◆ Human Brain Mapping 32:1961–1972 (2011) ◆

Predictability of Saccadic Behaviors is Modified by Transcranial Magnetic Stimulation Over Human Posterior Parietal Cortex

Chang-Mao Chao,[1,2,3] Philip Tseng,[1,4] Tzu-Yu Hsu,[1,3,5] Jia-Han Su,[6] Ovid J.L. Tzeng,[1,3,5,7] Daisy L. Hung,[1,3,5] Neil G. Muggleton,[8] and Chi-Hung Juan[1,5,9]*

[1]*Institute of Cognitive Neuroscience, National Central University, Jhongli, Taiwan*
[2]*Department of Life Science, National Central University, Jhongli, Taiwan*
[3]*Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan*
[4]*Department of Psychology, University of California, Santa Cruz, California*
[5]*Laboratories for Cognitive Neuroscience, National Yang-Ming University, Taipei, Taiwan*
[6]*Department of Computer Science and Information Engineering, National Central University, Jhongli, Taiwan*
[7]*Institute of Linguistics, Academia Sinica, Taipei, Taiwan*
[8]*Institute of Cognitive Neuroscience & Department of Psychology, University College London, London, United Kingdom*
[9]*Institute of Network Learning Technology, National Central University, Jhongli, Taiwan*

Abstract: Predictability in the visual environment provides a powerful cue for efficient processing of scenes and objects. Recently, studies have suggested that the directionality and magnitude of saccade curvature can be informative as to how the visual system processes predictive information. The present study investigated the role of the right posterior parietal cortex (rPPC) in shaping saccade curvatures in the context of predictive and non-predictive visual cues. We used an orienting paradigm that incorporated manipulation of target location predictability and delivered transcranial magnetic stimulation (TMS) over rPPC. Participants were presented with either an informative or uninformative cue to upcoming target locations. Our results showed that rPPC TMS generally increased saccade latency and saccade error rates. Intriguingly, rPPC TMS increased curvatures away from the distractor only when the target location was unpredictable and decreased saccadic errors towards the distractor. These effects on curvature and accuracy were not present when the target location was predictable. These results dissociate the strong contingency between saccade latency and saccade curvature and also indicate that rPPC plays an important role in allocating and suppressing attention to distractors when the target demands visual disambiguation. Furthermore, the present study suggests that, like the frontal eye fields, rPPC is critically involved in determining saccade curvature

Contract grant sponsor: National Science Council, Taiwan; Contract grant numbers: 97-2511-S-008-005-MY3, 99-2410-H-008-022-MY3, 96-2413-H-008-001-MY3, 98-2410-H-008-010-MY3, 98-2517-S-004-001-MY3, 97-2511-S-008-008-MY5; Contract grant sponsor: UK Medical Research Council; Contract grant sponsor: National Science Council, Taiwan, Fulbright scholarship; Contract grant numbers: 98-2918-I-008-011.

*Correspondence to: Chi-Hung Juan, Institute of Cognitive Neuroscience, National Central University, No. 300, Jhongda Rd., Jhongli 320, Taiwan. E-mail: chijuan@cc.ncu.edu.tw

Received for publication 14 May 2010; Revised 5 August 2010; Accepted 12 August 2010

DOI: 10.1002/hbm.21162

Published online 21 January 2011 in Wiley Online Library (wileyonlinelibrary.com).

and the generation of saccadic behaviors under conditions of differing target predictability. *Hum Brain Mapp 32:1961–1972, 2011.*

Key words: predictability; parietal cortex; TMS; saccades; curvatures; visual search

INTRODUCTION

Predictabilities in the visual environment provide a powerful cue for efficient processing of scenes and objects. For example, when walking into a familiar living room, there is no need to visually inspect every object. The gist, as well as the identities of seen objects, predicts the locations and identities of other objects. Behavioral studies have shown that these predictive cues can efficiently guide attention explicitly or implicitly and also facilitate visual search [Brockmole et al., 2006; Chun and Jiang, 1998; Peterson and Kramer, 2001]. Visual recognition also benefits from such predictability as objects are recognized more accurately in their familiar and semantically coherent context [Davenport and Potter, 2004], presumably because visual predictability limits the number of perceptual interpretations on the basis of prior likelihood. Indeed, utilizing predictive information is advantageous as it offsets the computational load for the visual system [for a review see Summerfield and Egner, 2009].

One way to study how the visual system takes advantage of the predictive information is to look at the intervening path that the eyes travel to reach its destination. These eye movement trajectories are often not straight, never like fastballs that shoot straight to the target; instead, these trajectories are found to be curved. The directionality and magnitude of these curvatures are useful here because many researchers have suggested that they reveal the dynamic competition between target selection and distractor suppression that the visual system must resolve [van der Stigchel et al., 2006; Walker and McSorley, 2008]. Specifically, the directionality of these curvatures to the target can often be determined by the presence and location of a distractor so that the trajectories either curve towards [McPeek et al., 2003; McPeek, 2006] or away [Doyle and Walker, 2001; McSorley et al., 2004; Sheliga et al., 1994; Tipper et al., 2001] from the distractor. McPeek [2003] explained deviation "toward" as a result of unresolved competition between elements in a visual scene. When two possible targets are positioned in close proximity, the neural populations of these targets are combined into one mean population, resulting in an averaged vector that travels between the distractor and the intended target [McPeek et al., 2003; Port and Wurtz, 2003; Tipper, 1997; Tipper et al., 2001]. Sheliga [1994] explained the "away" curvatures with a suppression hypothesis that treats the opposite saccade direction as a result of one's effort to inhibit an eye movement to the distractor location. Thus, the saccade trajectory would deviate away from the distractors due to over-inhibition.

Recently, studies have shown that predictability in the visual environment can also interact with saccade curvature. For example, Walker et al. [2006] used a predictive (directionally specific arrow) or uninformative (directionally neutral hourglass) cue to make target locations either predictable or unpredictable, respectively. They found that saccades curved toward the distractor when target location was unpredictable and away from the distractor when target location was predictable. This finding revealed a qualitative difference between two patterns of eye movements that was determined solely by the presence of a predictive cue. This provides insights into the competing processes between target selection and distractor suppression. Presumably, when target location was predictable, the distractor location was suppressed and did not capture attention. In contrast, when target location was unpredictable, the target and distractor competed to capture attentional resources.

The Frontal Eye Field

The neural substrates of these behaviors are less clear. Many studies have shown that FEF and PPC are critical for visual attention and eye movements [e.g., Chambers and Heinen, 2010; Chambers et al., 2004; Juan et al., 2004, 2008; Morris et al., 2007; Muggleton et al., 2003; Prime et al., 2008, 2009; Rushworth and Taylor, 2006; Schenkluhn et al., 2008; Taylor et al., 2007]. Recently, Walker and colleagues [2009] used TMS to probe the causal relationship between FEF and saccade curvature. The authors applied single-pulse TMS during a left- or rightward saccade and found that TMS to the right FEF increased saccadic curvature away from the distractor location. This finding is similar to those of McPeek et al. [2006], who suggested that higher FEF activity on distractor would lead to saccades curving towards the distractor, and vice versa. Walker and colleagues provided convincing evidence showing that TMS interference with FEF indeed led to greater away curvatures. These studies suggested a role of FEF in the representation of salience.

