

Parietal Lobe Contribution to Mental Rotation Demonstrated with rTMS

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Abstract

■ A large number of imaging studies have identified a role for the posterior parietal lobe, in particular Brodmann's area 7 and the intraparietal sulcus (IPS), in mental rotation. Here we investigated whether neural activity in the posterior parietal lobe is essential for successful mental rotation performance by observing the effects of interrupting this activity during the execution of a mental rotation task. Repetitive transcranial magnetic stimulation (rTMS) was applied to posterior parietal locations estimated to overlie Brodmann's area 7 in the right and the left hemisphere, or to a posterior midline location (sham condition). In three separate experiments, rTMS (four pulses, 20 Hz) was delivered at these locations either 200–400, 400–600, or

600–800 msec after the onset of a mental rotation trial. Disrupting neural activity in the right parietal lobe interfered with task performance, but only when rTMS was delivered 400 to 600 msec after stimulus onset. Stimulation of the left parietal lobe did not reliably affect mental rotation performance at any of the time points investigated. The time-limited effect of rTMS was replicated in a fourth experiment that directly compared the effects of rTMS applied to the right parietal lobe either 200–400 or 400–600 msec into the mental rotation trial. The results indicate that the right superior posterior parietal lobe plays an essential role in mental rotation, consistent with its involvement in a variety of visuospatial and visuomotor transformations. ■

INTRODUCTION

Recent years have seen a great increase in the number of functional imaging studies concerned with the neural underpinnings of spatial transformations. One of the most popular paradigms used in these investigations has been that of mental rotation (Shepard & Metzler, 1971). In one version of this task, subjects decide whether two 3-D figures presented in different orientations are identical or mirror images of each other. In an alternative version of the task, subjects have to judge whether a rotated letter is normal or mirror-reversed (Cooper & Shepard, 1973). Response times tend to increase linearly as a function of the angular distance between the two objects or, in the case of single alphanumeric characters, of the angular distance to the upright position. This suggests that people imagine the objects passing through intermediate orientations, in a manner analogous to observing a physical object rotating through space.

Most functional imaging studies have revealed robust activations in the parietal lobes, most often centered on the intraparietal sulcus (IPS), as well as regions of the frontal and occipital cortex (Jordan, Heinze, Lutz, Kanowski, & Jancke, 2001; Vingerhoets et al., 2001;

Harris et al., 2000; Carpenter, Just, Keller, Eddy, & Thulborn, 1999; Kosslyn, Digirolamo, Thompson, & Alpert, 1998; Alivisatos & Petrides, 1997; Richter, Ugurbil, Georgopoulos, & Kim, 1997; Tagaris et al., 1997; Cohen et al., 1996; Tagaris et al., 1996). Although parietal lobe activations have been demonstrated in all these studies, the relative involvement of the left and right parietal lobes remains somewhat controversial. The majority of studies have demonstrated bilaterally symmetrical parietal activations (Jordan et al., 2001; Carpenter et al., 1999; Kosslyn et al., 1998; Richter et al., 1997; Tagaris et al., 1997; Cohen et al., 1996; Tagaris et al., 1996). A couple of studies reported exclusively left parietal activations (Vingerhoets et al., 2001; Alivisatos & Petrides, 1997), whereas in one study the activation was restricted to the right parietal lobe, centered on the IPS (Harris et al., 2000), and in another it was bilateral but with a predominantly right-sided focus (Podzbenko, Egan, & Watson, 2002). It is still not clear whether these differences in patterns of activation are due to differences in the stimuli and paradigms used by different researchers (Jordan et al., 2001; Vingerhoets et al., 2001), or whether they are due to other extraneous factors such as eye movements, attention shifts, or differences in cognitive strategy (see Harris et al., 2000, for an extensive discussion of these issues). Furthermore, a widely acknowledged limitation of functional imaging

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experiments is that they cannot differentiate between regions that are “essential” for a cognitive task and regions that are recruited by the task without playing a critical role in it. To answer the latter question, it is necessary to show that disrupting activity in a brain region interferes with the ability to perform the task under investigation. Studies of patients with brain lesions can go some way in answering this question, but they are often limited by the fact that lesions are large, thus involving a number of different structures, and it is difficult to replicate the effects of a particular lesion in more than one patient.

In the present study we have used repetitive transcranial magnetic stimulation (rTMS) to investigate the involvement of the parietal lobe in mental rotation. TMS is a method of delivering electrical stimulation through the intact skull by inducing a rapidly changing magnetic field at the scalp. This produces synchronous activity in a subpopulation of neurons located under the stimulating coil, with the net result of disrupting any pattern of activity that was occurring at the time of the stimulation (see Jahanshahi & Rothwell, 2000; Walsh & Cowey, 2000, for a review). Thus, TMS provides a systematic and replicable way of disrupting activity in a restricted area of cortex and observing the behavioral effects. Furthermore, TMS can be applied at different time points during the execution of a cognitive task, and thus it can also provide valuable information about when a particular brain region is involved in that task.

The first aim of this study was to determine the relative contribution of the right and left parietal lobes to mental rotation. We delivered rTMS over the superior parietal lobe, in the vicinity of the IPS (see Figure 1), because this is the parietal region most consistently activated by mental rotation tasks in imaging studies. The superior parietal lobe is also an obvious candidate from a theoretical stance, because neurons in this region are known to implement a variety of visuospatial and visuomotor transformations (Snyder, Batista, & Andersen, 2000; Colby, 1999). The second aim of the study was to determine the time course of the parietal involvement in mental rotation, by applying rTMS at different time points during the execution of a mental rotation task.

