Hemispheric Asymmetry in the Remapping and Maintenance of Visual Saliency Maps: A TMS Study

Martijn Gerbrand van Koningsbruggen[1], Shai Gabay[2], Ayelet Sapir[1], Avishai Henik[2], and Robert D. Rafal[1]

Abstract

■ Parietal cortex has been implicated in the updating, after eye movements, of a salience map that is required for coherent visual experience and for the control of visually guided behavior. The current experiment investigated whether TMS over anterior intraparietal cortex (AIPCx), just after a saccade, would affect the ability to update and maintain a salience map. In order to generate a salience map, we employed a paradigm in which an uninformative cue was presented at one object in a display to generate inhibition of return (IOR)—an inhibitory tag that renders the cued object less salient than others in the display, and that slows subsequent responses to visual transients at its location. Following the cue, participants made a saccade to either left or right, and we then probed for updating of the location of IOR by measuring manual reaction time to targets appearing at cued location of the cued compared to an uncued object. Between the time of saccade initiation and target appearance, dual-pulse TMS was targeted over right (Experiment 1) or left AIPCx (Experiment 2), and a vertex control side. Updating of the location of IOR was eliminated by TMS over right, but not the left, AIPCx, suggesting that right parietal cortex is involved in the remapping of IOR. Remapping was eliminated by right AIPCx, regardless of whether the saccade was made to the left (contralateral), or right (ipsilateral) visual field, and regardless of which field the target appeared in. We conclude that right AIPCx is the neural substrate for maintaining a salience map across saccades, and not simply for propagating an efference copy of saccade commands. ■

INTRODUCTION

Although the retinal input changes dramatically with every eye movement, our visual experience is coherent. This consistency is hypothesized to be achieved by a remapping mechanism that uses corollary discharge as an "extra-retinal signal" to compensate for each saccade (Sommer & Wurtz, 2008). This remapping mechanism integrates information across successive fixations into a spatial consistent percept. The current experiments investigated the role of human parietal cortex in remapping visual saliency maps by applying TMS just after an eye movement.

Duhamel, Colby, and Goldberg (1992) reported the first neurophysiological evidence of neurons in monkey lateral intraparietal (LIP) cortex that remapped their receptive fields either before or after eye movements. During a task requiring continuous fixation, neurons in LIP only respond to visual stimuli presented within their retinotopic receptive field. However, in an experiment that involved eye movements, in which a stimulus was presented outside a neuron's receptive field, and in which the monkey was instructed to make a saccade which would bring the stimulus into the receptive field, a subset of the LIP neurons responded to stimuli at the location of the *future* receptive field before saccade initiation. Subsequent studies have reported neurons with similar properties in monkey superior colliculus (Walker, Fitzgibbon, & Goldberg, 1995), frontal eye field (FEF; Umeno & Goldberg, 1997, 2001), striate, and extrastriate cortex (Nakamura & Colby, 2002). More important to the current investigation, Duhamel, Colby, et al. (1992) and Duhamel, Goldberg, Fitzgibbon, Sirigu, and Grafman (1992) also observed LIP neurons that responded to "remembered" targets. When a briefly flashed stimulus was presented outside their receptive fields before a saccade, the neurons responded after the saccade brought this location into their receptive field, even though this location no longer contained the stimulus. Duhamel et al. concluded that visual memory has a retinotopic representation, which is updated after every saccade. More recently, it has been shown that LIP neurons do not simply remap visual stimuli but, more specifically, remap the saliency of the visual stimulus (Gottlieb, Kusunoki, & Goldberg, 1998).

There is converging evidence implicating human parietal cortex in saccade updating from neuropsychological, TMS, and fMRI investigations. Patients with lesions in parietal cortex are impaired when executing the second saccade of a double-step saccade task. In this task, two saccades are made to sequentially flashed targets, each of which disappears before the first eye movement. The first saccade can be made on the basis of retinotopic coordinates. However,

[1]Bangor University, UK, [2]Ben-Gurion University of the Negev, Beer-Sheva, Israel

an accurate second saccade requires updating of the location of the second target based on the motor vector of the first saccade. Failure to update the location faithfully results in inaccurate saccades to the second target or, if no extraretinal signal is generated at all, the second saccade either cannot be executed at all, or will be made to the *retinal* location of the target. In a task in which the two targets were presented in opposite visual fields, patients with both left and right parietal lesions were impaired in the second saccade when the first was directed contralesionally (Heide, Blankenburg, Zimmermann, & Kompf, 1995). Recent fMRI studies have confirmed and extended the involvement of parietal cortex in spatial updating (Medendorp, Goltz, & Vilis, 2005, 2006; Medendorp, Goltz, Vilis, & Crawford, 2003; Merriam, Genovese, & Colby, 2003).

Several TMS studies have investigated the role of parietal cortex in remapping. Because the current study uses TMS, these studies are discussed in more detail below. van Donkelaar and Muri (2002) found that right parietal TMS 150 msec, but not earlier, after the onset of the first saccade of a double-step paradigm impaired accuracy of the second saccade. Right TMS only impaired performance if the first saccade was to the left and the second saccade to the right. Morris, Chambers, and Mattingley (2007) used a more focal figure-of-eight coil and found that a posterior part of the intraparietal sulcus (IPS), close to the transverse occipital sulcus, and not a more anterior part, was involved in updating in a variant of the double-step paradigm. Other studies have found that TMS over parietal cortex also impairs the detection of displacement of visual targets that moved during a saccade (Chang & Ro, 2007) and transsaccadic memory of visual feature (Prime, Vesia, & Crawford, 2008).