The Posterior Parietal Cortex

In addition to the mounting evidence that points to FEF involvement as an important factor in saccade curvatures, it is likely that these curvatures are determined by multiple brain regions [Ellison et al., 2007]. Specifically, the posterior parietal cortex (PPC) is likely to play an important role in saccade curvatures due to its functions in visuomotor control [Ellison and Cowey, 2006; Morris et al., 2007; Nobre et al., 1997], updating spatial mapping [Andersen et al., 1985; Merriam et al., 2003; Morris et al., 2007], and shifting spatial attention [Ashbridge et al., 1997; Chambers et al., 2004; Constantinidis and Steinmetz, 2005; Ellison et al., 2003; Heilman and Van Den Abell, 1980; Mesulam, 1981; Mevorach et al., 2006; Rushworth and Taylor, 2006; Schenkluhn et al., 2008; Tseng et al., 2010]. Konen and Kleiser [2004] also pointed out that target predictability and unpredictability can effectively modulate rPPC activation, which led them to hypothesize that rPPC is critically involved in the switching of spatial attention [Heilman and Van Den Abell, 1980; Mesulam, 1981]. Recently, a TMS study by Hodsoll and colleagues [2009] tested rPPC's role in attentional capture tasks [Ellison et al., 2003; Ellison and Cowey, 2007] and found that disrupted rPPC activity lessened the magnitude of attentional capture.

The Current Study

The present study sought to investigate the role of rPPC in terms of distractor-modulation. It has been shown that neural activity in monkey LIP (the area homologous to human PPC) can represent predictive information such as the weighted likelihood of certain shape-combinations that can lead to reward [Yang and Shadlen, 2007]. Therefore, given PPC's crucial role in processing predictive information and in attentional capture, it is plausible to assume that it is also critically involved in processing meaningful information that is predictive of future events. According to Hodsoll et al. [2009], when rPPC activation is low or disrupted, attentional capture decreases. Since attentional capture is the main source of distractor effects, if we combine this with the Walker et al. [2006] findings on curvature, it can be predicted that interference with rPPC activity should decrease the salience of a distractor, thereby pushing saccade curvature further away from the distractor [as predicted by Walker et al., 2006; c.f., McSorley et al., 2009]. In other words, decreased rPPC activity should restrict attention mostly to the target by preventing attentional capture from the distractor, thereby pushing curvatures further away from the distractor. To test this hypothesis, we employed theta burst TMS (theta TMS) over rPPC and used the same paradigm as Walker et al. [2006]. If rPPC is critical in allocating attention to distractors, then rPPC TMS should have an impact in two ways. First, in the unpredictable condition, it should drive saccade curvature further from the distractor location so that the overall pattern mimics that of the predictable condition. Second, it should improve accuracy in the unpredictable condition by decreasing the salience of the distractors. Conversely, saccade curvatures and performance should not deviate as much in the predictable condition as the distractors in this condition are already largely ignored.

METHODS

Participants

The experiment used a within-subject design. Eleven participants (four male and seven female; 20–26 years old; mean age = 21.6) took part in the experiment across three conditions (rPPC TMS, M1 TMS, no TMS). All participants were randomly chosen from a pool of undergraduate students from the National Central University. All had normal or corrected to normal vision and gave informed consent form prior to the experiment. Participants received monetary reward upon the completion of the experiment. The experiments were approved by Institutional Review Board of the Chang-Gung Memorial Hospital, Taoyuan, Taiwan.

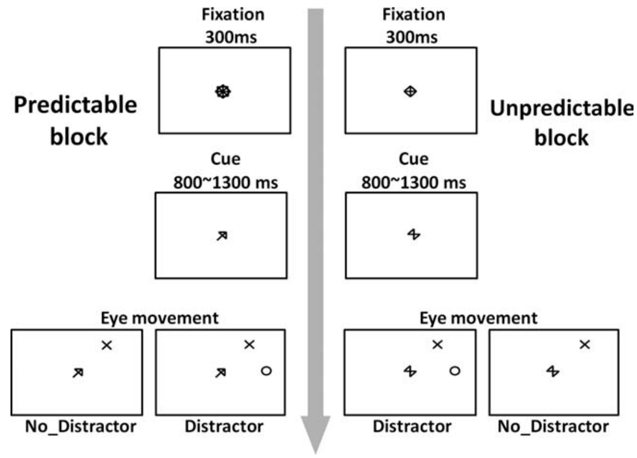

Figure 1.
Experimental paradigm. The experiment consisted of two blocks, where block 1 provided a neutral cue (hourglass; unpredictable) to target location (the "X") and block 2 provided a directionally specific cue (arrow; predictable) to the upcoming target location.

Apparatus and Stimuli

Stimuli were presented on a 19-inch CRT monitor with resolution of 1024 * 768 pixels and vertical refresh rate of 100 Hz. Participants sat 85 cm in front of the monitor, which was positioned at eye level. The position of the left eye was recorded using an EyeLink II tracker (SR Research, Mississauga, Ontario, Canada) with a 500 Hz sampling rate. A 9-point calibration was carried out in every participant prior to the formal collection of data. Saccades were defined by a significant elevation in eye movement velocity ($>30^\circ/s$) and acceleration ($>8000^\circ/s^2$). The direction of saccades and saccadic curvature were recorded throughout the experiment.

The stimuli used in the experiment are illustrated in Figure 1. There were four possible positions for targets and distractors [c.f., 8 positions in Walker et al., 2006]. Target positions were 10° away from the fixation, and were arranged circularly with 45° between locations. The target (a cross), distractor (unfilled circle), and the fixation (diamond) were all 1° in size. Target positions were constrained to four locations on the diagonal (oblique) axes because the oblique saccade trajectory is greater than that for horizontal and vertical saccades [Viviani and Swensson, 1982]. In addition, Walker et al. [2006] also observed that oblique saccades showed greater saccade trajectories in predictable and unpredictable conditions. When a distractor was present, it appeared either in the clockwise or counterclockwise immediately adjacent to the target location.

Experiment Design and Procedure

The entire experiment consisted of three conditions: rPPC TMS, no TMS, and M1 TMS. All conditions were within-subject, and were run on three different days. The materials, stimuli, and procedures were identical across all conditions. Thus, the only difference between these three conditions was the TMS site. The orders of the rPPC TMS and no TMS conditions were counterbalanced between every participant. The M1 TMS condition was added as another control to ensure the specific TMS effects over the PPC, and was always run after the other two conditions.

Within each condition (rPPC TMS, no TMS, and M1 TMS), there were two blocks of trials: one block for the predictive condition and one for the non-predictive condition. The sequence of these blocks was counterbalanced across subjects. In the rPPC and M1 TMS conditions, theta burst TMS was applied at the beginning of both blocks. Participants then rested for 5 min [Hubl et al., 2008] before participating in the formal experiment. The two blocks were also separated by 1 h of rest for the participants. Each block lasted ~13 min. This ensured that the experiment length did not exceed the duration of the theta burst TMS effect [Huang et al., 2005].

Each block began with 40 practice trials, followed by 120 formal trials. The 120 formal trials consisted of 40 no-distractor trials and 80 distractor trials. The saccade curvatures from the no-distractor trials served as baseline for determining whether the curvatures from the distractor trials were "toward" or "away" curvatures. In other word, a distractor-induced curvature that traces between the baseline curvature and the distractor location would be categorized as a "toward" curvature because it curved towards the distractor more in comparison to when the distractor was absent. The reverse is true for "away" curvatures. This subtraction method was adopted from Walker et al.'s original study [2006].

Each trial started with a fixation (a diamond in block 1 and a complex diamond in block 2) for 300 ms, followed either by a directionless cue (hourglass, Condition 1), or a directional cue (arrow, Condition 2). The directional cue was 100% valid [Walker et al., 2006]. After a random delay ranging from 800 to 1300 ms, the target and distractor appeared simultaneously while the cue was still present. Participants were instructed to fixate at the center fixation until target onset and make a saccade to the target within 1 s.

