100 ms and then disappeared. After a 200 ms cue-target interval, the target was presented (not shown in catch trials) and remained visible until the subjects responded by pressing one button, or for 2,000 ms if there was no response. Subjects were instructed to maintain fixation throughout the trial and to make responses with their right hand as rapidly as possible. All of the stimuli were presented on a 19-inch computer screen at a viewing distance of 90 cm. Each subject was first given a set of practice trials, which

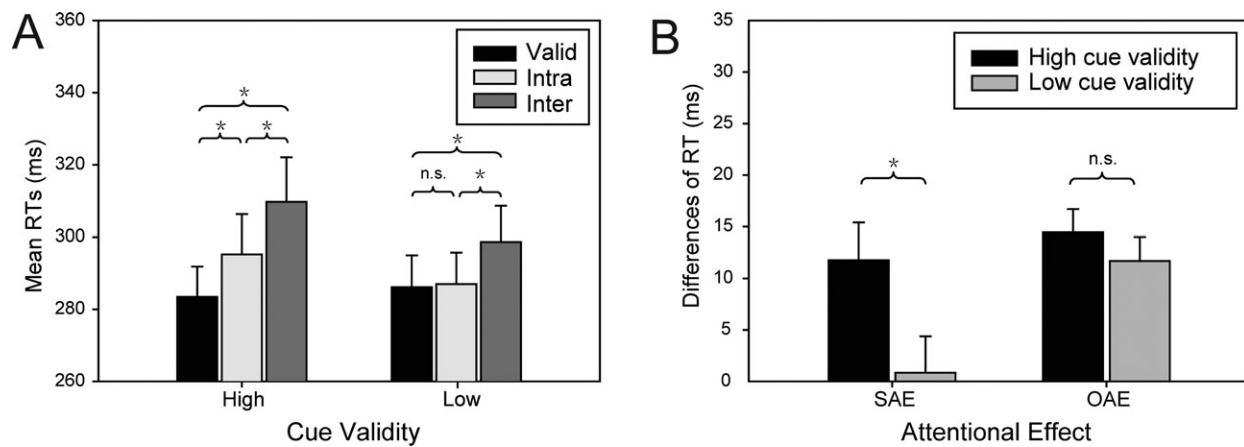


Figure 2.

Results of Experiment 1. **A:** Mean reaction times for valid, intra, and inter conditions under both high and low cue validity. **B:** SAE and OAE under different cue validity conditions. Error bars indicate SEMs. “*” indicates $P < 0.05$ and “n.s.” indicates $P > 0.05$.

were randomly selected from the experimental conditions, and began the formal experiments after making 20 consecutive correct responses during the training. In Experiment 1, each subject completed two sessions with different cue validities (high or low) on separate days. Subjects were encouraged to use the information of cue validity to direct their attention covertly. The order of two sessions was counterbalanced across subjects. In the high-cue-validity session, there were 640 trials in six blocks. Of all 544 target-present trials, the target appeared at three possible locations: the cued end of the rounded rectangle (valid condition), the other end of the cued rounded rectangle (intra condition), and the equidistant end of the other rounded rectangle (inter condition), with percentages of 65%, 17.5%, and 17.5%, respectively. The remaining 96 trials were catch trials in which no target appeared. In the low-cue-validity condition, there were 480 trials in four blocks. Of all 384 target-present trials, the percentages of the valid, intra, and inter were 50%, 25%, and 25%, respectively. The remaining 96 trials were catch trials.

RESULTS AND DISCUSSION

Mean RTs were analyzed for each condition. RTs of less than 150 ms or 3 standard deviations from the mean of each condition for each individual were removed from the analysis ($< 3\%$). The mean hit rate on target-present trials was 97% ($\pm 3\%$), and the mean false-alarm rate was 2% ($\pm 2\%$).