To this end, we first carried out three separate experiments, in which we examined the effect of applying rTMS to the right and the left parietal lobe, compared to a posterior midline location (sham condition). In each experiment, rTMS was given at a different time during a mental rotation trial: (1) 200–400 msec after the trial onset, (2) 400–600 msec into the trial, or (3) 600–800 msec into the trial. The results of these three initial experiments suggested an interesting pattern of results. First, compared to sham stimulation at a posterior midline location, the only discernable effects of rTMS on mental rotation performance occurred when stimulation was applied to the

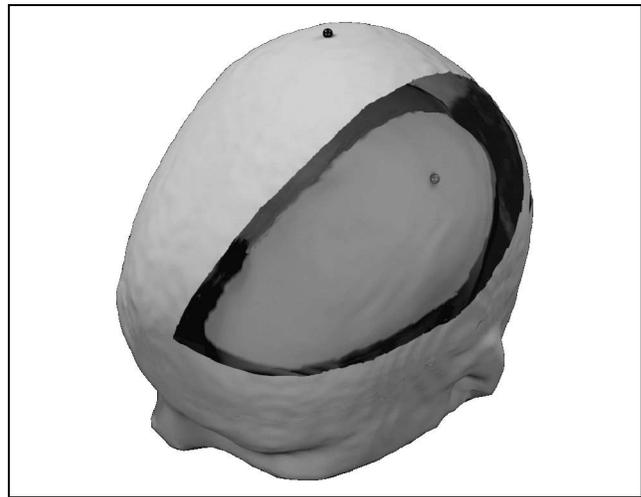


Figure 1. The stimulated site located halfway between P4 and CP4 (10-20 International EEG system) is depicted on a scalp model, together with the perpendicular projection halfway between P3 and CP3 depicted on a cortical model. The Talairach coordinates of this site, calculated with the Softaxic Navigator software, are $x = \pm 34$, $y = -64$, $z = 50$, corresponding to the superior parietal lobule (Brodmann’s Area 7). The head models were obtained by averaging the magnetic resonance images of 152 subjects using the Statistical Parametric Mapping (SMP96) software.

right superior parietal lobe, but not to the left parietal lobe. Second, this effect of right parietal stimulation was not seen at all time intervals investigated here. There was absolutely no effect on performance when rTMS was delivered in the later part of a mental rotation trial (600 to 800 msec after the stimulus onset). On the other hand, stimulating the right parietal lobe 400–600 msec after trial onset interfered with task performance, while the effects of rTMS applied 200–400 msec following trial onset were somewhat inconclusive. These findings were followed up in a fourth experiment, which used a more powerful within-subject design and directly compared the effects of rTMS versus sham stimulation delivered to the right parietal lobe 200–400 and 400–600 msec after the onset of a mental rotation trial.

RESULTS

Inspection of the subjects’ accuracy rates revealed no differences between stimulation conditions in any of the experiments. Therefore, the accuracy measures were not considered further, and the results focus on the subjects’ reaction time (RT). The RTs reported here are for correct responses only; however, essentially the same results were obtained when all responses were considered. In each of the experiments, RTs were averaged for each subject, condition, and orientation angle, and the data were analyzed using repeated-measures ANOVA. Follow-up comparisons of conditions were carried out where appropriate.

Experiment 1 (rTMS at 200–400 msec)

In this experiment, rTMS was delivered to the left parietal lobe (“left” condition), right parietal lobe (“right” condition), and the posterior midline (“sham” condition) in a time window 200–400 msec after the onset of a mental rotation trial (see Methods and Figure 1 for details of placement of the TMS coil). The results are summarized in Figure 2, and appear to indicate that RTs in the right condition were generally somewhat faster than in the left and sham conditions, with no differences between the latter two conditions. An ANOVA with stimulation (three levels: left, right, sham) and angle (four levels: 0°, 60°, 120°, 180°) revealed a significant increase in RT across orientation angles, $F(3,24) = 45.98$, $p < .01$, as predicted for a mental rotation task. However, there was no significant effect of stimulation, $F(2,16) = 2.49$, $p = .11$, or interaction between stimulation and angle, $F(6,48) = 1.41$, $p = .23$. Given the pattern of results depicted in Figure 2, we also carried out post hoc pairwise comparisons of conditions to rule out the possibility that there might be some subtle differences that were not picked up by the overall analysis. We failed to find any reliable differences between right and sham, $F(1,8) = 3.19$, $p = .11$, or between right and left conditions, $F(1,8) = 4.13$, $p = .08$.

Thus, while we cannot completely rule out an effect of rTMS applied to the right superior parietal lobe in this

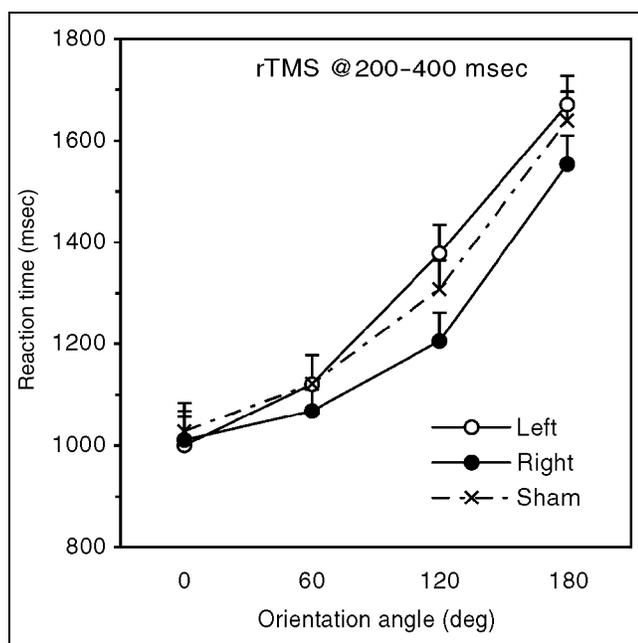


Figure 2. Mean RTs across orientation angles for mental rotation of alphanumeric characters in Experiment 1. Trains of rTMS (four pulses, 20 Hz) were delivered to the left superior parietal lobe, the right superior parietal lobe, or to a posterior midline location (sham condition) 200–400 msec after stimulus presentation. Error bars represent within-subject standard error of the mean (Loftus & Masson, 1994).