In an experiment motivating the current research, Sapir, Hayes, Henik, Danziger, and Rafal (2004) demonstrated that human parietal cortex is also involved in updating visual saliency maps across eye movements. To generate a salience map, the experiment employed an paradigm in which an exogenous cue engendered an inhibitory tag at the location of the cue, resulting in slower responses to targets presented at the previously cued location (inhibition of return, IOR; Posner, Rafal, Choate, & Vaughn, 1985). IOR has been hypothesized to contribute to the elaboration of a salience map that can guide efficient visual exploration by favoring novel locations (Klein, 1988, 2000; Posner et al., 1985). Sapir et al. (2004) exploited the fact that the location of this inhibitory tag is updated after a saccade (Tipper, Grison, & Kessler, 2003; Danziger, Fendrich, & Rafal, 1997; Maylor & Hockey, 1985; Posner & Cohen, 1984).

In the IOR paradigm employed by Sapir et al. (2004), one of four boxes was briefly cued to generate an inhibitory tag and, after a saccade was made to a new location, a target requiring a manual detection response was presented at either the retinal location of the cue, the environmental location of the cue, or at corresponding uncued locations. They tested five patients with a unilateral lesion involving superior parietal cortex and healthy controls. Healthy control participants showed inhibitory tagging (IOR) at the remapped, environmental location of the cue, as well as a smaller inhibitory effect at the retinal location. The patients' results revealed no evidence of updating the location of the inhibitory tag, that is, IOR was observed only at the retinal location of the cue.

In contrast to the results of double-step saccade paradigms summarized above, the deficit in remapping was bilateral; that is, it occurred for targets in both the ipsilesional and contralesional visual field, and after both ipsilesional and contralesional saccades. Interestingly, abolished remapping of the inhibitory tag was found in the three patients with a right hemisphere lesion but not in the two left hemisphere patients. However, due to the small sample size, this was not statistically tested. Sapir et al. (2004) interpreted their results to indicate that parietal cortex was not simply the source of the corollary discharge that provides the extra-retinal signal for saccade remapping, but that it may also provide the neural substrate for maintaining a salience map across saccades.

The patients studied by Sapir et al. (2004) all had chronic lesions. It is not clear whether the effects reported in those patients reflect the normal function of parietal cortex, or are the consequence of brain reorganization. Moreover, Sapir et al. studied only two patients with left parietal lesions and three with right parietal lesions, and therefore, could not draw definitive conclusions about possible hemispheric asymmetries for maintaining salience maps. Here we employed dual-pulse TMS to transiently disrupt the function of parietal cortex, and to compare the effects of right and left parietal TMS in order to test for a hemispheric asymmetry in two experiments: In Experiment 1, TMS was applied over right parietal cortex, whereas TMS was given over left parietal cortex in Experiment 2. The parietal stimulation site, over superior parietal cortex, corresponded to the area of lesion overlap in the patients studied by Sapir et al. A TMS vertex control site was also stimulated in each experiment. The timing of the TMS pulses, 150 and 250 msec after saccade onset, was based on the observations of van Donkelaar and Muri (2002).

METHODS

Participants

Fourteen subjects (9 women) participated in Experiment 1 in which TMS was applied over either right parietal cortex, or the vertex. A different group of 14 subjects (7 women; mean age) participated in Experiment 2 in which TMS was applied over either left parietal cortex, or the vertex. Six subjects of (3 of whom had participated in Experiment 1, the other 3 participated in Experiment 2) participated also in a control experiment in which inhibitory tagging without eye movement was tested. Written informed consent was obtained from each participant. In addition, subjects filled in a safety screening questionnaire for TMS (Keel, Smith, & Wassermann, 2001). Ethics approval was

obtained from the School of Psychology at the Bangor University, UK. Participants received £10/hour for their participation.

Apparatus

A limbus tracker (ASL 210, Bedford, MA) was used to monitor horizontal eye position at a rate of 1000 Hz. The eye movement recording device was calibrated by a three-point calibration every 20 trials. A chin and cheek rest was used to reduce head movements. The analogue output of the eye tracker was processed on-line to determine the onset of saccades. When the velocity of saccades reached 50°/sec, a TTL pulse was sent to stimulus PC which recorded the saccadic latency and direction. Next, the stimulus PC send out two TTL pulses to the TMS stimulator to trigger the dual TMS pulse. On each trial, two TMS pulses were given, 150 and 250 msec after the onset of the eye movement. Presentation software (Neurobehavioral Systems, Albany, CA) was used for stimulus presentation and triggering of the TMS machine. Stimuli were presented on an IIyama vision master pro 512 monitor (200 Hz). A response device connected to the game port was used to record manual reaction times (RTs).