We first carried out a two-way repeated measures analysis of variance (ANOVA) with cue validity (high or low) and target type (valid, intra or inter) as within-subject factors. The main effect of target type was significant ($F_{(2,24)} = 20.21$, $P = 0.0001$). Importantly, there was a significant interaction between cue validity and target type ($F_{(2,24)} = 8.04$;

$P = 0.009$) (Fig. 2A), suggesting that cue validity affected target detection across conditions. Further analysis was conducted to test whether cue validity affects the magnitudes of SAE and OAE. As in previous study, SAE was defined by subtracting RTs in the valid condition from those in the intra condition, and OAE was characterized by differences in RTs between the intra and inter conditions. As shown in Figure 2B, the magnitude of SAE was significantly larger under high cue validity compared to low cue validity ($T_{(12)} = 2.99$, $P = 0.011$). Actually, under low cue validity, SAE disappeared ($T_{(12)} = 0.24$, $P > 0.05$). In contrast, robust OAEs were found for both high- and low-cue-validity conditions (all P 's < 0.05), and the magnitude of OAE were not affected by the different levels of cue validity ($T_{(12)} = -1.37$, $P > 0.05$) (Fig. 2B).

Thus, consistent with previous findings, when cue validity was high, a significantly larger SAE was observed, corresponding to the endogenous modulation, whereas low cue validity resulted in a decrease in endogenous modulation and correspondingly an SAE decrease. The present data, therefore, confirmed that SAE and OAE in an informative peripheral cueing paradigm reflect the endogenous and exogenous processes, respectively.

EXPERIMENT 2

In Experiment 2, to examine the role of dorsal PPC in endogenous orienting, we applied rTMS over right and left PPC sub-regions immediately before participants had to perform the same task as that in Experiment 1. Only the high cue validity was adopted to make sure that robust SAE and OAE can be achieved in Experiment 2. After TMS, a decrease in the magnitude of SAE or OAE would be interpreted as the consequence of the disruption of endogenous or exogenous processing, respectively.

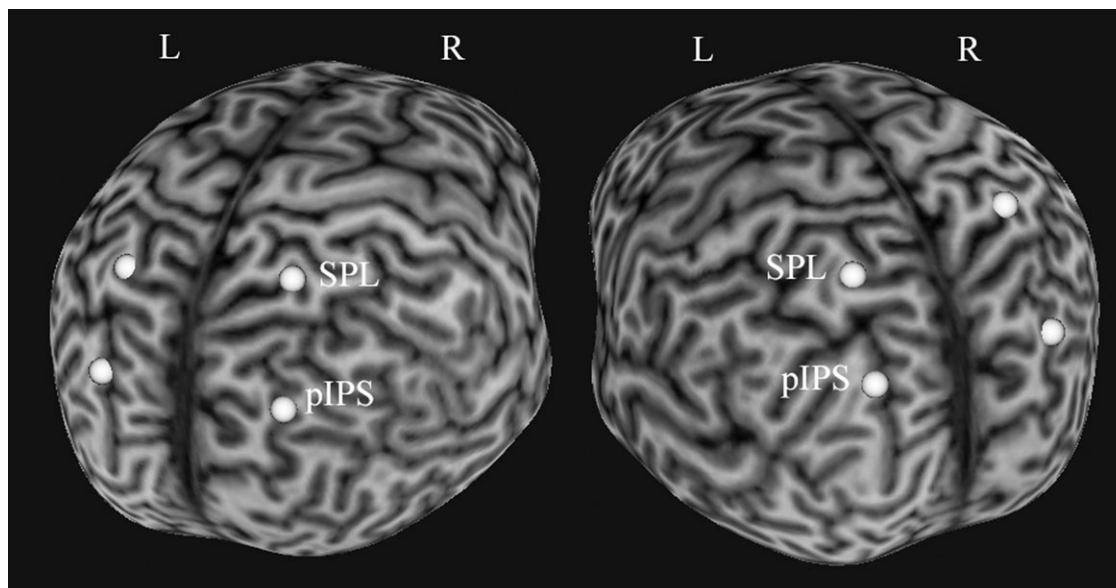


Figure 3.

TMS sites relative to individual magnetic resonance images of one subject as extrapolated using a frameless stereotaxic system.

MATERIALS AND METHODS

Subjects

Seventeen right-handed subjects (3 males and 14 females; aged 19–26 years; all right-handed) who had normal or corrected-to-normal vision took part in Experiment 2. Written informed consents were obtained from all subjects in accordance with requirements of the Institutional Review Board of Beijing MRI Center for Brain Research and were treated in accordance with the Declaration of Helsinki. Nine subjects received left parietal stimulation, and eight subjects received right parietal stimulation. One subject who received left parietal stimulation was excluded from further analysis because of a high false-alarm rate (>10%).