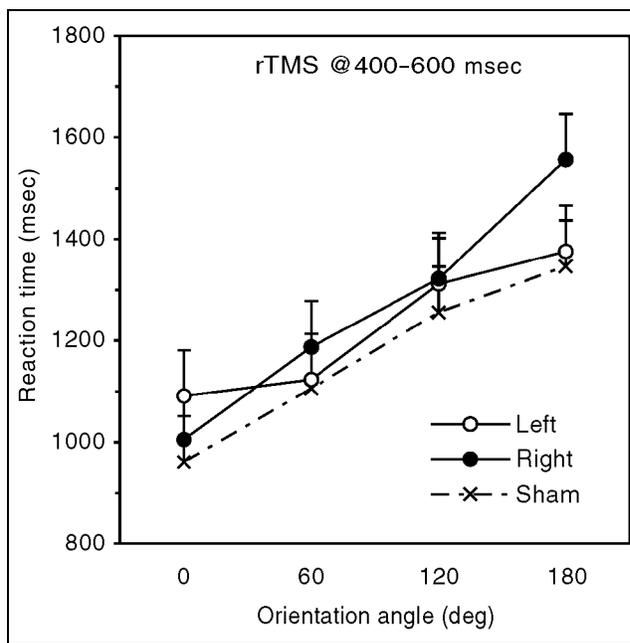


Figure 3. Mean RTs across orientation angles for mental rotation of alphanumeric characters in Experiment 2. Trains of rTMS (four pulses, 20 Hz) were delivered to the left superior parietal lobe, the right superior parietal lobe, or to a posterior midline location (sham condition) 400–600 msec after stimulus presentation. Error bars represent within-subject standard error of the mean.

early time window, this effect was not statistically reliable. On the other hand, there was no evidence that rTMS delivered to the left parietal lobe had any effect at all on mental rotation performance.

Experiment 2 (rTMS at 400–600 msec)

The RT results for this experiment, in which stimulation was delivered to the left parietal, right parietal and posterior midline sites 400–600 msec after trial onset, are summarized in Figure 3. As can be seen from this figure, this time stimulation of the right parietal lobe appeared to slow down mental rotation compared to the left and sham conditions.

An ANOVA with stimulation and angle as within-subject factors revealed a significant main effect of angle, $F(3,24) = 19.10$, $p < .01$, but no overall effect of stimulation, $F(2,16) = 1.26$, $p = .31$. The Stimulation \times Angle interaction approached, but failed to reach, statistical significance, $F(6,48) = 2.01$, $p = .08$. Given the pattern of results depicted in Figure 3, we carried out more detailed analyses of the data using contrasts that measured differences between pairs of conditions across rotation angles (equivalent to the Stimulation \times Angle interaction, but with only two levels on the stimulation factor). There was a significant difference between right and sham, $F(1,8) = 5.73$, $p < .05$, indicating a steeper increase in RTs across orientation angles in the right

condition compared to sham. There was no difference between left and sham, $F(1,8) = .67, p = .44$, and the difference between left and right just failed to reach statistical significance, $F(1,8) = 4.27, p = .07$.

The results of this experiment were interesting and encouraging, because they suggested that rTMS applied to the right parietal lobe 400–600 msec after stimulus onset may interfere with the subjects' ability to perform mental rotation compared to a sham stimulation condition. In contrast, similar to the findings of Experiment 1, there was no evidence that rTMS of the left parietal lobe had an effect on mental rotation performance.

Experiment 3 (rTMS at 600–800 msec)

The RT results for this experiment, in which stimulation was delivered in a later time window 600–800 msec after trial onset, are presented in Figure 4. There was no discernable effect on mental rotation performance when rTMS was applied to either the left or the right superior parietal lobe in this time window. An ANOVA with stimulation and angle as within-subject factors confirmed the expected main effect of angle, $F(3,24) = 12.69, p < .01$, but found no overall effect of stimulation, $F(2,16) = .26, p = .78$, and no interaction between stimulation and angle, $F(6,48) = .28, p = .61$. Therefore, we conclude that rTMS applied 600–800 msec after stimulus onset had no effect on mental rotation performance.

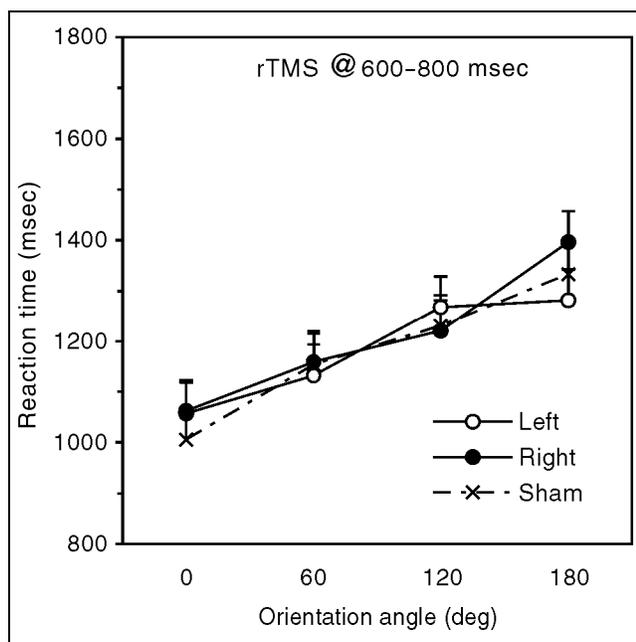


Figure 4. Mean RTs across orientation angles for mental rotation of alphanumeric characters in Experiment 3. Trains of rTMS (four pulses, 20 Hz) were delivered to the left superior parietal lobe, the right superior parietal lobe, or to a posterior midline location (sham condition) 600–800 msec after stimulus presentation. Error bars represent within-subject standard error of the mean.