Transcranial Magnetic Stimulation

A MagStim Super Rapid with a 70-mm figure-eight coil was used for the TMS. The hand area of motor cortex was first localized in the left hemisphere. The motor threshold then was determined by finding the minimum amount of TMS intensity that was required to elicit a visible hand twitch in the relaxed right hand. Stimulation was set to 120% of the MT. All subjects participated in two sessions, separated by at least 1 week. In Experiment 1, subjects received TMS over either the vertex (control site) or a right parietal location that was 3 cm to the right and 4 cm posterior relative to the vertex, with the order of TMS location counterbalanced across subjects. In Experiment 2, subjects received TMS over either the vertex, or a left parietal site that was 3 cm to the left and 4 cm posterior relative to the vertex. A similar criterion for parietal cortex stimulation has been used in previous investigations (Chang & Ro, 2007; Kapoula, Yang, Coubard, Daunys, & Orssaud, 2004, 2005; van Donkelaar & Muri, 2002). All subjects were naive to the purpose of the study and location of stimulation. Vertex stimulation and parietal stimulation locations were relatively close to each other, and only one location was stimulated in each session, subjects did not report feeling any differences between sessions.

Procedure

The experiment was conducted in a dimly lit room. The distance between the monitor and the subjects was 57 cm. The stimulus display consisted of three small white fixation points (0.1° × 0.1°) on a black background, one presented in the center, and the other two presented 10° to the right or left of the center. A white unfilled box (3° × 3°) was presented 5° above and below each fixation point. The six boxes and the two peripheral fixation points were presented throughout the experiment. The stimulus display and the trial structure are shown in Figure 1.

Each trial began with the onset of a central fixation point. If the subject did not fixate at the central fixation point within 250 msec, the trial was aborted and an error sound was presented. After 1000 msec, a noninformative cue was presented in one of the midline boxes, either above or below the central fixation. The cue was a thickening of the line for 200 msec. A right or left arrow (1°) was presented at central fixation 300 msec after cue offset. The arrow was presented for 200 msec. Subjects were instructed to move their eyes as fast as possible in the direction of the arrow toward either the left or right peripheral fixation point. If subjects made a saccade in the wrong direction, or did not make a saccade within 500 msec, the trial was aborted and an error sound was presented. Following the eye movement, subjects were required to keep fixation at the indicated peripheral fixation point. After 700 or 900 msec, a target was presented either above or below the central fixation point (i.e., a SOA of either 700 or 900 msec). The target was presented until the subject responded by pressing a button with their right index finger, or for 1000 msec (see Figure 1 for a graphical illustration of the trial structure). Although both the cue and targets were always presented in the box above, or below initial central fixation, there were an additional four boxes. The additional boxes were presented because pilot testing revealed that this led to a reliable remapped IOR. Following a training session of 20 trials, a total of 176 trials were presented, with 10% catch trials. Catch trials were exactly the same as the other trials (i.e., including TMS), except that no target was presented.

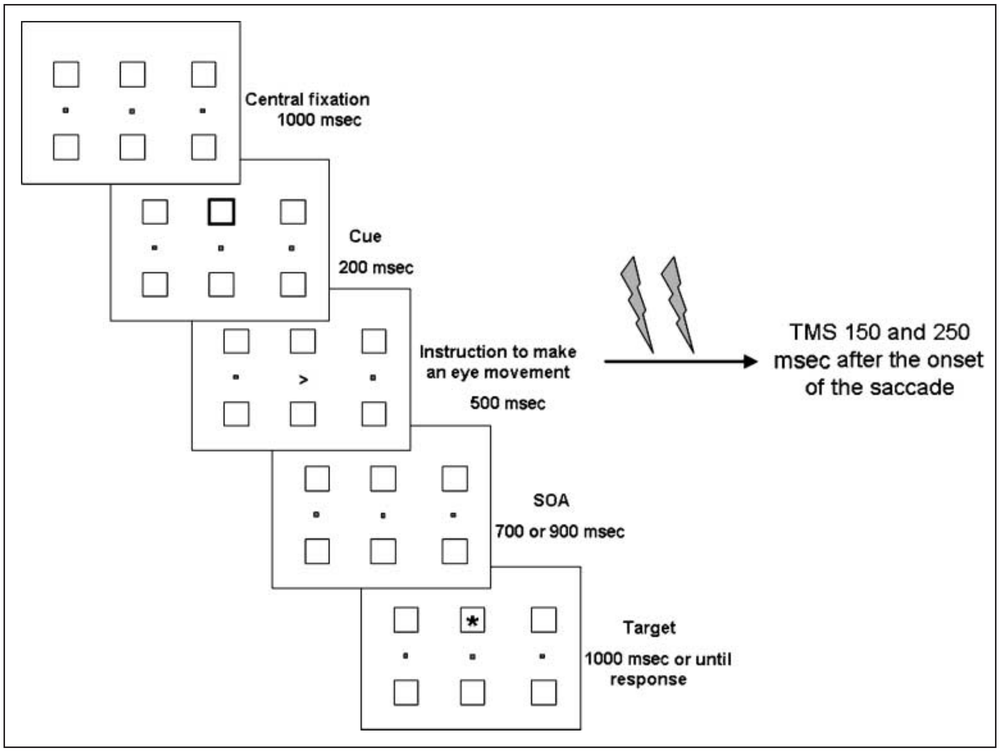
All subjects participated in two sessions: one session with either right parietal TMS (Experiment 1) or left parietal TMS (Experiment 2), and one with TMS over the vertex. Each session took around 60 min, and the order of sessions was counterbalanced across subjects. The intertrial interval was set to 4000 msec, in order to make sure that the time between two successive TMS trains was never shorter than 5000 msec to conform with safety guidelines (Wassermann, 1998; Chen et al., 1997). Sapir et al. (2004) probed for IOR at both retinal and environmental locations. However, because of the long intertrial interval required, in the current study the TMS sessions were 60 min long, and it was not practical to test for both retinal and environmental IOR. Therefore, we only tested environmental IOR in this experiment.