Stimuli and Procedure

The visual stimuli and procedure were identical to those in Experiment 1. There were three sessions in Experiment 2, including two TMS sessions and one no-TMS (baseline condition) session. There was at least one week between each TMS session. To minimize the possible sound induced spatial cueing effects [Spence and Santangelo, 2009] or/and sound induced visual illusion [Shams et al., 2000] resulted from the TMS stimulation, a train of five-pulse TMS (pulse gap 100 ms) was applied at the onset of each trial, followed by a delay of 500–1,000 ms before the cue onset (see Fig. 1).

A long interval between TMS stimulation and the cue onset was used to minimize the possible auditory and somatosensory influences of TMS that might lead to an artificial hemisphere asymmetry. In TMS sessions, 27% of the valid trials were given TMS stimulations to match the

number of stimulations in the intra and inter conditions. This TMS protocol maintained the TMS effect during the entire block while keeping the stimulations to a minimum.

Transcranial Magnetic Stimulation

The stimulator was a Magstim Super Rapid stimulator (Magstim Company, UK), delivering current to a 70 mm figure-of-eight coil. Pulses were delivered at an intensity of 65% of maximum output of the stimulator at 10 Hz for 500 ms [Beck et al., 2006; Campana et al., 2002; Muggleton et al., 2006; Stewart et al., 2001].

TMS was applied over four sites of the PPC: left and right SPL, and left and right posterior intraparietal sulcus (pIPS). They were localized in each subject on the basis of sulcal landmarks from individual MRI scans and projected to the scalp surface using TMS-MRI co-registration. Prior to testing, a T1-weighted MRI scan was obtained from each subject using a 3 Tesla Siemens MRI scanner. As illustrated in Figure 3, the pIPS was defined as the posterior region of the intraparietal sulcus (adjacent to the posterior part of the angular gyrus), and the SPL was defined as the medial mid-point of the superior parietal gyrus, between the anterior IPS and the longitudinal fissure [Chambers et al., 2006; Muggleton et al., 2003, 2008; Schenkluhn et al., 2008]. The pIPS sites were located slightly lateral to the angular gyrus; therefore, the posterior SPL would not be affected by pIPS stimulation. The mean Montreal Neurological Institute (MNI) coordinates of the bilateral pIPS and SPL were $-28 -70 37$ (SD = 4.5 4.0 9.6, left pIPS), $-25 -61 55$ (SD = 6.1 7.3 5.9, left SPL), $38 -68 32$ (SD = 6.3 2.6 8.4, right pIPS),