Taken together, the results of these experiments suggest that rTMS delivered to the right superior parietal lobe may have an effect on mental rotation, whereas stimulating the same location in the left parietal lobe did not interfere with task performance at all. Moreover, this effect was most reliably obtained when rTMS was delivered around 400–600 msec following the onset of a mental rotation trial, although we cannot completely discount the possibility that rTMS also had some effect during an earlier time period, 200–400 msec after trial onset. The next experiment attempted to replicate these effects in a more powerful within-subject experiment.

Experiment 4

In this experiment, we only stimulated the right superior parietal lobe, because the previous experiments had demonstrated that rTMS delivered to the left superior parietal lobe did not have an effect on mental rotation performance. We also concentrated only on the two time windows when rTMS appeared most likely to interfere with mental rotation performance, namely 200–400 and 400–600 msec after trial onset, and manipulated the timing of TMS within subjects. Limiting the conditions in this manner allowed us to increase the number of trials in each condition (and thus experimental power) while keeping the number of stimulation trials administered to each subject within a reasonable limit. Performance during right parietal rTMS was compared to performance during a sham condition, in which sham stimulation was applied at the same right parietal site.

A repeated-measures ANOVA with stimulation (two levels: TMS vs. sham), delay (two levels: 200 vs. 400 msec), and angle (4 levels: 0°, 60°, 120°, 180°) as within-subject factors revealed a significant main effect of stimulation, $F(1,5) = 8.95, p < .05$, and a significant Stimulation \times Delay interaction, $F(1,5) = 25.12, p < .01$, in addition to the predicted significant effect of angle, $F(3, 15) = 29.17, p < .01$. Stimulation and delay did not interact with angle, indicating that RT increased across orientation angles in a similar fashion in all conditions.

Pairwise comparisons of conditions revealed a significant difference between TMS and sham stimulation at 400–600 msec, $F(1,5) = 42.49, p < .01$, but no difference between TMS and sham stimulation at 200–400 msec, $F(1,5) = .17, p = .70$. There was also a significant difference between TMS applied at 400–600 msec and TMS applied at 200–400 msec, $F(1,5) = 14.67, p < .05$, but no difference between the two sham conditions, $F(1,5) = 1.54, p = .27$. These results are summarized in Figure 5.

Thus, we replicated the effect found in Experiment 2, namely an increase in RT when rTMS was applied to the right parietal lobe 400–600 msec into a mental rotation trial. Furthermore, this experiment demonstrated unequivocally that the effect of TMS was confined to

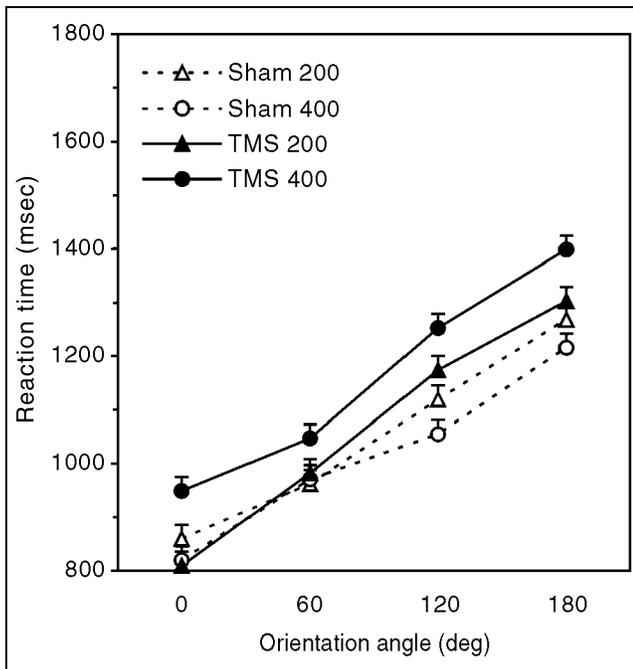


Figure 5. Mean RTs across orientation angles for mental rotation of alphanumeric characters in Experiment 4. Trains of either rTMS or sham stimulation (four pulses, 20 Hz) were delivered to the right superior parietal lobe either 200–400 or 400–600 msec after stimulus presentation. Error bars represent within-subject standard error of the mean.

this time window, as rTMS administered at an earlier time, 200–400 msec after stimulus onset, did not interfere with the subjects' mental rotation performance.

DISCUSSION

In this study, we investigated the effects of rTMS delivered to the left and right superior parietal lobes at different times during a mental rotation task. In two separate experiments, we found that disrupting neural activity in the right superior parietal lobe in a time window 400–600 msec after stimulus onset interfered with the mental rotation of alphanumeric characters. In contrast, stimulation of the left superior parietal lobe did not reliably affect mental rotation performance at any of the time points investigated here. These findings strongly suggest that the right superior parietal lobe plays an essential role in mental rotation, whereas the left superior parietal lobe does not appear to be critically involved in this process.

Our results are consistent with neuropsychological evidence that lesions to the right parietal lobe impair mental rotation abilities (Passini, Rainville, & Habib, 2000; Ditunno & Mann, 1990). They also support the findings of two recent imaging studies that have demonstrated exclusive, or predominant, right-sided superior parietal lobe activation during mental rotation of alphanumeric characters (Podzbenko et al., 2002; Harris

et al., 2000). In these studies, which used a parametric approach, changes in cerebral blood flow and BOLD response in the right superior parietal lobe, particularly within the IPS, were significantly correlated with the mental rotation demands of the task. Another study using the same paradigm found a similar correlation between the degree of mental rotation required and the duration of an event-related potential (ERP) component recorded at a right parieto-occipital site (Pegna et al., 1997). The systematic relationship identified between neural activity in the right posterior parietal lobe and the amount of mental rotation performed strongly suggests that this region implements the actual spatial transformations that constitute the imagined rotation. The present results strengthen this conclusion.