TMS Parameters

In all TMS conditions (rPPC TMS and M1 TMS), we applied theta TMS before the formal experiment. It has been shown that theta TMS can suppress motor evoked potentials in the primary motor cortex for more than 20 min [Huang et al., 2005]. Theta TMS can also selectively excite or inhibit neural activities of different brain regions [Silvanto et al., 2007], making it a suitable method for studying higher cognitive functions [e.g., Nyffeler et al., 2006; Silvanto et al., 2007]. We used a Magstim Super-Rapid Stimulator and a figure-of-8 coil to deliver rPPC TMS. The site of theta TMS stimulation was point P4 10-20 on the electroencephalograph coordinate [Mevorach et al., 2006]. The stimulation site was also confirmed with subjects' structure MRI with the Brainsight system (Rogue Research, Montreal, Canada). Our participants wore goggles with a tracker attached, enabling them to be co-registered with their structural image using a mounted Polaris infrared tracking system (Northern Digital, Waterloo, Canada), subsequently allowing the skull point overlying the stimulated region to be identified. The site was in the vicinity of rPPC areas used for the investigation of the functional role of PPC in visual search tasks [e.g., Ashbridge et al., 1997; Beck et al., 2006; Ellison et al., 2003, 2007; Kalla et al., 2008; Tseng et al., 2010], which corresponds to point P4 (right parietal) on the 10-20 electroencephalography coordinate system. This was also the method used to localize rPPC in Hodsoll et al.'s study, thus making the present paradigm more consistent with their methods [Hodsoll et al., 2009; Mevorach et al., 2006]. Although this method may be less precise than individual site localization using fMRI [see Sack et al., 2009 for a comparison of localization methods], it nevertheless facilitates comparison with previous findings while also being considerably less time consuming and resource intensive. Participants received 3 pulses of stimulation given at 50 Hz repeated starting every 200 ms for 20 s at 40% of maximum output (40% of the maximum output of 2 Tesla) [Huang et al., 2005], which was well below each individual participants' motor threshold (the lowest of which was 53%). A fixed stimulation level was used because it has proven successful and replicable in many studies and over a wide range of tasks [e.g., Ashbridge et al., 1997; Chen et al., 2009; Ellison and Cowey, 2007; Hung et al., 2005; Kalla et al., 2008; Muggleton et al., 2003; Muggleton et al., 2010a,b; Rushworth et al., 2002] and because motor cortex excitability does not provide a good guide to TMS thresholds in other cortical areas [Stewart et al., 2001].

Data Analysis

Saccade latency was defined as the interval between target onset and the initiation of a saccadic eye movement (in milliseconds). If saccadic latency was lower than 100 ms or higher than 800 ms, the trial was identified as an outlier and removed from analysis (no-TMS: 0.1%; rPPC TMS: 0.1%; M1 TMS: 0.1% trials excluded).

Saccade curvature was computed by taking the area under the curve that was formed by the saccade trajectory and dividing it by the distance between the saccadic starting and ending position [e.g., Ludwig and Gilchrist, 2002]. Trials with curvature more than two standard deviations away from the mean curvature were identified as outliers and removed from further analysis (no-TMS: 3%; rPPC TMS: 3%; M1 TMS: 3%). Since saccade trajectories are never straight, the curvatures from the no-distractor condition were used to serve as the baseline curvatures and were subtracted from the curvatures from trials with a distractor. Positive values indicated saccade trajectories toward the distractor, whereas negative values indicated saccade trajectories away from the distractor location.

Accurate saccades were defined as saccades that landed within a computer-defined square boundary ($4.6° \times 4.6°$) centered on the target. Saccades that landed outside the square were identified as error saccades (no-TMS: 8%; rPPC TMS: 14%; M1 TMS: 10%). These error saccades were further divided into three categories. The first two types were undershoot and overshoot errors where saccades failed to land within the pre-defined target square boundary. The last type of errors was distractor-induced error in which saccades first landed within a pre-defined triangular area toward the distractor before making a second saccade to the target. The triangular boundaries were defined by drawing an equilateral triangle (11.5° visual degrees on all three sides) that projected outwards from the fixation point (vertex) towards the distractor, covering an angle of 45°(in geometrical angle). This equilateral triangle was bisected by the distance (extending 10° visual degrees) between the fixation and the distractor so that the 45° opening was composed by one boundary that projected 22.5° to the left and one boundary 22.5° to the right in the vertically positioned distractor (or up and down for horizontally positioned distractors) from the fixation point. We used this equilateral triangle to define the distractor-induced errors because these error saccades, although induced by the distractors (as shown by their initial trajectories), did not always land in close proximity to the distractors. Thus, a square boundary around the distractor locations would not have been sensitive enough to capture these error saccades.

RESULTS

Saccade Latency

A three-way ANOVA was performed to investigate whether TMS, target predictability, and visual field had an effect on saccade latency in the distractor condition (see Fig. 2). There was a significant effect of TMS [$F(2,20) = 7.8$, $P < 0.05$], but no effect of visual field [$F(1,10) = 1.37$, $P > 0.05$] and predictability[$F(1,10) = 4.42$, $P > 0.05$], with no interaction between them [$ps > 0.05$]. For the effect of TMS, saccade latencies on average were longer in the rPPC TMS condition, regardless of target predictability and visual field. There was no significant difference between left and right visual field even under the predictability or TMS ($ps > 0.05$). Furthermore, in the no-distractor condition, we conducted a three-way ANOVA to investigate whether TMS and target predictability and visual field had an effect on saccade latency (see Fig. 2). There was a significant effect of TMS [$F(2,20) = 6.85$, $P < 0.05$] but no effect on visual field [$F(1,10) = 1.19$, $P > 0.05$] and no effect of predictability[$F(1,10) = 2.40$, $P > 0.05$], with no interaction between them ($P > 0.05$). The results revealed the rPPC TMS prolonged the saccade latency not only in the distractor condition but in the no-distractor condition as well. This prolonged latency by rPPC TMS has previously been observed in intentional [Muri et al., 1996] and reflexive saccades [Kapoula et al., 2001], and is likely due to PPC's function in motor planning [Sabes et al., 2000; Snyder et al., 1997; Morris et al., 2007]. This suggests that theta TMS causes a slower execution of motor planning despite target predictability.

Saccade Curvature

A three-way ANOVA was carried out to investigate whether rPPC TMS, target predictability, and visual field had an effect on curvature (see Fig. 3). There was a significant effect of TMS [$F(2,10) = 8.01$, $P < 0.05$] but no effect of visual field [$F(1,10) = 1.27$, $P > 0.05$] and predictability [$F(1,10) = 0.28$, $P > 0.05$], with an interaction between predictability and TMS [$F(1,10) = 7.04$, $P < 0.05$]. As illustrated in Figure 3, there was a significant effect of rPPC TMS when target location was unpredictable regardless of visual fields, but not when target location was predictable, but this effect was not observed in M1 TMS condition. Because no difference was found between the left and right visual field, we combined the visual fields for subsequent analyses.