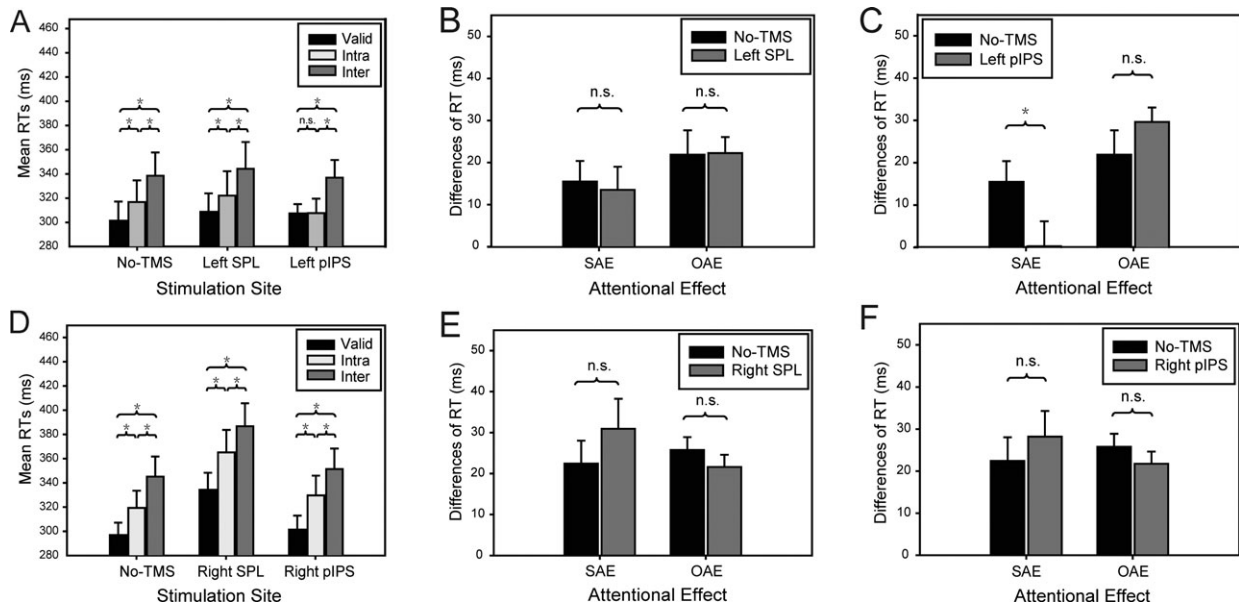


Figure 4.

Results of Experiment 2. **A:** Mean reaction times for valid, intra, and inter conditions in left-parietal stimulation group. **B, C:** SAE and OAE for left SPL stimulation, left pIPS stimulation, and no-TMS condition. **D:** Mean reaction times for valid, intra, and inter conditions in right-parietal stimulation group. **E, F:** SAE and OAE for right SPL stimulation, right pIPS stimulation, and no-TMS condition. Error bars indicate SEMs. “*” indicates $P < 0.05$ and “n.s.” indicates $P > 0.05$.

and 25 –57 57 (SD = 3.5 6.0 6.0, right SPL), respectively [see also Driver et al., 2010; Gobel et al., 2006; Morris et al., 2007; Ruff et al., 2008; Schenkluhn et al., 2008]. We used a frameless stereotaxy system (BrainSight, Rogue Research, Montreal, Canada) to position the coil over the location of these sites marked on each subject’s MRI. For each site, the coil was placed tangential to the scalp surface, with the virtual cathode over the region of interest.

RESULTS AND DISCUSSION

Mean RTs were analyzed for each condition. RTs of less than 150 ms or those out of 3 standard deviations from the mean of each condition for each individual were removed from the analysis (<4%). In the left parietal stimulation group, the hit rates for the no-TMS condition, SPL stimulation, and pIPS stimulation were 97.01% ($\pm 0.91\%$), 97.40% ($\pm 0.61\%$), and 96.63% ($\pm 1.02\%$), respectively. The false alarm rate for the no-TMS condition, SPL stimulation, and pIPS stimulation were 2.34% ($\pm 1.74\%$), 2.08% ($\pm 1.08\%$), and 2.60% ($\pm 1.67\%$), respectively. In the right parietal stimulation group, the hit rates for the no-TMS condition, SPL stimulation, and pIPS stimulation were 97.37% ($\pm 1.23\%$), 97.63% ($\pm 1.15\%$), and 97.50% ($\pm 1.35\%$), respectively. The false alarm rates for the no-TMS condition, SPL stimulation, and pIPS stimulation were 2.34% ($\pm 2.14\%$), 0.78% ($\pm 0.48\%$), and 0.91% ($\pm 1.17\%$), respectively. The hit rates and false alarm rates did not significantly differ across all conditions (all P ’s > 0.05).

In subsequent analyses, data were pooled for the valid conditions with and without TMS, which made our analyses more comparable to previous pre-cueing studies that had more trials in the valid condition than in the invalid condition. Any effects of TMS here could not be explained by this operation, because the combination of these two conditions should only weaken the impact of TMS rather than increase it.

The mean RTs for correct responses were initially analyzed in a three-way mixed ANOVA. The within-subject factors were target type (valid, intra, or inter) and TMS site (no-TMS, SPL, or pIPS). Side of parietal lobule stimulated (left or right) was a between-subject factor. We found significant main effects of target type ($F_{(2,28)} = 54.40, P < 0.0001$) and TMS site ($F_{(2,28)} = 3.92, P = 0.033$). Importantly, there was a significant three-way interaction ($F_{(4,56)} = 3.18, P = 0.045$). To unravel this interaction, separate analyses were performed for left- and right-parietal stimulation.