Our failure to obtain evidence that the left superior parietal lobe plays an essential role in mental rotation is somewhat surprising given that many functional imaging studies and some studies of patients with brain lesions have found evidence for left parietal lobe involvement in mental rotation tasks (e.g., Jordan et al., 2001; Vingerhoets et al., 2001; Carpenter et al., 1999; Alivisatos & Petrides, 1997; Cohen et al., 1996; Morton & Morris, 1995; Mehta & Newcombe, 1991). By comparing our findings to studies of brain-lesioned patients, we might conclude that larger lesions, encompassing areas outside that stimulated in the present study, can cause mental rotation deficits. This possibility could be investigated in future studies by using TMS to systematically stimulate other locations within the parietal lobes. Alternatively, it is possible that we did not find an effect of left parietal stimulation because this region does not participate in mental rotation during the periods investigated here. However, this seems unlikely given that, across three experiments, we covered a rather extensive time window ranging between 200 and 800 msec after the onset of the stimulus. Moreover, the effect of TMS on the right parietal cortex was relatively time specific, and one would expect functionally equivalent regions to be involved in a task at roughly the same time. Failure to obtain such evidence argues for a functional asymmetry as regards the participation of the superior parietal lobe in mental rotation, at least as far as this paradigm is concerned (see also Podzbenko et al., 2002; Harris et al., 2000; Pegna et al., 1997).

The majority of studies that have identified a possible contribution of the left parietal lobe in mental rotation have used the Shepard and Metzler (1971) paradigm, which requires the simultaneous comparison of two rather complex stimuli. This paradigm would be more likely to induce eye movements and attention shifts between the stimuli—two processes that are likely to recruit the superior parietal lobes bilaterally (Anderson et al., 1994; Corbetta, Miezin, Shulman, & Petersen, 1993). Other factors that might lead to differential activation of the left parietal lobe may include the cognitive elaboration of different types of stimuli (e.g.,

complex 3-D objects vs. 2-D figures and letters vs. body parts), or a failure to isolate just the mental rotation component of the task through the experimental design (see Harris et al., 2000, for extensive discussion of these issues). Thus, the left parietal activations seen in some imaging experiments may be related to factors other than mental rotation *per se*.

One of the stated aims of this study was to characterize the time course of the parietal involvement in mental rotation. We found that the critical period in which the right parietal lobe played a role in mental rotation occurred in a time window 400–600 msec after the presentation of the stimulus. This is consistent with the results of several ERP studies of mental rotation, which found a pronounced negative potential over the parietal sites (especially right) between 400 and 600 msec after stimulus onset (Yoshino, Inoue, & Suzuki, 2000; Pegna et al., 1997; Peronnet & Farah, 1989). This timing seems appropriate when one considers that the visual stimulus first needs to be processed by lower-level visual areas and recognized before one can attempt to verify its handedness through mental rotation. By 600 msec poststimulus onset, rTMS no longer had an effect on mental rotation performance, suggesting that the parietal cortex had ceased to play a critical role at this stage of the task. Conversely, a recent TMS study found that stimulation delivered to the left primary motor cortex around 650 msec after the presentation of the stimulus disrupted mental rotation of hand stimuli, whereas the same TMS pulse delivered at 400 msec had no effect (Ganis, Keenan, Kosslyn, & Pascual-Leone, 2000). Although Ganis et al. (2000) tested mental rotation of pictures of hands and feet, which may preferentially recruit the motor cortex, there is good evidence that motor processes play a role in the mental rotation of abstract figures as well (Jordan et al., 2001; Vingerhoets et al., 2001; Richter et al., 2000; Wexler, Kosslyn, & Berthoz, 1998; Wohlschlagel & Wohlschlagel, 1998; Tagaris et al., 1997). Combining Ganis et al.'s findings with those of the present experiments would suggest an information processing flow that proceeds from the right superior parietal cortex at around 400–600 msec to the primary motor cortex at around 650 msec. One could reasonably speculate on an interaction between parietal and motor regions of the brain, in which neurons in the superior parietal cortex map the coordinate transformations that constitute the imagined rotation and then pass these transformation parameters on to motor centers, which elaborate movement signals consistent with these visuomotor transformations (Snyder et al., 2000).

A final issue that merits discussion here is a possible role for the superior parietal lobe in mirror-image discrimination, over and above its role in mental rotation. The findings of this study are somewhat inconclusive in this regard. On the one hand, in Experiment 2, rTMS only affected processing of rotated stimuli, in particular

those rotated by 180°, implying a selective effect on the mental rotation component of the task. By contrast, when rTMS was given at 400–600 msec in Experiment 4 it affected the subjects' performance on all trials, including those in which the stimuli were upright. Given that upright stimuli supposedly do not require any rotation, this latter result would suggest that TMS interfered with the mirror-discrimination process that has to be performed on every trial, rather than with the mental rotation component of the task.

One explanation for these apparently discrepant results may lie in the slight differences in coil orientation in the two experiments. There is some evidence that mental rotation and mirror-image discrimination are subserved by neighboring, even overlapping, regions of the right superior parietal lobe (Harris et al., 2000; Alivisatos & Petrides, 1997). Therefore, it is possible that by altering the orientation of the TMS coil we stimulated slightly different neuronal populations that were more or less involved in mirror-image discrimination. Alternatively, it is possible that TMS affected the same neuronal population in both experiments, but the coil orientation used in Experiment 4 resulted in more effective stimulation, leading to a stronger effect on performance across all angles used in the experiment, whereas the effect of TMS in Experiment 2 was weaker and, therefore, only apparent for the more difficult angles.