In addition to the effect of TMS on saccade latency, we were also interested in the development of saccade curvature over time to examine its effects on target predictability. Therefore, we divided all saccades into five groups (bins) based on their latency [see also Mulckhuyse et al., 2009]. The latency range of each bin was customized for each individual so that each of the five bins contained approximately 20% of saccades for each participant. As shown in Figure 4, this categorization allowed us to investigate whether there was a curvature difference between saccades that initiated either early or late. We conducted a three-way ANOVA that incorporated TMS (three levels), target predictability (two levels), and bins (five levels) on saccade curvature. There was a significant main effect of all three variables: TMS [$F(2,20) = 3.76$, $P < 0.05$], target predictability [$F(1,10) = 8.68$, $P < 0.05$], and bins [$F(4,40) = 8.91$, $P < 0.05$]. Most importantly, we observed a

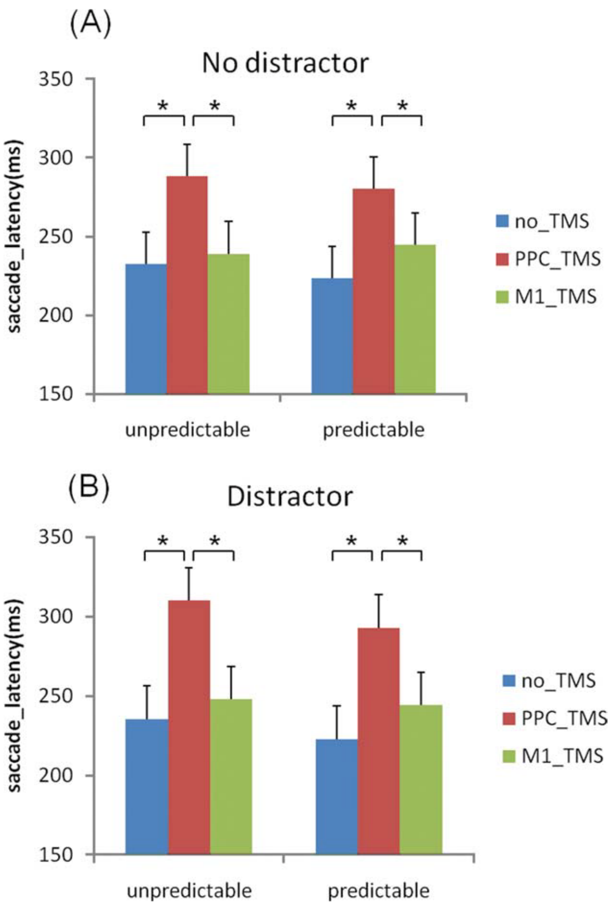

Figure 2.

Saccade latency differences. The *Y* axis shows saccade latency in ms. Overall, rPPC TMS delayed saccade latency regardless of target predictability and visual field and distractor condition. This is consistent with rPPC's role in motor and spatial attention. Error bars denote a 95% confidence interval. *Indicates significant post hoc *P* values less than 0.05.

significant interaction between TMS and target predictability [$F(2,10) = 6.66$, $P < 0.05$].

Interestingly, theta rPPC TMS pushed saccade curvatures further away from the distractor only when target location was unpredictable (see Fig. 4a). It had no influence on saccade curvature when target location was predictable. It is important to note that TMS prolonged saccade latency in the predictable condition without affecting saccade curvature (see Fig. 4b). In other words, the association between a prolonged saccade latency and increased degrees of curvature can be lessened by rPPC TMS.

To investigate the different amount of curvatures that are induced by TMS and target predictability, we illustrated the saccade traces from these experimental conditions (see Fig. 5). As shown in Figure 5, there was no difference between rPPC TMS, no-TMS and M1 TMS saccade traces in the predictable condition. However, when target location was unpredictable, rPPC TMS made the saccade trace further away from the distractor than no-TMS condition and M1 TMS condition, suggesting increased inhibition of the distractor.

Saccade Accuracy

We used a two-way ANOVA to examine the effect of target predictability and TMS on accuracy. There was a main effect of TMS [$F(2,10) = 5.32$, $P < 0.05$] and predictability [$F(1,10) = 10.6$, $P < 0.05$; see Fig. 6a], with no interaction between them ($P > 0.05$). These results suggest that rPPC TMS indeed impaired motor attention regardless of target predictability (TMS effect).

To investigate the effect of TMS on the ability of distractors to capture attention [see Hodsoll et al., 2009] in this paradigm, we compared the number of distractor-induced error saccades across different conditions (see Fig. 6b). When target location was predictable, distractor-induced errors accounted for 1% of overall errors in the no-TMS condition, 4% in the M1 TMS condition and 5% in the PPC TMS condition (the remaining errors were due to saccade overshoot/undershoot: 99%, 96%, and 95% in the no-TMS, M1 TMS and PPC TMS block, respectively). This difference was not significant in a separate t-test [no TMS: 1%; M1 TMS: 4%; PPC TMS: 5%; $t(10) = -1.11$, $P > 0.05$]. Interestingly, when target location was unpredictable, rPPC TMS reduced the number of distractor-induced errors from 50% (no TMS) to 28% (rPPC TMS) and 38%

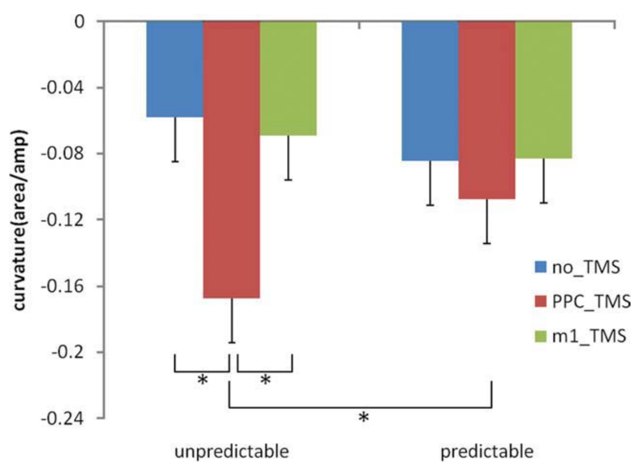

Figure 3.

Saccade curvatures. The *Y* axis shows saccade curvatures where positive and negative values indicate curvature towards and away from the distractors, respectively. rPPC TMS significantly increased the magnitude of away curvatures in the unpredictable condition regardless of visual field. This implies increased suppression on distractor locations. Error bars denote a 95% confidence interval. *Indicates significant post hoc *P* values less than 0.05.

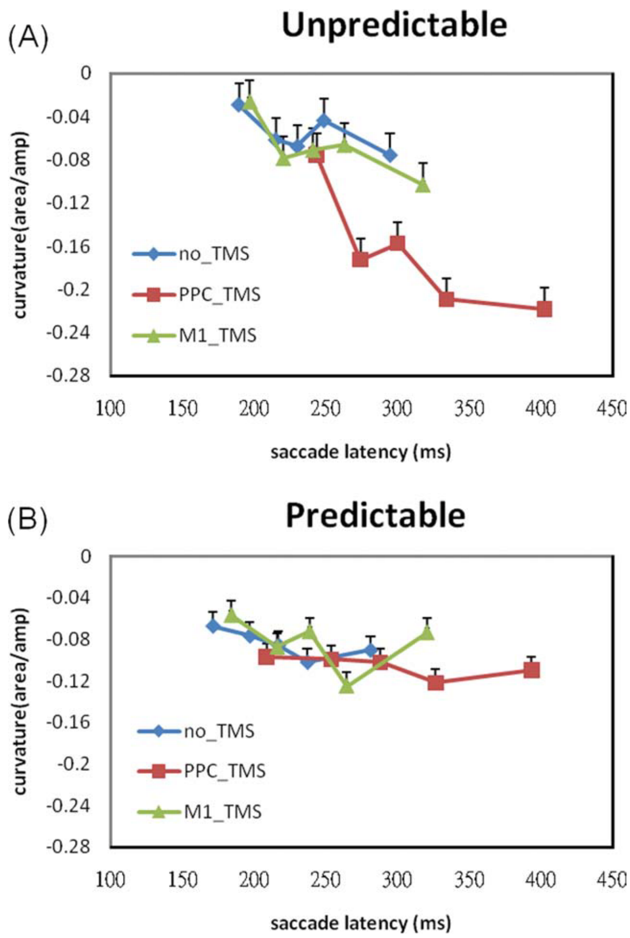

Figure 4.