RESULTS

TMS Location

Because the stimulation site was based on skull landmarks (3 cm lateral and 4 cm posterior to the vertex, we acquired

Figure 1. Trial structure and stimulation sequence for a cued target with a saccade to the right between the cue and target presentation. Note that the colors are inverted for illustration purposes.



a T1-weighted anatomical MRI scan of six subjects (4 from Experiment 1) to more precisely specify the anatomical location target with TMS in a sample of our subjects. Irrespective of the experiment in which the subject had participated, a marker (vitamin E capsule) was placed over both the right and left parietal stimulation side prior to the MRI scan. Brainsight Software was used to process the MRI scans. Figure 2 shows that the parietal TMS was over the rostral superior parietal lobule, including the anterior part of the IPS. This is in accordance with region of maximum overlap in the Sapir et al. (2004) study.

Results Experiment 1

Errors

There were two different types of errors subjects could make: an eye movement error, or a manual keypress error. A failure to keep fixation at the center, a blink, an eye movement which was not in the right direction or was too slow (>500 msec), or a failure to keep fixation at the peripheral fixation point after a successful eye movement were all classified as eye movement errors. We used such a strict criterion as TMS was given relative to the saccade onset. Subject made an average of 6.5% eye movement errors, which did not differ between TMS conditions (right parietal, or vertex), saccade direction (left or right), or the interaction between these two ($F < 1$). All trials with a saccade error were aborted. Responses faster than 90 msec or slower than 750 msec were all classified as keypress errors, and omitted from the analyses. Subjects made a very small number of manual keypress errors (1.5%), and were therefore not further analyzed. Catch trials were omitted from the analyses as well.

Saccadic Reaction Times

The overall mean saccadic RT was 306 msec (SD = 24 msec). Thus, on average, the two TMS pulses were given 456 msec and 556 msec after the onset of the arrow (i.e., 150 and 250 msec after the saccade onset). Mean saccade RTs were computed for each participant in each condition and were analyzed with a repeated measures analysis of variance (ANOVA) with TMS condition (right parietal or vertex) and saccade direction (left or right) as factors. TMS did not affect saccade latencies [$F(1, 13) < 1$]. The interaction between TMS condition and saccade direction was also not significant [$F(1, 13) < 1$]. However, the leftward directed saccades were significantly faster (302 msec) than rightward directed saccades (309 msec) [$F(1, 13) = 7.48$, $p < .05$, $\eta_p^2 = .37$]. Although the difference was statistically reliable, it was only 7 msec, that is, the TMS pulses were almost given at the same time for left and right saccades.

Manual Reaction Times

Anticipatory responses (faster than 90 msec) and slow responses (slower than 750 msec) were excluded from the analysis. Note, that if subjects did not execute the saccade correctly, the trial would have been aborted. Mean RT for each subject in each condition was computed and analyzed in a repeated measures ANOVA with TMS condition (right parietal or vertex), saccade direction (left or right), cue (previously cued or uncued box), and SOA (700 or 900 msec)