The present results cannot distinguish between these two alternatives and, in fact, an attempt to separate mental rotation from mirror-image discrimination in this fashion may be misguided. Indeed, the fact that mental rotation is most consistently induced when subjects must discriminate between mirror images (Pierret & Peronnet, 1994; Shepard & Cooper, 1982), as well as the fact that the two processes lead to similar patterns of brain activation, attests to the intimate relationship between these processes. Furthermore, Ilan and Miller (1994) have demonstrated that mental rotation is not purely inserted into a mirror-normal discrimination task. They showed that subjects take longer to decide whether an upright character is normal or mirror-reversed when this character is presented amongst rotated stimuli, compared to when it occurs in a block of only upright characters. This slowing was attributed to a "rotational uncertainty," which led the subjects to set up, or maintain readiness for, mental rotation (Ilan & Miller, 1994). Thus, the rTMS effect found for all angles in Experiment 4 could still be explained by an interference with a mental rotation mechanism.

In conclusion, the results obtained in this study extend previous evidence that mental rotation is correlated preferentially with activity in the right parietal lobe (Podzbenko et al., 2002; Harris et al., 2000; Pegna et al., 1997) by demonstrating that the right superior parietal lobe plays an essential role in mental rotation. We have further determined that the involvement of the right superior parietal lobe in mental rotation was relatively

limited to a period between 400 and 600 msec following the onset of the stimulus. Further studies of this sort, targeting other brain regions known to be involved in mental rotation, should clarify their relative contributions to mental rotation, as well as the sequence of operations performed by different areas in the execution of mental rotation tasks.

METHODS

Subjects

A total of 33 right-handed subjects participated in this study. Nine subjects (6 men, 3 women) aged 26–39 years (mean = 31), with a mean Edinburgh Handedness Inventory score of 72.0, took part in Experiment 1. Nine subjects (3 men, 6 women) aged 20–44 years (mean = 30), with a mean Edinburgh Handedness Inventory score of 93.2, took part in Experiment 2. Nine subjects (5 men, 4 women) aged 24–51 years (mean = 33.6), with a mean Edinburgh Handedness Inventory score of 91.2, took part in Experiment 3. Six subjects (2 men, 4 women) aged 27–37 years (mean = 31), with a mean Edinburgh Handedness Inventory score of 89.0, took part in Experiment 4. Five subjects were common to Experiments 1 and 2. All were free from family history of epilepsy or other neurological disorders. Informed consent was obtained prior to the experiment, in accordance with the declaration of Helsinki, and the protocol was approved by the local ethics committee for research with human subjects.

Experimental Apparatus

The experiment was designed and conducted using MEL Professional software (Psychology Software Tools, University of Pittsburgh, PA). The stimuli were generated by a portable PC computer and were rear projected on a screen positioned 150 cm in front of the subject. This computer also triggered the TMS stimulator at the appropriate time. Responses were recorded via a compatible button box, which recorded RTs with 1-msec accuracy. Throughout the experiment, the subject's head was stabilized with a combination of a chin rest and a head support bar. The coil was fixed in position with the aid of an articulated mechanical arm.

Stimuli

For the first three experiments, the stimuli were six asymmetric alphanumeric characters (F, G, R, 2, 4, 5) presented either in their canonical form or mirror-reversed. Three other characters (P, Q, 7) were used for practice trials. For Experiment 4, the “4” was replaced with “P,” because the subjects in the previous experiments had found the “4” particularly difficult, and the practice trials used the same stimuli as the exper-

imental trials (i.e., the stimuli used in both the experimental and the practice trials in Experiment 4 were F, G, P, R, 2, 5). The characters were white, and were presented on an indigo background. They were rotated in 60° steps in the frontal plane, ranging from 0° to 180°. For stimuli rotated by 60° or 120°, half were rotated clockwise and half anticlockwise, and the data from corresponding angles were combined. This was done in order to maximize the number of possible different angles used in the experiment, drawing on previous findings that subjects mentally rotate along the shortest path and RTs are symmetrical around 180° (Shepard & Cooper, 1982). The six characters were evenly distributed amongst orientations and conditions, with half the stimuli being presented in their canonical form and half mirror-reversed.

rTMS Protocol

rTMS was applied using a Magstim Rapid with a figure-of-eight (double 70 mm) coil, which can induce a maximum magnetic field of 2.2 T at the scalp site. Before the experiment, individual resting excitability thresholds of stimulation were determined by stimulating the left motor cortex and measuring the amplitude of contractions evoked by a single TMS pulse in the contralateral first interosseus dorsalis muscle. The threshold was defined as the minimum intensity that induced a visible contraction in the tested muscle, as agreed by two experimenters on at least three trials. The stimulation intensity used during the experiment was set at 110% of each subject's threshold. For our group of subjects, the mean stimulation intensity was 68% (maximum 75%) of the maximum output of the TMS coil, which is well within the National Institute of Neurological Disorders and Stroke (NINDS) guidelines on safety of rTMS (Wasserman, 1998). During the experiment, rTMS was delivered using a train of four pulses with a frequency of 20 Hz (i.e., lasting a total of 200 msec).

The subjects wore a close-fitting Lycra skullcap on which the positions of Cz, CP3, P3, CP4, and P4 from the International 10/20 EEG system were reproduced. The cap was positioned such that the Cz marking corresponded to the individual's measured Cz, thus ensuring that the position of the reference points was constant across subjects. Three additional points were marked on the cap, corresponding to the stimulation sites used in the study. Two sites, which were estimated to overlie the posterior superior parietal lobe, in the vicinity of the IPS, were marked in the left and right hemispheres, at positions halfway between P3 and CP3 and halfway between P4 and CP4, respectively (see Figure 1). The location of these points was then reconstructed using the Softaxic Navigator software, and yielded Talairach coordinates $x = \pm 34, y = -64, z = 50$, corresponding to Brodmann's area 7, in the superior parietal lobule

(Talairach & Tournoux, 1988). The stimulation site for the sham condition used in Experiments 1–3 was on the midline at the same horizontal level as the parietal sites. In Experiment 4, the sham stimulation was applied to the P4/CP4 (right parietal) site described above.