Saccade latency and curvature in five bins. Latency is plotted in ms on the *X* axis. The *Y* axis plots saccade curvatures where positive and negative values indicate curvatures toward and away from the distractors, respectively. In the unpredictable block, rPPC TMS made saccade initiation slower (shifting rightward) and saccade curvature further away (curving downward). In the predictable condition, rPPC TMS made saccade initiation slower (shifting rightward) and but did not change the saccade curvature. Error bars denote a 95% confidence interval.

(M1 TMS) (the remaining errors were due to saccade overshoot/undershoot: 50% and 72% and 62% in the no-TMS, rPPC TMS and M1 TMS block, respectively). This decrease in distractor-induced errors was marginally significant in the rPPC TMS condition [no TMS: 50%; rPPC TMS: 28%; $t(10) = 2.16$, $P = 0.057$; see Fig. 6b] but not in the M1 TMS condition [$t(10) = 0.31$, $P > 0.05$;]. As shown in Figure 7, the error saccades were further categorized into three kinds of errors: distractor-induced error, overshoot and undershoot. There was no significant difference between rPPC TMS, no-TMS and M1 TMS under the overshoot [no TMS: 30%; rPPC TMS: 35%; M1 TMS: 25%] and undershoot [no TMS: 20%; rPPC TMS: 37%; M1 TMS: 37%] [$ps > 0.05$] categories. However, the reduction in distractor-induced errors was marginally significant [no TMS: 50%; rPPC TMS: 28%; $P = 0.057$]. Thus, the critical finding here is that rPPC TMS did not reduce the number of overall errors (due to a disruptive effect of TMS on motor planning), but did reduce the number of distractor-induced errors (see Fig. 7). This finding supports Hodsoll et al.'s [2009] attentional capture account, which we discuss in detail below.

DISCUSSION

The aim of the present study was to investigate the role of rPPC in evaluating predictive or non-predictive

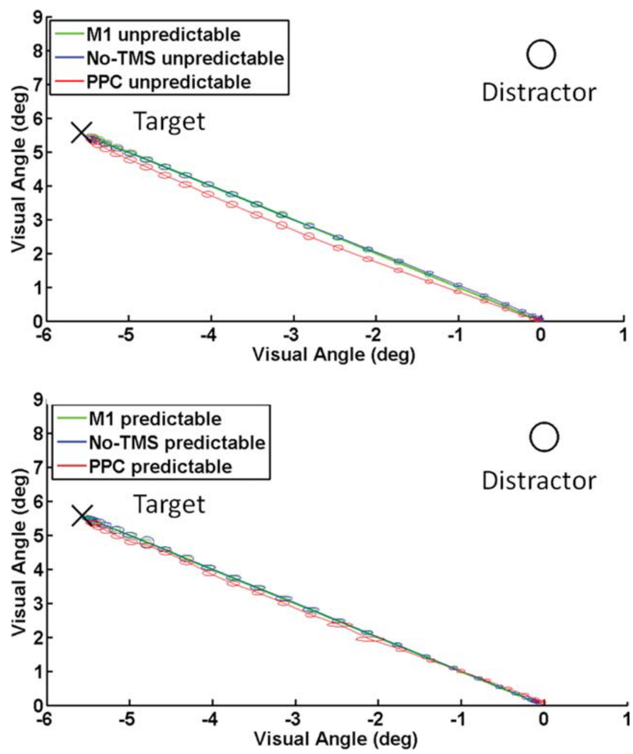

Figure 5.

Saccade traces in the predictable and unpredictable condition. The blue lines represent averaged trace from the no-TMS condition and the green lines came from the M1 TMS condition and the red lines from the PPC TMS condition. Each line is composed of 26 points. The ellipse on each line is the each point 95% confidence interval (the ellipses denote the horizontal and vertical 95% confidence interval). The theta TMS pushed saccade curvature further away from the distractor in the unpredictable condition than in the predictable condition. This increase of magnitude in the away curvatures can only be explained by target unpredictability, as its effect is above and beyond the disruptive effect of TMS in motor planning (wider gap between the three traces in the unpredictable condition than in the predictable condition).

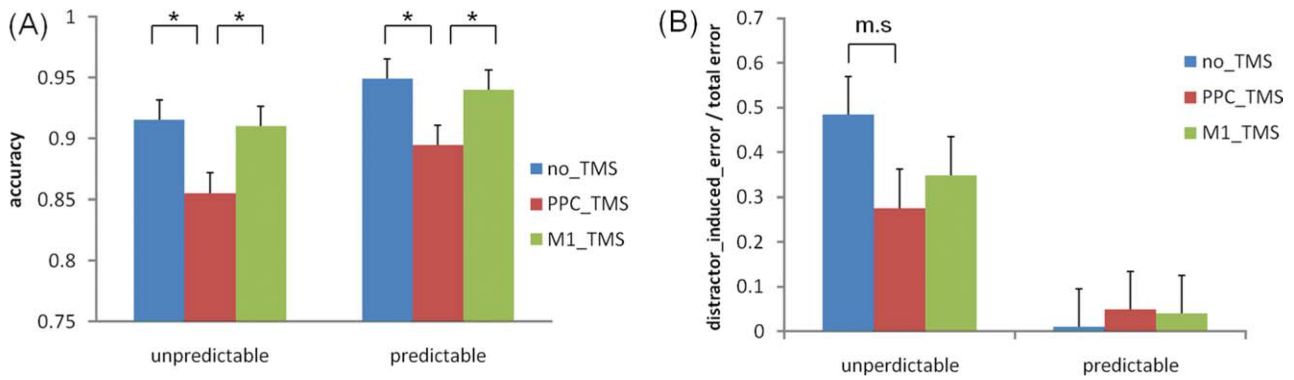

Figure 6.

Overall saccade accuracy and the break-down of saccade errors. As expected, saccades accuracy was always higher in the predictable condition than the unpredictable condition. rPPC TMS increased saccade errors in both the predictable and unpredictable condition. Specifically, rPPC TMS produced more errors in the unpredictable condition than the predictable condition (a). But when we break down these errors, rPPC TMS actually decreased the amount of errors that were caused by the distractors (b). We think these two effects can be explained by rPPC's function in spatial attention (more errors) and attentional capture (less distractor-induced errors). Error bars are 95% confidence interval. *Indicates significant post hoc *P* values less than 0.05.[m.s.] denotes marginal significant ($p = 0.057$).

information when one intends to make an eye movement. We applied the paradigm of Walker et al. [2006], in which target location predictability was manipulated with an endogenous central cue, and coupled it with theta burst TMS delivered to rPPC to elucidate the role of this area in predictable and unpredictable situations. Saccade curvature was used as an index of the effect of predictability and disrupted rPPC activity [Walker et al., 2006]. The critical