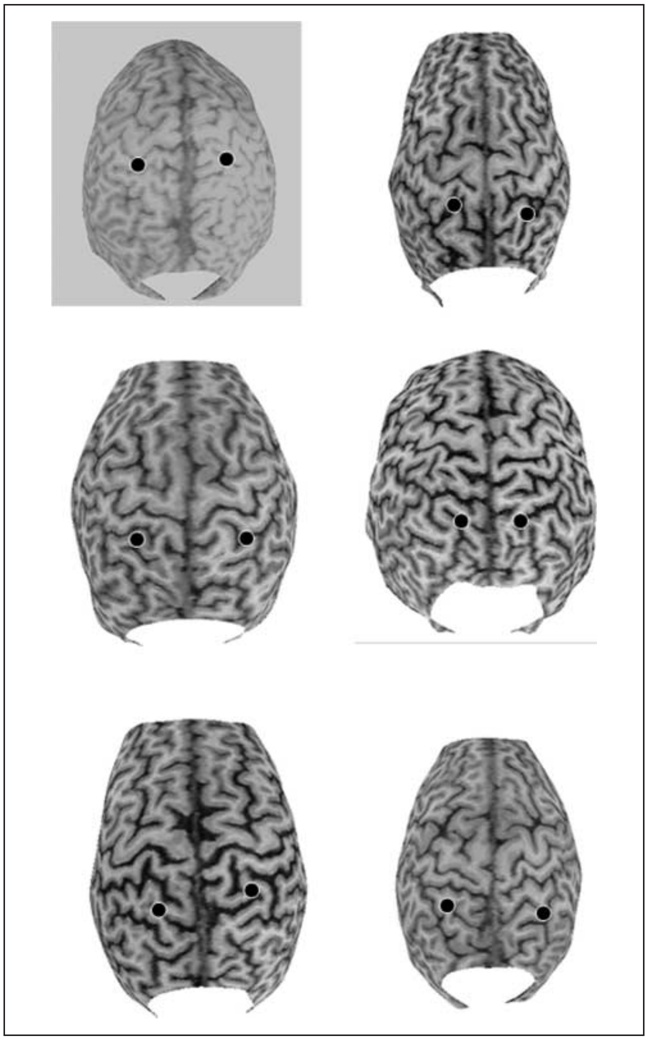


Figure 2. The 3-D-rendered structural MRI scans of the six scanned subjects. On each scan, the two possible TMS locations are marked: 4 cm posterior and 3 cm to the right and left relative to the vertex.

as within-subject factors. There were only two significant effects. RTs were slower [$F(1, 13) = 7.24$, $p < .05$, $\eta_p^2 = .36$] for cued targets (296 msec) than for uncued targets (291 msec), that is, there was a significant IOR. As shown in Figure 3, the interaction between cue and TMS location was also significant [$F(1, 13) = 24.72$, $p < .01$, $\eta_p^2 = .66$], indicating that the site of TMS affected IOR.

Two pairwise comparisons were performed to investigate the interaction between cue (previously cued or uncued) and TMS location (vertex or right parietal). There was a significant effect of cue on RTs during vertex stimulation [$t(13) = 5.64$, $p < .001$], that is, there was a significant IOR of 11 msec. However, when TMS was administered over right parietal cortex, there was no significant difference in RT for cued and uncued targets ($t < 1$).

No other effects were significant, including the interaction between TMS × Cue × Saccade direction ($F < 1$), indicating that the remapping impairment induced by right parietal stimulation was independent of the direction of the eye movement.

Results Experiment 2

Errors

Subject made an average of 6.7% eye movement errors, which did not differ between TMS condition, saccade direction, or the interaction between these two ($F < 1$). Subjects made a very small number of manual keypress errors (1.9%), and were therefore not further analyzed.

Saccadic Reaction Times

The overall mean saccadic RT was 335 msec ($SD = 39$ msec). Thus, on average, the two TMS pulses were given 485 and 585 msec after the onset of the arrow, that is, 150

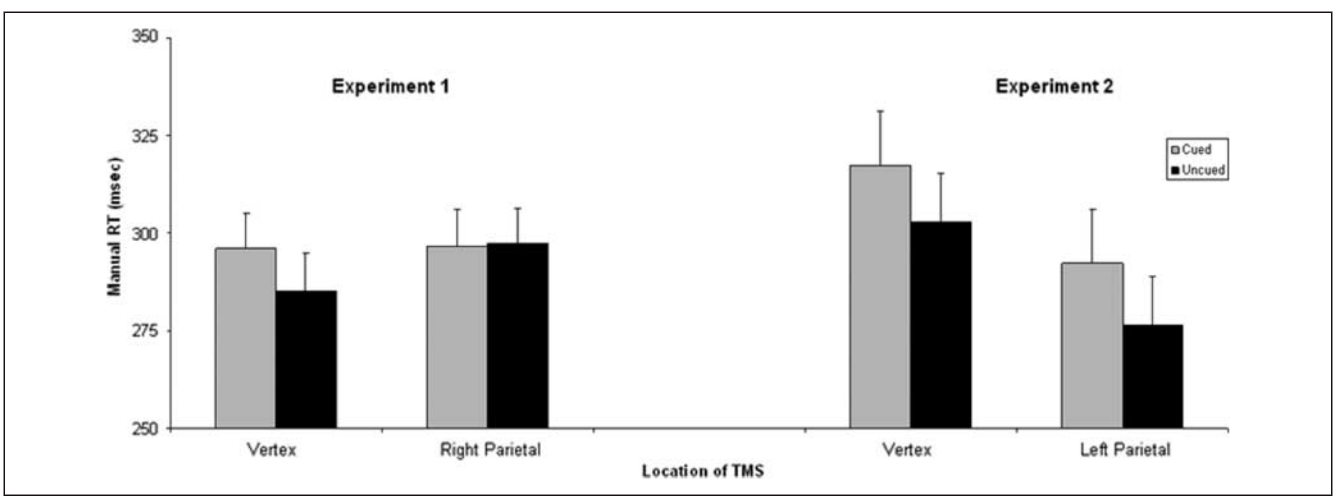


Figure 3. The mean manual RT for cued (gray) and uncued (black) targets for each TMS location. The data for Experiment 1 (right parietal and vertex TMS) are on the left. The data for Experiment 2 (left parietal and vertex TMS) are on the right. Error bars reflect within-subjects standard error of the mean (Loftus & Masson, 1994) calculated for each experiment separately.

and 250 msec after the saccade onset. Mean saccade RT was computed for each subject in each condition and analyzed with a repeated measures ANOVA with TMS (left parietal or vertex) and saccade direction (left or right) as within-subject factors. There were no significant effects ($F < 1$ in all cases).