Procedure

Experiments 1–3

The three experiments followed the same procedure, the only differences being the timing of the TMS relative to stimulus onset and the number of trials in each experiment. The subjects sat at a table in a dimly lit room and wore earplugs. Before the start of the experiment, they completed a block of 24 practice trials. During the practice block, the TMS coil was placed near the subject, and trains of stimulation were delivered with the same intensity and timing as in the subsequent experimental trials, in order to accustom them to the noise produced by the stimulator. The practice block was followed immediately by the experimental blocks. Each experimental block had 32 trials (8 trials per orientation angle), randomly intermixed. Experiment 1 comprised six experimental blocks (two blocks per condition: left parietal, right parietal, and midline sham, administered in a randomized, counterbalanced, ABCCBA order). In Experiments 2 and 3, only three blocks of 32 trials were administered (one per condition), with the order counterbalanced across subjects. We did this to reduce the number of stimulations received by each subject, given that some subjects had already participated in Experiment 1. Each block of trials lasted approximately 5 min, with a short break of 2–3 min between conditions while the experimenter repositioned the coil over the next site.

In the left and right stimulation conditions, the coil was positioned tangential to the scalp, with the handle pointing down and the virtual cathode overlying the relevant site. In the sham condition, the coil was turned over (thus reversing the direction of the magnetic field) and a 20-mm-thick plywood shield of the same shape and size as the coil was fastened to the back of the coil and placed against the subject's scalp. In addition, rather than being tangential to the scalp, the shielded coil was oriented at approximately 45° to the scalp. This ensured that no magnetic stimulation reached the brain during the sham condition, and controlled for the noise and sensation of the coil against the head although the subjects did not feel the muscle contraction that one sometimes gets with real TMS.

Individual trials began with a fixation dot appearing in the center of the screen for 1 sec, to serve as a cue, followed by the stimulus. In the upright orientation, the stimulus was displayed 1.1° above the fixation dot and together they subtended a visual angle of approximately 6°; at other orientations the whole display was rotated (with the dot serving as pivot), such that the character

was displaced radially by 1.1° from the fixation dot. rTMS was delivered at a specified time relative to stimulus onset: either 200–400 msec later (Experiment 1), 400–600 msec later (Experiment 2), or 600–800 msec later (Experiment 3). The stimulus remained on the screen until the subject responded, or for a maximum of 2.5 sec, and was followed by a blank screen for 7 sec. This ensured that the stimulations were well spaced in time, thus minimizing any risk associated with rTMS, in accordance with the NINDS guidelines (Wasserman, 1998). Subjects decided, as quickly as possible, whether each stimulus was normal or mirror-reversed and responded by pressing two buttons with the index or middle finger of their right hand (index for mirror-image stimuli, middle finger for normal stimuli).

Experiment 4

The general procedure was identical to the first three experiments, with the following exceptions. First, in this experiment, rTMS and sham stimulation were both delivered to the right parietal site, and there was no stimulation of the left parietal lobe. Second, the orientation of the coil was changed slightly in this experiment, such that the handle of the coil was approximately parallel to the long axis of the temporal lobe, pointing toward the temporal pole.

There were four experimental blocks, two of rTMS and two of sham stimulation, administered in a counterbalanced ABAB order. On half the trials in each block, rTMS (or sham stimulation) was delivered 200–400 msec after the onset of the trial, and on the other half it was delivered 400–600 msec into the trial, with the two types of trials randomly intermixed. Each experimental block comprised 64 trials, 16 in each of the 0°, 60°, 120° and 180° orientations. The experimental trials were preceded by a longer practice block of 64 trials.

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REFERENCES

- Alivisatos, B., & Petrides, M. (1997). Functional activation of the human brain during mental rotation. *Neuropsychologia*, *35*, 111–118.
- Anderson, T. J., Jenkins, I. H., Brooks, D. J., Hawken, M. B., Frackowiack, R. S. J., & Kennard, C. (1994). Cortical control of saccades and fixation in man. A PET study. *Brain*, *117*, 1073–1084.