Left Parietal Stimulation Group

A two way repeated measures ANOVA was conducted with TMS condition (no-TMS or SPL stimulation) and target type (valid, intra, or inter) as within-subject factors. The results showed a significant main effect of target type ($F_{(2,14)} = 22.04, P = 0.001$). The interaction was not significant ($F < 1$) (Fig. 4A). Further analysis revealed that, compared with no-TMS condition, TMS over left SPL had

no effects on either exogenous or endogenous processes ($T_{(7)} = 0.10, P > 0.05; T_{(7)} = 0.31, P > 0.05$) (Fig. 4B).

Similar analysis was used for the comparison between left pIPS stimulation and no-TMS condition. The main effect of target type was significant ($F_{(2,14)} = 17.77, P = 0.002$). Importantly, the interaction was also significant ($F_{(2,14)} = 5.25, P = 0.021$) (Fig. 4A). Analysis of simple interaction effects revealed that left pIPS stimulation, as compared with no-TMS condition, reduced and even eliminated the magnitude of SAE ($T_{(7)} = 3.44, P = 0.011$), whereas the magnitude of OAE was not affected ($T_{(7)} = 1.70, P > 0.05$) (Fig. 4C), suggesting that endogenous processes, but not exogenous processes, were severely interrupted by left pIPS stimulation. The decrease of SAE observed with the left pIPS disruption was not due to the possible non-specific effects of TMS on following cue-target sequences, because the left SPL disruption shared the similar TMS-related discomfort, noise, or muscle twitches, but showed no decrease of SAE.

Right Parietal Stimulation Group

A two-way repeated measures ANOVA was conducted with TMS condition (no-TMS or right SPL stimulation) and target type (valid, intra or inter) as within-subject factors. The results revealed a significant main effect of target type ($F_{(2,14)} = 34.24, P = 0.0003$). The main effect of TMS condition was also significant ($F_{(1,7)} = 5.70, P = 0.048$), showing that the right SPL stimulation, as compared with no-TMS condition, produced an overall increase in RTs for target detection ($P < 0.05$) (Fig. 4D). No significant interaction was found ($F_{(2,14)} = 2.53, P > 0.05$). Similar analysis was used for the comparison between right pIPS stimulation and no-TMS condition. Only a main effect of target type was significant ($F_{(2,14)} = 37.80, P = 0.0002$). The interaction was not significant ($F_{(2,14)} = 1.61, P > 0.05$) (Fig. 4D). Further analysis revealed that right parietal stimulation (SPL or pIPS), as compared with no-TMS condition, has no effect on either SAE or OAE (all P 's > 0.05) (Fig. 4E,F). Hence, these results suggest that right SPL stimulation might interfere with task-related arousal or vigilance rather than with specific voluntary or reflexive processes.

CONCLUSION

To summarize, in the present study, we found that (i) disruption of left pIPS diminished and even eliminated SAE, but did not affect OAE, suggesting that left pIPS has a pivotal role in endogenous spatial orienting, but not in exogenous processing; (ii) disruption of right SPL resulted in an overall increase in RTs across conditions, but had no effects on either SAE or OAE, indicating the right SPL involvement in arousal and/or vigilance; and (iii) disruption of left SPL or right pIPS has no reliable effects on target detection in the present study.

The present study provides support for the hypothesis that two functionally distinct neural systems mediate endogenous (voluntary) and exogenous (involuntary) orienting [Corbetta and Shulman, 2002; Fu et al., 2005a,b; Mayer et al., 2004]. As found in the present study, applying TMS over dorsal PPC did not affect the attentional effects of exogenous orienting, but disrupted endogenous processes. The results are thus in line with the findings of previous neuroimaging, electrophysiological and lesion studies [Bisley and Goldberg, 2003; Bressler et al., 2008; Corbetta and Shulman, 2002; Driver and Vuilleumier, 2001; Hopfinger et al., 2000; Mort et al., 2003; Posner et al., 1987; Sylvester et al., 2007; Szczepanski et al., 2010], suggesting that the dorsal PPC controls the voluntary deployment of attention, but is not engaged in exogenous orienting. However, several lines of neuroimaging studies have reported common activations when the two modes of orienting are directly compared [Corbetta et al., 1993; Kim et al., 1999; Nobre et al., 1997; Rosen et al., 1999]. One possibility is that these studies often utilized different behavioral paradigms to elicit endogenous and exogenous orienting component, which may introduce other confounding effects (e.g., attentional set, arousal, or alerting state) into these neuroimaging results. In the present study, by studying the endogenous and exogenous processes within a single task, these confounding factors are controlled as far as possible. The current results therefore provide direct evidence suggesting that endogenous and exogenous processing recruited separate cortical areas.