Manual Reaction Times

Mean manual RTs for each subject in each condition were computed and analyzed in a repeated measures ANOVA, with TMS (left parietal or vertex), saccade direction (left or right), cue (previously cued or uncued box), and SOA (700 or 900 msec) as within-subject factors performed to study the effects of left parietal TMS. RTs were slower RTs for cued targets (305 msec) than for uncued targets (290 msec), indicating that there was a significant IOR of 15 msec [$F(1, 13) = 19.45, p < .01, \eta_p^2 = .6$]. IOR was larger at the short SOA (21 msec) than at the long SOA (9 msec) [$F(1, 13) = 7.01, p < .05, \eta_p^2 = .35$].

There was also a significant interaction between Saccade direction × TMS [$F(1, 13) = 5.61, p < .05, \eta_p^2 = .30$]. In order to study this interaction, four pairwise comparisons were conducted. RTs were significantly faster after a saccade to the left (280 msec) than after a saccade to the right (289 msec) when left parietal TMS was administered [$t(13) = 5.96, p < .01$]. There were no other significant effects. Most important, the interaction between TMS × Cue was not significant ($F < 1$), suggesting that TMS to the left parietal and TMS to the vertex have similar effects. Figure 3 shows that there is a significant IOR after left parietal TMS, which is comparable to that observed after control stimulation at the vertex; that is, left parietal TMS does not influence the remapping of the inhibitory tag.

Comparing the Results of Experiments 1 and 2

Two different ANOVAs were performed to compare the effects of right and left PPC TMS, with experiment as a between-subjects factor. One ANOVA compared the effect of vertex TMS for both experiments, whereas the other ANOVA compared the effect of parietal TMS for both experiments. The reason for comparing the vertex stimulation between experiments was to determine whether there is a baseline difference between the groups. The mixed effect repeated measures ANOVA with experiment (1 or 2) as a between-subjects factor, and saccade direction (left or right), cue (previously cued or uncued box), and SOA (700 or 900 msec) as within-subject factors revealed only a significant effect of cue [$F(1, 26) = 20.91, p < .01, \eta_p^2 = .45$], reflecting longer latencies for targets at cued (307 msec) than at uncued (294 msec) locations. There were no other significant effects, including no main effect of experiment, or interactions with the experiment factor. Thus, the groups in Experiments 1 and 2 did not differ from each other in the vertex condition.

The same ANOVA was performed for parietal TMS. There was a significant effect of cue [$F(1, 26) = 8.10, p < .01, \eta_p^2 = .24$] and a significant Cue × Experiment interaction [$F(1, 26) = 9.70, p < .01, \eta_p^2 = .27$]. The source of this interaction was examined by comparing the size of IOR for both experiments. As expected, the size of the IOR was significantly larger in Experiment 2 (left parietal TMS; 16 msec) than in Experiment 1 (right TMS; −1 msec) [$t(26) = 3.11, p < .01$]. The effect of saccade direction was also significant [$F(1, 26) = 5.05, p < .05, \eta_p^2 = .16$], as was the interaction between saccade direction and experiment [$F(1, 26) = 6.52, p < .05, \eta_p^2 = .20$]. Follow-up *t* test found that there was no effect of saccade direction in Experiment 1 (right parietal TMS; RT was 297 msec independent of saccade direction). However, in Experiment 2

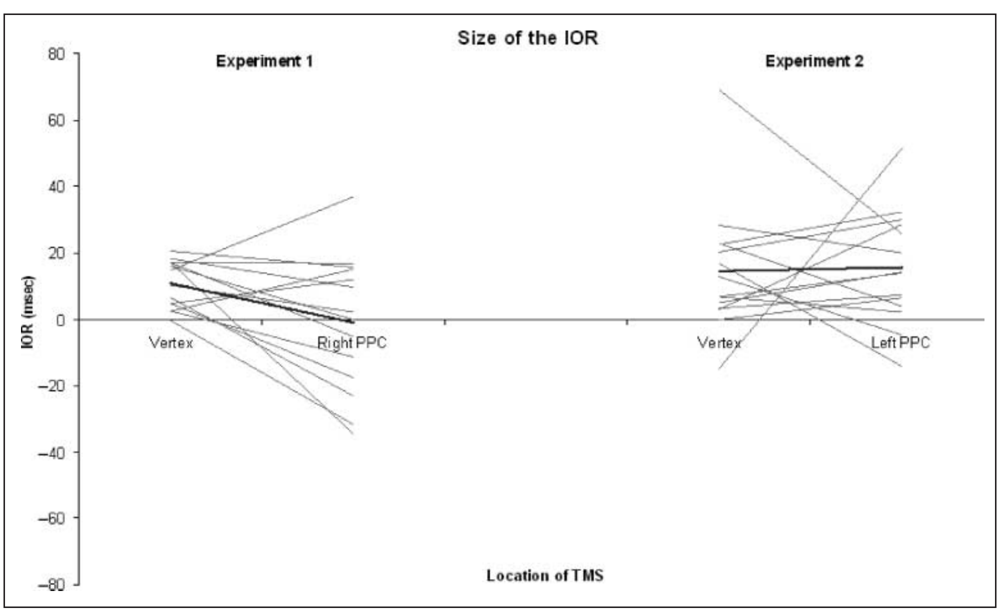


Figure 4. The mean size of IOR (thick black line) and individual subject data (thin gray lines). The data for Experiment 1 are on the left, and for Experiment 2 on the right.