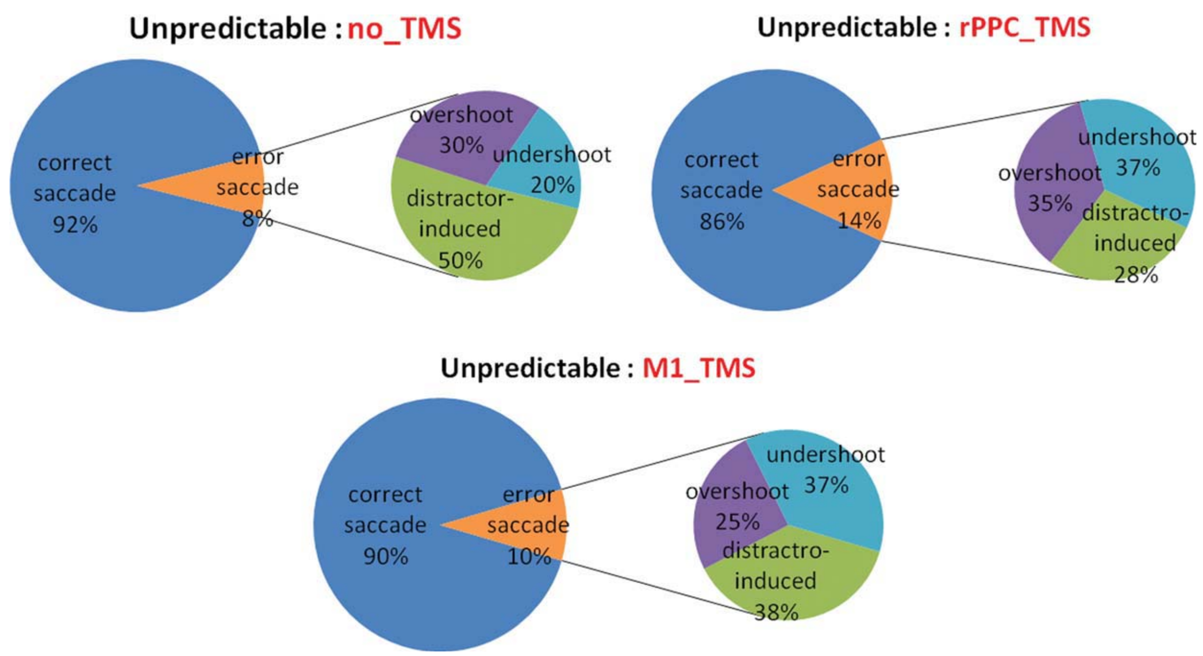

Figure 7.

Error saccade distribution in the no-TMS, rPPC TMS, and M1 TMS conditions from the unpredictable block. These error saccades were further divided into three categories: undershoot, overshoot, and distractor-induced error. Specifically, rPPC TMS decreased the number of distractor-induced errors.

finding was the dissociation between saccade latency and saccade curvature when we introduced the variable of target predictability. In terms of saccade latency, when theta TMS was applied to rPPC, saccade latencies were elevated but this effect did not differ between the predictable and the unpredictable conditions. On the other hand, when considering the curvature data, theta rPPC TMS increased the magnitude of away curvature only in the unpredictable condition and not in the predictable condition. Since recent studies have suggested that saccades with long latencies usually tend to curve further away from the distractor [McSorley et al., 2009; Mulckhuyse et al., 2009], one would predict this latency and curvature contingency should be manifested in our curvature results. Thus, we observed a dissociation of the saccade latency and saccade curvature relationship that was caused by specific TMS effects that were dependant on target location predictability.

Our findings here are in line with the many known functions of rPPC in visual attention, namely visuomotor control [Ellison and Cowey, 2006; Ellison et al., 2003, 2007; Morris et al., 2007; Nobre et al., 1997; Prime et al., 2008], updating spatial mapping [Andersen et al., 1985; Merriam et al., 2003; Morris et al., 2007], and shifting spatial attention [Ashbridge et al., 1997; Chambers et al., 2004; Constantinidis and Steinmetz, 2005; Ellison et al., 2003; Heilman and Van Den Abell, 1980; Mesulam, 1981; Mevorach et al., 2006; Rushworth and Taylor, 2006; Rushworth et al., 2001; Schenkluhn et al., 2008; Tseng et al., 2010]. Specifically, a recent TMS study by Hodsoll and colleagues [2009] tested the role of rPPC in attentional capture tasks [Ellison et al., 2003; Ellison and Cowey, 2007] and found that disrupted rPPC activity lessened the magnitude of attentional capture. Their findings suggest that rPPC is critically involved in the reflexive orienting of attention to salient stimuli. Therefore, when TMS disrupted rPPC activity, participants could better focus on the target, possibly due to decreased salience of the distractor. This implies that increased suppression of distractors can be induced by interference with rPPC activity, which should directly impact saccade curvature. Chambers and colleagues [2004] have suggested two critical times periods (fast: 90–120 ms; slow: 210–240 ms) for parietal involvement in automatic shifts of attention to salient stimuli, both of which are well within the saccade latencies reported here. Consequently, rPPC TMS can reduce the amount and magnitude of attentional capture by decreasing the salience of singleton distractors. Together, these findings are consistent with what we report here: theta TMS over rPPC led to increased curvature away from the distractor when target location was unpredictable, presumably because of the increased suppression and decreased salience of the distractor.

In our experiment, the key underlying difference between the predictable and unpredictable condition was the competition between the target and distractor for attention. In the predictable condition, there was no significant TMS effect on saccade curvature because the cue had directed attentional allocation to the probable location much earlier. Thus, target-distractor competition had long been resolved by the time of target onset. In contrast, when target location was unpredictable, target and distractor were competing to capture attention. Since TMS interfered with rPPC involvement in attentional capture, the effect of the distractor was lessened. This led to an increased suppression of the distractor, which was reflected in the increased curvature away from it even more so than when target location was predictable.

Saccade Accuracy and Latency

Although saccade curvature was the measure of primary interest, our saccade accuracy and latency data are also of importance as they validate the effect of theta TMS. In accuracy data we observed a dissociation between the numbers of motor and distractor-induced errors in accuracy data: rPPC TMS increased the overall error rate from 8% to 14% (including overshoot and undershoot) but decreased the proportion of distractor-induced errors from 50% to 28% (see Fig. 7). This is an important dissociation because rPPC is critically involved in motor planning [Nobre et al., 1997] and spatial attention [Ashbridge et al., 1997]. Therefore, any effect that is based on the disruption of rPPC should always come at the cost of certain degrees of accuracy in spatial attention. Here, we observed an overall increase in error rate when theta TMS was applied to rPPC, which validates the disruptive effect of TMS on rPPC. But most importantly, the simultaneous reduction in distractor-induced errors suggests a decreased distractor salience when target location was not cued, thus leading to fewer distractor-induced errors in comparison to the no-TMS condition. Therefore, it is possible that the effect of rPPC TMS lies in decreasing the "unpredictability" of the unpredictable condition, making it more similar to the predictable condition by decreasing the salience of the distractor.

In terms of latency, rPPC TMS prolonged saccade latency regardless of target predictability or the visual field of which the distractor appeared. In fact, the same TMS effect was also observed in the no-distractor condition. That is, TMS lengthened saccade latency regardless of target predictability (predictable and unpredictable) and visual fields (left and right) even when there was no distractor present. This non-specific disruptive effect of rPPC TMS had previously been observed in intentional [Muri et al., 1996] and reflexive saccades [Kapoula et al., 2001], which can be understood in terms of the role of the PPC in motor planning [Sabes et al., 2000; Snyder et al., 1997; Morris et al., 2007]. We think this general TMS effect also points to the predictability effects of saccade curvature being caused by something more than just motor preparation. That is, we observed a non-specific TMS effect on saccade latency, presumably due to rPPC involvement in motor preparation, and a predictability-specific TMS effect on saccade curvature that is likely an additive effect over and above general saccade planning and motor preparation. In summary, combining the overall increase in saccade latency and error rate (including overshoot and undershoot saccade) in the TMS condition, we conclude that theta TMS caused a slower and impaired execution of motor planning regardless of target predictability.