The present data reveal previously unseen functional dissociations between dorsal PPC sub-regions. The left pIPS is necessary for deploying attention orienting in an endogenous way, whereas the right SPL appears to be crucial for arousal. On the other hand, the present data also strengthen the notion that there is lateralized functionality of the parietal cortex for endogenous orienting. Previous studies suggested that a left-hemispheric network (including the IPS) displayed activity in response to cues that increased linearly with increased cue validity [Hahn et al., 2006; Vossel et al., 2006]. Here, by using TMS, the present study provides direct evidence to establish such causal relationships.

In the present study, we did not observe a significant impairment of visual orienting after the right PPC stimulation as did some early studies for right-hemispheric rTMS [e.g., Ashbridge et al., 1997; Hilgetag et al., 2001]. This divergence may be due to the different experimental protocol used in current study, which prevents direct comparison and reconciliation with these studies. First, the experimental paradigm used here was different from those used in previous studies, which may introduce differences as well as similarities in the attentional mechanisms in these paradigms. Further investigations are still needed to explore the contributions of PPC sub-regions to different attentional protocols. Second, it should be noted that current TMS protocol, in which the TMS pulses were delivered 500–1,000 ms before the onset of cue, was carefully

designed to avoid the interference from the auditory artifact from TMS. It might be argued that the current pattern of results could be specifically originated from the timing of TMS delivery, since the physiological basis of the after-effects of current TMS protocol remains unknown and further studies using combined TMS-EEG technology would be necessary to evaluate the validity of this protocol. Nevertheless, it can be ruled out by the fact that the same TMS protocol was used for all conditions, and different response patterns have been observed after TMS stimulations over different cortical sites. However, future TMS experiments using theta burst stimulation or 1 Hz stimulation, which has better theoretical and neurophysiological foundation, would help to confirm the differential contributions of PPC sub-regions to visual orienting.

The left parietal areas, particularly the supramarginal gyrus (SMG), also play a direct role in motor attention [Rushworth et al., 1997, 2001a,b, 2003], the current pattern of results, however, could not be originated from the disruption of motor attention. The Euclidean distance between the left SMG site reported by Rushworth et al. (2001a) (Talairach and Tournoux coordinates: $-52, -36, 56$) and the left pIPS site in current study (Talairach and Tournoux coordinates: $-28, -66, 38$) was approximately 4.2 cm, which was within the resolution of TMS [Paus et al., 1997, 1998; Walsh and Cowey, 1998]. In addition, SMG and pIPS are not anatomically interconnected [Catani et al., 2002, 2005; Cavada and Goldman-Rakic, 1989a,b]. The left pIPS stimulation in our study, therefore, was unlikely to affect motor attention.

The right SPL involvement in arousal and/or vigilance is in agreement with the findings that non-lateralized attentional impairments are associated with right parietal damage. For example, neglect patients need more time than normal individuals to respond to visual targets, even in their ipsilesional, non-neglected space, which represents arousal or vigilance deficits. A recent study on perceptual rivalry, using TMS in combination with highly sensitive correlational methods such as voxel-based morphometry (VBM) and the fractional anisotropy (FA) analyses, also confirmed that SPL regions play a causal role in generating consciously perceptual switches between competing interpretations [Kanai et al., 2010]. Thus, the interpretation that the right SPL is engaged in arousal or vigilance fits well with the assumption of the right-hemisphere arousal system postulated by Posner et al. [Posner, 1987; Posner and Petersen, 1990].

Taken together, the present data extend the understanding of the functions of the PPC in voluntary modulation and attentional control processes, especially addressing the role of the left PPC in the voluntary control of attention orienting.

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