(left parietal TMS), RTs were faster after a saccade to the left (280 msec) than after a saccade to the right (289 msec) [$t(13) = 5.96, p < .01$]. No other effects were significant. The individual and mean sizes of IOR are displayed in Figure 4.

Control Experiment

The current result suggests that right parietal TMS impairs remapping of the inhibitory tag regardless of the direction of eye movements. However, the conditions in this study do not allow us to rule out the possibility that right parietal TMS abolishes IOR in general and not only the remapping of the inhibitory tag. Sapir et al. (2004) also presented targets at retinal cued locations, for which no remapping was required. Like the healthy controls, the patients' RTs were slower for the cued retinal location. This finding demonstrated that patients had a normal IOR, but that this IOR was lost when they were required to remap the inhibitory tag. Because there were no such targets presented at the retinal location of the cue in the current experiment (i.e., subjects were always required to remap the inhibitory tag), we performed a control experiment in a few participants, in which no remapping was required.

The procedure was identical, except that subjects were not required to make an eye movement. Instead of an arrow, an equal sign of the same size was presented, and subjects were instructed to maintain central fixation. The TMS pulses were given relative to their mean saccadic RTs of the previous experiment. We recruited six subjects who had participated in either Experiment (3 had participated in Experiment 1 and the other 3 in Experiment 2). They participated in one vertex and one right parietal TMS session.

RTs were subject to a 2 (TMS) × 2 (cue) × 2 (SOA) repeated measures ANOVA. The main effect of cue was significant [$F(1, 5) = 16.43, p = .01, \eta_p^2 = .77$], reflecting the slow RTs to valid than for invalid trials (i.e., IOR). There was no interaction between TMS site and cue, and a paired-samples t test confirmed that there was no significant difference in the size of IOR during vertex stimulation (11 msec) and parietal stimulation (10 msec) [$t(5) = 0.16, p = .88$]. This result confirms that right parietal TMS does not influence IOR when there is no need to update the saliency map.

DISCUSSION

The results of these experiments converge with those reported in neurological patients (Sapir et al., 2004), implicating the rostral superior parietal lobule in updating saliency maps after eye movements. They also demonstrate a hemispheric asymmetry in representing salience maps. TMS over the right, but not the left, rostral superior parietal lobule prevented remapping of the inhibitory tag after either left or right saccades. This remapping deficit was regardless of whether the target appeared in the field ipsilateral or contralateral to the right parietal stimulation site. Our results also converge with another recent TMS study reporting that stimulation over the right, but not left, hemisphere, at a more dorsal site over the IPS than the one used here (i.e., at the P3 electrode site), disrupted transsaccadic working memory (Prime et al., 2008).

As was the case in the case of the patients studied by Sapir et al. (2004), the absence of environmental IOR was a result of a slower detection RT at invalidly cued locations. There was no difference between right parietal cued, right parietal uncued, and vertex cued targets. One possible explanation for this effect is that the cued location has a reduced saliency, and that TMS impaired the updating of the whole saliency map, resulting in lower saliency and longer RTs for all possible target locations. Another possibility is that IOR occurs because the other target location becomes more salient, and that this benefit has been disrupted.

Chang and Ro (2007) showed that TMS over right parietal cortex impaired perisaccadic displacement detection. Performance was only affected when the probe was presented in the left visual field, subjects were required to make a contralateral saccade, and TMS was given just before the saccade. They hypothesized that the reason that TMS affects perception is that TMS introduces external noise into the PPC representation. In the current study, the absence of a remapped inhibitory tag might be caused by that TMS-introduced noise into the parietal representation as Chang and Ro (2007) hypothesized. When subjects were not required to make eye movements (control experiment), or TMS was applied over left PPC, the inhibitory tag was remapped, making it less likely that TMS introduces just noise. To further investigate this issue, it would be interesting to study whether right PPC TMS affects retinal IOR. However, patients with a parietal lobe lesion show preserved retinal IOR. This further supports the idea that parietal lobe disruption interferes with remapping rather than just degrading location information.

The TMS pulses were given 150 and 250 msec after the onset of the eye movement. This time interval was chosen based on previous research indicating that this is the critical time of spatial updating in an ERP study (Bellebaum, Hoffmann, & Daum, 2005), in single-unit recordings (Gottlieb et al., 1998; Duhamel et al., 1992), and in previous studies using the double-step saccade paradigm (Morris et al., 2007; van Donkelaar & Muri, 2002). Although, no other time points were tested, it is interesting to note that there was no effect of SOA (700 or 900 msec) in right parietal TMS group. This indicates that once the representation of the inhibitory tag is affected by TMS, it cannot be regained. Further research is needed to definitively specify the critical time that TMS must be applied to disrupt remapping.

Like the patient study of Sapir et al. (2004), but unlike previous patient (Heide & Kompf, 1998; Heide et al., 1995; Duhamel et al., 1992) and TMS (Morris et al., 2007; van Donkelaar & Muri, 2002) studies employing the double-step saccade paradigm, disruption of remapping occurred when saccades were directed toward the ipsilateral as well as contralateral fields. In double-step saccade studies, the deficit has been observed only when saccades were directed

contralateral to the disrupted cortex. The current results suggest that parietal cortex is not simply responsible for generating an extra-retinal signal necessary for updating a salience map of the visual field, but that right parietal cortex is critical for maintaining a durable, transsaccadic representation of that map across the visual field.