The Directions and the Degrees of Saccade Curvatures

One interesting discrepancy between our results and those from Walker et al. [2006] is the overall direction of saccade curvatures. Walker et al. [2006] observed curvatures toward the distractor when target location was cued and away from the distractor when target was not cued. In the present study, when no TMS was applied, we also observed a similar trend of increased magnitude of away curvature in the predicable condition than that in the unpredictable condition. However, we did not observe curvature toward the distractor in the unpredictable condition. There are two possible explanations. First, we only used four possible target positions in the interest of decreasing the number of trials for the TMS experiment, whereas Walker et al. used eight. This is because in our experiment the target and distractor locations were programed not to overlap spatially (distractors in the vertical and horizontal axes but the target in the oblique axis), whereas Walker et al.'s study did not impose this restriction on their stimuli locations. Thus our task was more "predictable" than Walker et al.'s version because our participants could focus on the oblique axis (target location) and ignore the horizontal and vertical axes (distractor location) even in the unpredictable condition. Therefore, if the level of unpredictability would have an impact on performance, the degree of unpredictability for our targets was less than that from Walker et al.'s setup. Second, our observed saccade latency was on average 40 ms longer than the latencies reported by Walker et al. This signifies that there could have been more top-down involvement in the present experiment, which led to an increase in curvature away from distractors [Van der Stigchel et al., 2007]. Indeed, studies have shown that longer saccade latency tends to correlate with away curvatures [McSorley et al., 2009; Mulckhuyse et al., 2009]. Specifically, a recent study by Walker and colleagues [McSorley et al., 2009] using a similar orienting paradigm also found that saccades within the latency range of 260–280 ms tend to curve away from the distractor, which is consistent with our findings. Together, these discrepancies should account for our observed "away" curvatures regardless of target predictability. One recent study has shown that the probability of a saccade location can effectively modulate saccade latency [Liu et al., 2010]. It remains to be tested whether the extent of predictability would not only affect the degrees of saccade curvatures but also the directions of them.

CONCLUSION

The present study suggests that in addition to rFEF, rPPC is also critically involved in the processes of determining saccade curvature. More specifically, when targets locations were unpredictable and attentional selection of target was required, rPPC TMS decreased distractor-induced errors and increased curvature away from the distractors. Our findings thus also suggest that rPPC may be critically involved in processing predictive and non-predictive information. Monkey neurophysiology has already shown that area LIP (equivalent to the vicinity of human PPC) can encode behaviorally relevant objects [Gottlieb et al., 1998] and even the color of a cue if it is associated with an eye movement [Toth and Assad, 2002]. Furthermore, target predictability can have a significant effect in modulating LIP activity [Konen et al., 2004]. Recently, Yang and Shadlen [2007] reported that neural activity in LIP can represent predictive information such as the weighted likelihood that certain shape-combinations can lead to reward. Therefore, PPC is not only crucial to spatial attention, but may also be involved in processing meaningful information that is predictive of future events. The predictability effects may be highly related to the attentional effects observed in many studies [e.g., Geng and Behrmann, 2002, 2005; Liu et al., 2010; Summerfield and Egnar, 2009]. Together, these results suggest that rPPC is critical in processing probability-related behaviors, and our findings here demonstrate this effect in terms of modulation of saccade curvature.

REFERENCES

Andersen RA, Essick GK, Siegel RM (1985): Encoding of spatial location by posterior parietal neurons. Science 230:456–458.

Ashbridge E, Walsh V, Cowey A (1997): Temporal aspects of visual search studied by transcranial magnetic stimulation. Neuropsychologia 35:1121–1131.

Beck DM, Muggleton N, Walsh V, Lavie N (2006): Right parietal cortex plays a critical role in change blindness. Cereb Cortex 16:712–717.

Brockmole JR, Castelhano MS, Henderson JM (2006): Contextual cueing in naturalistic scenes: Global and local contexts. J Exp Psychol Learn Mem Cogn 32:699–706.

Chambers CD, Payne JM, Stokes MG, Mattingley JB (2004): Fast and slow parietal pathways mediate spatial attention. Nat Neurosci. doi: 10.1038/nn2303.

Chambers CD, Heinen K (2010): TMS and the functional neuroanatomy of attention. Cortex 46:114–117.

Chen CY, Muggleton NG, Tzeng OJ, Hung DL, Juan CH (2009): Control of prepotent responses by the superior medial frontal cortex. Neuroimage 44:537–545.

Chun MM, Jiang Y (1998): Contextual cueing: Implicit learning and memory of visual context guides spatial attention. Cogn Psychol 36:28–71.

Constantinidis C, Steinmetz MA (2005): Posterior parietal cortex automatically encodes the location of salient stimuli. J Neurosci 25:233–238.

Davenport JL, Potter MC (2004): Scene consistency in object and background perception. Psychol Sci 15:559–564.

Doyle M, Walker R (2001): Curved saccade trajectories: Voluntary and reflexive saccades curve away from irrelevant distractors. Exp Brain Res 139:333–344.

Ellison A, Rushworth M, Walsh V (2003): The parietal cortex in visual search: A visuomotor hypothesis. Suppl Clin Neurophysiol 56:321–330.

Ellison A, Cowey A (2006): TMS can reveal contrasting functions of the dorsal and ventral visual processing streams. Exp Brain Res 175:618–625.

Ellison A, Cowey A (2007): Time course of the involvement of the ventral and dorsal visual processing streams in a visuospatial task. Neuropsychologia 45:3335–3339.

Ellison A, Lane AR, Schenk T (2007): The interaction of brain regions during visual search processing as revealed by transcranial magnetic stimulation. Cereb Cortex 17:2579–2584.

Geng JJ, Behrmann M (2002): Probability cuing of target location facilitates visual search implicitly in normal participants and patients with hemispatial neglect. Psychol Sci 13:520–525.

Geng JJ, Behrmann M (2005): Spatial probability as an attentional cue in visual search. Percept Psychophys 67:1252–1268.

Gottlieb JP, Kusunoki M, Goldberg ME (1998): The representation of visual salience in monkey parietal cortex. Nature 391:481–484.

Heilman KM, Van Den Abell T (1980): Right hemisphere dominance for attention: The mechanism underlying hemispheric asymmetries of inattention (neglect). Neurology 30:327–330.

Hodsoll J, Mevorach C, Humphreys GW (2009): Driven to less distraction: rTMS of the right parietal cortex reduces attentional capture in visual search. Cereb Cortex 19:106–114.

Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC (2005): Theta burst stimulation of the human motor cortex. Neuron 45:201–206.

Hung J, Driver J, Walsh V (2005): Visual selection and posterior parietal cortex: Effects of repetitive transcranial magnetic stimulation on partial report analyzed by Bundesen's theory of visual attention. J Neurosci 19:9602–9612.

Hubl D, Nyffeler T, Wurtz P, Chaves S, Pflugshaupt T, Luthi M, von Wartburg R, Wiest R, Dierks T, Strik WK, Hess CW, Muri RM (2008): Time course of blood oxygenation level-dependent signal response after theta burst transcranial magnetic stimulation of the frontal eye field. Neuroscience 151:921–928.

Juan CH, Shorter-Jacobi SM, Schall JD (2004): Dissociation of spatial attention and saccade preparation. Proc Natl Acad Sci USA 101:15541–15544.

Juan CH, Muggleton NG, Tzeng OJ, Hung DL, Cowey A, Walsh V (2008): Segregation of visual selection and saccades in human frontal eye fields. Cereb Cortex 18:2410–2415.