- Carpenter, P. A., Just, M. A., Keller, T. A., Eddy, W., & Thulborn, K. (1999). Graded functional activation in the visuospatial system with the amount of task demand. *Journal of Cognitive Neuroscience*, *11*, 9–24.
- Cohen, M. S., Kosslyn, S. M., Breiter, H. C., Digirolamo, G. J., Thompson, W. L., Anderson, A. K., Bookheimer, S. Y., Rosen, B. R., & Belliveau, J. W. (1996). Changes in cortical activity during mental rotation: A mapping study using functional MRI. *Brain*, *119*, 89–100.
- Colby, C. L. (1999). Parietal cortex constructs action-oriented spatial representations. In N. Burgess, K. J. Jeffrey, & J. O'Keefe (Eds.), *The hippocampal and parietal foundations of spatial cognition* (pp. 104–126). New York: Oxford University Press.
- Cooper, L. A., & Shepard, R. N. (1973). The time required to prepare for a rotated stimulus. *Memory and Cognition*, *1*, 246–250.
- Corbetta, M., Miezin, F. M., Shulman, G. L., & Petersen, S. E. (1993). A PET study of visuospatial attention. *Journal of Neuroscience*, *13*, 1202–1226.
- Ditunno, P. L., & Mann, V. A. (1990). Right hemisphere specialization for mental rotation in normals and brain damaged subjects. *Cortex*, *26*, 177–188.
- Ganis, G., Keenan, J. P., Kosslyn, S. M., & Pascual-Leone, A. (2000). Transcranial magnetic stimulation of primary motor cortex affects mental rotation. *Cerebral Cortex*, *10*, 175–180.
- Harris, I. M., Egan, G. F., Sonkila, C., Tochon-Danguy, H., Paxinos, G., & Watson, J. D. G. (2000). Selective right parietal lobe activation during mental rotation: A parametric PET study. *Brain*, *123*, 65–73.
- Ilan, A. B., & Miller, J. (1994). A violation of pure insertion: Mental rotation and choice reaction time. *Journal of Experimental Psychology: Human Perception and Performance*, *20*, 520–536.
- Jahanshahi, M., & Rothwell, J. (2000). Transcranial magnetic stimulation studies of cognition: An emerging field. *Experimental Brain Research*, *131*, 1–9.
- Jordan, K., Heinze, H.-J., Lutz, K., Kanowski, M., & Jancke, L. (2001). Cortical activations during the mental rotations of different visual objects. *Neuroimage*, *13*, 143–152.
- Kosslyn, S. M., Digirolamo, G. J., Thompson, W. L., & Alpert, N. M. (1998). Mental rotation of objects versus hands—neural mechanisms revealed by positron emission tomography. *Psychophysiology*, *35*, 151–161.
- Loftus, G. R., & Masson, M. E. J. (1994). Using confidence intervals in within-subject designs. *Psychonomic Bulletin and Review*, *1*, 476–490.
- Mehta, Z., & Newcombe, F. (1991). A role for the left hemisphere in spatial processing. *Cortex*, *27*, 153–167.
- Morton, N., & Morris, R. G. (1995). Image transformation dissociated from visuospatial working memory. *Cognitive Neuropsychology*, *12*, 767–791.
- Passini, R., Rainville, C., & Habib, M. (2000). Spatio-cognitive deficits in right parietal lesion and its impact on wayfinding: A case study. *Neurocase*, *6*, 245–257.
- Pegna, A. J., Khateb, A., Spinelli, L., Seeck, M., Landis, T., & Michel, C. M. (1997). Unraveling the cerebral dynamics of mental imagery. *Human Brain Mapping*, *5*, 410–421.
- Peronnet, F., & Farah, M. J. (1989). Mental rotation: An event-related potential study with a validated mental rotation task. *Brain and Cognition*, *9*, 279–288.
- Pierret, A., & Peronnet, F. (1994). Mental rotation and mirror-image discrimination. *Perceptual and Motor Skills*, *78*, 515–524.
- Podzbenko, K., Egan, G. F., & Watson, J. D. G. (2002). Widespread dorsal stream activation during a parametric mental rotation task, revealed with functional magnetic resonance imaging. *Neuroimage*, *15*, 547–558.
- Richter, W., Somorjai, R., Summers, R., Jarmasz, M., Menon, R. S., Gati, J. S., Georgopoulos, A. P., Tegeler, C., Ugurbil, K., & Kim, S.-G. (2000). Motor area activity during mental rotation studied by time-resolved single-trial fMRI. *Journal of Cognitive Neuroscience*, *12*, 310–320.
- Richter, W., Ugurbil, K., Georgopoulos, A., & Kim, S. G. (1997). Time-resolved fMRI of mental rotation. *NeuroReport*, *8*, 3697–3702.
- Shepard, R. N., & Cooper, L. A. (1982). *Mental images and their transformations*. Cambridge: MIT Press.
- Shepard, R. N., & Metzler, J. (1971). Mental rotation of three-dimensional objects. *Science*, *171*, 701–703.
- Snyder, L. H., Batista, A. P., & Andersen, R. A. (2000). Intention-related activity in the posterior parietal cortex: A review. *Vision Research*, *40*, 1433–1441.
- Tagaris, G. A., Kim, S. G., Strupp, J. P., Andersen, P., Ugurbil, K., & Georgopoulos, A. P. (1996). Quantitative relations between parietal activation and performance in mental rotation. *NeuroReport*, *7*, 773–776.
- Tagaris, G. A., Kim, S. G., Strupp, J. P., Andersen, P., Ugurbil, K., & Georgopoulos, A. P. (1997). Mental rotation studied by functional magnetic resonance imaging at high field (4 Tesla)—Performance and cortical activation. *Journal of Cognitive Neuroscience*, *9*, 419–432.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. Stuttgart: Thieme.
- Vingerhoets, G., Santens, P., Van Laere, K., Lahorte, P., Dierckx, R. A., & De Reuck, J. (2001). Regional brain activity during different paradigms of mental rotation in healthy volunteers: A positron emission tomography study. *Neuroimage*, *13*, 381–391.
- Walsh, V., & Cowey, A. (2000). Transcranial magnetic stimulation and cognitive neuroscience. *Nature Reviews: Neuroscience*, *1*, 73–79.
- Wasserman, E. M. (1998). Risk and safety of repetitive transcranial magnetic stimulation: Report on suggested guidelines from the International Workshop on the safety of Repetitive Transcranial Magnetic Stimulation, June 5–7, 1996. *Electroencephalography and Clinical Neurophysiology*, *108*, 1–16.
- Wexler, M., Kosslyn, S. M., & Berthoz, A. (1998). Motor processes in mental rotation. *Cognition*, *68*, 77–94.
- Wohlschlagel, A., & Wohlschlagel, A. (1998). Mental and manual rotation. *Journal of Experimental Psychology: Human Perception and Performance*, *24*, 397–412.
- Yoshino, A., Inoue, M., & Suzuki, A. (2000). A topographic electrophysiologic study of mental rotation. *Cognitive Brain Research*, *9*, 121–124.