This interpretation of the current results is consistent with observations from neurophysiological recording in LIP of nonhuman primates, demonstrating that this area is concerned specifically with remapping of objects that are salient by virtue of either a recent appearance or because they are designated as targets of visual search (Gottlieb et al., 1998). Moreover, updating of the receptive fields of LIP neurons is independent of whether the saccade is directed ipsilateral or contralateral to the neuron's receptive field, and whether the object is updated within or between hemispheres (Heiser & Colby, 2006).

It is possible that separate regions of the IPS may be responsible for generating the extra-retinal signal and for maintaining a remapped representation. A recent TMS study (Morris et al., 2007), using an adaptation of the double-step saccade paradigm, reported inaccurate second saccades after stimulation of a posterior area of right parietal cortex, but not after TMS of a more rostral site that approximated the region stimulated in the current investigation. We might speculate that the more posterior part of parietal cortex is necessary for generating an extra-retinal signal, such that its inactivation only affects performance after contralateral saccades, whereas more anterior parts of right parietal cortex maintain durable representation of the remapped salience map after a saccade in either direction. However, it is notable that the effect specific to PPC in the Morris et al. (2007) experiment was an increase in variability in the second saccade end point, suggestive perhaps of a degraded representation of the location of the second target. There was no evidence that TMS of this site resulted in saccades to the *retinal* location of the second target, as might be expected if TMS prevented the generation of a critical extra-retinal signal. Further TMS experiments, over the more posterior site examined by Morris et al., using the kind of paradigm used here, or the transsaccadic memory paradigm employed by Prime et al. (2008), may seek further evidence for a dissociation of function along parietal cortex that may contribute to updating and maintaining salience maps across saccades.

A TMS study targeting FEF that examines the remapping of IOR may also be informative. Lesions of the FEF have been reported to not disrupt performance on double-step saccades (Heide et al., 1995). However, parietal cortex receives remapping signals from the colliculo-thalamic-FEF circuit elucidated by Sommer and Wurtz (2006), and these signals may be critical for the encoding of a durable salience map.

All previous TMS studies using the double-step saccade paradigm have, to our knowledge, only stimulated the right parietal lobe (Morris et al., 2007; van Donkelaar & Muri, 2002), and further research is needed to clarify whether there may be hemispheric asymmetries in saccade remapping in this paradigm.

The patient research using the double-step saccade paradigm, reported by Heide et al.'s (1995) lab, does suggest that the left parietal lobe participates in saccade remapping. In a double-step saccade task, in which the first and second targets occurred in opposite visual fields, patients with left parietal lesions did show a deficit, although patients with right parietal lesions were more impaired. fMRI studies have not revealed hemispheric updating asymmetries (Medendorp et al., 2003; Merriam et al., 2003): Representations of stimuli presented to the right hemisphere are remapped to the left hemisphere after left saccades, and representations of stimuli presented to the left hemisphere are remapped to the right hemisphere after right saccades.

Although there is, then, evidence for a role of both hemispheres in saccade remapping, there is also evidence that their contributions may differ. Heide et al. (1995) also tested parietal lesioned patients on a within-hemifield double-step saccade task, in which both targets were presented in the same visual field. In this task, in which no between-hemispheric spatial updating was necessary, an asymmetric effect of right and left parietal lesions was observed. In addition to impaired performance on the between-hemifield task, patients with right parietal lesions also had an impairment in the within-hemifield condition in the left visual field. An ERP study by Bellebaum et al. (2005) also provided evidence for different contributions of left and right hemisphere in saccade remapping. Bellebaum et al. reported a larger slow positive wave when remapping was required, starting between 150 and 200 msec after first saccade onset. Source analysis showed that whereas the source was restricted to right PPC in trials with leftward first saccades, left and right PPC were both involved in rightward trials.

Further research is needed to specify the circumstances under which left parietal cortex may be involved in updating salience maps. Future studies, using the paradigm employed here, will test for hemispheric asymmetries in salience updating when the stimuli to be updated are presented to either the left or right visual field, when vertical saccades are made, and when stimuli must be remapped either within or between hemispheres.

In conclusion, these observations converge with those made in neurological patients with chronic lesions of parietal cortex implicating this region as a neural substrate for maintaining the spatial constancy necessary for a coherent continuity of visual experience. They also suggest a special role for the right parietal lobe, at least under the conditions of the current experiments. The observation that remapping was disrupted when saccades were executed toward the field ipsilateral as well as contralateral to cortical disruption suggests that parietal cortex is not involved simply in generating the corollary discharge that provides the extra-retinal signal needed for remapping the visual scene. Rather, the results implicate parietal cortex as a

neural substrate that uses the extra-retinal signal to maintain a continuous salience map across saccades.

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Reprint requests should be sent to Martijn Gerbrand van Koningsbruggen, School of Psychology, Brigantia Building, Penrallt Road, Bangor, Gwynedd LL572AS, UK, or via e-mail: Martijn_van_koningsbruggen@hotmail.com.

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