Kalla R, Muggleton NG, Juan CH, Cowey A, Walsh V (2008): The timing of the involvement of the frontal eye fields and posterior parietal cortex in visual search. Neuroreport 19:1067–1071.

Kapoula Z, Isotalo E, Muri RM, Bucci M-P, Rivaud-Pechoux S (2001): Effects of transcranial magnetic stimulation of the posterior parietal cortex on saccades and vergence. Neuroreport 12:4041–4046.

Konen CS, Kleiser R, Wittsack HJ, Bremmer F, Seitz RJ (2004): The encoding of saccadic eye movements within human posterior parietal cortex. Neuroimage 22:304–314.

Liu CL, Chiau HY, Tseng P, Hung DL, Tzeng OJL, Muggleton NG, Juan CH (2010): The antisaccade cost is modulated by contextual experience of location probability. J Neurophysiol 103:1438–1447.

Ludwig CJ, Gilchrist ID (2002): Measuring saccade curvature: A curve-fitting approach. Behav Res Methods Instrum Comput 34:618–624.

McPeek RM, Han JH, Keller EL (2003): Competition between saccade goals in the superior colliculus produces saccade curvature. J Neurophysiol 89:2577–2590.

McPeek RM (2006): Incomplete suppression of distractor-related activity in the frontal eye field results in curved saccades. J Neurophysiol 96:2699–2711.

McSorley E, Haggard P, Walker R (2004): Distractor modulation of saccade trajectories: Spatial separation and symmetry effects. Exp Brain Res 155:320–333.

McSorley E, Haggard P, Walker R (2009): The spatial and temporal shape of oculomotor inhibition. Vision Res 49:608–614.

Merriam EP, Genovese CR, Colby CL (2003): Spatial updating in human parietal cortex. Neuron 39:361–373.

Mesulam MM (1981): A cortical network for directed attention and unilateral neglect. Ann Neurol 10:309–325.

Mevorach C, Humphreys GW, Shalev L (2006): Opposite biases in salience-based selection for the left and right posterior parietal cortex. Nat Neurosci 9:740–742.

Morris AP, Chambers CD, Mattingley JB (2007): Parietal stimulation destabilizes spatial updating across saccadic eye movements. Proc Natl Acad Sci USA 104:9069–9074.

Muggleton NG, Juan CH, Cowey A, Walsh V (2003): Human frontal eye fields and visual search. J Neurophysiol 89:3340–3343.

Muggleton NG, Chen CY, Tzeng OJ, Hung DL, Juan CH (2010a): Inhibitory control and the frontal eye fields. J Cogn Neurosci 22:2804–2812.

Muggleton NG, Juan CH, Cowey A, Walsh V, O'Breathnach U (2010b) Human frontal eye fields and target switching. Cortex 46:178–184.

Mulckhuyse M, Van der Stigchel S, Theeuwes J (2009): Early and late modulation of saccade deviations by target distractor similarity. J Neurophysiol 102:1451–1458.

Muri RM, Vermersch AI, Rivaud S, Gaymard B, Pierrot-Deseilligny C (1996): Effects of single-pulse transcranial magnetic stimulation over the prefrontal and posterior parietal cortices during memory-guided saccades in humans. J Neurophysiol 76:2102–2106.

Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD (1997): Functional localization of the system for visuospatial attention using positron emission tomography. Brain 120:515–533.

Nyffeler T, Wurtz P, Lüscher HR, Hess CW, Senn W, Pflugshaupt T, von Wartburg R, Lüthi M, Müri RM (2006): Repetitive TMS over the human oculomotor cortex: Comparison of 1-Hz and theta burst stimulation. Neurosci Lett 409:57–60.

Peterson MS, Kramer AF (2001): Attentional guidance of the eyes by contextual information and abrupt onsets. Percept Psychophys 63:1239–1249.

Prime SL, Vesia M, Crawford JD (2008): Transcranial magnetic stimulation over posterior parietal cortex disrupts transsaccadic memory of multiple objects. J Neurosci 28:6938–6949.

Prime SL, Vesia M, Crawford JD (2009): TMS over human frontal eye fields disrupts trans-saccadic memory of multiple objects. Cereb Cortex. doi: 10.1093/cercor/bhp148.

Rushworth MF, Ellison A, Walsh V (2001): Complementary localization and lateralization of orienting and motor attention. Nat Neurosci 4:656–661.

Rushworth MF, Taylor PC (2006): TMS in the parietal cortex: Updating representations for attention and action. Neuropsychologia 44:2700–2716.

Sabes PN (2000): The planning and control of reaching movements. Curr Opin Neurobiol 10:740–746.
Sack AT, Cohen Kadosh R, Schuhmann T, Moerel M, Walsh V, Goebel R (2009): Optimizing functional accuracy of TMS in cognitive studies: A comparison of methods. J Cogn Neurosci 21:207–221.
Schenkluhn B, Ruff CC, Heinen K, Chambers CD (2008): Parietal stimulation decouples spatial and feature-based attention. J Neurosci 28:11106–11110.
Sheliga BM, Riggio L, Rizzolatti G (1994): Orienting of attention and eye movements. Exp Brain Res 98:507–522.
Silvanto J, Muggleton NG, Cowey A, Walsh V (2007): Neural activation state determines behavioral susceptibility to modified theta burst transcranial magnetic stimulation. Eur J Neurosci 26:523–528.
Stewart LM, Walsh V, Rothwell JC (2001): Motor and phosphene thresholds: A transcranial magnetic stimulation correlation study. Neuropsychologia 39:415–419.
Summerfield C, Egner T (2009): Expectation (and attention) in visual cognition. Trends Cogn Sci 13:403–409.
Snyder LH, Batista AP, Andersen RA (1997): Coding of intention in the posterior parietal cortex. Nature 386:167–170.
Taylor PC, Nobre AC, Rushworth MF (2007): FEF TMS affects visual cortial activity. Cereb Cortex 17:391–399.
Tipper SP, Howard LA, Jackson SR (1997): Selective reaching to grasp:evidence for distractor interference effects. Vis Cogn 4:1–38.
Tipper SP, Howard LA, Paul MA (2001): Reaching affects saccade trajectories. Exp Brain Res 136:241–249.
Tseng P, Hsu TY, Muggleton NG, Tzeng OJL, Hung DL, Juan CH (2010): Posterior parietal cortex mediates encoding and maintenance processes in change blindness. Neuropsychologia 48:1063–1070.
Toth LJ, Assad JA (2002): Dynamic coding of behaviourally relevant stimuli in parietal cortex. Nature 415:165–168.
Van der Stigchel S, Meeter M, Theeuwes J (2006): Eye movement trajectories and what they tell us. Neurosci Biobehav Rev 30:666–679.
Van der Stigchel S, Meeter M, Theeuwes J (2007): Top-down influences make saccades deviate away: The case of endogenous cues. Acta Psychol 125:279–290.
Viviani P, Swensson RG (1982): Saccadic eye movements to peripherally discriminated visual targets. J Exp Psychol Hum Percept Perform 8:113–126.
Walker R, McSorley E, Haggard P (2006): The control of saccade trajectories: Direction of curvature depends on prior knowledge of target location and saccade latency. Percept Psychophys 68:129–138.
Walker R, Mcsorley E (2008): The influence of distractors on saccadetarget selection: Saccade trajectory effects. J Eye Movement Res 7:1–13.
Walker R, Techawachirakul P, Haggard P (2009): Frontal eye field stimulation modulates the balance of salience between target and distractors. Brain Res 1270:54–63.
Yang T, Shadlen MN (2007): Probabilistic reasoning by neurons. Nature 447:1075–1080.